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OBESIDADE E SÍNDROME METABÓLICA EM CRIANÇAS

PRÉ-PÚBERES DOS 7 AOS 9 ANOS DE IDADE

OBESITY AND METABOLIC SYNDROME IN 7-9 YEARS-OLD

PRE-PUBERTAL CHILDREN

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Ao Paulo.

Aos meus Pais.

“Every child deserves to be born well, to be physically fit, and to achieve self-responsibility for good health habits”

(de Bright Futures Children's Health Charter)

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LISTA DE ABREVIATURAS

AGL: Ácidos gordos livres

AGS: Ácidos gordos saturados

Apo A-I: Apolipoproteína A-I

Apo B: Apolipoproteína B

CDC: *Centers for Disease Control and Prevention*

DCV: Doenças cardiovasculares

DM2: Diabetes Mellitus tipo 2

DTG: Diminuição da tolerância à glicose

HC: Hidratos de carbono

HDL: Lipoproteína de alta densidade (high density lipoprotein)

HMW: Adiponectina de elevado peso molecular (high molecular weight)

HOMA-IR: *Homeostasis model assessment of insulin resistance*

IDF: *International Diabetes Federation*

IGF-1: Insulin-like growth factor-1

IMC: Índice de massa corporal

IOTF: *International Obesity Task Force*

LDL: Lipoproteína de baixa densidade (low density lipoprotein)

NCEP/ATPIII: *National Cholesterol Education Program Adult Treatment Panel III*

NCHS: *National Center for Health Statistics*

NHANES: *National Health and Nutrition Examination Survey*

OMS: Organização Mundial de Saúde

Perc_{IMC}: Percentis de índice de massa corporal

PTGO: Prova de tolerância oral à glicose

SM: Síndrome Metabólica

TrG: Tratamento em grupo

TRI: Tratamento individual

VLDL: Lipoproteína de muito baixa densidade (very low density lipoprotein)

z-IMC: z-score do índice de massa corporal

RESUMO

Nas últimas décadas, a prevalência de obesidade infantil alcançou proporções epidémicas, tornando-se um sério problema de Saúde Pública. À medida que a prevalência de obesidade em idade pediátrica aumenta, as implicações para a saúde também se tornam mais evidentes devido às diversas comorbilidades que esta acarreta, nomeadamente alterações do perfil lipídico, do metabolismo da insulina e da glicose, hipertensão arterial, síndrome metabólica (SM), entre outros.

Dada a escassez de dados nacionais relativos a esta temática, foi objectivo desta dissertação avaliar a prevalência de obesidade e SM numa amostra de crianças portuguesas entre os 7 e os 9 anos de idade, residentes no concelho de Aveiro, bem como avaliar o efeito de um programa de intervenção nos estilos de vida, nomeadamente no comportamento alimentar e na actividade física, sobre os parâmetros antropométricos e bioquímicos.

Para tal, foram avaliadas antropometricamente 905 crianças de 13 escolas do concelho de Aveiro, tendo sido convidadas a colaborar no restante estudo as que apresentavam um percentil de IMC superior a 95. As crianças que aceitaram participar foram distribuídas aleatoriamente por 2 grupos de estudo: o de tratamento individual e o de tratamento em grupo, ambos baseados na educação alimentar (plano alimentar estruturado ou sessões de educação alimentar, respectivamente) e na promoção da actividade física. Durante o período de 1 ano foram estudadas 61 crianças, tendo-se procedido à recolha de dados demográficos, antropométricos, bioquímicos, bem como dados referentes à ingestão alimentar e à prática de actividade física.

A prevalência de excesso de peso e obesidade foi verificada em, respectivamente, 17,2% e 14,0% segundo os critérios do *Centers for Disease Control and Prevention* e em 20,0% e 8,1% segundo os critérios da *International Obesity Task Force*, encontrando-se entre as mais elevadas da Europa. Estes resultados são semelhantes aos verificados em outros estudos com representatividade nacional.

A presença de SM foi avaliada, nas 82 crianças que aceitaram participar no estudo, segundo a definição do *National Cholesterol Education Program Adult Treatment Panel III* modificada por Cook e col. para a idade pediátrica. Constatou-se que 15,8% das crianças apresentavam três ou mais critérios desta síndrome, verificando-se uma correlação significativa entre o número de critérios da SM e o z-score de IMC ($p=0,411$; $p<0,001$). Pelo contrário, nenhuma das crianças normoponderais foi diagnosticada com SM. Todas as crianças com excesso de peso apresentaram obesidade abdominal, enquanto que a presença de 2, 3 e 4 dos restantes critérios da SM se verificou, respectivamente, em 50%, 11% e 4,9% das crianças. Destes critérios, destaca-se a presença de valores elevados de tensão arterial em 62,6% das crianças avaliadas. Não se registou qualquer alteração da glicemia em jejum.

As crianças com SM manifestaram maior frequência de resistência à insulina, bem como níveis de leptina mais elevados, comparativamente com as crianças obesas sem SM. Usando a regressão logística, verificou-se que a concentração de insulina se apresentou como o único factor preditivo positivo da SM ($p=0,045$), enquanto a apolipoproteína A-I ($p=0,007$) e o estágio de puberdade ($p=0,043$) se mostraram como factores preditivos negativos.

Na primeira avaliação verificou-se que a distribuição de macronutrientes se enquadra nas recomendações do *Institute of Medicine* para esta faixa etária, nomeadamente com 46,6% do valor energético total de HC, 31,8% de lípidos e 21,1% de proteínas. Exceptuam-se os ácidos gordos saturados (12,6%) e os açúcares totais (19,4%) que se apresentaram acima das recomendações, enquanto o consumo médio de fibra de 14,8 g (desvio-padrão 3,7 g) se situou abaixo das recomendações.

O tempo despendido na actividade física extra-curricular mostrou-se reduzido, principalmente nas crianças do sexo feminino ($9,4\pm 11,4$ min/dia vs. $21,7\pm 17,0$ min/dia; $p=0,005$) e nas com SM ($3,0\pm 6,4$ min/dia vs. $17,2\pm 15,5$ min/dia; $p=0,004$).

Por regressão logística, a gordura total ingerida apresentou-se como um factor preditivo positivo da SM ($p=0,031$), ao contrário dos ácidos gordos saturados que curiosamente se mostraram como um factor preditivo negativo ($p=0,025$) desta síndrome. Para além disso, o tempo despendido na actividade física extra-curricular ($p=0,031$) e as horas de sono ($p=0,033$) destacaram-se também como factores preditivos negativos da SM.

Apesar de não se terem observado alterações significativas quer na ingestão alimentar quer na prática de actividade física, o programa de intervenção conduziu a resultados significativos, ainda que modestos, na perda ponderal e na regressão de alguns parâmetros associados à SM. A presença de obesidade diminuiu de 83,6% para 59%, acompanhada de uma diminuição dos valores tensionais elevados para 49,1%. Das dez crianças inicialmente diagnosticadas com SM, cinco deixaram de apresentar esta síndrome, enquanto quatro foram diagnosticadas ao final do ano de estudo. Nestas últimas verificou-se um aumento do IMC ao longo deste período, ao contrário das primeiras em que este parâmetro diminuiu. O tratamento em grupo, comparativamente com o tratamento individual, foi aquele que apresentou uma evolução mais favorável dos diversos parâmetros antropométricos e bioquímicos.

Assim, esta investigação documenta uma elevada prevalência de excesso de peso nas crianças entre os 7 e os 9 anos de idade, bem como de SM nas crianças com obesidade. A intervenção dirigida à correcção dos estilos de vida, nomeadamente dos hábitos alimentares e da actividade física, traduziu-se numa melhoria ainda que modesta dos diversos parâmetros avaliados, o que demonstra a importância destas medidas na redução do risco futuro.

ABSTRACT

In the past decades, the prevalence of childhood obesity has increased worldwide, reaching epidemic proportions and becoming a serious public health problem. As childhood obesity increases, the health implications also become more evident due to several comorbidities, namely dyslipidemia, hypertension, disarrangements in insulin and glucose metabolism, metabolic syndrome (MS), among others, known risk factors for the development of diabetes and cardiovascular diseases in adulthood.

Given the paucity of national data concerning this theme, it was an aim of this thesis to determine the prevalence of obesity and MS in a sample of Portuguese children between 7-9 years-old living in Aveiro, and to evaluate the effect of a lifestyle intervention program, with nutrition counselling and physical activity promotion, on anthropometric and metabolic measures.

Therefore, 905 children from 13 schools in Aveiro were anthropometrically evaluated, and the children with a BMI percentile above 95 were invited to collaborate in the further study. Those who agreed to participate were randomly assigned to two groups: the individual-based treatment and the group-based treatment, both consisting in nutrition counselling (prescription of a healthy eating plan or participation in nutrition education sessions, respectively) and in physical activity promotion. During the 1-year study period 61 children were studied and demographic, anthropometric and biochemical data, as well dietary intake and physical activity levels were collected.

Overweight and obesity were present in 17.2% and 14.0%, respectively, of the evaluated children according to the *Centers for Disease Control and Prevention* criteria, and in 20.0% and 8.1% according to the *International Obesity Task Force* criteria, which are among the highest in Europe. These results are similar to those found in other studies with national representativeness.

MS was evaluated in 82 children that agreed to participate in the study and was defined according to the *National Cholesterol Education Program Adult Treatment Panel III* (NCEP/ATPIII) criteria modified by Cook et al. for the pediatric age. It was found that 15.8% of the children presented 3 or more components of the MS. Moreover, a significant correlation was confirmed between the BMI z-score and the number of MS components ($p=0.411$; $p<0.001$). On the other hand, none of the normal weight children was diagnosed with MS. All overweight subjects presented abdominal obesity, while 2, 3 and 4 of the other MS criteria were presented respectively in 50%, 11% and 4.9%. Elevated blood pressure levels were verified in 62.6% of the children. None of the children presented impaired fasting glucose.

The children with MS showed a higher frequency of insulin resistance and higher leptin levels compared with obese children without MS. By logistic regression, insulin levels ($p=0.045$) presented as the only positive predictor of MS, while apolipoprotein A-I ($p=0.007$) levels and puberty ($p=0.043$) showed to be negative predictors.

At baseline, the macronutrient profile observed in children was in accordance with the recommendations of the *Institute of Medicine* for this age group, namely with 46.6% of the total energy intake as carbohydrates, 31.8% as fat and 21.1% as proteins. Saturated fatty acids (12.6%) and total sugars (19.4%) intake was above the recommendations, while the average fibre intake of 14.8 g (standard-deviation 3.7 g) stood below it.

A reduced time spent in extra-curricular physical activities was observed, especially in girls (9.4 ± 11.4 min/day vs. 21.7 ± 17.0 min/day; $p=0.005$) and in MS-children (3.0 ± 6.4 min/day vs. 17.2 ± 15.5 min/day; $p=0.004$).

By logistic regression, total fat intake presented as a positive predictor of MS ($p=0.031$), while, surprisingly, a higher saturated fatty acids intake was a predictor of a lower risk of this syndrome ($p=0.025$). Also, the time spent in extra-curricular physical activities ($p=0.031$) and the hours of sleep ($p=0.033$) were negative predictive factors of MS.

Although no significant changes were observed in either dietary intake or in time spent in physical activities, the intervention program presented significant results, albeit modest, in weight loss and in regression of some of the characteristics associated with MS. The prevalence of obesity decreased from 83.6% to 59%, accompanied by a decrease to 49.1% in high blood pressure levels. Of the 10 children initially diagnosed with this syndrome, 5 no longer presented it at 1-year, while 4 children were newly diagnosed. Among those children who no longer presented MS it was observed an improvement in their BMI over this period, while in the children newly diagnosed this parameter has increased. The group-based treatment seems to be more successful, with positive anthropometric and biochemical outcome measures.

This research documents a high prevalence of excess weight in children between 7-9 years-old, such as of MS in children with obesity. The lifestyle intervention program has resulted in an improvement, albeit moderate, of several parameters, which supports the importance of these approaches in reducing future health risks.

INTRODUÇÃO

I. OBESIDADE

A obesidade, segundo a Organização Mundial de Saúde (OMS), é definida como a acumulação anormal ou excessiva de gordura corporal que pode comprometer a saúde do indivíduo e diminuir a esperança de vida ⁽¹⁾.

As origens da obesidade remontam há pelo menos cerca de 30.000 anos, altura em que a sobrevivência do mais apto ditava que os indivíduos que armazenassem mais energia de forma mais eficiente sobreviveriam ao jejum e à fome que se seguiriam aos tempos de abundância. Esta eficiência energética tem sido atribuída aos chamados '*thrifty genes*' ou genes 'poupadores de energia' ⁽²⁾.

Desde o início dos anos 80, com a relativa abundância energética, a prevalência de obesidade mais que triplicou em diversos países a nível mundial. Em 1998, a OMS designou a obesidade como uma epidemia global. Na realidade, cerca de 1 bilião de adultos apresentam excesso ponderal, dos quais 300 milhões são obesos ⁽³⁾.

OBESIDADE INFANTIL

DEFINIÇÃO E PREVALÊNCIA

A crescente prevalência da obesidade a nível mundial não se verifica apenas na idade adulta. Nas últimas décadas, a prevalência de obesidade infantil atingiu também proporções epidémicas, tornando-se um sério e crescente problema de Saúde Pública ⁽⁴⁻⁶⁾.

Desde 1997, o Índice de Massa Corporal (IMC) tem sido considerado como a principal medida de avaliação da obesidade na população pediátrica ⁽⁷⁻⁹⁾. Apesar de o método ideal de avaliação da adiposidade ainda não exista ⁽¹⁾, o IMC é um método antropométrico simples, conveniente, reprodutível e não dispendioso ^(7, 10, 11). Apresenta uma forte correlação com a percentagem de gordura corporal ^(9, 12-14), bem como com a presença de factores de risco cardiovascular ⁽¹⁵⁻¹⁸⁾. Contudo, a sua utilização na criança e adolescente apresenta algumas limitações, de que são exemplos o aumento do peso e

estatura em resposta ao desenvolvimento, e consequentemente o aumento do IMC, bem como as diferenças existentes entre sexos na composição corporal no início da puberdade e na velocidade de crescimento ^(7, 13, 19). A fase da puberdade acompanha-se de alterações no tamanho, forma e composição corporal, sendo que 50% do peso corporal do adulto é ganho neste período ^(20, 21). Observa-se um dimorfismo sexual marcado, associado a um perfil hormonal distinto, com um aumento de massa gorda nas raparigas entre os nove e os vinte anos, enquanto nos rapazes ocorre um aumento da massa muscular e óssea, acompanhado da diminuição da massa gorda após os treze anos de idade ⁽²¹⁻²³⁾. Desta forma, a utilização do IMC em crianças e adolescentes requer informação adicional relativa à idade e ao sexo ^(19, 24).

Apesar da utilização frequente do IMC na idade pediátrica, não existe uma definição de obesidade universalmente aceite ⁽⁸⁾. Na realidade, devido ao processo de crescimento e desenvolvimento em crianças e adolescentes ^(8,11), o IMC não pode ser utilizado nesta faixa etária como o é no adulto com recurso a pontos de corte. Assim, têm sido desenvolvidas tabelas de percentis de IMC ($Perc_{IMC}$) específicas para a idade e sexo, e respectivas curvas, de modo a avaliar a evolução deste parâmetro ao longo do tempo. Todavia, quer pela existência de tabelas de $Perc_{IMC}$ nacionais, quer pelos diferentes pontos de corte a partir dos quais se define obesidade, diferentes autores, em diferentes países, utilizam diferentes definições ^(7, 8, 16, 24, 25). Como é óbvio, este aspecto dificulta a comparação das taxas de prevalência entre países e entre os vários estudos.

Em 2000, a partir de censos (NHANES – *National Health and Nutrition Examination Survey*) realizados na população norte-americana, o *Centers for Disease Control and Prevention* (CDC) actualizou as tabelas de $Perc_{IMC}$ específicas para o sexo e para a idade (dos 2 aos 20 anos de idade) criadas em 1977 pelo *National Center for Health Statistics* (NCHS) e utilizadas até então ⁽²⁶⁾. Foi definido como ‘risco de sobrecarga ponderal’ o $Perc_{IMC}$ superior ou igual a 85 e inferior a 95, e como ‘sobrecarga ponderal’ o $Perc_{IMC}$ superior ou igual a 95, terminologia esta entretanto corrigida para ‘sobrecarga ponderal’

(Perc_{IMC} superior ou igual a 85 e inferior a 95) e ‘obesidade’ (Perc_{IMC} superior ou igual a 95)⁽²⁶⁾. Por sua vez, a *International Obesity Task Force* (IOTF) define ‘sobrecarga ponderal’ e ‘obesidade’ a partir dos pontos de corte definidos por Cole e col.⁽²⁷⁾. Estes autores utilizam percentis decorrentes dos pontos de corte de 25 e 30 Kg/m² utilizados na população adulta que definem, respectivamente, sobrecarga ponderal e obesidade. Estes percentis foram estimados a partir de dados obtidos em indivíduos entre os 6 e os 18 anos de idade, em diferentes estudos, em diferentes anos e em diferentes países, designadamente EUA, Brasil, Grã-Bretanha, Singapura, Hong-Kong e Holanda⁽²⁷⁾. Actualmente, ambas as definições (CDC e IOTF) são empregues em todo o mundo na avaliação da obesidade infantil. Em 2007, a OMS actualizou as suas curvas de referência para o peso, altura e IMC específicas para o sexo e idade, acrescentadas agora também da faixa etária dos 5 aos 19 anos⁽²⁸⁾. Tal como os dados do CDC, esta actualização compreende apenas crianças norte-americanas, com a característica de terem sido alimentadas com leite materno⁽²⁸⁾. É de salientar que as curvas da OMS pretendem traduzir a forma como as crianças devem crescer, com uma alimentação e nutrição adequadas, em vez de descreverem o seu crescimento num determinado tempo e local⁽²⁹⁾.

Por deliberação da Direcção-Geral de Saúde, em Portugal são utilizadas as curvas do CDC, cuja actualização foi implementada no Boletim de Saúde Infantil e Juvenil em 2006⁽³⁰⁾.

Apesar das dificuldades inerentes à avaliação da prevalência da obesidade na idade pediátrica devido às diferentes metodologias empregues, um facto óbvio pode ser sublinhado, o número de crianças e adolescentes com sobrecarga ponderal e obesidade tem vindo a aumentar nas últimas décadas em todo o mundo. Dados de um relatório da IOTF publicado em 2004, estimavam a presença de sobrecarga ponderal/obesidade a nível mundial em 1 em cada 10 crianças⁽⁵⁾. Ainda segundo este relatório, o aumento da prevalência foi mais acentuado nos países desenvolvidos, dos quais se destacam os EUA

em que a prevalência de sobrecarga ponderal mais que duplicou e a de obesidade quadruplicou nos últimos quarenta anos. Nos países em vias de desenvolvimento, este incremento na prevalência foi de menor magnitude ⁽⁵⁾. Num estudo transversal realizado entre 2001 e 2002 em crianças e adolescentes (10 a 16 anos de idade) de 34 países maioritariamente Europeus, os autores constataram ser Malta (33,3%) e os EUA (31,9%) os países com maior prevalência de excesso de peso ⁽³¹⁾. De acordo com este estudo, Portugal era o oitavo país com maior prevalência de excesso de peso, sendo que cerca de 15% dos jovens avaliados apresentavam sobrecarga ponderal e 3% obesidade. Wang e Lobstein estimaram, numa análise a diversos estudos publicados ao longo de 15 anos, que no corrente ano de 2010 apresentarão excesso de peso cerca de 46% das crianças em idade escolar no continente Americano, cerca de 38% na Europa, cerca de 27% no Pacífico Oeste e cerca de 22% no Sudeste Asiático ⁽⁶⁾.

Estudos realizados em vários países da União Europeia traduzem este preocupante aumento da prevalência de sobrecarga ponderal e obesidade nos mais jovens, de tal modo que actualmente a obesidade infantil é considerada a doença pediátrica mais comum neste continente ^(5, 32-34). Em 2002, a IOTF apontava que em média 1 em cada 6 crianças europeias apresentava excesso de peso ⁽⁴⁾, relação esta actualizada em 2004 para 1 em cada 4 crianças, o que corresponde a 14 milhões de crianças com excesso de peso ⁽³⁵⁾. Dados mais recentes, reportados no relatório anual de 2009 da *EU Platform on Diet, Physical Activity and Health* apontam aproximadamente para 22 milhões de crianças europeias (cerca de 30%) com sobrecarga ponderal, número este que aumenta em cada ano em cerca de 400.000 crianças ⁽³⁶⁾. A existência de padrões complexos nos dados da prevalência mostra uma variação com o tempo, a idade, o sexo e a região geográfica ⁽⁵⁾. Na realidade, Lobstein e col. verificaram uma prevalência de sobrecarga ponderal superior nos países do Sul da Europa (20 a 35%) comparativamente com os do Norte (10 a 20%) ⁽⁵⁾, facto este confirmado recentemente ⁽³³⁾. As razões deste gradiente geográfico não são claras, mas sugerem que, independentemente de diferenças genéticas, as variáveis

ambientais são importantes factores preditivos de obesidade, operando de forma complexa intra e inter-países ^(5, 32).

Em Portugal, num estudo transversal com representatividade nacional, realizado entre 2002 e 2003 em crianças entre os 7 e os 10 anos de idade, Padez e col. verificaram uma prevalência de 20,3% de sobrecarga ponderal e 11,3% de obesidade, segundo os critérios da IOTF ⁽³⁷⁾. De acordo com este estudo, Portugal classifica-se em 2º lugar no *ranking* europeu da obesidade infantil (31,5%), após a Itália (36%) e logo seguido da Grécia (31%) e Espanha (30%) ⁽³⁷⁾. Recentemente, no âmbito do *European Childhood Obesity Surveillance Initiative* da OMS, foi aplicado a nível nacional o estudo COSI-Portugal tendo sido observada uma prevalência de 18,1% de sobrecarga ponderal e 13,9% de obesidade, com base nos critérios definidos pelo CDC, em crianças do 1º ciclo do Ensino Básico ⁽³⁸⁾.

Curiosamente, e apesar de na maioria dos países se verificar o aumento da prevalência de obesidade pediátrica, nos últimos anos alguns países, como os EUA ⁽³⁹⁾, França ⁽⁴⁰⁾, Suíça ⁽⁴¹⁾ e Suécia ⁽⁴²⁾, têm relatado uma estabilização da mesma.

Embora a definição de obesidade se reporte ao valor do IMC, esta implica necessariamente a existência de um valor anormal de gordura corporal total.

O desenvolvimento do tecido adiposo tem início no feto, sendo os primeiros vestígios deste tecido detectáveis entre as 14 e as 16 semanas de gestação. O segundo trimestre parece corresponder ao período da adipogénese, verificando-se no terceiro trimestre a presença de adipócitos nos principais locais de deposição de gordura, apesar de estas células serem ainda relativamente pequenas ⁽⁴³⁾.

O recém-nascido apresenta em média cerca de 10-15% de massa gorda, aumentando para 30% aos seis meses de idade e diminuindo gradualmente durante a primeira infância ⁽⁴⁴⁾. Entre os cinco e os oito anos de idade ocorre o ressalto adipocitário, período em que se reinicia o aumento progressivo do IMC, após a diminuição verificada no

primeiro ano de vida, seguido das alterações associadas à puberdade em que as diferenças entre os sexos se tornam aparentes, conforme já descrito ^(23, 45).

O tecido adiposo é constituído não apenas por adipócitos, mas também por outros tipos celulares, nomeadamente macrófagos, pré-adipócitos, fibroblastos, células imunes e vasculares, entre outras ⁽⁴⁶⁾. Quando presente em redor das vísceras abdominais, o tecido adiposo denomina-se de visceral ou intra-abdominal e é diferente daquele presente na região glúteo-femoral e nas paredes abdominal anterior e posterior, denominado de tecido adiposo subcutâneo ^(47, 48). O tipo de adipócitos, a sua função endócrina, actividade lipolítica, bem como a resposta à insulina e a outras hormonas difere entre estes dois tipos de tecido ⁽⁴⁷⁾. No que respeita à sua distribuição anatómica, esta também apresenta padrões distintos de acordo com o sexo ⁽⁴⁹⁾. Em geral, durante a adolescência, o tecido adiposo subcutâneo aumenta no tronco nos rapazes, enquanto nas raparigas aumenta na região glúteo-femoral, verificando-se assim uma distribuição central no sexo masculino - fenótipo andróide - e uma mais periférica no sexo feminino - fenótipo ginóide ^(22, 49).

A acumulação subcutânea de gordura representa o depósito fisiológico normal para o excesso de ingestão energética (excessos alimentares) acompanhado de uma capacidade limitada de gasto energético (sedentarismo). Actua como um receptáculo metabólico em que o excesso de ácidos gordos livres (AGL) e glicerol são armazenados sob a forma de triglicerídeos nos adipócitos ^(43, 50), representando cerca de 80% de toda a gordura corporal no adulto ⁽⁵¹⁾ e cerca de 90% na criança ⁽⁵²⁾. Quando a capacidade de armazenamento deste tecido é ultrapassada, devido à incapacidade de aumento do tamanho (hipertrofia) ou do número de adipócitos (hiperplasia), a gordura acumula-se em áreas fora do tecido subcutâneo, nomeadamente a nível visceral ^(47, 53). Devido à sua localização anatómica, o fluxo sanguíneo proveniente do tecido adiposo visceral é drenado directamente para o fígado através da veia porta, permitindo o acesso hepático a AGL e outras moléculas secretadas por este tecido, em contraste com o tecido subcutâneo cuja drenagem se efectua para a circulação sistémica ^(46, 54). As diferenças anatómicas e

fisiológicas existentes contribuem para a explicação do risco cardiovascular e metabólico associado à obesidade abdominal ⁽⁴⁷⁾.

O tecido adiposo é hoje em dia considerado um órgão endócrino metabolicamente activo ⁽⁵⁵⁾. Os adipócitos sintetizam e secretam um vasto número de substâncias com actividade autócrina e/ou parácrina ou endócrina, denominadas de adipocinas. Estas regulam diversos mecanismos fisiológicos, nomeadamente o apetite, balanço energético, imunidade, sensibilidade à insulina, angiogénese, pressão arterial, metabolismo lipídico, inflamação, entre outros ^(46, 55, 56). Desta forma, a produção desregulada destas moléculas participa na patogénese das comorbilidades associadas à obesidade ^(57, 58). Têm sido inúmeras as adipocinas descritas onde se incluem a leptina, adiponectina, resistina, adipsina, inibidor do activador do plasminogénio-1, citocinas, factores de crescimento, entre outras ⁽⁵⁵⁻⁵⁸⁾. De destacar a leptina e a adiponectina, ambas de interesse no âmbito desta investigação.

A leptina, descrita em 1994 ⁽⁵⁹⁾, é expressa e secretada fundamentalmente pelo tecido adiposo subcutâneo em quantidade proporcional à percentagem de massa gorda ^(60, 61), funcionando assim como um sinal adipostático. Esta hormona actua em receptores específicos localizados no sistema nervoso central, regulando o apetite e aumentando o gasto energético ^(61, 62). Para além disso, actua também a nível periférico onde desempenha importantes papéis na angiogénese, imunidade, reprodução e metabolismo ⁽⁶²⁻⁶⁴⁾. A sua concentração plasmática é geralmente superior no sexo feminino comparativamente com o masculino ^(65, 66). A incapacidade da leptina em suprimir o apetite e promover a perda de peso na obesidade, apesar dos seus níveis estarem elevados, é reconhecida como resistência à acção da leptina e pode estar associado a um aumento do risco metabólico e cardiovascular ^(61, 64, 67). Em resposta à restrição energética e à perda de peso, os níveis de leptina diminuem rapidamente ^(61, 68).

A adiponectina, também descrita como Acrp30, Adipo Q, apM1 ou GBP28, ao contrário das restantes adipocinas apresenta uma concentração diminuída com o aumento

da percentagem de massa gorda, estando associada inversamente à obesidade e suas complicações ⁽⁶⁹⁻⁷¹⁾. A sua concentração é elevada, representando 0,01% das proteínas plasmáticas ⁽⁷⁰⁾, e encontra-se presente em circulação sob três isoformas: trímero, hexâmero e multímero, também denominadas respectivamente de baixo peso molecular (*low molecular weight*: LMW), médio peso molecular (*medium molecular weight*: MMW) e elevado peso molecular (*high molecular weight*: HMW). Cada forma oligomérica apresenta propriedades biológicas distintas, activando diferentes vias de sinalização intracelular, porém a adiponectina-HMW é considerada a de maior actividade biológica ^(72, 73). A concentração plasmática de adiponectina é superior no sexo feminino comparativamente com o masculino, o que parece estar associado aos diferentes níveis de hormonas sexuais ^(74, 75). Mediante a ligação aos seus receptores (AdipoR1 e AdipoR2) ⁽²⁶¹⁾, esta desempenha importantes funções a nível do metabolismo glicídico com aumento da sensibilidade à insulina e diminuição do fluxo hepático de glicose, bem como do metabolismo lipídico, exercendo funções anti-diabetogénicas, anti-aterogénicas e anti-inflamatórias ^(71, 73, 76).

A comunicação estabelecida entre o tecido adiposo e os restantes sistemas é bidireccional, sendo as principais mensagens integradas a nível hipotalâmico, onde o balanço energético é controlado ⁽⁴⁶⁾. A título de exemplo, e no âmbito do presente trabalho, destaca-se a grelina. Este péptido é secretado pelas células do estômago e duodeno, e deve o seu nome à acção estimuladora sobre a secreção da hormona de crescimento ⁽⁷⁷⁾. Funciona também como estimulador do apetite e da ingestão alimentar, verificando-se um aumento pré-prandial dos seus níveis, seguido de uma diminuição pós-prandial ⁽⁷⁸⁻⁸⁰⁾. A sua concentração plasmática está diminuída na obesidade, parecendo funcionar como um sinal adipostático ^(80, 81). Outras funções da grelina, nomeadamente a nível do metabolismo glicídico e lipídico estão também descritas ^(82, 83), o que demonstra a complexa rede de interacções associada à regulação do peso e da composição corporal.

FACTORES ETIOLÓGICOS

A obesidade é uma doença complexa e multifactorial. Na sua génese estão envolvidos factores genéticos, hormonais, metabólicos e ambientais ⁽⁸⁴⁻⁸⁶⁾.

O alarmante aumento verificado nas últimas décadas na prevalência da obesidade não é justificável apenas pelo ambiente genético, pois para além de este ser relativamente estável, o período de tempo necessário para que se registasse uma mudança no genoma não foi o suficiente. Assim, os principais responsáveis por esta epidemia parecem ser factores ambientais que exercem a sua acção em indivíduos geneticamente susceptíveis ^(5, 6, 87). Na realidade, este flagelo representa a interacção entre o ambiente interno e o ambiente externo *obesogénico*, altamente favorecedor de um estilo de vida sedentário e do consumo excessivo de energia ^(5, 86, 87).

A compreensão da problemática da obesidade e dos factores predisponentes para a mesma é imprescindível para uma actuação mais eficaz e precisa na prevenção e tratamento desta epidemia.

FACTORES GENÉTICOS E FAMILIARES

É frequente os indivíduos atribuírem o seu excesso de peso à genética. E, na realidade, os genes não só podem, como influenciam o peso corporal. Certos indivíduos são portadores de genes ‘poupadores de energia’ (*thrifty genes*), manifestando maior susceptibilidade para a acumulação de gordura corporal ⁽⁸⁸⁾. No entanto, os defeitos genéticos associados à obesidade contribuem apenas para explicar uma fracção desta epidemia ^(87, 89). Estudos com gémeos têm demonstrado uma heritabilidade do IMC e adiposidade entre 40 a 70%, e em trabalhos com crianças adoptadas o seu IMC correlaciona-se com o dos seus pais biológicos e não com o dos seus pais adoptivos ^(90, 91). Estes achados apontam para a influência do componente genético na regulação do peso corporal, porém sem desvalorizar a capital importância dos factores ambientais no desenvolvimento desta patologia ^(92, 93).

Neste sentido, a presença de obesidade familiar é um importante factor preditivo do desenvolvimento de excesso de peso na criança ⁽⁹⁴⁻⁹⁶⁾. Crianças cujos familiares são obesos têm um risco duas a três vezes superior de desenvolverem obesidade, comparativamente com crianças cujos familiares são normoponderais, e este risco aumenta se ambos os pais forem obesos ⁽⁹⁷⁾. A influência da obesidade parental na obesidade da criança provavelmente resulta não só da partilha de factores genéticos, mas também de factores ambientais ^(95, 98), pois os pais além de agentes educadores são também agentes criadores do ambiente que rodeia a criança. Diversos estudos têm demonstrado que o IMC materno exibe uma maior associação com o IMC dos descendentes, comparativamente ao IMC paterno ^(94, 99). Isto reflecte as relações mãe-criança que se desenvolvem durante o período intra-uterino ⁽¹⁰⁰⁾, mas também poderá reflectir o facto de ser geralmente a mãe a responsável pela alimentação familiar, em especial dos filhos.

FACTORES ASSOCIADOS AO DESENVOLVIMENTO

O crescimento linear e a maturação física são processos dinâmicos que envolvem alterações moleculares, celulares e somáticas ⁽²⁰⁾. De acordo com Dietz ⁽¹⁰¹⁾, existem pelo menos três períodos críticos ao longo do desenvolvimento e crescimento do indivíduo que parecem determinar o risco de desenvolvimento da obesidade: o período fetal, do ressalto adipocitário e da adolescência.

O ambiente intra-uterino tem sido amplamente associado ao risco de obesidade prematura, no entanto os mecanismos precisos deste efeito não estão ainda completamente esclarecidos. Na 2ª Guerra Mundial, durante o cerco alemão à cidade de Amesterdão, a população foi sujeita a significativa restrição alimentar, de tal modo que durante um período de cerca de 6 meses a sua ingestão energética diminui de aproximadamente 1500 kcal para 500 kcal. Os indivíduos que foram expostos *in utero* a esta privação foram avaliados antropometricamente aos 18 anos de idade, tendo-se verificado uma baixa prevalência de obesidade naqueles que sofreram esta exposição no

último trimestre da gestação, enquanto que naqueles expostos no 1º e 2º trimestre se observou um aumento na prevalência ⁽¹⁰²⁾. Os dois primeiros trimestres da gravidez são caracterizados pelo desenvolvimento neurológico, nomeadamente a nível hipotalâmico. Neste sentido, a resposta à ingestão energética poderá ser definida pela capacidade de resposta do hipotálamo, do sistema nervoso simpático e da função endócrina ^(103, 104) à disponibilidade intra-uterina de substrato ⁽¹⁰²⁾. Durante a desnutrição materna, o feto restringe o seu crescimento e adapta o seu metabolismo no sentido da poupança energética, de modo a permitir a sua sobrevivência num ambiente extra-uterino escasso de nutrientes. Contudo, esta adaptação, inicialmente benéfica, fará com que quando expostos a maior disponibilidade alimentar esta se traduza em maior deposição de tecido adiposo ^(105, 106). O último trimestre da gestação representa o período de replicação adipocitária e de aumento do tecido adiposo, pelo que uma menor ingestão energética neste período levaria a menor deposição de tecido adiposo e subsequente magreza ⁽¹⁰²⁾.

O peso ao nascer também tem sido associado ao risco de desenvolvimento de obesidade ^(94, 107), exibindo uma curva em U ou J, isto é, recém-nascidos com baixo peso ou com peso elevado estão mais predispostos a serem obesos ⁽¹⁰⁰⁾. Esta associação parece dever-se à ocorrência de determinados estímulos numa fase precoce do desenvolvimento humano, que induzem alterações endócrinas e metabólicas que irão persistir ao longo da vida ⁽¹⁰⁶⁾. No entanto em alguns estudos, os resultados não são conclusivos ^(94, 108). Como exemplo, um peso elevado ao nascer pode ocorrer em recém-nascidos de mulheres diabéticas, nomeadamente com diabetes gestacional, em que a hiperglicemia materna induz um aumento dos níveis de insulina fetal. Este ambiente hiperinsulinémico parece suscitar uma programação metabólica a nível do hipotálamo que afectaria o balanço energético pós-natal, com maior risco de obesidade ⁽¹⁰⁹⁾.

O ressalto adipocitário, quando ocorre precocemente, encontra-se associado a um aumento do risco de obesidade na idade adulta, no entanto esta associação não é independente do IMC durante os primeiros anos de vida ^(108, 110, 111). Segundo Rolland-

Cachera e col., isto pode dever-se a uma deposição mais rápida de gordura nas crianças com um ressalto precoce ⁽¹¹¹⁾. Em termos sociais, este período coincide com o momento de entrada para a escola, com provável diminuição da actividade física e aumento das actividades sedentárias, bem como com a crescente ingestão de alimentos energéticos, eventualmente sem supervisão familiar.

Na adolescência, como já referido, verificam-se alterações da composição corporal e da distribuição da gordura corporal em ambos os sexos. Nas raparigas assiste-se a um incremento na percentagem de massa gorda, enquanto que nos rapazes, apesar de esta percentagem diminuir, verifica-se a sua maior deposição a nível central ⁽²⁰⁻²²⁾. Vários estudos sugerem que até cerca de 80% dos adolescentes com sobrecarga ponderal poderão tornar-se adultos obesos ^(103, 104, 108), sendo que o risco parece ser superior nas raparigas relativamente aos rapazes ^(103, 104). Este aspecto provavelmente está associado ao maior ganho de massa gorda, cerca de 5-6 kg, que ocorre neste sexo durante este período ⁽²²⁾. Observa-se também um risco aumentado de obesidade quanto mais precoce for o início da puberdade ^(112, 113). Poder-se-á ainda deduzir uma interligação entre a precocidade do ressalto adipocitário e da puberdade ⁽¹¹⁴⁾, visto que a precocidade do ressalto, estando na dependência de um aumento da gordura corporal, conduzirá a uma acumulação excessiva e irreversível de adiposidade, associado à mudança da composição corporal típica da adolescência, conduzindo a um maior risco de obesidade.

A ocorrência de obesidade em idade pediátrica apresenta uma forte persistência na idade adulta ⁽¹¹⁵⁾. Esta persistência aumenta à medida que a criança e o adolescente são mais velhos, conforme constatou Whitaker e col. em crianças entre os 6 e os 9 anos e em adolescentes entre os 10 e os 14 anos, em que 69% e 83%, respectivamente, dos que apresentavam obesidade, mantiveram-na na idade adulta ⁽⁹⁷⁾.

FACTORES AMBIENTAIS

Se considerarmos que a obesidade surge de um desequilíbrio entre a ingestão energética e o seu subsequente dispêndio energético, então poderemos considerar como factores ambientais *major* as modificações no padrão alimentar e na actividade física da população, que se traduzem num balanço energético positivo, tal como descrito no relatório da OMS ⁽¹¹⁶⁾.

INGESTÃO ALIMENTAR

As fases da infância e adolescência correspondem a períodos-chave para a aquisição de padrões alimentares adequados que promovam um crescimento saudável e um adequado desenvolvimento intelectual. Porém, a longo prazo os padrões alimentares desajustados nesta faixa etária podem gerar doenças crónico-degenerativas, como hipertensão arterial, diabetes mellitus tipo 2 (DM2), doenças cardiovasculares (DCV), arteriosclerose, osteoartrose, alguns tipos de cancro e obesidade ^(116, 117). No entanto, conforme vários autores constataam em diversos estudos epidemiológicos, a associação entre dieta ou a ingestão específica de um nutriente e o desenvolvimento de obesidade não é clara e os resultados não são consensuais ^(5, 118-121). Este facto aponta para a necessidade de desenvolvimento da investigação nesta área, contribuindo para um melhor conhecimento.

O rendimento das famílias, o preço dos alimentos, as preferências e crenças individuais, tradições culturais, bem como outros factores geográficos, sociais e económicos interagem de forma complexa moldando o consumo alimentar ⁽¹¹⁶⁾. Na realidade, as alterações que têm ocorrido a nível do padrão alimentar nos últimos 30 anos, quer quantitativas quer qualitativas, contribuem para a epidemia da obesidade que hoje se verifica ^(116, 122).

Em termos globais, estas alterações correspondem a uma maior disponibilidade e acessibilidade de alimentos, a uma diminuição no preço relativo dos alimentos e a um

aumento nas porções servidas e/ou ingeridas ⁽¹²²⁾. A análise da *FAO Statistical Database* (FAOSTAT) mostra que a ingestão energética medida em kcal por dia e *per capita* tem vindo a aumentar a nível mundial, verificando-se que a disponibilidade de calorias por dia e *per capita* a partir de meados da década de 60 para a década de 90 aumentou globalmente em cerca de 450 kcal ⁽¹¹⁶⁾. Este acréscimo observou-se também nos países europeus, onde a disponibilidade energética aumentou cerca de 17% entre 1961 e 2001 ^(116, 123). Em Portugal, segundo dados da Balança Alimentar Portuguesa, este aumento foi de 6% entre 1990 e 2003 ⁽¹²⁴⁾.

Estudos populacionais longitudinais em idade pediátrica têm demonstrado que, apesar da modificação dos hábitos alimentares, a ingestão energética não tem sofrido alterações significativas nos últimos 30 anos que justifiquem por si só o aumento da prevalência de obesidade. Assim, no *Bogalusa Heart Study*, um estudo prospetivo de uma população pediátrica norte-americana do Louisiana, verificou-se que nas crianças com 10 anos de idade a ingestão energética permaneceu relativamente estável entre 1973 e 1988 ⁽¹²⁵⁾. Após comparação de três inquéritos nacionais norte-americanos – NHANES I (1971-1974), NHANES II (1976-1980) e NHANES III (1988-1994), foram constatados resultados semelhantes ⁽¹²⁶⁾, e a mesma tendência verificou-se no NHANES (1999-2000) ⁽¹²⁷⁾. A análise de dados relativos à ingestão alimentar em crianças e adolescentes europeus durante os últimos 30 anos, permitiram concluir que apesar de a ingestão energética ser variável em relação à idade e sexo, não se verificou qualquer tendência óbvia para um aumento ou diminuição da energia ingerida ⁽¹²⁸⁾. Contudo, é de ressaltar que a avaliação da ingestão alimentar, quer em crianças quer em adultos, está sujeita a diversos viés ^(128, 129, 130). O aporte energético por si só não parece ser assim o principal contribuinte para o aumento da prevalência de excesso de peso ⁽¹¹⁸⁾. Neste sentido, importa conhecer qual a contribuição de cada macronutriente para o valor energético total diário e para a problemática da obesidade.

À partida, o consumo excessivo de lípidos parece ser um forte candidato como factor etiológico no ganho de peso. Pensa-se que a ingestão de gordura esteja associada a um aumento da ingestão alimentar devido à sua baixa saciação, elevada palatibilidade e densidade energética, e fraca regulação metabólica ⁽¹³¹⁾. Vários estudos transversais demonstram uma associação significativa entre a ingestão lipídica e a adiposidade ⁽¹³²⁻¹³⁴⁾. Porém, estudos longitudinais, quer em crianças quer em adultos, apresentam resultados contraditórios ^(119, 135, 136). Berkey e col., num estudo com a duração de 1 ano envolvendo crianças e adolescentes norte-americanos (9-14 anos de idade), não demonstraram qualquer relação entre a evolução do IMC e a ingestão de lípidos, tendo inclusive verificado uma redução da ingestão dos mesmos no decurso do estudo ⁽¹³⁷⁾. Em contrapartida, Maffei e col. constataram em crianças pré-púberes uma associação positiva entre a percentagem de lípidos e o excesso de peso, mesmo após ajuste para o metabolismo basal, e não verificaram qualquer associação com a ingestão energética e os restantes macronutrientes ⁽¹³³⁾. Recentemente tem sido dada particular atenção ao tipo de gordura alimentar, e um maior consumo de gordura saturada tem sido demonstrado em crianças obesas ⁽¹³⁸⁾. Porém, segundo dados dos diversos NHANES, a ingestão deste tipo de gordura tem vindo a decrescer, tal como sucede com a ingestão lipídica total ^(126, 127). Estes aparentes dados contraditórios podem dever-se à dificuldade na quantificação da gordura alimentar e contribuem para a incerteza do papel da gordura no desenvolvimento da obesidade.

Apesar de existirem poucos estudos que abordam o papel do teor proteico da dieta, este tem sido proposto como capaz de modular a percentagem de gordura corporal ⁽¹³³⁾. A ingestão proteica aos 2 anos de idade mostrou-se associada a um IMC superior quando do ressalto adipocitário ⁽¹³⁹⁾, bem como a uma maior precocidade do mesmo ⁽¹⁴⁰⁾, o que por sua vez se encontra associado ao desenvolvimento de obesidade. Outros estudos, por seu lado, não encontraram associação entre o aporte proteico durante a infância e o desenvolvimento posterior de massa gorda ⁽¹³⁵⁾. Dados do *Bogalusa Heart Study* mostram que a ingestão proteica em crianças com 10 anos de idade aumentou cerca de 7,5% entre

1973 e 1994 ⁽¹²⁵⁾. O mesmo se verifica em adolescentes de países do sul da Europa, incluindo Portugal ⁽¹⁴¹⁾. Em termos metabólicos, a proteína é um nutriente insulínico, estimulando a secreção de insulina e de *insulin-like growth factor-1* (IGF-1), promotores da adipogénese e da lipogénese ⁽¹⁴⁰⁾.

Relativamente aos hidratos de carbono (HC) tem-se verificado um aumento da sua ingestão em crianças e adolescentes norte-americanos ^(125, 127). Uma das possíveis razões deste aumento encontra-se na dependência directa das recomendações relativas à redução do aporte lipídico da dieta, e à sua substituição crescente pelos HC. No entanto, é de salientar que esta substituição nas crianças e adolescentes se faz preferencialmente à custa de HC simples, em detrimento dos complexos ^(125, 142). Em países do Sul da Europa, Cruz aponta para o facto de a ingestão de açúcares adicionados contribuir para mais de 10% do valor energético total ⁽¹⁴¹⁾. Neste sentido, existem diversos aspectos que indicam um aumento do índice glicémico do actual padrão alimentar dos mais jovens nos últimos anos, tais como o aumento no consumo de *snacks* e de refrigerantes, sendo que a ingestão destes últimos ultrapassa os 8% do aporte energético total em adolescentes norte-americanos ^(118, 125, 143). No entanto, alguns estudos em crianças e adolescentes têm demonstrado uma associação negativa entre o IMC e a percentagem de HC da dieta ^(132, 144).

ACTIVIDADE FÍSICA

Nas últimas décadas várias modificações nos estilos de vida tiveram como resultado a redução da actividade física por parte quer dos adultos, quer das crianças e adolescentes. Actualmente, as crianças deslocam-se fundamentalmente em transportes públicos ou de carro, o tempo dedicado à actividade física na escola diminuiu, e em casa os pais têm receio de que as crianças brinquem no exterior, remetendo-as para actividades sedentárias como ver televisão e jogar no computador ^(32, 128, 145, 146). Assim, podemos considerar como factores capazes de aumentar o risco de obesidade dois aspectos

aparentemente interligados, a diminuição da actividade física e o aumento das actividades sedentárias ^(146, 147, 114).

De acordo com dados do NHANES III, as crianças (6-11 anos) e adolescentes (12-19 anos) que reportaram passar maior número de horas a ver televisão ou a jogar computador eram os que apresentavam maior IMC ⁽¹⁴⁹⁾. Num estudo transversal envolvendo 34 países europeus, incluindo Portugal, os autores constataram em 29 países (88%) que a probabilidade de ter excesso de peso era significativamente menor, mediante um efeito dose-resposta, com uma participação maior na actividade física. Paralelamente, observaram um maior grau de sobrecarga ponderal para um maior tempo de visualização de televisão em 22 (65%) dos países avaliados ⁽³¹⁾. Segundo Ekelund e col., o tempo passado a ver televisão e a frequência da prática de actividade física, constituem factores distintos e independentemente associados com a obesidade e o risco metabólico ⁽¹⁵⁰⁾. Um aspecto importante associado à visualização da televisão, para além da redução do gasto energético diário, é a associação frequente a uma ingestão alimentar aumentada, nomeadamente ao consumo de alimentos de elevada densidade energética e baixa densidade nutricional ^(151, 152).

Todavia, os estudos longitudinais apresentam por vezes resultados contraditórios. Enquanto alguns demonstram uma relação inversa entre a actividade física, o IMC e a adiposidade ⁽¹⁵³⁻¹⁵⁵⁾, outros não ^(119, 156). Assim, torna-se difícil concluir que a diminuição da actividade física seja a principal causa da prevalência aumentada de excesso ponderal, muito embora seja inquestionável a sua intervenção. Na realidade, o efeito da actividade física na prevenção e tratamento da obesidade deve-se não só ao impacto da mesma no dispêndio energético, mas também ao seu papel na regulação energética e na ingestão alimentar, promovendo a oxidação de substratos e modulando o peso e a composição corporal ⁽¹⁵⁷⁾.

COMPLICAÇÕES ASSOCIADAS AO EXCESSO DE PESO

A obesidade representa um grave problema de Saúde Pública devido às diversas comorbidades que acarreta com atingimento de vários órgãos e sistemas (cardiovascular, respiratório, endócrino, renal, gastrointestinal, reprodutor e músculo-esquelético) ^(5, 34, 103, 109, 158). À medida que a prevalência de obesidade em idade pediátrica aumenta, as suas implicações para a saúde também se tornam mais evidentes ^(34, 158). Assim, não só na idade adulta, mas também já na criança e adolescente, o excesso de gordura corporal está relacionado directamente com alterações do perfil lipídico, do metabolismo da insulina e da glicose, hipertensão arterial, síndrome metabólica (SM), entre outros, considerados factores de risco para o desenvolvimento DM2 e DCV na idade adulta ⁽¹⁵⁹⁻¹⁶¹⁾. Lobstein e Jackson-Leach, utilizando dados da prevalência de obesidade de 2006, estimaram que na Europa cerca de 27.000 crianças obesas apresentavam DM2 e mais de 400.000 tinham tolerância anormal à glicose; cerca de 1 milhão eram susceptíveis de apresentarem um conjunto de factores indicadores de DCV, nomeadamente hipertensão ou dislipidemia presente em 1.1 milhões de crianças, e SM presente em aproximadamente 1.2 milhões. Adicionalmente, 1.4 milhões de crianças obesas apresentavam esteatose hepática ⁽³⁴⁾. De acrescentar que o excesso ponderal na idade pediátrica pode ainda ser acompanhado de distúrbios psicológicos que se podem manifestar em doenças do comportamento alimentar, baixa auto-estima e comportamento social desajustado ^(162, 163).

Estes resultados vão de encontro à relação existente entre a obesidade nas primeiras décadas de vida e as elevadas taxas de morbilidade e mortalidade em adultos ^(4, 103, 164-165). Mesmo após normalização ponderal o risco de doença no adulto persiste, o que sugere o desenvolvimento de alterações não totalmente reversíveis durante a obesidade na infância e adolescência ^(164, 166). Assim, a obesidade nesta faixa etária obriga a uma atenta avaliação metabólica e cardiovascular, de modo a prevenir o desenvolvimento precoce de DCV, DM2, entre outras ⁽¹⁶⁶⁻¹⁶⁸⁾.

ALTERAÇÕES DO PERFIL LIPÍDICO

A epidemia da obesidade em idade pediátrica faz-se acompanhar de um perfil lipídico anormal, situação que se pensava ter início na idade adulta e ser expressa na infância apenas como uma anormalidade genética ⁽¹⁶⁹⁾.

Dados do *Bogalusa Heart Study* mostram que as crianças obesas são 2,4, 3 e 7,1 vezes mais propensas a valores aumentados, respectivamente, de colesterol total, de lipoproteínas de baixa densidade (*low density lipoproteins* – LDL), e de triglicerídeos. Relativamente às lipoproteínas de alta densidade (*high density lipoproteins* – HDL), estas são 3,4 vezes mais propensas a valores diminuídos ⁽¹⁷⁰⁾. Num estudo recente realizado em crianças obesas (7 a 12 anos de idade), os autores verificaram que cerca de metade da população apresentava um perfil lipídico anormal, quando comparado com uma população de referência. Para além disso, as crianças com maior z-score do IMC (z-IMC) e menor aptidão física apresentavam as concentrações mais elevadas de triglicerídeos e mais reduzidas de HDL ⁽¹⁷¹⁾.

Um aspecto importante no desenvolvimento de um perfil lipídico anormal é a acumulação de gordura a nível abdominal, sabendo-se que já na idade pediátrica um perímetro da cintura elevado está associado a concentrações superiores de triglicerídeos, LDL, colesterol total e insulina, bem como valores elevados de pressão arterial ⁽¹⁷²⁾. O tecido adiposo abdominal tem elevada actividade lipolítica, drenando directamente no sistema porta hepático os AGL e glicerol, com consequente aumento da síntese de triglicerídeos e de lipoproteínas de muito baixa densidade (*very low density lipoproteins* – VLDL), reflectindo-se num aumento dos níveis plasmáticos de LDL e diminuição de HDL ⁽¹⁷³⁾.

Estudos prospectivos têm demonstrado que não só os valores das lipoproteínas persistem fortemente desde a infância e adolescência até à idade adulta ^(174, 175), mas também que valores adversos das lipoproteínas no início da vida podem induzir alterações arteriais que contribuem para o desenvolvimento de aterosclerose no adulto ⁽¹⁷⁶⁻¹⁷⁸⁾.

Neste sentido, segundo a *American Academy of Pediatrics*, a obesidade é um factor de risco para o desenvolvimento de dislipidemia, pelo que em crianças com sobrecarga ponderal se deve proceder ao rastreio de alterações nos lípidos plasmáticos, independentemente da história familiar ⁽¹⁷⁹⁾. Contudo, é reconhecido que a dislipidemia observada em crianças e adolescentes obesos possui origens quer genéticas, quer ambientais ⁽¹⁸⁰⁾.

ALTERAÇÕES DA PRESSÃO ARTERIAL

Não só no adulto mas também na criança, o excesso ponderal está associado com o aumento da pressão arterial. No *Muscatine Study* e no *Bogalusa Heart Study*, o aumento do IMC mostrou uma relação consistente com valores tensionais elevados ^(170, 181, 182). Neste último estudo, os dados mostram que as crianças obesas são 4,5 e 2,4 vezes mais propensas a apresentarem valores aumentados de pressão arterial sistólica e diastólica, respectivamente ⁽¹⁷⁰⁾. Assim, em paralelo com a obesidade, também a hipertensão pediátrica registou um aumento epidemiológico nos últimos anos ⁽¹⁸³⁾. Num estudo transversal realizado em crianças e adolescentes norte-americanos, Falkner e col. verificaram uma prevalência de hipertensão entre 4,3 a 6,5% em crianças dos 2 aos 10 anos de idade, valor este que quase duplicou para 7,8 a 11,2% nas obesas. O mesmo se verificou nos indivíduos dos 11 aos 19 anos de idade, com uma prevalência de hipertensão entre 9,5 a 11,8% do total da amostra e de 18,5 a 20,8% nos obesos ⁽¹⁸⁴⁾.

As origens da hipertensão em crianças e adolescentes obesos permanece ainda por clarificar, no entanto crê-se que esta seja em parte devida a uma combinação de 3 mecanismos: disfunção autonómica, resistência à insulina e anormalidades na função e estrutura vascular ⁽¹⁸³⁾. A leptina parece também desempenhar um papel no aumento da pressão arterial, nomeadamente por estimulação da actividade simpática ⁽⁶⁴⁾. De acrescentar também outros factores predisponentes de hipertensão, tais como factores genéticos e factores ambientais ⁽¹⁸⁵⁾, entre os quais a ingestão de sal ⁽¹⁸⁶⁾.

A pressão arterial na infância e o IMC demonstraram ser, consistentemente, os factores preditivos mais fortes dos valores tensionais do adulto, em todas as idades e em ambos os sexos ⁽¹⁸¹⁾. Assim, a hipertensão na idade pediátrica persiste até à idade adulta ⁽¹⁸⁷⁾ e tem sido associada com o espessamento da camada íntima-média carotídea ⁽¹⁷⁶⁾, hipertrofia ventricular esquerda ⁽¹⁸⁸⁾ e formação de placas fibrosas ⁽¹⁸⁹⁾, todos factores determinantes de eventos cardiovasculares adversos no adulto ⁽¹⁸⁵⁾. Neste sentido, a intervenção precoce reveste-se de extrema importância na prevenção da DCV futura ⁽¹⁸⁷⁾.

ATEROSCLEROSE

A aterosclerose inicia-se na infância e desenvolve-se silenciosamente durante décadas antes de ocorrerem os eventos clínicos associados, tais como enfarte do miocárdio ou acidente vascular cerebral ⁽¹⁷⁸⁾.

A combinação de obesidade, hipertensão arterial e dislipidemia aumenta dramaticamente a incidência de lesões ateroscleróticas iniciais, tais como estrias lipídicas e placas fibrosas, nas artérias carótidas e coronárias de crianças e adolescentes ^(170, 182). No *Bogalusa Heart Study*, após a autópsia de crianças e adultos jovens com idades compreendidas entre os 2 e os 39 anos, os autores demonstraram que a prevalência de estrias lipídicas e placas fibrosas nas artérias aorta e coronárias aumentava com a idade e correlacionava-se positivamente com o z-IMC, a concentração plasmática de triglicédeos e colesterol total, e os valores de pressão arterial ⁽¹⁸⁹⁾. De referir ainda que, segundo este estudo, a combinação de vários factores de risco aumentava exponencialmente o grau de envolvimento da superfície íntima arterial ⁽¹⁸⁹⁾. No *PDAY (Pathological Determinants of Atherosclerosis in Youth) Study*, a análise *post-mortem* de mais de 3.000 indivíduos (15 a 34 anos de idade) demonstrou a associação entre a progressão das lesões ateromatosas e a presença de obesidade e de tolerância anormal à glicose ⁽¹⁹⁰⁾.

A associação entre o IMC e a presença de disfunção endotelial e disfunção vascular periférica tem sido constatada por vários autores, verificando-se em crianças obesas uma

maior espessura da camada íntima-média carotídea ^(178, 191, 192). Paralelamente, uma diminuição da *compliance*, uma reduzida distensibilidade e uma diminuída função endotélio-dependente e independente, são frequentemente encontradas em crianças com obesidade severa ^(192, 193). Também a resistência à acção da insulina, normalmente presente em obesos, está associada com o grau de disfunção endotelial e contribui para o processo de aterogénese ^(173, 194).

Num estudo populacional, Baker e col. verificaram que por cada aumento de uma unidade no z-IMC, o risco de desenvolver um evento coronário aumentava significativamente nos rapazes entre os 7 e os 13 anos de idade e nas raparigas entre os 10 e os 13 anos, mais acentuadamente em ambos os sexos por volta dos 13 anos. Segundo os autores, mesmo um pequeno ganho de peso é suficiente para aumentar o risco de doença coronária ⁽¹⁹⁵⁾. Assim, recomenda-se que a prevenção a longo prazo da aterosclerose deve começar cedo na vida do indivíduo e concentrar-se nos vários factores de risco cardiovascular ⁽¹⁸⁵⁾.

ALTERAÇÕES DO PERFIL GLICÉMICO, RESISTÊNCIA À INSULINA E DIABETES MELLITUS TIPO 2

A complicação metabólica mais grave da obesidade pediátrica é a DM2 ^(109, 173). Na realidade, durante a infância e adolescência a obesidade é a principal causa de resistência periférica à insulina e encontra-se intimamente relacionada com o desenvolvimento de alterações no metabolismo da glicose ⁽¹⁹⁶⁾. Estas alterações não são sintomatologicamente aparentes nas fases iniciais da doença, mas podem ser confirmadas por avaliação bioquímica ⁽¹⁸⁵⁾.

Potenciais candidatos à ligação entre obesidade e as alterações no metabolismo da glicose incluem concentrações elevadas de AGL e citocinas pró-inflamatórias derivadas do tecido adiposo, bem como concentrações diminuídas de adiponectina, que podem mediar uma falência acelerada das células beta (β) pancreáticas ⁽¹⁹⁶⁾.

Nas últimas duas décadas, o aumento na prevalência de obesidade em crianças e adolescentes foi acompanhado de um aumento na prevalência de DM2 ⁽¹⁹⁷⁻¹⁹⁹⁾. Em 1996, cerca de um terço dos novos casos de diabetes diagnosticados em jovens norte-americanos (entre os 10 e 19 anos de idade) referiam-se a DM2, e mais de 90% destes indivíduos apresentavam um Perc_{IMC} superior a 90 ⁽²⁰⁰⁾. O ambiente genético desempenha também um papel no desenvolvimento desta patologia, sendo que entre 2002 e 2003 a proporção de DM2 entre os casos de diabetes recém-diagnosticada, na mesma faixa etária, variou de 14,9% em brancos não-hispânicos e 46,1% nos hispânicos, a 57,8% em afro-americanos e 86,2% nos índios americanos ⁽²⁰¹⁾.

Sinha e col. descreveram pela primeira vez as alterações no metabolismo glicídico presentes em crianças e adolescentes obesos: diminuição da tolerância à glicose (DTG) em 25% das crianças (4 a 10 anos de idade) e em 12% dos adolescentes (11 aos 18 anos de idade) obesos, bem como DM2 assintomática em 4% dos adolescentes ⁽²⁰²⁾. Na Europa, a prevalência de alterações no metabolismo da glicose é menor, nomeadamente no que respeita à DM2 (0,5% a 2%) ^(198, 199, 203).

Sob condições fisiológicas normais, a concentração plasmática de glicose permanece dentro de um intervalo estreito, quer em jejum, quer no estado pós-absortivo. Esta regulação precisa da glicemia é mantida mediante um delicado equilíbrio entre a secreção de insulina e a sensibilidade à insulina ⁽²⁰⁴⁾. Na presença de obesidade, a primeira manifestação que surge no metabolismo da glicose é a resistência à insulina ⁽²⁰⁵⁾. Esta corresponde à redução da capacidade dos tecidos sensíveis à insulina em poder utilizá-la normalmente, devido a alterações genéticas, metabólicas ou nutricionais ^(196, 206). Weiss e col. verificaram que crianças e adolescentes obesos com DTG apresentavam profunda resistência periférica à insulina, com acumulação intramiocelular aumentada de lípidos e aumento da gordura visceral ⁽²⁰⁷⁾. A secreção de adipocinas pelo tecido adiposo, nomeadamente visceral, também parece ser responsável pelo desenvolvimento da resistência à insulina ^(208, 209). Contudo, e apesar de em jovens obesos se presenciar níveis

plasmáticos aumentados de triglicerídeos e insulina, os níveis de glicose geralmente estão normais ^(210, 211). Isto sugere que a DTG, também denominada de pré-diabetes, se desenvolve mais tardiamente ⁽²¹²⁾.

Nas fases iniciais da DTG, as células β pancreáticas são capazes de compensar a resistência à insulina através de um aumento da sua produção, sendo esta hiperinsulinemia compensatória capaz de manter a glicemia dentro da normalidade. Num trabalho envolvendo a realização de um *clamp* hiperinsulinémico-euglicémico em adolescentes, Sinaiko e col. demonstraram uma correlação significativamente positiva entre o IMC e a insulinemia em jejum, e negativa entre este parâmetro antropométrico e a sensibilidade à insulina ⁽²¹³⁾. Dados do *Bogalusa Heart Study* mostram que as crianças obesas são 12,6 vezes mais propensas a concentrações plasmáticas aumentadas de insulina ⁽¹⁷⁰⁾.

Porém, a dado momento as células pancreáticas entram em falência, o que resulta na secreção insuficiente de insulina, fazendo-se assim a transição de um quadro de resistência à insulina para uma situação de DM2 ^(196, 206). Este passo na progressão para a DM2 está também associado a um aumento do peso corporal ^(202, 212, 214). Weiss e col., ao reavaliar após 2 anos 117 crianças e adolescentes obesos (4 a 18 anos), verificaram que dos 33 indivíduos com DTG, 8 tinham desenvolvido DM2, correspondendo a cerca de 7% do total da amostra. De salientar que aqueles que desenvolveram DM2 apresentaram um aumento significativo do peso e do IMC ⁽²¹²⁾. Segundo estes autores, o estado de tolerância à glicose é altamente dinâmico e pode sofrer deterioração rapidamente. No entanto esta progressão não é regra, pois uma parte dos indivíduos obesos com resistência à insulina não desenvolve DM2. Este facto sugere que a predisposição genética é um factor catalisador importante ⁽¹⁷³⁾.

Durante a puberdade verifica-se uma diminuição transitória da sensibilidade à insulina e consequente aumento da resistência à acção desta hormona, possivelmente devido ao aumento nos níveis de hormona de crescimento e IGF-1, o que pode agravar a possível resistência à insulina presente no obeso, acelerando a progressão para DM2 ⁽²¹⁵⁾.

A sequência do desenvolvimento destas alterações, as causas da falência das células pancreáticas e a natureza dos sinais provenientes dos tecidos resistentes à insulina que falham na capacidade de produzir uma resposta adequada das células β , continuam a ser objecto de debate e investigação quer na idade adulta, quer na idade pediátrica ⁽²¹⁶⁾.

SÍNDROME METABÓLICA (SM)

A SM é reconhecida como o agrupamento da obesidade e de alterações metabólicas, tais como a hiperinsulinemia e resistência à insulina, intolerância à glicose, hipertensão arterial, níveis séricos elevados de triglicérideos e diminuição dos níveis de HDL ⁽²¹⁷⁾, entre outras.

Uma síndrome define-se como a reunião de factores que ocorrem em conjunto com maior frequência do que por mero acaso e cuja causa é frequentemente incerta. A SM cumpre estes critérios, pois a coexistência dos seus componentes parece ser mais frequente do que seria de esperar, e o seu agrupamento parece adicionar um risco cardiovascular substancial, para além dos factores de risco individuais ^(217, 218).

Pelo já exposto nas secções anteriores, a obesidade pode ser considerada o expoente máximo de facilitação para o desenvolvimento de SM, quer pela comorbilidade metabólica, quer pela comorbilidade cardiovascular a ela associada ^(103, 180, 185). Em crianças e adolescentes obesos, Weiss e col. verificaram que o aumento de 0,5 no z-IMC está associado a um aumento de cerca de 50% no risco de SM ⁽²¹⁰⁾.

Efectivamente, até há pouco tempo a SM era entendida como uma patologia do adulto, no entanto é cada vez mais frequente a sua observação em idade pediátrica, impulsionada pela crescente epidemia da obesidade ^(210, 211, 219).

No âmbito da presente investigação, este assunto será abordado com maior detalhe na secção seguinte.

II. SÍNDROME METABÓLICA

A evolução da SM está enraizada no conceito de resistência à insulina e suas consequências, bem como no reconhecimento do tecido adiposo como um órgão heterogêneo e fisiologicamente activo ⁽²²⁰⁾.

As primeiras descrições referentes à coexistência dos vários componentes da SM surgiram no início do século XX. Assim, nos anos 20 os austríacos Hitzenberger e Richter-Quittner, o sueco Kylin, e o espanhol Marañon publicaram quase simultaneamente artigos em que descreviam a coexistência de hipertensão arterial e diabetes em adultos e propuseram a existência de mecanismos comuns ao desenvolvimento de ambas as patologias. Posteriormente, Kylin acrescenta a uricemia e descreve a ‘síndrome hipertensão-hiperglicemia-hiperuricemia’. Na década de 60, Camus (1966) descreve a ‘tri-síndrome metabólica’ que incluía gota, diabetes e dislipidemia, enquanto que Avogaro e Crepaldi (1967) descrevem a ‘síndrome plurimetabólica’ que reunia dislipidemia, obesidade, diabetes, hipertensão e doença coronária. A associação entre o aumento da prevalência destas patologias com a nutrição e estilos de vida é descrita por Mehnert e Kuhlmann (1968), a que denominam de ‘síndrome da abundância’. O termo ‘síndrome metabólica’ surge pela primeira vez em 1981, por Hanefeld e Leonhardt, reunindo DM2, hiperinsulinemia, obesidade, hipertensão, dislipidemia, gota e trombofilia, que se desenvolvem num contexto de predisposição genética e influências ambientais, levando ao desenvolvimento de aterosclerose ^(220, 221). Em 1988, durante a *Banting Lecture* na *American Diabetes Association* (ADA), Reaven descreve a resistência à insulina como um factor etiológico comum a várias situações clínicas, nomeadamente DTG, hiperinsulinemia, hipertensão, níveis plasmáticos elevados de VLDL e diminuídos de HDL, definindo assim a ‘síndrome X’ ⁽²²²⁾. Salienta ainda o facto dos indivíduos com esta síndrome apresentarem risco aumentado de aterosclerose, bem como o papel de factores genéticos e ambientais (obesidade e sedentarismo) no agravamento da resistência à insulina. Um ano mais tarde,

Kaplan acrescenta a adiposidade central aos sintomas enumerados por Reaven, resumizando a SM em quatro componentes: adiposidade central, DTG, hipertrigliceridemia e hipertensão, denominando-a de ‘quarteto mortal’ ^(220, 221). Durante os anos 90, DeFronzo e Ferrannini, bem como Haffner, aplicaram a designação ‘síndrome de resistência à insulina’ procurando sublinhar o forte papel causal da resistência à insulina no desenvolvimento das várias componentes da síndrome. Desde então vários cientistas têm contribuído para a melhor compreensão dos vários aspectos da SM ⁽²²¹⁾, apesar de ainda hoje o seu conhecimento ser limitado.

Paralelamente a esta evolução dos conceitos da SM, assistiu-se sempre à dificuldade na sua definição. Só em 1988 surge a primeira definição internacional pela OMS ⁽²²³⁾, em que o principal componente é a resistência à insulina, identificada pela presença de DM2 ou DTG. Para além desta, o diagnóstico de SM requeria a presença de pelo menos dois dos seguintes componentes: hipertensão, hipertrigliceridemia, níveis reduzidos de HDL, obesidade (classificada pelo IMC ou pela razão perímetro da cintura/perímetro da anca) e microalbuminúria. Várias definições se seguiram, porém actualmente as mais utilizadas são a do *National Cholesterol Education Program/Adult Treatment Panel III* (NCEP/ATPIII) que surge em 2001 ⁽²²⁴⁾, e a da *International Diabetes Federation* (IDF) que surge em 2005 ⁽²²⁵⁾. Recentemente, na tentativa de uniformizar a definição da SM, membros de várias organizações internacionais acordaram nos cinco critérios para o diagnóstico da mesma (hipertensão, alterações do metabolismo da glicose, dislipidemia (HDL e triglicérideos) e obesidade abdominal) e na existência de um ponto de corte para cada um deles, excepto no que respeita ao perímetro da cintura em que pontos de corte nacionais/regionais poderão ser usados e para o qual são necessários mais estudos ⁽²¹⁷⁾.

Os críticos do conceito da SM apontam como principais limitações: a) ambiguidade dos critérios descritos e seus pontos de corte; b) incerteza da resistência à insulina como factor etiológico unificador; c) ausência de uma base clara para a inclusão/exclusão de

outros factores de risco cardiovasculares; d) variabilidade e dependência do valor de risco cardiovascular consoante os factores de risco presentes; e) risco associado à SM não parecer ser maior que a soma das partes; f) tratamento da SM como um todo não ser diferente do tratamento de cada um dos seus componentes; g) ausência de clareza no valor médico do diagnóstico da SM ⁽²²⁶⁻²²⁸⁾. De acrescentar que a SM não é um indicador de risco absoluto, pois não contém muitos dos factores que o determinam, tais como idade, sexo, tabagismo, entre outros ⁽²²⁶⁾.

Neste sentido, o reconhecimento da SM como uma doença tem sido dificultado pela ausência de uma definição consensual para o seu diagnóstico, pelo debate contínuo acerca da sua etiologia e patogénese, e incerteza acerca do seu tratamento ⁽²²⁰⁾.

SÍNDROME METABÓLICA NA IDADE PEDIÁTRICA

DEFINIÇÃO E PREVALÊNCIA

A dificuldade de consenso na definição da SM na população adulta manifesta-se também na população pediátrica. Apesar dos mecanismos fisiopatológicos e os vários componentes desta entidade se encontrarem já presentes nesta faixa etária, várias tentativas têm sido feitas para caracterizar a SM ^(219, 229). Khoury e col., em 1980, no *Cincinnati Lipid Research Clinic's Princeton Study*, foram talvez os primeiros a demonstrar o agrupamento de factores de risco para DCV em crianças e adolescentes entre os 6 e os 19 anos de idade ⁽²³⁰⁾. Mais tarde, Smoak e col. relataram também a coexistência de factores de risco cardiovasculares em crianças e adultos jovens no *Bogalusa Heart Study* ⁽²³¹⁾.

Têm sido vários os obstáculos à existência de uma definição coerente e consensual na idade pediátrica, nomeadamente: o uso de pontos de corte para adultos ou um conjunto único de pontos de corte para todas as idades durante a infância/adolescência; o facto de os distúrbios metabólicos observados nas crianças serem quantitativamente moderados; a ausência da definição de um limite normal de concentração de insulina durante a infância/adolescência; a resistência à insulina fisiológica da puberdade; a ausência da

definição de pontos de corte para o perímetro da cintura associados à morbilidade da obesidade ou ao SM em crianças; e as diferenças entre etnias nas concentrações basais dos lípidos plasmáticos ⁽²¹⁹⁾.

De acordo com a literatura, verifica-se que a maioria dos trabalhos recorre às definições descritas para a população adulta com correcção de alguns critérios, nomeadamente através de percentis específicos para a idade e para o sexo, estando identificadas 46 definições, algumas delas originais ^(210, 211, 232-237). Esta variabilidade é devida em parte às modificações do crescimento e desenvolvimento que ocorrem na infância e adolescência e que tornam complicada a definição de pontos de corte para os vários factores de risco. Algumas das várias definições reconhecidas estão descritas no Quadro 1, sendo que as mais utilizadas são a definição de Cook e col. ⁽²³⁴⁾ e mais recentemente a da IDF ⁽²³⁷⁾. No primeiro caso, os autores adaptaram a definição do NCEP/ATPIII com correcção de alguns critérios, nomeadamente pressão arterial, perímetro da cintura e lípidos plasmáticos, através de percentis específicos para idade e para o sexo, sendo necessária a presença de pelo menos três dos critérios definidos para o seu diagnóstico ⁽²³⁴⁾. Já a definição da IDF assenta, tal como no adulto, na presença obrigatória de obesidade abdominal, definida por um valor superior ao percentil 90, acrescida de pelo menos dois dos restantes critérios. Esta definição distingue três grupos etários, justificados pelas distintas características do desenvolvimento relacionado com a idade: dos 6 aos 10 anos; dos 10 aos 16 anos; e superior a 16 anos. Crianças com idade inferior a 6 anos foram excluídas da definição pela escassez de dados específicos para esta faixa etária, e em crianças menores de 10 anos, segundo os autores, a SM não deve ser diagnosticada devendo ser apenas transmitida uma mensagem de alerta para a redução de peso ⁽²³⁷⁾.

Esta variabilidade nas definições e critérios utilizados, traduz-se na dificuldade em comparar diferentes estudos e determinar a prevalência de SM na idade pediátrica ^(238, 239).

Quadro 1 (A e B) – Definições da SM descritas para a idade pediátrica.**A**

Cook e col. ⁽²³⁴⁾	de Ferranti e col. ⁽²³²⁾	Cruz e col. ⁽²³³⁾	Weiss e col. ⁽²¹⁰⁾	Viner e col. ⁽²⁴⁰⁾
PC ≥P90 (NHANES III)	PC >P75	PC ≥P90 (NHANES III)	z-IMC ≥2.0	IMC ≥P95
Gli ≥110 mg/dl	Gli ≥110 mg/dl	DTG (PTGO)	DTG (PTGO)	Gli ≥110 mg/dl ou DTG (PTGO) ou hiperinsulinemia
TG ≥110 mg/dl (NCEP)	TG ≥100 mg/dl	TG ≥P90 (NHANES III)	TG >P95 (NGHS)	TG ≥150 mg/dl ou HDL <35 mg/dl ou col-total ≥P95
HDL ≤40mg/dl (NCEP)	HDL <50mg/dl	HDL ≤P10 (NHANES III)	HDL <P5 (NGHS)	
PA ≥P90 (NHBPEP)	PA >P90	PA >P90 (NHBPEP)	PA >P95 (NHBPEP)	PA ≥P95
≥3 critérios	≥3 critérios	≥3 critérios	≥3 critérios	≥3 critérios

B

IDF ⁽²³⁷⁾		
6-10 anos	≥10 aos 16 anos	≥16 anos
Pcintura ≥P90	Pcintura ≥P90	≥94 cm (rapazes Euroid) ≥80 cm (raparigas Euroid)
	Gli ≥100 mg/dl ou DM2	Gli ≥100 mg/dl ou DM2
	TG ≥150 mg/dl	TG ≥150 mg/dl
	HDL <40 mg/dl	HDL <40 mg/dl (rapazes) HDL <50 mg/dl (raparigas)
	PAS ≥130 ou PAD ≥85 mmHg	PAS ≥130 ou PAD ≥85 mmHg
	Obesidade abdominal + ≥2 critérios	Obesidade abdominal + ≥2 critérios

PC: Perímetro da cintura; IMC: índice de massa corporal; z-IMC: z-score IMC; Gli: glicose em jejum; DTG: diminuição da tolerância à glicose; PTGO: prova de tolerância oral à glicose; DM2: diabetes mellitus tipo 2; TG: triglicerídeos; HDL: lipoproteínas de alta densidade; col-total: colesterol total; PA: pressão arterial; PAS: pressão arterial sistólica; PAD: pressão arterial diastólica. NHANES III: third National Health and Nutrition Examination Survey; NCEP: National Cholesterol Education Program; NGHS: National Growth and Health Study; NHBPEP: National High Blood Pressure Education Program.

No *Bogalusa Heart Study*, os autores verificaram uma prevalência de 3,6% de SM em crianças e adolescentes entre os 8 e os 17 anos de idade ⁽²⁴¹⁾. Dados do NHANES III (1988-1994) mostraram em adolescentes (12-19 anos de idade) uma prevalência de SM de 4,2%, aumentando para 6,8% naqueles com Perc_{IMC} superior ou igual a 85 e inferior a 95

Kg/m² e para 28,7% nos obesos ⁽²³⁴⁾. No NHANES 1999-2000, esta prevalência aumentou para 6,4%, atingindo cerca de 1/3 dos indivíduos obesos ⁽²⁴²⁾. Mais recentemente, Johnson e col. ⁽²⁴³⁾ confirmaram novo aumento da prevalência de SM para 8,6% em adolescentes participantes do NHANES 2001-2006. Um outro estudo, utilizando os mesmos dados do NHANES III mas pontos de corte diferentes para os diversos componentes da SM, mostrou uma prevalência de quase 10%, enquanto nos adolescentes com Perc_{IMC} superior ou igual a 85 Kg/m² a prevalência foi de 31,2%, isto é, 1 em cada 3 adolescentes com sobrepeso apresentava SM ⁽²³²⁾. Weiss e col. ⁽²¹⁰⁾, utilizando outros critérios em crianças e adolescentes (4-20 anos de idade), confirmaram a maior prevalência de SM nos indivíduos obesos, verificando uma prevalência de 38,7% nos indivíduos com obesidade moderada (z-IMC 2,0 a 2,5) e de 49,7% nos indivíduos com obesidade grave (z-IMC>2,5), enquanto nenhum dos normoponderais apresentava SM. Num estudo comparativo entre oito definições de SM, observou-se uma variação significativa da sua presença entre 6% a 39% em crianças e adolescentes obesos, sendo que apenas 2% destes cumpriam os critérios de SM em todas as definições utilizadas ⁽²³⁹⁾.

Na Europa, a prevalência de SM tem-se mostrado inferior à descrita para os EUA. Ekelund e col. ⁽²⁴⁴⁾ demonstraram uma prevalência de 0,2% e de 1,4% aos 10 e aos 15 anos de idade, respectivamente, segundo os critérios descritos pela IDF. Contudo, quando na presença de obesidade esta síndrome atingiu os 16,4%, segundo a mesma definição, podendo chegar aos 35,7% recorrendo a outras definições ⁽²⁴⁵⁾. Em crianças mais jovens, entre os 7 e os 9 anos de idade, Dubose e col. verificaram a presença de SM em 5% da amostra ⁽²⁴⁶⁾. Considerando crianças com excesso ponderal (6-9 anos de idade), esta prevalência aumenta para valores entre 39% a 60%, consoante a definição utilizada ⁽²⁴⁷⁾. Neste sentido, diversos autores têm alertado para a necessidade de uniformização dos critérios e definição da SM ^(219, 239, 247).

Apesar da dificuldade inerente à comparação entre estudos, constata-se que a prevalência de SM na idade pediátrica é relativamente baixa ^(211, 241, 242). Porém, se considerarmos os indivíduos obesos esta perspectiva é bastante alterada ^(210, 211, 232, 233, 242).

Para além da obesidade, o sexo e a etnia também influenciam a prevalência de SM ^(210, 211, 234, 248), contudo nem todos os trabalhos são conclusivos. De um modo geral, a SM é menos prevalente no sexo feminino do que no masculino ^(210, 234, 242), e também nos indivíduos de raça negra ⁽²³⁴⁾. Estes últimos apresentam um perfil lipídico mais favorável, porém ao utilizar critérios específicos para a etnia, a prevalência torna-se similar à raça caucasiana ^(210, 219). Os factores genéticos e ambientais que podem contribuir para as diferenças étnicas observadas na resistência à insulina e nos outros componentes da SM são ainda mal compreendidos ⁽²¹⁹⁾. Além disso, a base fisiopatológica e as características desta síndrome são também influenciadas pelo crescimento e puberdade ⁽²⁴⁹⁾.

Apesar do valor preditivo da SM não estar ainda estabelecido nas populações mais jovens, a evidência indica que os factores de risco individuais persistem até à idade adulta e tendem a evoluir clinicamente, principalmente se a presença de obesidade se mantiver ou agravar ^(210, 247). Alguns estudos têm demonstrado a persistência do fenótipo da SM ao longo do tempo ⁽²⁵⁰⁻²⁵³⁾. Num estudo prospectivo, as crianças com SM apresentaram maior prevalência desta síndrome (68,8%) e de DM2 (15,6%) 25 a 30 anos mais tarde quando adultos, comparativamente com os seus pares ⁽²⁵²⁾. Porém, não é de esperar que a sensibilidade dos componentes da SM na infância em relação ao adulto seja muito elevada, uma vez que o desenvolvimento desta síndrome é bastante dependente dos estilos de vida ^(229, 253).

O crescente número de casos de obesidade, resistência à insulina, DM2 e DCV em crianças e adolescentes é preocupante e, enquanto a correcção do estilo de vida é fundamental, o reconhecimento precoce e o tratamento intensivo dos componentes da SM são recomendados ⁽¹⁸⁵⁾.

ETIOPATOGENIA

A patogénese da SM é extremamente complexa e, até à data, não totalmente compreendida. A interacção entre o sedentarismo, o padrão alimentar e a obesidade durante a infância e adolescência, juntamente com o ambiente intra-uterino e factores genéticos têm sido sugeridos como factores contribuintes para o seu desenvolvimento ⁽²⁵⁴⁾.

Conforme descrito anteriormente, a definição de SM proposta por Reaven assentava na resistência à acção da insulina e não incluía qualquer parâmetro associado com a obesidade. As definições mais recentes, nomeadamente a proposta pela IDF, defendem que a obesidade, particularmente a abdominal, é um factor importante para o desenvolvimento da SM ⁽²⁵⁴⁾. Para melhor entender a fisiopatologia desta síndrome, Chen e col. avaliaram as relações entre o agrupamento dos componentes metabólicos na infância e o risco de doença cardiovascular na idade adulta no *Bogalusa Heart Study* ⁽²⁵⁵⁾. As associações mais fortes com a doença cardíaca na idade adulta foram observadas para a resistência à insulina e obesidade, sugerindo que estes podem ser os mecanismos subjacentes ao agrupamento dos componentes da SM. Embora ambos pareçam ser importantes, isto não nega a possibilidade de outros factores desempenharem um papel etiológico ⁽²²⁹⁾. Na realidade, nem todas as crianças com obesidade ou com resistência à insulina desenvolvem esta síndrome ^(211, 219, 246).

RESISTÊNCIA À INSULINA

Muitos acreditam ser a resistência à insulina o factor-chave na patogénese da SM ^(219, 256), e as diferentes sensibilidades dos diversos tecidos à insulina provavelmente contribuem para a variabilidade da expressão desta síndrome ⁽²¹⁹⁾.

Na realidade, os efeitos da insulina sobre o metabolismo glicídico e a homeostasia energética dependem directamente da normal capacidade das células β pancreáticas em segregar esta hormona, bem como da normal sensibilidade dos tecidos à acção da mesma

(204, 257). Além disso, defeitos na sinalização intracelular da insulina conduzem à resistência à acção desta hormona (258).

Embora a patogénese exacta da desregulação das vias de sinalização da insulina seja ainda desconhecida, os AGL parecem estar envolvidos (256). A nível hepático, a acumulação de AGL torna este órgão resistente à insulina, o que se traduz num aumento da síntese de triglicerídeos e de VLDL (256, 259). Paralelamente, um desequilíbrio entre a síntese e a degradação de HDL parece também estar na dependência da resistência à insulina, contribuindo para concentrações inferiores desta lipoproteína (173, 259). No músculo esquelético, a deposição lipídica intramiocelular é responsável por alterações na sinalização intracelular da insulina (207, 260), enquanto nos adipócitos a resistência à insulina induz a estimulação da lipólise (259). O pâncreas, de modo a manter a normoglicemia, e em resposta à resistência à acção da insulina, aumenta a síntese e secreção desta (hiperinsulinismo), o que promove a acumulação de AGL, agravando a já existente resistência e gerando assim um ciclo vicioso (256). Assim, a deposição ectópica de gordura pode conduzir e inclusive agravar a resistência à insulina, tal como verificado em adolescentes obesos com maior proporção de tecido adiposo visceral (207, 261). Este facto, como já referido, está associado à elevada actividade lipolítica da gordura visceral que contribui para o aumento da concentração de AGL (256, 259).

Outros factores descritos como favorecedores da resistência à insulina incluem citocinas pró-inflamatórias, como o factor de necrose tumoral-alfa (TNF- α) e a interleucina-6 (IL-6) (257, 259, 262), enquanto a adiponectina se associa a uma melhoria da sensibilidade à insulina (262, 263).

Concentrações elevadas de insulina, em resposta à resistência dos tecidos, têm sido associadas com os diversos componentes da SM na idade pediátrica (173, 210, 264), nomeadamente alterações do metabolismo da glicose, dislipidemia, obesidade abdominal e hipertensão arterial. No que respeita a este último componente, a insulina parece desenvolver um efeito directo sobre o sistema nervoso simpático, aumentando o tónus

vascular e consequentemente os valores tensionais ^(185, 256, 257). Além disso, o hiperinsulinismo parece levar à retenção crónica de sódio a nível renal, bem como à estimulação do crescimento do músculo liso vascular ^(185, 256).

Se a resistência à insulina é o factor causal, o resultado, ou ambos, das anomalias da SM é um aspecto que ainda se encontra em investigação.

OBESIDADE

A obesidade é não só um critério de SM, mas também um importante factor causal ⁽²⁴¹⁾. Conforme descrito, cada componente da síndrome agrava com o aumento do peso corporal, independentemente da idade, sexo e estágio pubertário ⁽²¹⁰⁾.

Poder-se-ia afirmar que a principal e mais frequente causa de resistência à insulina em idade pediátrica é a obesidade ^(214, 264, 265). Todavia, o grau de obesidade *per se* não é o mais importante determinante do grau de resistência à insulina. De facto, é possível observar adolescentes com obesidade severa mas com metabolismo glicídico normal ⁽²⁶¹⁾, bem como outros com menor grau de excesso de peso mas com um fenótipo metabólico adverso ⁽²⁶⁶⁾, pelo que a localização dos depósitos de gordura é um factor essencial ⁽⁴⁸⁾.

Na realidade, a deposição lipídica no tecido adiposo visceral e nos tecidos periféricos (músculo e fígado) está associada, pela sua lipotoxicidade, ao desenvolvimento de efeitos metabólicos adversos característicos da SM ^(48, 262, 265). Cali e Caprio verificaram a presença de um risco 5 vezes superior de SM em adolescentes com deposição visceral de gordura ⁽²⁶⁷⁾. Recentemente, alguns estudos têm demonstrado que o perímetro da cintura é um factor preditivo independente de resistência à insulina em crianças ⁽²⁶⁸⁻²⁷⁰⁾. Segundo Brambilla e col. ⁽²⁷¹⁾, este parâmetro antropométrico está mais associado à gordura visceral, enquanto o IMC está mais associado à gordura subcutânea.

Algumas adipocinas estão aumentadas na obesidade, sendo a sua expressão e secreção moduladas pela hipertrofia dos adipócitos e pelos factores inflamatórios que envolvem o tecido adiposo ^(272, 273), actuando como mediadores dos distúrbios associados à

adiposidade ^(219, 273, 274). As crianças obesas, tal como no adulto, apresentam resistência à acção da leptina ^(275, 276). A hiperleptinemia resultante relaciona-se directamente com a resistência à insulina e com os índices da SM em crianças ^(275, 277). Em contrapartida, a secreção de adiponectina está diminuída na presença de obesidade ^(71, 278, 279), pelo que tem sido demonstrada como um marcador independente de SM na população pediátrica ^(280, 281).

Recentemente surgiu o termo ‘adiposopatia’ que se define por um tecido adiposo ‘doente’ devido a um balanço energético positivo, presente em indivíduos genética e ambientalmente susceptíveis ⁽²⁸²⁾. Assim, parece ser a obesidade, nomeadamente a obesidade central e a deposição ectópica de gordura, acompanhada de uma susceptibilidade aumentada à resistência à acção da insulina, potenciais factores favorecedores do desenvolvimento da SM em idade pediátrica ⁽²¹¹⁾.

III. TERAPÊUTICA DA OBESIDADE E SÍNDROME METABÓLICA

A obesidade, de acordo com o já descrito, está associada a diversas complicações e riscos para a saúde da criança, bem como para a morbilidade e mortalidade na idade adulta ^(34, 103, 166). Neste sentido, a prevenção é vista universalmente como a melhor estratégia para reverter a actual epidemia da obesidade, especialmente nos mais jovens ^(86, 168, 283). Na presença de obesidade, nomeadamente em crianças com Perc_{IMC} superior a 95 ou superior a 85 com comorbilidades, o tratamento é mandatório ⁽¹⁶⁸⁾.

A correcção dos hábitos alimentares constitui a pedra basilar no tratamento da obesidade. Os principais objectivos da intervenção dietética são fornecer o aporte energético e nutricional adequado ao correcto desenvolvimento e crescimento, auxiliando a criança a desenvolver e manter hábitos alimentares saudáveis. Paralelamente, a incorporação de actividade física regular constitui outro pilar do tratamento, sendo fundamental na prevenção do ganho de peso, bem como na perda ponderal ^(157, 168).

Numa meta-análise recente, as intervenções destinadas ao tratamento da obesidade apresentaram eficácia a curto-prazo, porém com evidência limitada, enquanto o impacto do tratamento a longo-prazo na saúde das crianças e adolescentes permanece ainda pouco claro ⁽²⁸⁴⁾.

O tratamento da SM em idade pediátrica assenta nos mesmos princípios do tratamento da obesidade, pois a combinação da intervenção alimentar e actividade física parece ser aquela que apresenta melhores benefícios em termos dos componentes da SM ⁽²¹⁹⁾. Neste sentido, tem-se verificado que em crianças e adolescentes obesos a adopção de estilos de vida saudáveis está associada a uma melhoria dos factores de risco cardiovasculares e metabólicos reconhecidos na SM, tanto mais eficaz quanto maior a perda ponderal ^(285, 286).

OBJECTIVOS

A identificação precoce das crianças obesas e em risco de desenvolver SM é crucial para a prevenção de doenças crónicas na infância e na idade adulta, tais como DM2 e DCV. No entanto, a maior parte dos estudos é realizada em crianças e adolescentes obesos seguidos em contexto clínico, geralmente com obesidade severa.

Dada a escassez de dados nacionais relativos a esta temática, nomeadamente em crianças com idade inferior a 10 anos, este projecto pretende avaliar a prevalência de obesidade e SM numa amostra de crianças portuguesas, bem como avaliar a resposta às intervenções terapêuticas propostas.

Deste modo, são objectivos do presente trabalho:

1. Avaliar a prevalência de excesso ponderal e obesidade numa amostra de crianças portuguesas, com idade compreendida entre os 7 e os 9 anos, residentes no concelho de Aveiro;
2. Avaliar a prevalência de SM nas crianças obesas, bem como eventuais patologias associadas, procurando esclarecer a associação entre obesidade e os componentes da SM;
3. Intervir sobre os factores de risco extrínsecos ao indivíduo, em especial na ingestão alimentar, mediante tratamento individualizado com prescrição de terapêutica nutricional ou tratamento em grupo com participação em sessões de educação alimentar, e promoção da actividade física;
4. Avaliar a resposta, relativamente à obesidade e SM, ao tratamento instituído.

ARTIGO 1

**PREVALENCE OF OVERWEIGHT AND OBESITY AMONG 7-9 YEAR-OLD
CHILDREN IN AVEIRO, PORTUGAL: COMPARISON BETWEEN
IOTF AND CDC REFERENCES**

Prevalence of overweight and obesity among 7–9-year-old children in Aveiro, Portugal: comparison between IOTF and CDC references

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Abstract

Objective: To estimate the prevalence of overweight and obesity in schoolchildren from Aveiro, Portugal, according to two criteria: the International Obesity Task Force (IOTF) and the US Centers for Disease Control and Prevention (CDC) cut-offs.

Design: Weight, height and waist circumference were measured. Using the BMI, gender- and age-specific prevalences of overweight and obesity were determined according to the IOTF cut-offs extrapolated from an adult BMI of 25 and 30 kg/m² and the CDC cut-off values of 85th and 95th BMI percentile.

Setting: Aveiro, Portugal.

Subjects: A random representative sample of 905 children (457 boys; 448 girls) aged 7–9 years.

Results: The prevalence of excess weight (overweight and obesity) was lowest according to IOTF cut-offs compared to CDC (28.1% *v.* 31.2%), especially obesity (8.1% *v.* 14.0%). However, the CDC and IOTF criteria have a strong agreement (Cohen's $k=0.755$; $P<0.001$). There were significant differences in excess weight between boys and girls according to the CDC (26.9% *v.* 35.7%; $P=0.003$). Obese children are younger and the majority present abdominal obesity.

Conclusions: The present study shows a high prevalence of excess weight in Aveiro children, similar to other Portuguese regions and among the highest in Europe, especially in the female gender. The IOTF cut-off values give a lower prevalence of excess weight, namely obesity.

Keywords
Children
Obesity
Portugal
Prevalence

The prevalence of childhood obesity is increasing at a dramatic rate, especially in economically developed countries^(1–3). According to international definitions, 10% of the world's school-aged children is estimated to be overweight, a quarter of which is obese^(2,4). Recent data indicate that in Europe, 31.8% of schoolchildren were estimated to be overweight, including 7.9% estimated to be obese^(1,3), with a higher prevalence of overweight youth in Southern Europe^(5,6). The significant linear trends in the annual increments indicate that the rate of change of prevalence is itself increasing. The predicted prevalence for 2010 will be 38.2% for overweight, of which 10% reports to obesity^(1,3).

In Portugal, weight and height are not assessed regularly at the national level. In a recent review, fifteen individualised studies reported overweight and obesity, in Portugal, in children and adolescents aged 2–15 years⁽⁷⁾. In a sample

of 5511 children (7–9-year-old), a prevalence of overweight between 19.1% and 21.4% and of obesity between 10.2% and 12.3% was reported, respectively, in boys and girls⁽⁸⁾.

Obesity has important consequences as it increases the risk of other chronic diseases, including dyslipidaemia, hypertension, CVD, insulin resistance and diabetes. Moreover, obesity influences the physical, social and psychological development of children⁽⁹⁾. Approximately one-third of overweight children and one-half of overweight adolescents remain obese as adults^(3,10). Therefore, prevention of obesity in these age groups should be a public health priority.

There is no widely agreed standard for classifying overweight and obesity in paediatric age, however the use of a universal classification may facilitate international comparisons^(2,11). The BMI is the most practical and widely used index to identify overweight and obese children and adolescents for survey purposes⁽¹²⁾. The

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International Obesity Task Force (IOTF) recommends the use of BMI cut-off points of Cole *et al.*⁽¹³⁾. These were derived from the BMI cut-off points of 25 and 30 kg/m² at an age of 18 years and by extrapolating these along the equivalent BMI-for-age centile lines in a multinational data set of children aged 6–18 years⁽¹³⁾. The US Centers for Disease Control and Prevention (CDC) recommends the sex- and age-specific 85th and 95th BMI percentile as the cut-offs to define overweight and obesity in children and adolescents⁽¹⁴⁾. Both methods are routinely employed to assess childhood obesity⁽¹⁵⁾, nevertheless previous research^(16,17) showed that they yield different prevalences for overweight and obesity.

The present study has been carried out in order to estimate the prevalence of overweight and obesity in 7–9-year-old children from Aveiro and to compare the IOTF and CDC sex-specific BMI-for-age reference values.

Subjects and methods

The study was carried out in public primary schools of Aveiro in a sample of 7–9-year-old children. This age group was chosen for physiological reasons, as it precedes puberty⁽¹⁸⁾. The study protocol was approved by each group of schools (forty public primary schools scattered within seven groups of schools).

Aveiro is the fifth most populous district in Portugal. Its gross domestic product (GDP) per capita represents 90% of the national average, with low levels of poverty⁽¹⁹⁾.

Participants

The number of children enrolled at 2nd and 3rd grade (corresponding to children aged between 7 and 9 years) was identified (*n* 1799) at the beginning of 2005/2006 academic year. A random sample of schools was extracted with the restriction of having at least one school from each group of schools. The probability of selection of one school was proportional to the number of students in the 2nd and 3rd grade. From a total of forty, thirteen schools were selected (see Appendix). A representative sample of 980 children was obtained, corresponding to all students in the 2nd and 3rd grade of the sampled schools. The survey was carried out from January to March 2006 and 931 children were evaluated, of which 98.8% were Caucasian. Twenty-six children were excluded (twenty-five were older than 9 years; one suffered from Down syndrome). Therefore, our sample consists of 905 children (92.4% of the initial sample).

Anthropometric measures

In each school, two trained staff (one nutritionist and one nurse) measured height, weight and waist circumference according to standardised procedures⁽²⁰⁾. Weight was measured to the nearest 0.1 kg using an electronic column scale (SECA-780; Seca Ltd, Hamburg, Germany); height was measured to the nearest 0.1 cm using a stadiometer

(SECA-220, Seca Ltd), with the head in the Frankfurt horizontal plane; waist circumference was measured at the mid-point between the iliac crest and the lower edge of the ribs at the end of a normal expiration. Age was calculated in decimal units based on the date of the survey relative to birth date. Overweight and obesity were defined using the IOTF cut-offs proposed by Cole *et al.*⁽¹³⁾ derived from BMI cut-points of 25 and 30 kg/m² and the CDC sex- and age-specific 85th and 95th BMI percentile⁽¹⁴⁾. The term overweight in the present study does not include obese children. Abdominal obesity was defined using the sex and age-specific 95th waist circumference percentile by McCarthy *et al.*⁽²¹⁾.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences statistical software package version 14.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were executed by computing the mean and standard deviation for continuous variables, or frequencies for ordinal and nominal variables. Pearson and Spearman correlation coefficients were computed to evaluate the degree of association between variables. Independent samples *t* test and ANOVA were performed on scale variables to evaluate the differences between two or more groups, respectively. The Mann–Whitney *U* test was used in ordinal variables to evaluate the differences between two groups. To study the independence between nominal categorical variables, the χ^2 test was used. Cohen's *k* was calculated in order to measure the agreement between the IOTF and CDC criteria. The IOTF criteria were computed using the Excel add-on ImsGrowth⁽²²⁾ and CDC criteria were computed using the tables provided by the Centers for Disease Control and Prevention webpage⁽²³⁾.

Results

The analysis involves 905 children aged 7–9 years, of whom 457 (50.5%) were boys and 448 (49.5%) were girls. The characteristics of the sample are shown in Table 1. There are no significant differences in age and anthropometric characteristics between boys and girls.

The prevalence of overweight and obesity by gender according to IOTF and CDC is shown in Table 2. The prevalence of excess weight (overweight and obesity) was lowest according to IOTF (28.1% *v.* 31.2%), especially in the obese group (8.1% *v.* 14.0%). The IOTF and CDC criteria have a strong agreement (Cohen's *k* = 0.755, *P* < 0.001), however with higher prevalence of obesity when using the CDC. According to IOTF, the prevalence of excess weight was highest among girls, without significance (*Z* = −1.794, *P* = 0.073). Also, according to the CDC criteria, the prevalence of both overweight and obesity was highest among girls (35.7% *v.* 26.9%), with significant differences between genders for the CDC criteria

Table 1 Descriptive characteristics of the 7–9-year-old Portuguese children living in Aveiro, according to gender

	Boys (n 457)		Girls (n 448)		95% CI	P
	Mean	SD	Mean	SD		
Age (years)	8.23	0.70	8.24	0.64	–0.06, 0.11	0.588
Weight (kg)	29.86	6.07	29.90	6.78	–0.08, 0.90	0.887
Height (cm)	130.01	6.21	129.38	6.40	–1.42, 0.22	0.151
BMI (kg/m ²)	17.53	2.54	17.71	2.90	–0.18, 0.53	0.344
Z-score BMI	0.33	0.70	0.25	0.56	–0.06, 0.19	0.299
Waist circumference (cm)	59.87	6.37	59.28	7.27	–1.48, 0.30	0.195

There are no significant differences between boys and girls in relation to all studied variables.

Table 2 Prevalence of overweight and obesity among 7–9-year-old Aveiro children according to the IOTF and the CDC sex-specific BMI-for-age reference values and gender

	Boys (n 457)		Girls (n 448)		All (n 905)	
	n	%	n	%	n	%
IOTF						
Overweight	85	18.6	96	21.4	181	20.0
Obese	30	6.6	43	9.6	73	8.1
CDC						
Overweight	74	16.2	82	18.3	156	17.2
Obese	49	10.7	78	17.4	127	14.0

IOTF, International Obesity Task Force; CDC, US Centers for Disease Control and Prevention.

There were significant differences between genders for the CDC criteria (Mann–Whitney $Z = 2.966$, $P = 0.003$) but no differences were found for the IOTF (Mann–Whitney $Z = -1.794$, $P = 0.073$) for the mean rank of the BMI group (normal, overweight and obese).

($Z = 2.966$, $P = 0.003$) for the mean rank of the BMI group (normal, overweight and obese).

Obese children are younger (8.25 (SD 0.67) years in normal weight *v.* 8.08 (SD 0.63) years in obese according to IOTF, and 8.15 (SD 0.64) years in obese according to CDC), although the correlation between age and Z-score BMI is very weak ($R = -0.084$, $P < 0.011$). There is no statistical difference in age ($P = 0.588$) and Z-score BMI ($P = 0.300$) according to gender. Abdominal obesity (Table 3) is present in 84.9% and 83.5% of obese children according to IOTF ($\rho = 0.608$; $P < 0.001$) and CDC criteria ($\rho = 0.639$; $P < 0.001$), respectively. Waist circumference is strongly associated with BMI ($R = 0.922$; $P < 0.001$).

According to the school environment (ten rural schools: 458 children; three urban schools: 447 children), the prevalence of excess weight is similar in both school types (IOTF: 27.51% in rural *v.* 28.57% in urban; CDC: 33.63% *v.* 32.14%). There is no statistical difference between gender, age and Z-score BMI according to rural or urban environment ($P = 0.154$; $P = 0.519$; $P = 0.185$) and according to each school ($P = 0.116$; $P = 0.188$; $P = 0.092$).

Discussion

Our study presents the first estimates on prevalence of overweight and obesity in children living in Aveiro. These

Table 3 Waist circumference percentile distribution in 7–9-year-old normal weight, overweight and obese children according to the IOTF and the CDC sex-specific BMI-for-age reference values

	Waist circumference percentiles					
	<90th		≥90th–95th		≥95th	
	n	%	n	%	n	%
IOTF						
Normal weight (n 617)	499	80.9	62	10.0	56	9.1
Overweight (n 181)	40	22.1	28	15.5	113	62.4
Obese (n 73)	11	15.1	0	0.0	62	84.9
CDC						
Normal weight (n 613)	511	83.4	55	9.0	47	7.7
Overweight (n 156)	42	26.9	35	22.4	79	50.6
Obese (n 127)	20	15.7	1	0.8	106	83.5

IOTF, International Obesity Task Force; CDC, US Centers for Disease Control and Prevention.

Spearman correlation between waist circumference percentile and IOTF criteria: $\rho = 0.608$ ($P < 0.001$). Spearman correlation between waist circumference percentile and CDC criteria: $\rho = 0.639$ ($P < 0.001$).

data constitute a representative sample of 7–9-year-old schoolchildren, although randomisation was school- and not individually based. We found a high prevalence of excess weight (overweight and obesity) between 28% and 31% according to the criteria used (IOTF and CDC, respectively), which is estimated to be among the highest in Europe⁽¹⁾. This prevalence is in accordance with Padez *et al.*⁽⁸⁾, which found 31.5% of excess weight according to IOTF (20.3% overweight and 11.3% obesity *v.* 20.0% overweight and 8.1% obesity in our study).

The prevalence of overweight in our sample is slightly higher when using IOTF reference (20.0% *v.* 17.2%). However, a higher prevalence of obesity, almost twofold, was found when using the CDC charts (8.0% *v.* 14.0%). Several authors also have found a higher prevalence of obesity when using the CDC reference. Lobstein *et al.* showed that 10.7% of boys and 14.0% of girls (6–11-year-old) were obese according to IOTF, while according to CDC criteria obesity increased to 19.9% in boys and 17.6% in girls (data from the National Health and Nutrition Examination Survey 2003–2004). In contrast, the IOTF reference yielded a higher percentage of overweight compared to CDC (21% and 23.6% for IOTF *v.* 16.6% and 20.4% for CDC, respectively in boys and girls)⁽²⁴⁾. In a national sample of 6–12-year-old Swiss children, 3.85%

and 3.72% of boys and girls were obese based on IOTF reference, whereas 7.63% and 5.91% were obese based on CDC⁽¹⁷⁾. In the Pro Children Study, the authors also found that CDC criteria consistently estimated higher proportions of obesity than IOTF⁽²⁵⁾. These two definitions differ in data sets, smoothing methods and approaches to set cut-offs^(16,26). The IOTF BMI cut-off points derived from a multinational (Brazil, United Kingdom, Hong-Kong, Singapore, the Netherlands and USA) data set of children⁽¹³⁾. While the CDC2000 growth charts were created to update the 1977 National Center for Health Statistics charts using data from five cross-sectional child growth surveys, involving US nationally representative samples⁽¹⁴⁾. For 6–12-year-olds, the IOTF cut-offs are generally higher than the CDC ones. For boys, the mean differences between the CDC and IOTF references for overweight and obesity are around 0.5 and 1.5–2.0 kg/m², respectively. For girls, the two sets of reference values are similar for overweight, but the IOTF cut-offs are near 1.0 kg/m² higher⁽¹⁶⁾. Therefore, the IOTF definition of obesity tends to be more cautious and according to several studies its sensitivity for obesity is poorer when compared to CDC definition^(17,27). This can lead to an underestimation of obesity prevalence. Although the IOTF reference has a slightly stronger capacity for predicting obesity and metabolic disorders in young adulthood⁽¹⁵⁾, the CDC criteria, being broader, might have the advantage of identifying more children who will benefit from an early intervention, even at the risk of creating false positives.

Differences in gender are generally small and there is no suggestion that either males or females consistently predominate within particular age groups, or according to particular overweight definitions^(28,29). In almost all cases, the gender differences were not statistically significant⁽²⁸⁾. Nevertheless, in our study we found a higher prevalence of excess weight in girls, statistically significant according to CDC. This might be related to gender differences in physical activity, since boys are generally more active than girls⁽²⁸⁾. However, physical activity levels were not evaluated in our study.

Researchers should be aware of the differences between IOTF and CDC criteria, since they will yield different prevalence rates. Each one has its advantages and limitations, and should be used taking into account its possible limitations⁽¹⁶⁾.

Despite the small age interval of the sample, the prevalence of obesity was higher in younger children, which could be an indicator of a future increase in the prevalence of obesity. It also shows the importance of an early intervention in order to prevent the increase in weight and its consequences.

In our sample, the majority of obese children present abdominal obesity. According to other authors, waist circumference is a useful measure of the abdominal obesity that is more closely related to cardiovascular risk and metabolic syndrome than overall obesity^(30,31).

Therefore, waist circumference measurement might be a simple tool to help identify children at risk.

The school environment might be associated with socio-economic status of families, but we did not find differences in the prevalence of excess weight between children from schools in rural and in urban areas. In the rural area, schools are smaller and children generally come from families that work mainly in agriculture and factories, with a lower education level. In the urban area, children generally come from families that work mainly in the services industry, normally with higher education level. A limitation of our study is that we did not evaluate the family socio-economic status and the parent's education. In industrialised societies, adults with a low/medium education level and less qualified occupations are at risk of excess weight, and also influence the diet and lifestyle of their families, which leads to a greater risk for their children⁽³²⁾. Lower socio-economic status may also be related to decreased physical activity in children and adolescents⁽³³⁾.

In summary, the prevalence of excess weight in Portuguese schoolchildren living in Aveiro is high, especially in the female gender, and among the highest in Europe. Our data confirm that the CDC charts give a higher prevalence of obesity, compared to the IOTF. The majority of obese children present abdominal obesity, which can be associated with cardiometabolic risk. It is clear that the obesity epidemic calls for an urgent action, to set up surveillance programmes and preventive strategies in order to contain the increasing number of obese children.

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Appendix

Public primary schools of Aveiro and children enrolled at 2nd and 3rd grade and evaluated per school

Schools	Population (n)	Sample (n)	Prob. (%)	Schools	Population (n)	Sample (n)	Prob. (%)
<i>Group I</i>				<i>Group IV (cont.)</i>			
School 1	90	81	5.0	School 21	4	0	0.2
School 2	164	0	9.1	School 22	15	0	0.8
School 3	40	0	2.2	School 23	6	0	0.3
School 4	29	0	1.6	School 24	9	0	0.5
School 5	183	168	10.2	School 25	9	0	0.5
<i>Group II</i>				<i>Group V</i>			
School 6	120	119	6.7	School 26	26	0	1.4
School 7	56	47	3.1	School 27	18	0	1.0
School 8	37	0	2.1	School 28	37	0	2.1
School 9	39	0	2.2	School 29	12	0	0.7
School 10	23	21	1.3	School 30	31	20	1.7
School 11	63	61	3.5	School 31	64	47	3.6
<i>Group III</i>				<i>Group VI</i>			
School 12	52	70	2.9	School 32	22	21	1.2
School 13	25	0	1.4	School 33	13	0	0.7
School 14	34	0	1.9	School 34	36	0	2.0
School 15	17	0	0.9	School 35	28	0	1.6
School 16	9	0	0.5	School 36	22	0	1.2
School 17	36	0	2.0	School 37	17	17	0.9
School 18	14	0	0.8	<i>Group VII</i>			
<i>Group IV</i>				School 38	40	0	2.2
School 19	58	0	3.2	School 39	200	206*	11.1
School 20	60	53	3.3	School 40	41	0	2.3
<i>Total (I + II + III + IV + V + VI + VII)</i>					1799	931	100

Population = students from 2nd and 3rd grade (aged 7–9 years); Prob. = probability to be selected (%).

*School 39 had more students enrolled at the time of evaluation than when information was obtained.

ARTIGO 2

OBESITY AND METABOLIC SYNDROME IN 7-9 YEARS-OLD PORTUGUESE SCHOOLCHILDREN



RESEARCH

Open Access

Obesity and metabolic syndrome in 7-9 years-old Portuguese schoolchildren

Carla Pedrosa^{*1,2}, Bruno MPM Oliveira¹, Isabel Albuquerque², Carlos Simões-Pereira², Maria D Vaz-de-Almeida¹ and Flora Correia^{1,3}

Abstract

Background: Body fat is related to changes in lipid profile, blood pressure and metabolism of insulin and glucose, known as the metabolic syndrome (MS). The aim of this study was to estimate the prevalence of metabolic syndrome (MS) and its components among overweight and obese Portuguese schoolchildren, and to identify associated clinical and biochemical characteristics.

Methods: A total of 82 children (14 overweight and 68 obese; 40 boys and 42 girls) aged 7-9 years, underwent anthropometric measurements. A blood sample was obtained to assess biochemical parameters. Insulin resistance (IR) was determined by the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR). MS was defined by the National Cholesterol Education Program Adult Treatment Panel III criteria modified by Cook.

Results: The prevalence of MS was 15.8%. Abdominal obesity was present in all children. Frequency of elevated blood pressure, low HDL-cholesterol and elevated triglyceride concentrations were 62.6%, 13.4% and 11.0%, respectively. None of the children presented impaired fasting glucose, however hyperinsulinemia (7.3%) and IR (8.5%) were observed. The number of components of MS was higher in children with higher z-BMI ($p = 0.411$; $p < 0.001$). MS was associated with higher leptin concentrations. No association was found with adiponectin or ghrelin levels. Leptin correlated positively with obesity, glucose metabolism, lipid profile, hepatic function and C-reactive protein, and negatively with HDL and Apolipoprotein A-I/B ratio.

Conclusions: This study shows a significant prevalence of MS among obese schoolchildren. Abdominal obesity and elevated blood pressure were the most frequent components of this syndrome. Dyslipidemia, IR and high levels of leptin were also associated with MS in this young group.

Background

In the past decades the prevalence of childhood obesity has increased worldwide, reaching epidemic proportions and becoming a serious and growing public health problem [1,2]. In Portugal, in a nationwide study, the prevalence of excess weight in 7-9 year-old children was 31.5% [3]. This is similar to what we found in a previous local study of 920 children from Aveiro (28%) [4].

The coexistence of obesity and metabolic disorders such as hyperinsulinemia, glucose intolerance, hypertension, high serum levels of triglycerides (TG) and decreased levels of high density lipoprotein (HDL), is known as metabolic syndrome (MS) [5]. This constella-

tion of symptoms, first described by Reaven [6], increases the risk for cardiovascular disease (CVD) and type 2 diabetes (DM2) [7]. Insulin resistance (IR) and an altered plasma lipid pattern are common pathophysiological features of MS, not only in adults but also in children and adolescents [7]. However, there is no consensus about the definition of MS in paediatric populations [8]. Many different MS criteria have been employed in children and adolescents, and the components and cut-offs used to diagnose this syndrome have varied considerably among studies [8-10]. Recently, a new consensus definition has been published, however according to it, in children younger than 10 years-old MS should not be diagnosed [11]. Changes in growth and development during childhood and adolescence make it difficult to choose a cut-off for risk factors [12]. Therefore, the prevalence varies

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according to the definitions used [8]. It has been reported to be relatively low in normal weight children (1% or less) contrary to what occurs in obese (18% to 50%) [13]. Moreover, MS is rapidly increasing in prevalence with rising childhood obesity and sedentary lifestyles worldwide [13]. In addition, parameters associated with MS have been shown to originate early in life [9], and tend to track into adulthood [14]. The recognition of MS in obese children, who have not yet developed cardiometabolic disorders, is of great importance from a clinical and public health perspective [15].

The MS has been widely studied in adults, however there is little research focusing on younger children (< 10 y old) [16]. Moreover, the absence of studies on MS in the paediatric Portuguese population led us to design the current study. The aims of this study were to determine the prevalence of MS and its individual components in a sample of Portuguese obese schoolchildren, and to identify clinical or biochemical characteristics associated with MS in our population.

Methods

Study Population

Recruitment of the study sample was population-based [4]. In brief, from a total of forty schools with 1799 schoolchildren enrolled at 2nd and 3rd grade (aged between 7-9 years), a random sample of 13 schools was selected and a representative sample of 980 children was obtained. Weight, height and waist circumference were evaluated in 905 children (457 boys and 448 girls). Of those, 127 (14%) were classified as obese ($\geq 95^{\text{th}}$ BMI percentile) according to the US Centers for Disease Control and Prevention (CDC) criteria [17], and were invited to participate in the study. Eighty-nine accepted the invitation and 82 (64.5% of the initial sample; 40 boys and 42 girls) allowed collection of blood.

Each parent gave written informed consent and children gave assent for participation. The study was approved by the Ethics Committee of the Hospital Infante D. Pedro. Assessments were carried out at the Department of Endocrinology, Diabetes and Nutrition.

None of the evaluated children suffered from primary dyslipidemia, hypertension, diabetes or glucose intolerance, secondary obesity, or were under pharmacological treatment.

Anthropometric Measures

Weight, height and waist circumference were measured according to standardized procedures [18]. All measurements were taken in underwear and without shoes. Weight was measured to the nearest 0.1 kg using an electronic column scale (SECA-780; Seca Ltd., Hamburg, Germany); height was measured to the nearest 0.1 cm using a stadiometer (SECA-220; Seca Ltd.), with the head

in the Frankfort horizontal plane; waist circumference (WC) was measured with a non-elastic, flexible tape measured at the mid-point between the iliac crest and the lower edge of the ribs at the end of a normal expiration. Age was calculated in decimal units based on the date of the survey relative to birth date. BMI was calculated with measured height and weight and was standardised (z-BMI) by using age- and gender-normative data from the CDC [17,19]. Abdominal obesity was defined using the sex and age-specific 90th waist circumference percentile by McCarthy *et al* [20]. Birth weight and length were obtained from the children health booklet.

Clinical and Biochemical Measures

A physical examination was performed looking for characteristic abnormalities, specifically acanthosis nigricans. Puberty status was assessed according to pubic hair in boys and pubic hair and breast development in girls [21,22]. Blood pressure (BP) was obtained on the right arm with the patient seated, after rest, using a digital sphygmomanometer (OMRON M6) and appropriate sized cuff. After three measurements, the lowest blood pressure value was chosen. Children were classified according to sex, height and age-specific charts [23].

Baseline blood samples were collected in the morning (8:00 to 9:00) after an overnight fast (10 to 12 hours) by venipuncture, after a local application of a topical anesthetic patch (EMLA). Plasma and serum were separated by centrifugation. The glucose oxidase method (Siemens Healthcare Diagnostics Inc., Newark, DE, USA) was used to determine blood glucose levels. Serum lipids (total cholesterol (T-chol), HDL, LDL, triglycerides) were measured using an enzymatic colorimetric method (Siemens Healthcare Diagnostics Inc.). Very low density lipoprotein (VLDL) was calculated using the principles of the Friedewald formula, and the Apolipoprotein A-I and Apolipoprotein B were measured by an immuno-turbidimetric assay (Olympus America Inc., Center Valley, PA, USA). Plasma liver enzyme (alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT)) levels were measured using an enzymatic colorimetric method (Siemens Healthcare Diagnostics Inc.), and C-reactive protein (CRP) was determined by a turbidimetric immunoassay (Siemens Healthcare Diagnostics Inc.). Plasma and serum were frozen until further analysis of insulin, C-peptide, leptin, adiponectin and ghrelin at an external laboratory (ENDOC LAB, Porto). Insulin and C-peptide were measured by luminescence immunometric assay (Siemens Healthcare Diagnostics Inc.). Insulin resistance was determined by the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) calculated as the product of the fasting plasma insulin level ($\mu\text{UI/ml}$) and the fasting plasma glucose level (mmol/l), divided by 22.5 [24].

Leptin, adiponectin and ghrelin were quantified by RIA (Linco Research Inc., St. Charles, MO, USA).

Definition of MS

MS was defined according to the National Cholesterol Education Program Adult Treatment Panel III criteria modified by Cook [10], with adjustment for fasting glucose according to the recent American Diabetes Association definition for impaired fasting glucose [25]. This definition was chosen since it is based in age- and gender-specific cutoffs and it has been used in several paediatric studies [8,26]. Thus, MS was considered if three or more of the following criteria were present: 1) abdominal obesity ($WC \geq 90^{\text{th}}$ percentile for age and sex) [20]; 2) fasting TG ≥ 110 mg/dl; 3) HDL ≤ 40 mg/dl; 4) systolic/diastolic BP $\geq 90^{\text{th}}$ percentile for age, sex and height [23]; 5) fasting glucose ≥ 100 mg/dl [25].

Statistical Analysis

Descriptive statistics were executed by computing the mean and standard deviation (SD) for scale variables, or frequencies for nominal variables. Pearson and Spearman correlation coefficients were computed to evaluate the degree of association between variables. To study the independence between nominal categorical variables Chi-square test was used. Independent samples t test was performed in scale variables to evaluate the differences between two groups. Mann-Whitney test was used in ordinal variables to evaluate the differences between two groups. The normality of scale variables was assessed using the Kolmogorov-Smirnov test. Non parametric tests were applied to variables with a distribution significantly different from the Normal. We considered a significance level of 0.05. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS version 14.0, 2005).

Results

The anthropometric and clinical characteristics of the 82 children (48.8% boys and 51.2% girls) are shown in Table 1. A statistical significant difference between genders was found for height, z-IMC, WC and the presence of acanthosis, with boys presenting higher values. Mean plas-matic concentration of total cholesterol (169.4 ± 27.1 mg/dl), HDL (50.1 ± 9.7 mg/dl), LDL (106.9 ± 23.2 mg/dl), TG (77.7 ± 47.3 mg/dl), insulin (8.6 ± 4.2 μ UI/ml), glucose (82.0 ± 6.7 mg/dl), AST (25.3 ± 4.9 U/L), ALT (20.3 ± 8.0 U/L) and GGT (15.6 ± 6.4 U/L) were within normal range for both genders. Plasma liver enzymes showed significant higher concentrations in boys: ALT (26.5 ± 5.5 vs 24.1 ± 4.0 U/L; $p = 0.021$), AST (22.8 ± 9.7 vs 17.8 ± 5.0 U/L; $p = 0.005$) and GGT (17.1 ± 8.1 vs 14.2 ± 3.6 U/L; $p = 0.043$). About three quarters of the sample were prepubertal (Tanner I: 74.4%; Tanner II: 25.6%). The prevalence

of MS in our children was 15.8%, without significant differences between boys and girls. None of the children fulfilled the five criteria of the MS.

Between the assessment at school and the first assessment at the Hospital, 14 (17.1%) children who were classified initially as obese ($\geq 95^{\text{th}}$ BMI percentile) became overweight (85-95th BMI percentile). In addition to the significantly higher values in anthropometric parameters, the levels of systolic BP (117.2 ± 9.1 vs. 111.9 ± 7.4 mmHg; $p = 0.047$) and C-peptide (1.0 ± 0.5 vs. 0.8 ± 0.3 ng/ml; $p = 0.010$) were also found significantly higher in obese children. Glucose, insulin and HOMA-IR showed a trend towards higher levels in obese subjects, as well as blood lipids (except HDL), leptin and GGT, without statistical significance (data not shown). None of the overweight children had 3 or more diagnostic criteria for MS or presented acanthosis. In obese, 13 (19.1%) presented MS and 18 (26.5%) presented acanthosis.

As shown in Table 2, BMI, z-BMI, WC, systolic BP and the presence of acanthosis were significantly higher in MS children than in non-MS sufferers. The number of components of MS was higher in children with higher z-BMI ($p = 0.411$, $p < 0.001$). We found significant differences between the presence and the absence of MS for several biochemical characteristics (Table 3). The number of criteria for MS correlated with several characteristics of the population, however most of these correlations were weak ($|p| < 0.5$), except for systolic BP ($p = 0.682$, $p < 0.001$).

All children presented abdominal obesity ($WC \geq 90^{\text{th}}$), while high BP ($\geq 90^{\text{th}}$) was the second most frequent component of MS (62.6%) (Figure 1). Frequency of high TG and low HDL was 13.4% and 11.0%, respectively. Abnormal fasting glucose values were not identified in any of the children, however IR occurred in 8.5% (23.1% in MS-children vs. 5.8% non-MS), hyperinsulinemia (plasma insulin >15 μ UI/ml) in 7.3% and acanthosis was present in 22.0%.

Leptin correlated positively ($p < 0.05$) with BMI, z-BMI, WC, insulin, HOMA-IR, C-peptide, T-chol, LDL, TG, Apolipoprotein B, ALT, GGT and CRP, and negatively with HDL and Apolipoprotein A-I/B, but most correlations were weak ($|R|, |p| < 0.5$). Adiponectin showed a negative ($p < 0.05$) but weak ($|R|, |p| < 0.5$) correlation with diastolic BP and birth weight, without any significant correlation with obesity. Also a negative ($p < 0.05$) and weak ($|R|, |p| < 0.5$) correlation was found between ghrelin and age, weight, BMI, systolic BP, insulin and HOMA-IR.

Discussion

Our study presents the first Portuguese report on the frequency of MS and associated metabolic complications among overweight and obese children aged 7-9 years. Since our study was population-based, not hospital-

Table 1: Descriptive characteristics of the population study, according to gender.

	Boys (n = 40)	Girls (n = 42)	P
Age (y)	8.7 ± 0.8	8.6 ± 0.7	0.721 ^a
Weight (kg)	43.5 ± 6.4	41.4 ± 6.0	0.128 ^a
Height (cm)	136.8 ± 5.9	134.2 ± 5.6	0.049 ^a
BMI (kg/m ²)	23.14 ± 2.22	22.85 ± 2.07	0.530 ^a
z-BMI	2.00 ± 0.29	1.86 ± 0.26	0.026 ^a
Waist circumference (cm)	74.1 ± 5.8	71.5 ± 5.9	0.044 ^a
Systolic BP (mmHg)	117.2 ± 8.1	115.4 ± 9.8	0.402 ^a
Diastolic BP (mmHg)	64.0 ± 10.9	61.9 ± 8.3	0.330 ^a
HOMA-IR	1.71 ± 0.90	1.79 ± 0.89	0.798 ^b
Birth weight (g)	3523 ± 429	3337 ± 472	0.072 ^a
Acanthosis (n; %)	13 (32.5%)	5 (11.9%)	0.024 ^c
Metabolic Syndrome (n; %)	6 (15.0%)	7 (16.7%)	0.836 ^c

Data presented as mean ± SD for continuous variables and as frequency (%) for dichotomous variables.

^a t-student test for the differences between genders.

^b Mann-Whitney for the differences between genders.

^c Chi-square test for the independence between gender and each variable.

based, the severity of obesity was moderate (z-BMI mean: 1.93 ± 0.28). We found a high prevalence of MS (19.1%) in obese children, while it was absent in the overweight. Nevertheless, all children presented abdominal obesity, a criterion of MS. The observed prevalence of MS in our study is similar to data from other European countries [8,15,26]. However, when considering the definition applied, large differences are noticed [8,15]. Thus, a consensual paediatric definition of MS is needed in order to

better compare studies and populations. Boys and pubertal subjects usually present higher frequencies of MS [9,10], however we did not found a significant difference in the prevalence of MS according to gender or pubertal status.

Childhood obesity is frequently associated with cardiovascular and metabolic disturbances [13]. In the present study, several biochemical parameters failed to present a significant difference between overweight and obese chil-

Table 2: Descriptive characteristics of the population study according to the presence or absence of MS.

	Without MS (n = 69)	With MS (n = 13)	P
Age (y)	8.7 ± 0.7	8.4 ± 0.8	0.167 ^a
Weight (kg)	41.9 ± 6.3	45.1 ± 5.2	0.091 ^a
Height (cm)	135.4 ± 5.9	136.2 ± 5.5	0.635 ^a
BMI (kg/m ²)	22.75 ± 2.13	24.23 ± 1.74	0.021 ^a
z-BMI	1.89 ± 0.26	2.15 ± 0.25	0.002 ^a
Waist circumference (cm)	72.1 ± 5.9	76.4 ± 5.0	0.016 ^a
Systolic BP (mmHg)	114.9 ± 8.3	123.5 ± 9.2	0.001 ^a
Diastolic BP (mmHg)	62.7 ± 10.2	63.9 ± 6.7	0.675 ^a
Birth weight (g)	3443 ± 442	3328 ± 546	0.412 ^a
Gender (M/F)	34/35	6/7	0.836 ^b
Tanner (I/II)	49/20	12/1	0.107 ^b
Acanthosis (n; %)	11 (15.9%)	7 (53.8%)	0.002 ^b

Data presented as mean ± SD for continuous variables and as frequency for dichotomous variables.

^a t-student test for the differences between absence or presence of MS.

^b Chi-square test for the independence between absence or presence of MS and each variable.

Table 3: Biochemical characteristics of the population study according to the presence or absence of MS.

	Without MS (n = 69)	With MS (n = 13)	P
Glucose (mg/dl)	81.8 ± 6.6	82.9 ± 7.4	0.580 ^a
Insulin (μU/ml)	8.1 ± 3.6	11.3 ± 6.3	0.037 ^b
C-Peptide (ng/ml)	0.9 ± 0.5	1.2 ± 0.5	0.044 ^b
HOMA-IR	1.64 ± 0.77	2.31 ± 1.25	0.028 ^b
T-chol (mg/dl)	167.6 ± 25.5	179.2 ± 33.9	0.156 ^a
HDL (mg/dl)	51.9 ± 8.9	40.4 ± 8.4	< 0.001 ^a
LDL (mg/dl)	104.5 ± 21.5	119.7 ± 28.3	0.030 ^a
Triglycerides (mg/dl)	63.4 ± 19.2	153.7 ± 74.7	< 0.001 ^b
VLDL (mg/dl)	12.7 ± 3.8	30.7 ± 14.9	< 0.001 ^b
T-chol/HDL	3.27 ± 0.50	4.54 ± 0.98	< 0.001 ^b
Apolipoprotein A-I (mg/dl)	126.2 ± 14.9	114.1 ± 14.7	0.008 ^a
Apolipoprotein B (mg/dl)	75.4 ± 13.8	87.7 ± 18.2	0.006 ^a
Apolipoprotein A-I/B	1.73 ± 0.37	1.36 ± 0.37	0.001 ^a
C-reactive protein (mg/dl)	0.38 ± 0.81	0.31 ± 0.23	0.283 ^b
Leptin (ng/ml)	10.6 ± 5.8	15.5 ± 7.8	0.011 ^a
Adiponectin (ng/ml)	26428.1 ± 12915.0	26136.9 ± 11291.1	0.940 ^a
Ghrelin (pg/ml)	1051.1 ± 420.3	985.1 ± 380.7	0.600 ^a
AST (U/L)	25.0 ± 6.3	26.8 ± 6.3	0.437 ^b
ALT (U/L)	19.4 ± 7.2	25.2 ± 10.3	0.011 ^b
GGT (U/L)	14.7 ± 4.1	20.6 ± 12.0	0.008 ^b

Data presented as mean ± SD.

^at-student test for the differences between absence or presence of MS.^bMann-Whitney for the differences between absence or presence of MS.

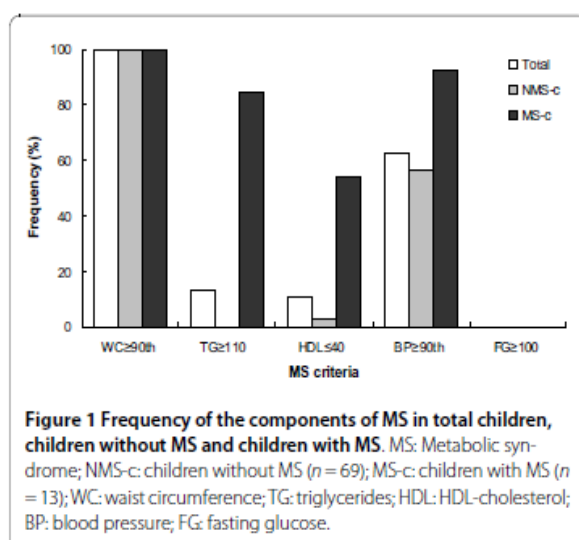
dren, except for systolic BP and C-peptide levels that were significantly higher in obese. This lack of difference may be due to the moderate grade of obesity and lower SD of z-BMI of our sample. We observed that children with MS presented higher z-BMI and largest significant differences in clinical and biochemical characteristics compared to those without MS. The reason why some obese children developed this syndrome, while others do not is still unknown [16]. This may be due to the presence of other underlying factors, such as IR. Indeed, IR seems to be an important pathophysiologic event contributing to MS, becoming more important than overall adiposity in the development of this syndrome [5,27]. In fact, in our study IR was lower in the obese relatively to MS-children. This alerts to the possibility that obese children with 2 or more MS components might form a high risk group within the obese population.

All evaluated children presented abdominal obesity, which is related with increased metabolic risk factors for DM2 and CVD [28]. Elevated BP was the second most common feature of MS, reaching about 2/3 of our sample, which is a remarkably high frequency. In obese children

from several European countries, a lower frequency (38%) was reported [15], similar to a study with US children (7-9 years-old) [16]. The differences found may be due to different methodology, since we used a digital sphygmomanometer which may overestimate blood pressure levels. It also may be due to distinct dietary habits in our population, namely sodium intake. Systolic BP was significantly ($p = 0.682$; $p < 0.001$) correlated to the number of factors of MS.

Dyslipidemia is less prevalent, however the lipid profile can be considered more 'atherogenic' in MS children, with higher TG, LDL, VLDL and apolipoprotein B, and lower HDL and apolipoprotein A-I. Indeed, it is well established that atherosclerosis begins in childhood and is associated with several risk factors for MS [26].

Although the younger age of our sample, the children with MS already presented acanthosis, elevated insulin and C-peptide levels and increased HOMA-IR. Despite this, fasting glucose levels were normal which reflects the range of abnormalities of glucose homeostasis associated with childhood obesity. In fact, even in the obese, high fasting glycemia is not common in the paediatric age [29].



This suggests that impaired glucose levels or pre-diabetes develops later than the other MS components, while IR is the earlier and predominant abnormality of glucose metabolism found in obesity [30]. Indeed, excess weight in children and adolescents may serve to accelerate the onset of DM2 in childhood [5].

Higher levels of hepatic enzymes (ALT, AST and GGT) were found in boys and in children with MS and obesity, although within normal range values. This gender-difference may be due to a larger liver mass in males [31]. Non-alcoholic fatty liver disease is considered the hepatic manifestation of the MS in adults [32]. Currently, this condition is related with child obesity and considered a major cause of abnormal liver function tests in paediatric populations [31,32].

In our sample, leptin levels were correlated to obesity, glucose metabolism, an 'atherogenic' lipid profile and to liver function. Consequently, the presence of MS was associated with significant higher levels of this adipose-tissue hormone. Leptin is described to be positively correlated with both BMI and fasting insulin levels [33]. Chronic insulin increase favours an increase in leptin, which in turn would perpetuate the increase in insulin and favour the onset of IR. This leptin-insulin association begins before puberty and may be connected to the onset of MS [33].

Bacha et al [34] reported that adiponectin is inversely associated with obesity and is an important determinant of insulin sensitivity and HDL in children. However, we did not verify these relations. This is possibly due to the small sample size and more homogeneous characteristics of our sample, without severe obese children. In this study, adiponectin levels showed a weak and negative correlation with diastolic BP and birth weight.

Ghrelin, an orexigenic peptide secreted by the stomach, is documented to be inversely correlated to obesity, insulin and IR indexes in children [35,36], such as confirmed in our study. The negative relationship between fasting ghrelin concentration and obesity might be explained by an inhibitory effect of insulin on ghrelin, since a higher IR is associated with visceral fat accumulation [35].

Conclusions

Our results showed a significant prevalence of MS and its cardiometabolic complications in Portuguese obese schoolchildren. Abdominal obesity was present in all children and the frequency of elevated BP levels was markedly high. None of the children presented impaired fasting glucose. The fact that the clustering of metabolic risk factors in childhood predicts the development of MS into adulthood highlights the importance of better understanding the longer-term health implications of this syndrome in children. Also, a consensual definition of paediatric MS is needed for proper screening, evaluation and treatment of children at risk or with MS. The implementation of preventive measures is urgently required since lifestyle modifications and weight loss may lead to favourable changes in risk factors.

List of abbreviations

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BMI: Body Mass Index; BP: Blood Pressure; CDC: Centers of Disease Control; CRP: C-reactive protein; CVD: Cardiovascular diseases; DM2: Type 2 Diabetes Mellitus; GGT: Gamma-glutamyltransferase; HDL: High density lipoprotein; HOMA-IR: Homeostasis model assessment of insulin resistance; IR: Insulin resistance; LDL: Low density lipoprotein; MS: Metabolic syndrome; SD: standard deviation; T-chol: Total cholesterol; TG: Triglycerides; VLDL: Very low density lipoprotein; WC: Waist circumference; z-BMI: standard deviation score of Body Mass Index.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

CP developed the study protocol, participated in children assessment, data analysis and writing the manuscript. BMPMO completed the statistical analysis and provided advice regarding interpretation and presentation of results. IA participated in children assessment and contributed to the revising of the manuscript. CSP and MDVA provided advice on study design and contributed to the writing of the manuscript. FC participated in protocol development, data analysis and contributed to the writing of the manuscript. All authors read and approved the final manuscript.

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ARTIGO 3

MARKERS OF METABOLIC SYNDROME IN OBESE CHILDREN BEFORE AND AFTER 1-YEAR LIFESTYLE INTERVENTION PROGRAM

Após revisão pelo *European Journal of Nutrition*

MARKERS OF METABOLIC SYNDROME IN OBESE CHILDREN BEFORE AND AFTER 1-YEAR LIFESTYLE INTERVENTION PROGRAM

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ABSTRACT

Purpose: Excess weight may be related to the development of adverse cardiometabolic risk factors in children. The aim of this study was to evaluate the effect of a lifestyle intervention program (nutrition and exercise counselling) on anthropometric parameters and metabolic syndrome (MS) components in Portuguese overweight/obese children.

Methods: A total of 83 overweight/obese children aged 7-9 years were assigned to a 1-year individual (IT) or group-based treatment (GT); 61 children (z-score BMI (zBMI): 1.93 ± 0.28 ; 27 boys and 34 girls) completed the program. Anthropometric and biochemical parameters were assessed at baseline, at 6-months and at 1-year.

Results: The overweight/obese children, compared to normal-weight ones, presented significantly higher blood pressure, total-cholesterol, total-cholesterol / high density lipoprotein cholesterol (HDL) ratio, triglycerides, Apolipoprotein B and C-reactive protein levels, while HDL and Apolipoprotein A-I were significantly lower. At baseline, the prevalence of MS was 16.4% in overweight/obese and 0% in normal-weight children. The number of components of MS was significantly higher in children with higher zBMI. Lifestyle intervention led to a significant improvement in zBMI, waist circumference/height ratio, HDL, triglycerides, Apolipoprotein A-I and Apolipoprotein B levels. The prevalence of MS decreased to 14.8%. The GT intervention seems to be more successful, with a significant decrease in zBMI and an increase in HDL and a lower drop-out rate.

Conclusions: Overweight/obese children have multiple risk factors associated with the MS. Lifestyle intervention, both individual and group-based treatment, led to an improvement in the degree of overweight/obesity and in MS components.

Keywords: children, Metabolic Syndrome, obesity, nutrition, lifestyle intervention.

INTRODUCTION

In the past decades the prevalence of childhood obesity has increased worldwide, reaching epidemic proportions and becoming a serious and growing public health problem [1]. An excessive increase in body mass index (BMI) during early childhood may be related to the development and acceleration of adverse cardiovascular and metabolic risk factors [2]. The constellation of symptoms such as hyperinsulinemia, glucose intolerance, hypertension, high plasma levels of triglycerides (TG), decreased levels of high density lipoprotein (HDL) cholesterol and obesity is known as metabolic syndrome (MS) [3]. This condition increases the risk for cardiovascular diseases (CVD) and type 2 diabetes (DM2) [3, 4]. The definition of MS is not consensual in paediatric populations [5]. Many different MS criteria have been employed and the cut-offs used to diagnose this syndrome in young have varied considerably among studies [4-7]. Recently, a new consensus definition has been published [8]. While the concept of MS has strengths in terms of professional and public health education and awareness, critics argue that it has some limitations [4, 9].

MS is rapidly increasing in prevalence with rising childhood obesity and sedentary lifestyles worldwide. It has been reported to be relatively low in normal-weight children (1% or less) contrary to what occurs in obese (18% to 50%) [10]. In addition, parameters associated with MS have been shown to originate early in life [7], and tend to track into adulthood [7, 11]. Data from the Princeton LRC Follow-up Study showed that the risk was almost 9-fold for CVD and almost 4-fold for DM2 in children with MS compared with children without MS [11]. A proper approach to reduce the obesity-related health risks, both in children and adults, is losing weight. Lifestyle programs that tackle diet and physical activity as well provide psychosocial support, may help prevent or reduce obesity and its associated comorbidities, including the MS [12-16].

The MS has been widely studied in adults and adolescents, however there is little research focusing on its prevalence during lifestyle intervention with younger children (<10 y old). The aims of our study were to evaluate the changes in the degree of overweight/obesity and in the prevalence of MS and its components in a sample of Portuguese overweight/obese schoolchildren enrolled in a 1-year outpatient lifestyle intervention program. We hypothesized that reduction of the degree of obesity will result in improvement of MS components, while increasing the degree of obesity will result in worsening of this syndrome.

SUBJECTS AND METHODS

Study Population

We invited to participate in the study 127 children classified as obese ($\geq 95^{\text{th}}$ BMI percentile) according to the US Centers for Disease Control and Prevention (CDC) [17]. These children were identified in a previous population-based study [18]. Eighty-three accepted the invitation and 61 (27 boys, 34 girls) concluded the 1-year study protocol. Between the assessment at school and the first visit at the Hospital Infante D. Pedro, 10 children initially classified as obese became overweight (85-95th BMI percentile). These children were also included in the study. The normal-weight (NW) children ($\leq 85^{\text{th}}$ BMI percentile; 7-9 year-old; 13 boys, 9 girls) were recruited from the outpatient Pediatric Clinic, and they performed only the baseline assessment. None of the children had primary dyslipidemia, hypertension, diabetes or glucose intolerance, secondary obesity, and were not receiving pharmacological treatment. Each parent gave written informed consent and children gave assent for participation. Assessments were done at the Department of Endocrinology, Diabetes and Nutrition. The study was approved by the Hospital Ethics Committee.

Study Protocol

The children were randomly assigned to one of the two treatments: an individual conventional treatment (IT) or a group-based treatment (GT). Since GT implies more visits, and due to staff and space limitations, GT was assigned with probability 1/3 and IT with probability 2/3. The main objective of both interventions was to promote lifestyle changes in children and their families, and consequently to stop weight gain and promote weight loss. At baseline, anthropometric and biochemical measurements were carried out to all children. In IT, a healthy eating plan meeting nutrient needs according to the recommended daily allowance (≈ 1800 Kcal) was prescribed and explained to children and their parents. The diet recommended the reduced intake of refined carbohydrates and saturated fats, with an increased consumption of vegetables and fruits. Additionally, physical activity was encouraged and sedentary behaviours, such as TV watching and computer/video game playing, were discouraged. Follow-up visits were held at 3- and 6-m and 1-y after the first visit. In GT, children and their parents participated in a group-based nutrition education program (4 children per group), which consisted of 4 consecutive sessions each of 60 minutes duration, conducted by a nutritionist. These sessions covered several topics regarding childhood obesity and comorbidities, healthy eating habits,

healthy cooking methods, portion size control, food labelling and physical activity promotion. The acquired knowledge was reinforced at each session and whenever necessary at follow-up visits that were held at 3- and 6-m and 1-y after the first visit. Forty-two children at the IT and 19 at the GT completed the 1-y follow-up visit.

Anthropometric Measures

Weight, height and waist circumference (WC) were measured according to standardized procedures [19]. Weight was measured to the nearest 0.1 kg using an electronic column scale (SECA-780); height was measured to the nearest 0.1 cm using a stadiometer (SECA-220); WC was measured to the nearest 0.1 cm at the mid-point between the iliac crest and the lower edge of the ribs at the end of a normal expiration. BMI was calculated with measured height and weight and was standardised (zBMI) by using age- and gender-normative data from the CDC [17, 20]. The term overweight/obese (OW/OB) includes children with a BMI percentile $\geq 85^{\text{th}}$. Abdominal obesity was defined using the sex and age-specific 90th WC percentile by McCarthy *et al* [21]. All measurements were repeated at each follow-up visit. Birth weight and length were obtained from the children's health booklet.

Clinical and Biochemical Measures

A physical examination was performed and puberty status was assessed according to Tanner stages [22]. Blood pressure (BP) was measured on the right arm with the patient seated, after rest, using a digital sphygmomanometer (OMRON M6) and appropriate sized cuff. After three measurements, the lowest blood pressure value was recorded. Children were classified according to sex, height and age-specific charts [23]. Baseline blood samples were collected in the morning (8:00 to 9:00) after an overnight fast (10 to 12 hours) and after a local application of a topical anaesthetic patch (EMLA). Plasma and serum were separated by centrifugation. The glucose oxidase method (Siemens Healthcare Diagnostics Inc., Newark, DE, USA) was used to determine blood glucose levels. Both serum lipids (total cholesterol (T-chol), HDL-cholesterol (HDL), LDL-cholesterol (LDL), triglycerides) and plasma liver enzymes (alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT)) levels were measured by enzymatic colorimetric methods (Siemens Healthcare Diagnostics Inc.). Apolipoprotein A-I and Apolipoprotein B were measured by an immunoturbidimetric assay (Olympus America Inc., Center Valley, PA, USA). C-reactive protein (CRP) was

determined using a turbidimetric immunoassay (Siemens Healthcare Diagnostics Inc.). Outcome measures were obtained at follow-up visits at 6-m and 1-y.

Physical activity

A questionnaire concerning children activities was applied at baseline and at 1-y follow-up visit. The children were asked, with the help of parents, about the time spent at school, watching TV, playing computer/video games and sleeping. The frequency and duration of physical activities performed at school and/or extracurricular were also quantified.

Family History

Parents were asked about the presence of overweight/obesity and associated co-morbidities such as diabetes, hypertension, dyslipidemia, CVD and hyperuricemia, as well as its presence in children's grandparents. The parents were not measured for height and weight.

Definition of MS

MS was defined according to the National Cholesterol Education Program Adult Treatment Panel III criteria modified by Cook [6], with adjustment for fasting glucose according to the recent American Diabetes Association definition for impaired fasting glucose [24]. This definition was chosen since it is based in age- and gender-specific cut-offs and it has been used in other paediatric studies [5, 25]. MS was considered if three or more of the following criteria were present: 1) abdominal obesity (WC $\geq 90^{\text{th}}$ percentile for age and sex) [21]; 2) fasting triglycerides ≥ 110 mg/dl; 3) HDL ≤ 40 mg/dl; 4) systolic/diastolic BP $\geq 90^{\text{th}}$ percentile for age, sex and height [23]; 5) fasting glucose ≥ 100 mg/dl [24].

Statistical Analysis

Descriptive statistics were executed. Pearson (R) and Spearman (ρ) correlation coefficients were used. Partial correlation was computed controlling for gender, age and Tanner stage. Chi-square test was used in nominal categorical variables. Independent samples t test was performed in continuous variables with normal distribution and Mann-Whitney test in those without normal distribution. General Linear Model (GLM) for repeated measures was used to compare the evolution of each of the variables, and time (baseline, 6-m and 1-y follow-up), treatment assignment (IT and GT) and

treatment X time interaction were included as fixed effects, controlling for gender and Tanner stage. The differences between 1-y follow-up and baseline values (Δ) were calculated. In order to reduce the number of variables, a principal components analysis on Δ of anthropometric, metabolic and physical activity variables was performed and the components to extract were selected applying Cattell's method (scree plot). The principal components extracted were used in a multivariate GLM to study the effect of both treatments, controlling for gender, age and Tanner stage. Normal distribution was assessed using the Kolmogorov-Smirnov test. We considered a significance level of 0.05. Analysis was performed using SPSS version 14.0, 2005.

For the purpose of sample size estimation, the primary outcome was a decrease in zBMI between baseline and 1-y follow-up. According to our previous experience, a standard deviation of zBMI near 0.35 and a dropout rate under 30% was estimated. From our baseline sample, the number of participants in the smaller treatment group (GT) was estimated to decrease from 25 to 18. From these assumptions, a power analysis was conducted using a sample size for each group of 18, obtaining an estimated power of 0.81 for a paired samples t-test.

RESULTS

Of the 83 OW/OB children that were evaluated at first visit, 73.5% (n=61) completed the program. No significant differences between dropouts (n=22) and those who finished the study were observed at baseline. The attrition rate was similar in both treatment types: 27.6% in IT and 24.0% in GT. The main reason referred to drop-out of the study was the lack of time due to school/work schedules. No statistical differences were found between the IT and GT subjects with respect to baseline parameters. The dropouts were excluded from the subsequent analysis.

Baseline Characteristics

The anthropometric and clinical characteristics of the 61 OW/OB (51 obese, 10 overweight) and 22 NW children are shown in Table 1. No differences were found between both groups in age and gender. Gestational data (weight, length and weeks of gestation) were also similar between groups. The OW/OB children presented significantly higher BP, T-chol, T-chol/HDL ratio, triglycerides (TG), Apolipoprotein B and C-reactive protein (CRP) levels; HDL and Apolipoprotein A-I were significantly lower. At baseline, the prevalence of MS was 16.4% in OW/OB children, without significant differences

between gender ($p=0.321$). None of the children fulfilled the five MS components. In NW children, MS was absent. Acanthosis nigricans was detected in 19.7% of the OW/OB children at baseline. Most children were prepubertal at baseline (Tanner stage: I - 70.5%; II – 29.5%). There were no statistical differences between gender, except for CRP (girls: 0.45 ± 0.91 mg/dl vs boys: 0.31 ± 0.77 mg/dl; $p=0.020$) and ALT (girls: 17.6 ± 4.9 U/L vs boys: 21.3 ± 7.3 U/L; $p=0.020$) in OW/OB children.

Primary Outcome

At follow-up, both groups showed a significant ($p<0.001$) decrease in zBMI (-0.18 and -0.25 in IT and GT, respectively) and in WC/height ratio, although weight and height increased (Table 2). This decrease was more pronounced in the GT subjects ($p=0.042$ for zBMI and WC/height ratio). An increase in zBMI was associated with an increase in WC ($R=0.783$; $p<0.001$), WC/height ratio ($R=0.781$; $p<0.001$) and GGT ($R=0.261$; $p=0.045$), and a decrease in HDL ($R=-0.357$; $p=0.006$).

Secondary Outcome

Along the study, we observed an improvement of HDL ($p=0.019$), higher in the GT children ($p=0.042$) (Table 3). TG levels evolved differently between genders ($p=0.001$) and between Tanner stages ($p=0.001$): it increased in time in girls (76.6 ± 41.8 mg/dl at baseline vs 82.4 ± 42.8 mg/dl after 1-y) and in stage II children (67.8 ± 31.6 mg/dl at baseline vs 83.3 ± 47.9 mg/dl after 1-y), while it decreased in boys (80.4 ± 65.1 mg/dl at baseline vs 67.7 ± 28.3 mg/dl after 1-y) and in stage I (73.2 ± 48.6 mg/dl at baseline vs 71.4 ± 31.5 mg/dl after 1-y). At 1-y, the MS prevalence decreased from 16.4% to 14.8% (Fig. 1), more significantly in boys ($p=0.030$). BP levels $\geq 90^{\text{th}}$ percentile decreased from 63.9% to 49.2% ($p=0.063$). No child presented impaired fasting glucose levels, and acanthosis decreased to 11.5% 1-y later. Children with higher than average zBMI presented a higher than average number of MS criteria ($p=0.418$, $p<0.001$). OW/OB children with MS presented higher zBMI (2.15 ± 0.20 vs 1.88 ± 0.23 ; $p=0.006$), systolic BP (120.9 ± 8.6 vs 114.5 ± 7.8 mmHg; $p=0.023$), TG (159.6 ± 85.2 vs 61.7 ± 18.6 mg/dl; $p<0.001$), T-chol/HDL (4.54 ± 0.99 vs 3.30 ± 0.53 ; $p=0.003$) and Apolipoprotein B levels (87.6 ± 16.9 vs 76.5 ± 14.2 mg/dl; $p=0.033$) than those without MS, while HDL (39.5 ± 8.8 vs 51.7 ± 8.6 mg/dl; $p<0.001$), Apolipoprotein A-I (111.4 ± 14.6 vs 124.9 ± 14.9 mg/dl; $p=0.011$) and Apo A-I/B ratio (1.31 ± 0.25 vs 1.69 ± 0.37 ; $p=0.003$) were lower.

Physical Activity and Sedentary Behaviour

OW/OB children had statistically fewer hours of sleep and spent more hours watching TV than NW ones (Table 4). OW/OB girls spent more time watching TV ($p=0.012$), while OW/OB boys spent more time playing computer ($p=0.001$) and in extra-curricular activities ($p=0.005$). Time devoted to extra-curricular exercise did not improve over time. No differences were found between the IT and GT subjects. MS children spent fewer hours in extra-curricular exercise, both at baseline (3.0 ± 6.4 vs 17.2 ± 15.5 min/day; $p=0.004$) and after 1-year (5.9 ± 10.9 vs 17.3 ± 14.6 min/day; $p=0.030$).

Family History

Overweight/obesity was present in 42.6% of the mothers, 37.7% of the fathers and 14.8% of both parents of the OW/OB children (65.6% had at least one of their parents with excess weight). In grandparents, excess weight was present in 63.9%. Other comorbidities were also referred, such as dyslipidemia (21.3% mother, 21.3% father, 39.3% grandparents), hypertension (9.8% mother, 8.2% father, 47.5% grandparents) and diabetes (0% mother, 1.6% father, 57.4% grandparents). In NW children, overweight/obesity was present in 19.0% of the mothers, 9.5% of the fathers and 4.8% of both parents.

Principal Components Analysis

Seven principal components (PCs) were extracted with eigenvalues above 1. The first PC (PC1) was correlated mainly with anthropometric variables (Δ weight, Δ BMI, Δ zBMI, Δ WC, Δ WC/height) and explained 24.0% of total variance (Table 5). The second PC (PC2) was correlated mainly with metabolic variables (Δ T-chol, Δ HDL, Δ LDL, Δ ApoA-I, Δ ApoB, Δ ALT, Δ GGT) and explained 21.6% of total variance. The other PCs explained less than 8%. The physical activities variables had very weak correlations with both PCs. The only exception was the association between physical activity at school and PC1 ($R=-0.450$). According to the multivariate GLM, no significant association between PC1 and PC2 and the Δ of the number of MS components ($p=0.639$) was found. Treatment type alone did not have a significant effect ($p=0.412$) but its interaction with gender did ($p=0.026$). For PC1, girls responded better to IT than to GT (-0.430 ± 1.220 vs 0.438 ± 1.029), while boys responded better to GT (0.160 ± 1.337 vs -0.773 ± 1.114). For PC2, girls did not showed large discrepancies between IT and GT (0.160 ± 1.257 vs 0.321 ± 1.060), while boys responded better to IT (-0.416 ± 1.377 vs 0.321 ± 1.148). No

significant differences between Tanner stages were found in both PCs, however children that evolved from stage I to stage II over 1-y period had significantly lower values in both ($p=0.023$).

DISCUSSION

Our study presents the first report on the impact of an outpatient lifestyle intervention on MS and their components among OW/OB Portuguese children aged 7-9 years, recruited from the general population. We found a high prevalence of MS (16.4%) in OW/OB children, while it was absent in the NW. Similar results were found by Dubose et al. [26]. In other European countries a similar prevalence of MS is found [5, 25, 27], however with differences when considering the definition applied [5, 27].

OW/OB children in comparison to NW ones presented several cardiovascular and metabolic risk factors. BP levels have shown to be strongly predicted by BMI [28], however when compared to other studies [26, 27], we found a greater prevalence of elevated BP levels. This may be due to distinct dietary habits in our population, namely high sodium intake [29]. Our results are in agreement with data from Bogalusa Heart Study that showed significantly higher levels of T-cholesterol, LDL and TG and lower HDL levels in overweight children [30]. CRP levels were also increased in our OW/OB subjects. This is in line with previous studies and seems to be related to an increased risk of CVD and diabetes [31]. Also, in our study, the number of children with 3 or more components of MS increased in parallel to the increasing severity of obesity. None of our children presented impaired fasting glucose levels. Indeed, our sample is very young and high fasting glycemia is not common in the paediatric age [32]. However, we found a high frequency (19.5%) of acanthosis nigricans, a known dermatologic feature of insulin resistance [33].

In this study, both approaches (IT and GT) were effective in zBMI change and, in general, clinical and metabolic parameters improved after 1-y. Since our study was not hospital-based, the severity of obesity was moderate (zBMI: 1.93 ± 0.28), which may also account to less severe comorbidities. WC/height ratio, an index associated with cardiovascular risk factors in children [30], reduced significantly at 1-y. Both zBMI and WC/height ratio showed a more pronounced decrease in children enrolled in the GT.

In addition to a reduction in zBMI, an improvement of blood pressure and lipid profile was also shown over time. BP levels $\geq 90^{\text{th}}$ percentile decreased by 23%, yet after 1-y we still found an alarming prevalence of elevated BP levels. In girls, we found an increase in TG levels at 1-y, which may be associated to the higher number of girls at Tanner stage II, since puberty is associated with an

increase in TG levels [34]. The relative normal baseline lipid levels in these children may have limited our ability to show a more substantial change. These results are in line with previous paediatric studies showing that a reduction in obesity leads to an improvement in CVD risks factors [12, 35].

Mostly in GT-children, we observed a fluctuation in the mean values of some parameters between the follow-up visits at 6-m and 1-y, namely an initial improvement followed by a small setback. This may be associated to more visits held in the first semester, allowing greater compliance between children and staff. This suggests the need for the development of continuous care models, helping maintaining initial weight loss [36].

A slight decrease of the MS prevalence was observed. However, in girls and in Tanner stage II children a higher prevalence of MS was found at 1-y. This may be explained by pubertal development, since it is associated with an increase in insulin resistance [37] and with several changes in plasma lipids [34], which are related to the risk of development of MS. Among those children who never developed MS (n=47) or no longer presented it after 1-y (n=5), most of them improved their zBMI, while among those who developed MS (n=4), all either worsen or maintained their degree of overweight/obesity. This is in accordance with a recent study which showed that the amount of overweight reduction is a predictive factor for the improvement of MS components [15]. The fact that MS phenotype tends to persist and worsen over time if no preventive actions are taken [7], highlights the value of diet and exercise intervention. Other authors obtained more significant results in response to lifestyle intervention [15, 35, 38], however those are accomplished with a stronger dietary restriction (1000-1200 kcal).

Besides small differences between the outcome measures in both interventions, the GT seems to be more successful, with a significant decrease in zBMI and an increase in HDL. A family-based group treatment has been described as more effective than individual treatment in the management of childhood obesity at long-term [13, 39, 40]. The response to the treatment, IT or GT, was different according to gender, which may also alert us to the need for different approaches at this age.

OW/OB children were more prone to sedentary activities. Indeed, OW/OB and MS subjects spent usually around 2 hours per day watching TV and playing computer or videogames, while only about 15 minutes in extra physical activities. Results from the Framingham Children's Study confirm that the number of hours spent watching television or playing videogames is an important risk factor for the development of excess body fat during childhood [41]. Boys are generally more active than girls [42], as we observed. The time devoted to extra-curricular exercise remained nearly constant over time.

Some of the reasons pointed out were the short time available, lack of appropriate infrastructures and insecurity in the practice of outdoor activities. On the other hand, an increase in physical activity performed at school had a positive effect in PC1, which may argue for a key role of school in promoting healthy lifestyles. Since sedentary and physical activities were obtained by self-report, this may limit the validity of these measures. Many intervention studies with exercise in their programs have shown that the combination of these approaches improves metabolic outcomes [13-15].

Overweight/obesity was present in about 2/3 of the family members of the OW/OB children. However, these may be underestimated since data on parents were obtained by self report. Other comorbidities were also reported, such as CVD and DM2, mainly in grandparents. Indeed, a family environment that promotes obesity and comorbidities in one member may be more likely to promote it in others [43]. The advantage of family interventions is that they address children and their parents. This is especially important for younger children, as our sample, since the influence of the parents on food habits and physical activity is higher on earlier ages [44].

Our study presents some limitations. First, the final sample size, despite an acceptable drop-out rate. Second, most children presented normal values at baseline for most of the metabolic parameters, which may contribute to decrease the statistical power for detecting significant differences over time. Third, both groups were subjected to treatment, not allowing us to compare the outcomes with children not enrolled in any.

In conclusion, our results showed a significant prevalence of MS and its components, namely abdominal obesity, higher blood pressure and dyslipidemia in Portuguese OW/OB children. Both treatment interventions led to a decrease in zBMI and a moderate improvement of those components, more effective in the GT. Even in the absence of weight loss, OW/OB children may improve their cardiovascular and metabolic risk profile by lifestyle changes – diet, exercise and behaviour therapies. This may lead to improved child health. The modest magnitude of the benefits observed argues for a longer-term and perhaps more intensive intervention. Hence, longer-term studies and larger cohorts are necessary to evaluate whether the improvements are clinically relevant, how the changes are incorporated into the lives of children and families and are sustained over time.

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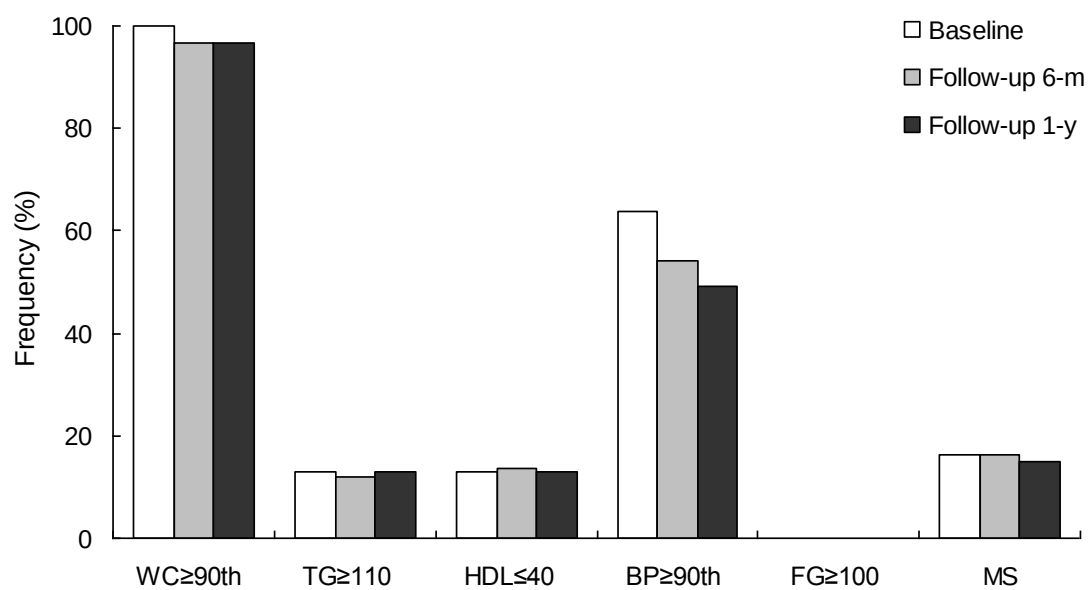
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Fig. 1 Prevalence of Metabolic Syndrome and its criteria at baseline and at the follow-up visits at 6-months and at 1-year in overweight/obese children



WC: waist circumference; TG: triglycerides; HDL: high density lipoprotein; BP: blood pressure; FG: fasting glucose; MS: metabolic syndrome.

Table 1 Anthropometric and metabolic characteristics of overweight/obese and normal-weight children

	OW/OB (n = 61)	NW (n = 22)	p
Gender			
Male	34 (55.7%)	13 (59.1%)	0.233 ^a
Female	27 (44.3%)	9 (40.9%)	
Metabolic Syndrome	10 (16.4%)	0 (0.0%)	0.043 ^b
Age (y)	8.6 ± 0.7	8.4 ± 0.7	0.133 ^b
Weight (kg)	42.0 ± 6.6	26.7 ± 3.1	<0.001 ^b
Height (cm)	134.9 ± 6.1	129.6 ± 5.8	0.001 ^b
BMI (kg/m ²)	22.94 ± 2.29	15.86 ± 1.06	<0.001 ^b
Z-score BMI	1.93 ± 0.28	-0.12 ± 0.62	<0.001 ^b
Waist circumference (cm)	72.8 ± 6.4	55.6 ± 3.7	<0.001 ^b
Systolic BP (mmHg)	115.6 ± 8.2	103.2 ± 9.9	<0.001 ^b
Diastolic BP (mmHg)	62.9 ± 9.6	53.8 ± 7.7	<0.001 ^b
Glucose (mg/dl)	80.7 ± 5.7	80.3 ± 6.2	0.749 ^b
T-chol (mg/dl)	169.6 ± 27.5	159.8 ± 15.3	0.046 ^b
HDL (mg/dl)	49.7 ± 9.7	55.2 ± 10.6	0.030 ^b
T-chol/HDL	3.51 ± 0.77	3.00 ± 0.67	0.008 ^b
LDL (mg/dl)	107.8 ± 23.8	97.6 ± 17.8	0.073 ^b
Triglycerides (mg/dl)	77.7 ± 52.1	52.3 ± 26.5	0.005 ^c
Apolipoprotein A-I (mg/dl)	122.7 ± 15.6	141.8 ± 10.5	0.010 ^b
Apolipoprotein B (mg/dl)	78.3 ± 15.1	69.4 ± 12.1	0.017 ^b
Apolipoprotein A-I/B (mg/dl)	1.62 ± 0.38	1.93 ± 0.41	0.085 ^b
C-reactive protein (mg/dl)	0.39 ± 0.84	0.11 ± 0.06	0.004 ^c
AST (U/L)	25.1 ± 5.0	26.8 ± 4.9	0.089 ^c
ALT (U/L)	19.3 ± 6.3	17.8 ± 4.4	0.552 ^c
GGT (U/L)	15.6 ± 6.8	17.1 ± 3.3	0.016 ^c
Birth weight (g)	3412 ± 457	3358 ± 455	0.638 ^b

Data presented as n (%) for gender and MS, and as mean ± standard-deviation (SD) for other variables. OW/OB: overweight/obese; NW: normalweight; BP: blood pressure; T-chol: total cholesterol; HDL: high density lipoprotein; LDL: low density lipoprotein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gama-glutamyltransferase.

Statistic tests comparing OW/OB children with controls: ^a Chi-square test; ^b t-student; ^c Mann-Whitney.

Table 2 Baseline and follow-up anthropometric and clinical characteristics of the population study according to treatment assignment

(n = 61)	Treat. type	Baseline	Follow-up 6-months	Follow-up 1-year	p^a		
					t	$t*T$	T
Weight (kg)	IT	42.6 ± 6.8	44.0 ± 7.3	46.5 ± 8.0	<0.001	0.431	0.270
	GT	40.7 ± 6.2	42.3 ± 6.9	43.9 ± 6.4			
BMI (kg/m ²)	IT	23.23 ± 2.52	23.08 ± 2.69	23.39 ± 2.77	0.842	0.579	0.107
	GT	22.30 ± 1.57	22.28 ± 1.75	22.14 ± 1.81			
zBMI	IT	1.96 ± 0.29	1.83 ± 0.34	1.78 ± 0.33	<0.001	0.582	0.042
	GT	1.86 ± 0.25	1.73 ± 0.35	1.61 ± 0.34			
WC (cm)	IT	73.6 ± 6.5	73.5 ± 6.9	74.9 ± 7.5	0.081	0.803	0.079
	GT	70.9 ± 6.0	71.1 ± 6.2	71.6 ± 5.6			
WC/height	IT	0.54 ± 0.04	0.53 ± 0.04	0.53 ± 0.04	<0.001	0.760	0.042
	GT	0.53 ± 0.03	0.52 ± 0.04	0.51 ± 0.03			
SBP (mmHg)	IT	115.2 ± 8.6	116.3 ± 8.8	114.3 ± 8.5	0.403	0.493	0.668
	GT	116.3 ± 7.5	111.9 ± 9.2	114.1 ± 9.9			
DBP (mmHg)	IT	62.3 ± 8.4	62.3 ± 8.4	60.5 ± 6.9	0.047	0.382	0.687
	GT	64.3 ± 12.0	58.4 ± 7.0	61.3 ± 6.5			

Data presented as mean ± standard-deviation (SD) for continuous variables. Treat. = Treatment; IT: individual treatment (n=42); GT: group-based treatment (n=19); WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure.

^a GLM repeated measures, controlling for gender and Tanner stage: t = time effect; T = treatment effect; $t*T$ = time X treatment interaction.

Table 3 Baseline and follow-up metabolic characteristics of the population study according to treatment assignment

(n = 61)	Treat. type	Baseline	Follow-up 6-months	Follow-up 1-year	<i>p</i> ^a		
					<i>t</i>	<i>t*T</i>	<i>T</i>
Glucose (mg/dl)	IT	80.7 ± 5.7	79.0 ± 6.2	77.4 ± 7.2	0.177	0.343	0.730
	GT	80.9 ± 6.2	78.7 ± 7.7	80.1 ± 10.8			
T-chol (mg/dl)	IT	166.0 ± 27.4	169.4 ± 27.2	168.6 ± 24.4	0.091	0.024	0.546
	GT	177.4 ± 26.8	170.6 ± 26.5	180.6 ± 30.4			
HDL (mg/dl)	IT	48.5 ± 9.9	49.8 ± 8.8	50.4 ± 10.6	0.019	0.235	0.042
	GT	52.4 ± 9.0	50.5 ± 9.7	55.9 ± 9.7			
T-chol /HDL ratio	IT	3.52 ± 0.79	3.48 ± 0.69	3.47 ± 0.76	0.377	0.413	0.145
	GT	3.47 ± 0.72	3.45 ± 0.67	3.30 ± 0.68			
LDL (mg/dl)	IT	105.4 ± 24.5	106.9 ± 21.9	105.4 ± 22.3	0.119	0.013	0.955
	GT	112.9 ± 21.9	107.4 ± 20.3	114.8 ± 26.4			
TG (mg/dl)	IT	79.2 ± 55.9	76.2 ± 27.8	77.2 ± 35.4	0.009	0.482	0.158
	GT	74.6 ± 43.8	65.1 ± 28.5	73.5 ± 42.1			
Apo A-I (mg/dl)	IT	121.5 ± 16.8	126.2 ± 16.8	122.9 ± 15.2	0.026	0.057	0.293
	GT	125.3 ± 12.6	122.2 ± 14.0	130.9 ± 14.2			
Apo B (mg/dl)	IT	77.2 ± 15.8	74.3 ± 13.8	75.1 ± 14.3	0.033	0.501	0.533
	GT	80.8 ± 13.4	75.9 ± 13.4	77.8 ± 14.5			

Data presented as mean ± standard-deviation (SD). Treat. = Treatment; IT: individual treatment (n=42); GT: group-based treatment (n=19); T-chol: total cholesterol; HDL: high density lipoprotein; LDL: low density lipoprotein; TG: triglycerides; Apo A-I: apolipoprotein A-I; Apo B: apolipoprotein B.

^a GLM repeated measures, controlling for gender and Tanner stage: *t* = time effect; *T* = treatment effect; *t*T* = time X treatment interaction.

Table 4 Sedentary and extra-curricular physical activities at baseline and at 1-year follow-up visit in overweight/obese and normal-weight children

	Overweight/Obese			Normal-weight			<i>p</i> ^a	<i>p</i> ^b
	Total (n=61)	Boys (n=27)	Girls (n=34)	Total (n=22)	Boys (n=13)	Girls (n=9)		
At baseline								
School (h/day)	7.3 ± 1.9	7.3 ± 2.2	7.4 ± 1.7	8.3 ± 0.8	8.1 ± 0.8	8.6 ± 0.7	0.141 ^c	0.001 ^c
Sleeping (h/day)	9.5 ± 0.7	9.4 ± 0.5	9.6 ± 0.8	10.2 ± 0.6	10.4 ± 0.7	9.9 ± 0.5	0.107 ^d	0.000 ^d
Watching TV (h/day)	1.7 ± 0.9	1.4 ± 0.6	2.0 ± 1.0	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	0.637 ^d	0.000 ^d
Playing computer/videogames (h/day)	0.6 ± 0.5	0.8 ± 0.5	0.4 ± 0.4	0.6 ± 0.4	0.6 ± 0.4	0.6 ± 0.4	0.621 ^d	0.450 ^d
Extra-curricular physical activities (min/day)	14.8 ± 15.3	21.7 ± 17.0	9.4 ± 11.4	19.0 ± 24.3	21.9 ± 24.8	14.8 ± 24.3	0.510 ^d	0.886 ^d
At 1-year follow-up								
Extra-curricular physical activities (min/day)	15.6 ± 14.6	24.4 ± 15.7	8.7 ± 9.0	-	-	-	<0.001 ^c	-

Data presented as mean ± standard-deviation (SD).

^a Significance level for the differences between boys and girls; ^b Significance level for the differences between overweight/obese and normal-weight children; ^c t-student test; ^d Mann-Whitney test.

Table 5 Correlation matrix between the principal components (PC) and the differences between baseline and 1-y follow-up variables (Δ)

Variables	PC1	PC2
Δ weight	0.860	-0.299
Δ height	0.095	-0.350
Δ BMI	0.906	-0.200
Δ zBMI	0.916	-0.207
Δ WC	0.865	-0.328
Δ WC/height	0.865	-0.263
Δ systolic BP	0.126	-0.097
Δ diastolic BP	0.046	-0.318
Δ glucose	-0.150	0.222
Δ total cholesterol	0.377	0.840
Δ HDL	-0.257	0.686
Δ LDL	0.394	0.807
Δ Triglycerides	0.401	0.372
Δ Apolipoprotein A-I	0.036	0.709
Δ Apolipoprotein B	0.458	0.694
Δ C-reactive protein	0.045	-0.080
Δ AST	-0.024	0.473
Δ ALT	0.045	0.567
Δ GGT	0.359	0.621
Δ physical activities at school	-0.450	-0.092
Δ extra-curricular physical activities	0.147	0.052

WC: waist circumference, BP: blood pressure; HDL: high density lipoprotein; LDL: low density lipoprotein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma-glutamyltransferase.

ARTIGO 4

METABOLIC SYNDROME, ADIPOKINES AND GHRELIN IN OVERWEIGHT AND OBESE SCHOOLCHILDREN: RESULTS OF A 1-YEAR LIFESTYLE INTERVENTION PROGRAM

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**METABOLIC SYNDROME, ADIPOKINES AND GHRELIN IN OVERWEIGHT AND
OBESE SCHOOLCHILDREN: RESULTS OF A 1-YEAR LIFESTYLE
INTERVENTION PROGRAM**

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ABSTRACT

The aim of this study was to evaluate the effect of a lifestyle intervention program (nutrition and exercise counselling) on MS components, adipokines (leptin, adiponectin) and ghrelin levels in overweight children. A total of 61 overweight children aged 7-9 years ($\geq 85^{\text{th}}$ BMI percentile; 27 boys/34 girls) were randomly assigned and completed a 1-year individual (IT) or group-based treatment (GT). Anthropometric and biochemical parameters were assessed at baseline, at 6-months and at 1-year. Twenty-two normal-weight children ($< 85^{\text{th}}$ BMI percentile; 7-9 year-old; 13 boys/9 girls) were also evaluated at baseline. Insulin resistance (IR) was determined by the Homeostasis Model Assessment of IR (HOMA-IR). Overweight children presented significantly higher blood pressure, triglycerides, Apolipoprotein B, insulin, HOMA-IR, leptin, C-reactive protein and homocysteine levels, while Apolipoprotein A-I was significantly lower. At baseline, MS was present in 10 overweight children, of which only 5 maintained it at 1-year. Leptin and ghrelin levels were associated with IR and MS components. MS was predicted by apolipoprotein A-I, insulin and pre-puberty. The lifestyle intervention led to a significant improvement in zBMI, waist circumference/height ratio and lipid profile. Changes in insulin, HOMA-IR, leptin and adiponectin were not significant. Ghrelin behaved differently between IT and GT. The GT intervention seems to be more successful, with a decrease in BMI z-score and an improvement of metabolic parameters.

In conclusion, overweight children have multiple risk factors associated with MS. A lifestyle intervention program seems to be an effective mean for reducing obesity and MS components and improving adipokines concentrations.

Keywords: childhood obesity, Metabolic Syndrome, leptin, adiponectin, ghrelin, lifestyle intervention.

ABBREVIATIONS

BMI: Body Mass Index

BP: Blood pressure

CDC: Centers for Disease Control and Prevention

CRP: C-reactive protein

CVD: Cardiovascular diseases

DM2: Type 2 Diabetes Mellitus

GT: Group-based treatment

HDL: High density lipoprotein

HOMA-IR: Homeostasis model assessment of insulin resistance

IT: Individual treatment

MS: Metabolic syndrome

SD: standard deviation

TG: Triglycerides

WC: Waist circumference

zBMI: Standard deviation score of Body Mass Index

INTRODUCTION

The prevalence of overweight and obesity among children has increased worldwide, reaching epidemic proportions and becoming a serious public health problem [40]. Increases in body mass index (BMI) during childhood may be related to the development and acceleration of adverse cardiometabolic risk factors [8], such as hypertension, dyslipidemia (high triglycerides (TG) and low high density lipoprotein (HDL) cholesterol, hyperinsulinemia and glucose intolerance, known as the metabolic syndrome (MS) [5]. This condition increases the risk for cardiovascular diseases (CVD) and type 2 diabetes (DM2) [5]. MS is rapidly increasing in prevalence with rising childhood obesity and sedentary lifestyles worldwide. It has been reported to be relatively low in normal-weight children (1% or less) contrary to what occurs in obese (18% to 50%) [32]. Notwithstanding, this prevalence can vary widely in paediatric populations depending on the definition used [4, 30, 43], which makes it difficult to fully understand the dimension of the problem. Recently, the International Diabetes Federation (IDF) presented a new consensus definition for children and adolescents [49].

The potential link between MS and obesity is probably related to a dysregulated adipocyte production of factors that participate in a proinflammatory and prothrombotic state [6]. This condition may induce insulin resistance leading to clinical and biochemical manifestation of MS. Adipose tissue release several adipokines, two of which, leptin and adiponectin, appear to play a role in glucose and lipid metabolism and energy homeostasis [20]. Elevated leptin and low adiponectin concentrations seem to correlate with a range of components of MS [38]. Ghrelin, a somatotrophic and orexigenic hormone, has been recognized as an important regulator of energy metabolism and serves as a physiological regulator of insulinemia and glycemia [12].

It is widely accepted that a proper approach to reduce the obesity-related risks in children is losing, or even maintaining, weight. Lifestyle programs may help prevent or reduce obesity and its associated comorbidities, including the MS, in youth [17, 25, 31]. There is little research focusing on MS components during lifestyle intervention with younger children (<10 y old). Besides, anthropometric parameters may not reflect all the positive changes associated with lifestyle modifications and the role of adipokines in MS development is not yet fully understood in children. Based on these aspects, the aims of our study were to: a) evaluate the changes in anthropometric, clinical and metabolic parameters in Portuguese overweight schoolchildren enrolled in a 1-year outpatient lifestyle intervention program; b) analyse the possible correlations between leptin, adiponectin, and ghrelin levels and MS components.

PATIENTS AND METHODS

Study Population

Recruitment of the study sample was population-based [28]. In brief, 905 children between 7-9 year-old (457 boys, 448 girls) were anthropometrically evaluated at school setting. Of those, 127 were classified as obese ($\geq 95^{\text{th}}$ BMI percentile) according to the US Centers for Disease Control and Prevention (CDC) [21] and were invited to participate in the study at the Hospital Infante D. Pedro. Eighty-three accepted the invitation and 61 (27 boys, 34 girls) concluded the 1-year study protocol (Figure 1). Between the assessment at school and the first visit at the Hospital, 10 children initially classified as obese became overweight (85-95th BMI percentile). These children were also included in the study. The control normal-weight children ($< 85^{\text{th}}$ BMI percentile; 7-9 year-old; 13 boys, 9 girls) were recruited from the outpatient Pediatric Clinic. They performed only the baseline assessment.

Each parent gave written informed consent and children gave assent for participation. Assessments were done at the Department of Endocrinology, Diabetes and Nutrition. The study was approved by the Hospital Ethics Committee.

None of the children had diagnosed primary dyslipidemia, hypertension, diabetes or glucose intolerance, secondary obesity, and were not receiving pharmacological treatment.

Study Protocol

The children were randomly assigned to one of the two interventions (Figure 1): an individual conventional treatment (IT) and a group-based treatment (GT). Since GT implies more visits to the Department and due to staff and space limitations, GT was assigned with probability 1/3 and IT with probability 2/3. The main objective of both interventions was to promote lifestyle changes in obese children and their families, and consequently to stop weight gain and even promoting weight loss. At baseline, anthropometric and biochemical measurements were carried out in all children. Follow-up visits were held at 3-months, 6-months and 1-year after the first visit. In IT, a healthy eating plan meeting nutrient needs according to the recommended daily allowance (~1800 kcal) was prescribed and explained to children and their parents. Additionally, physical activity was encouraged and sedentary behaviours, such as TV watching and computer/video game playing, were discouraged. In GT, children and their parents participated in group-based nutrition education sessions. These

consisted of 4 sessions, each of 60 minutes duration, distributed over the first study semester, conducted by a nutritionist. The children and their parents participated in all sessions. These sessions covered several topics regarding childhood obesity and comorbidities, healthy eating habits, healthy cooking methods, portion size control, food labelling and physical activity promotion. The acquired knowledge was reinforced in each session and whenever necessary at follow-up visits. Forty-two children at the IT and 19 at the GT completed the 1-year follow-up visit.

Anthropometric Measures

Weight, height and waist circumference were measured according to standardized procedures [46]. Weight was measured to the nearest 0.1 kg using an electronic column scale (SECA-780); height was measured to the nearest 0.1 cm using a stadiometer (SECA-220); waist circumference (WC) was measured to the nearest 0.1 cm at the mid-point between the iliac crest and the lower edge of the ribs at the end of a normal expiration. BMI was calculated with measured height and weight and was standardised (zBMI) by using age- and gender-normative data from the CDC [3, 21]. In this paper, the term overweight includes the obese children. Abdominal obesity was defined using the sex and age-specific 90th waist circumference percentile by McCarthy *et al* [24]. All measurements were repeated at each visit. Birth weight and length were obtained from the children's health booklet.

Clinical and Biochemical Measures

A physical examination was performed searching for abnormalities, such as acanthosis nigricans. Puberty status was assessed according to Tanner stages [36]. Blood pressure (BP) was measured on the right arm with the patient seated, after rest, using a digital sphygmomanometer (OMRON M6) and appropriate sized cuff. After three measurements, the lowest value was recorded. Children were classified according to sex, height and age-specific charts [27]. Baseline blood samples were collected in the morning (8:00 to 9:00) after an overnight fast (10 to 12 hours) by venipuncture, after a local application of a topical anaesthetic patch (EMLA). Plasma and serum were separated by centrifugation. The glucose oxidase method (Siemens Healthcare Diagnostics Inc., Newark, DE, USA) was used to determine blood glucose levels. Serum lipids levels were measured by enzymatic colorimetric methods (Siemens Healthcare Diagnostics Inc.). Apolipoprotein A-I and Apolipoprotein B were measured by an immuno-turbidimetric assay (Olympus America Inc., Center Valley, PA, USA). C-reactive protein (CRP) was determined using a turbidimetric immunoassay (Siemens Healthcare

Diagnostics Inc.). Plasma and serum were frozen until further analysis of insulin, C-peptide, leptin, adiponectin and ghrelin at an external laboratory (ENDOCLAB, Porto). Insulin and C-peptide were measured by luminescence immunometric assay and homocysteine by luminescence immuno-competitive assay (Siemens Healthcare Diagnostics Inc.). Insulin resistance was determined by the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) calculated as the product of the fasting plasma insulin level ($\mu\text{UI/ml}$) and the fasting plasma glucose level (mmol/l), divided by 22.5 [23]. Leptin, adiponectin and ghrelin were quantified by RIA (Linco Research Inc., St. Charles, MO, USA). Outcome measures were obtained at follow-up visits at 6-months and 1-year.

Physical activity

The children were asked about the time spent at school, watching TV, playing computer/video games and sleeping. The frequency and duration of physical activities performed at school and/or extracurricular were quantified.

Definition of MS

MS was defined according to the National Cholesterol Education Program Adult Treatment Panel III criteria modified by Cook [4], with adjustment for fasting glucose according to the recent American Diabetes Association definition for impaired fasting glucose [37]. This definition was chosen since it is based in age- and gender-specific cut-offs and it has been used in other paediatric studies [30]. MS was considered if three or more of the following criteria were present: 1) abdominal obesity ($\text{WC} \geq 90^{\text{th}}$ percentile for age and sex) [24]; 2) fasting triglycerides $\geq 110 \text{ mg/dl}$; 3) $\text{HDL} \leq 40 \text{ mg/dl}$; 4) systolic/diastolic BP $\geq 90^{\text{th}}$ percentile for age, sex and height [27]; 5) fasting glucose $\geq 100 \text{ mg/dl}$ [37].

Statistical Analysis

Descriptive statistics (median and range (min;max), and frequencies) were executed. Pearson and Spearman correlation coefficients were used. Partial correlation was computed to evaluate the degree of association between variables, controlling for gender, age and Tanner stage. To study the independence between nominal categorical variables Chi-square test was used. To evaluate the differences between two-groups, independent samples t test and Mann-Whitney test were performed, respectively, in continuous variables with normal distribution and without normal distribution.

Bonferroni correction was applied when multiple comparisons were performed. General Linear Model (GLM) for repeated measures was used to compare the evolution of each of the variables, and time (baseline, 6-m and 1-y follow up), treatment assignment (IT and GT) and treatment X time interaction were included as fixed effects, controlling for gender and Tanner stage. Logistic regression analysis was used to evaluate the difference in the prevalence of MS, considering the confounding effects of gender and Tanner stage. A reduced model was obtained by backward stepwise applying the likelihood test to eliminate independent variables at baseline. The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. We considered a significance level of 0.05. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS version 14.0, 2005).

For the purpose of sample size estimation, the primary outcome was a decrease in zBMI between baseline and 1-year follow-up. According to our previous experience, a standard deviation of zBMI near 0.35 and a dropout rate under 30% was estimated. From our baseline sample, the number of participants in the smaller treatment group (GT) was estimated to decrease from 25 to 18. From these assumptions, a power analysis was conducted using a sample size for each group of 18, obtaining an estimated power of 0.81 for a paired samples t-test.

RESULTS

Baseline Characteristics

The children that dropped out the study (n=22) were excluded from the analysis. There were no baseline significant differences between dropouts and those who finished the study. The anthropometric and metabolic characteristics of the 61 overweight (51 obese; 10 overweight) and 22 control children are shown in Table 1. Normal-weight children were all prepubertal, while 18 overweight children were at Tanner stage II. Overweight prepubertal children were significantly younger than those at Tanner II and presented higher ghrelin levels. Normal-weight subjects presented significantly lower blood pressure (BP), insulin, HOMA-IR, triglycerides (TG), Apolipoprotein B, leptin, C-reactive protein (CRP) and homocysteine levels when compared to overweight prepubertal ones, while Apolipoprotein A-I was significantly higher. Adiponectin levels were higher in overweight children compared to control, without statistical significance. Obese children ($\geq 95^{\text{th}}$ BMI) compared to overweight ones (85-95th BMI) showed lower HDL [1.22 (0.72;2.04) vs. 1.43 (1.19;1.73) mmol/L; p=0.046] and Apolipoprotein A-I [1.20 (0.9;1.64) vs. 1.32 (1.12;1.46) g/L; p=0.048] levels and higher

leptin [11.3 (2.3;40.2) vs. 6.3 (1.4;13.9) ng/mL; $p=0.009$]. There were no statistical differences between genders, except for CRP in overweight children. Gestational data (weight, length and weeks of gestation) were similar between groups (data not shown).

Ten overweight children presented MS, without significant dependence between genders ($p=0.321$) and Tanner stages ($p=0.256$). The number of components of MS was higher in children with higher zBMI ($p=0.418$, $p<0.001$). Indeed, overweight children with MS, by comparison with those without MS, presented higher systolic BP [119.5 (106.0;133.0) vs 114.0 (97.0;128.0) mmHg; $p=0.023$], TG [1.50 (0.67;3.75) vs 0.67 (0.36;1.14) mmol/L; $p<0.001$] and Apolipoprotein B levels [0.89 (0.61;1.16) vs 0.76 (0.42;1.15) g/L; $p=0.033$], while HDL [0.97 (0.72;1.50) vs 1.29 (0.90;2.04) mmol/L; $p<0.001$] and Apolipoprotein A-I [1.08 (0.90;1.34) vs 1.22 (0.94;1.64) g/L; $p=0.011$] concentrations were lower. Insulin, HOMA-IR and leptin were higher in MS, without statistical significance. Normal-weight children did not present MS.

Insulin resistance (HOMA-IR >2.5) was found in 13 overweight subjects and acanthosis in 32. Higher leptin levels [14.2 (10.6;24.7) vs. 9.9 (1.4;40.2) ng/mL; $p=0.014$] were associated with IR. Adiponectin was also lower in children with IR, but without significance [20.9 (11.1;39.9) vs. 25.4 (3.1;61.5) μ g/mL; ns].

Overweight children spent more hours watching TV [1.5 (0.2;4.5) vs. 1.0 (0.5;1.5) hours/day; $p<0.001$] and less time in extracurricular activity [8.6 (0.0;55.7) vs. 12.9 (0.0;90.0) min/day; ns] than normalweight ones. Time spent at extracurricular exercise was negatively correlated with leptin levels ($R=-0.294$; $p=0.021$).

MS related components, insulin, adipokines and ghrelin levels

At baseline, insulin levels were correlated positively with anthropometric variables and with TG levels (Table 2). Leptin showed a strong correlation with anthropometric variables and with those associated to glucose metabolism. By the contrary, ghrelin levels were negatively correlated with BMI, HOMA-IR and insulin. At baseline, adiponectin did not show any significant correlation with the above parameters, except for C-peptide ($R=-0.267$; $p=0.037$). When adjusted for gender and Tanner, ghrelin levels presented a correlation with systolic BP ($R=0.309$; $p=0.017$), while the other hormones maintained the previous associations. At 1-y, adiponectin presented a weak significant correlation with zBMI ($R=-0.283$; $p=0.026$).

To determine the relationship between the prevalence of MS and selected variables at baseline (age, zBMI, apolipoprotein A-I, apolipoprotein B, glucose, insulin, C-peptide, leptin, adiponectin and ghrelin), a logistic regression analysis was conducted. The final model showed that a higher prevalence of MS was predicted from children at Tanner stage I ($p=0.043$), with lower Apolipoprotein A-I levels ($p=0.007$) and with higher insulin ($p=0.045$) and leptin ($p=0.092$) concentrations (Table 4).

Anthropometric and Metabolic Health Outcomes

A similar drop-out rate was found in both interventions, 27.6% ($n=16$) in IT and 24.0% ($n=6$) in GT. The main reason referred to drop-out of the study was the lack of time due to school/work schedules. Eleven of the 43 prepubertal children at baseline were in Tanner stage II at 1-y. At baseline, no statistical differences were found between the IT and GT subjects with respect to anthropometric and metabolic variables (Table 3). At follow-up, both groups showed a significant decrease in zBMI (-0.18 and -0.25 in IT and GT, respectively) and in WC/height ratio. This difference was more pronounced in GT subjects ($p=0.042$ for zBMI and WC/height ratio). Diastolic BP improved ($p=0.047$) at 1-y in both groups. Insulin concentrations did not change significantly over time, however it behaved differently according to gender [girls: 48.6 (20.8;138.9) at baseline vs. 55.6 (20.8;250.0) pmol/L at 1-y; boys: 55.6 (13.9;187.5) at baseline vs 48.6 (13.9;152.8) pmol/L at 1-y; $p=0.013$]. HOMA-IR levels followed the behaviour of insulin. Along the study, we observed an improvement of HDL ($p=0.019$), higher in the GT subjects ($p=0.042$), and of TG ($P=0.009$). We have not verified any significant change in adipokines concentration, however a trend to lower leptin and higher adiponectin levels was shown in GT children. At 1-y, ghrelin increased significantly in GT children, while decreased in IT.

Over time, 5 of the initial 10 overweight children with MS no longer presented it, while 4 children were newly diagnosed at 1-y. In children with MS, insulin [48.6 (13.9;250.0) vs. 69.4 (48.6;201.4) pmol/L; $p=0.005$], HOMA-IR [1.3 (0.3;7.6) vs. 1.9 (1.2;5.1), $p=0.009$] and leptin [16.4 (5.4;32.3) vs. 8.3 (1.6;35.5) ng/mL; $p=0.021$] were significantly higher at 1-y, compared to children without MS. At the end of study, IR was present in 10 overweight children, while 19 presented acanthosis ($p<0.001$). Over time, ghrelin levels were lower in children with IR [578.5 (510.9;721.4) vs. 1062.9 (369.4;3627.9) pg/mL; $p=0.021$], as well as adiponectin, while leptin levels were higher, however both without statistical significance.

Time spent in extra-curricular activities did not improve significantly [8.6 (0.0;55.7) min/day at baseline vs. 12.9 (0.0;55.7) min/day at 1-y].

DISCUSSION

Childhood obesity is frequently associated with cardiovascular and metabolic disturbances [32]. To our knowledge, this is the first study assessing the impact of an outpatient lifestyle intervention on MS, adipokines and ghrelin levels in overweight Portuguese children aged 7-9 years. Parameters associated with MS have been shown to originate early in life [43], and tend to track into adulthood [16]. Therefore, it is important to understand the pathways leading to MS and how to prevent and treat it.

As described by others [16, 33, 41], our overweight children presented several cardiometabolic risk factors, namely dyslipidemia, higher blood pressure, CRP, homocysteine and insulin levels, and IR.

Leptin is an adipocyte-derived hormone, synthesized proportionately to fat mass. It is an important regulator of food intake and energy expenditure and also modulates insulin secretion and action [42]. Indeed, an independent association between IR and leptin, beginning in childhood, may become stronger with aging and chronic obesity [34]. We confirmed a significantly higher leptin concentration in overweight children, which correlated to waist circumference, insulin levels and HOMA-IR. It is recognized that a gender difference exists in leptin levels, with two- to threefold higher levels in women than men [42]. We also observed this difference, however it only became significant at 1-y. This may be associated with the initiation of puberty, which is related to an increase in body fat mass in girls in contrast to an increase in lean mass in boys [34, 42].

Adiponectin is a protein secreted exclusively by adipocytes, with insulin-sensitizing, anti-atherogenic and anti-inflammatory effects [45] that presents an inverse correlation with obesity [22]. Hypoadiponectinemia has been described as a possible marker for MS, IR and high cardiovascular risk in adults as in children [11, 22]. The mean adiponectin concentration measured by RIA in our children seems to be higher than those generally found in children and adolescents in previous reports [11, 38, 48]. This may be related to a genetic trait of our population. Unexpectedly, we found a trend to lower adiponectin concentration in normal-weight children. Differences in methodologies and blood collection procedures may account for the different results, although standardized procedures were used and measurements were executed in an accredited laboratory. Possible causes of the higher adiponectin levels observed can only be speculated. The assay used determines the total adiponectin concentration, whereas this circulates in distinct forms [45, 47]. High molecular weight (HMW) adiponectin has been described as the “active” form of this protein [45], and HMW or the ratio

HMW/total adiponectin and not total adiponectin *per se*, are associated with favourable metabolic effects [22, 47]. Besides, under pathophysiological conditions, such as obesity and diabetes, only HMW appears to be decreased [47]. Although non significant, we observed that insulin-resistant overweight subjects had the lowest adiponectin concentration, even compared to normal-weight, as expected. We might say that in a *milieu* of IR, both total adiponectin and HMW levels are decreased. This is in accordance with studies that argue that adiponectin is more associated with IR than with adiposity [15]. In several populations, functional single nucleotide polymorphisms and missense mutations have been identified in the adiponectin gene – *ADIPOQ* – which contribute to modulation of adiponectin levels and function [39].

A decrease in ghrelin levels with obesity, age and puberty has been recognized [44]. In relation to Tanner we confirmed this statement, however IT and GT children behaved differently over time regardless of zBMI decrease in both. We also observed a negative correlation between ghrelin, insulin and HOMA-IR. We may argue that the downregulation of ghrelin secretion may be a result of IR associated with excess weight. Indeed, it is reported that ghrelin is involved in the regulation of insulin secretion and is independently related to IR [1]. When adjusted for gender, ghrelin was inversely associated to systolic BP. It has been proposed that ghrelin has a beneficial effect on vasculature, since intravenous ghrelin injections decrease mean arterial BP and cardiac afterload in adults [26]. Thus, low ghrelin levels in obese children may promote the development of CVD.

Our overweight children presented a high prevalence of MS. The reason why some obese children developed this syndrome, while others do not is still unknown [9]. By logistic regression analysis, we observed that for each unit increase in apolipoprotein A-I, the *odds* of MS decreases by a factor of 0.9. This protein has antiatherogenic properties, stimulates glucose utilization and improves IR in peripheral tissues [14]. Insulin and leptin concentrations, and pre-puberty also predicted positively the MS. In the Young Finns Study [29], baseline insulin was higher in children who subsequently developed MS. IR is an important pathophysiologic event contributing to MS, becoming even more important than overall adiposity in the development of this syndrome [5]. In disagreement to what is described [11], we did not found any association between adiponectin levels and MS.

Both IT and GT reduced the degree of obesity and, in general, all other anthropometric and metabolic parameters slightly improved after 1-y. Since our study was population-based, the degree of obesity was not severe (zBMI: 1.93 ± 0.28), which also accounts for the minor changes observed. zBMI and WC/height showed a more pronounced decrease in children enrolled in the GT. Over time, an

improvement in lipid profile was also observed. Thus, a reduction in the degree of obesity in children can lead to an improvement in CVD risks factors [31]. Insulin and HOMA-IR did not change significantly, although it showed a trend to decrease in the GT. Overall, the number of children with IR decreased at 1-y. Leptin concentration did not improve significantly, mainly in the IT group. In a recent review, it is reported that 1% of weight reduction is sufficient to reach significant decrease in leptin levels [19]. Considering the global reduction obtained in zBMI at 1-y, we can argue that hormonal changes due to puberty, as insulin and IR, may have influenced the leptin levels. We verified a negative correlation between leptin and the time spent in extra-curricular exercise. Many of the intervention studies which include exercise have shown an improvement in metabolic outcomes [17, 25, 31]. However, although our interventions encouraged the increment in daily physical activity, the time devoted to these activities remained nearly constant at 1-y in the overweight children.

Bobbert et al [2] showed that the effect of moderate weight loss resulted in a relative increase of HMW adiponectin and a reduction on LMW. Altogether, several studies suggest that adiponectin levels are not as sensitive as leptin to the effect of dietary interventions [2]. Indeed, we could not confirm the effect of weight loss on adiponectin, as with ghrelin since its levels increased in GT while decreased in IT children over time. Other studies showed a rise in ghrelin concentration in response to weight loss [18], however this increase during weight reduction is considered to be responsible for compensatory mechanisms that make reduction of overweight difficult to be sustained [7].

MS phenotype tends to persist and worsen over time if no preventive actions are taken [43]. In our sample, the lifestyle intervention was associated with a small decrease of MS after 1-y. Among those children who never developed MS (n=47) or no longer presented it after 1-y (n=5), most of them improved their zBMI. In some studies more significant results are obtained, however they are accomplished with a marked dietary restriction (1000-1200 kcal) [31, 35].

Besides small differences between the outcome measures in both interventions, the GT seems to be more successful, with a more marked decrease in zBMI, insulin, HOMA-IR, leptin and an increase in HDL, adiponectin and ghrelin. Actually, a family-based group treatment was described by others as more effective than individual treatment in the management of childhood obesity at long-term [10, 17]. One advantage of family interventions is that they address both children and their parents.

Our study presents some limitations. First, the final sample size, despite an acceptable drop-out rate. Second, most children presented normal values for most metabolic parameters, which may have contributed to decrease the statistical power for detecting significant differences over time. Third, both

groups were subjected to an intervention, not allowing us to compare the outcomes with overweight children not enrolled in any treatment. Fourth, at 1-y almost half of the children entered puberty, which is associated with several hormonal changes.

In conclusion, our results showed a significant prevalence of MS in Portuguese overweight children. MS was predicted by apolipoprotein A-I, insulin levels and pre-puberty. Leptin and ghrelin were associated with components of MS and IR, however we did not find any relation between these conditions and adiponectin levels. We showed a higher adiponectin concentration in overweight children than in normal-weight. We attributed this unexpected finding to genetic factors. It would be interesting, in the future, to investigate the distribution of adiponectin isoforms, as well to confirm the presence of polymorphisms in our population. Both treatment interventions led to weight loss and a moderate improvement of cardiometabolic parameters and adipokines, more effective in the GT. The modest magnitude of the benefits observed argues for a longer-term and perhaps more intensive intervention.

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Table 1 Anthropometric and metabolic characteristics of overweight and control children at baseline

	Overweight (n = 61)			p ^a	Control (n = 22)	p ^b
	Tanner I (n = 43)	Tanner II (n = 18)				
Gender (Male / Female)	21 / 22	6 / 12		1.000 ^c	13 / 9	1.000 ^c
Metabolic Syndrome	9	1		n.a.	0	n.a.
Age (y)	8.4 (7.3;9.9)	9.3 (8.1;10.1)		<0.001 ^d	8.4 (7.1;9.4)	1.000 ^d
Weight (kg)	40.9 (31.1;52.1)	44.2 (35.7;65.9)		0.003 ^d	26.9 (20.9;31.8)	<0.001 ^d
Height (cm)	134.1 (124.6;145.3)	137.5 (126.6;151.0)		0.003 ^d	131.2 (116.5;139.1)	0.045 ^d
BMI (kg/m ²)	22.4 (19.7;28.1)	22.6 (20.9;31.2)		0.312 ^d	15.9 (13.8;18.4)	<0.001 ^d
Z-score BMI	1.94 (1.31;2.61)	1.88 (1.54;2.40)		1.000 ^d	-0.04 (-1.62;0.94)	<0.001 ^d
WC (cm)	71.0 (61.0;84.5)	72.8 (65.5;95.0)		0.297 ^d	55.1 (50.1;65.8)	<0.001 ^d
Systolic BP (mmHg)	118.0 (97.0;133.0)	111.5 (103.0;133.0)		0.951 ^d	104.0 (85.0;119.0)	<0.001 ^d
Diastolic BP (mmHg)	61.0 (42.0;100.0)	62.5 (52.0;77.0)		1.000 ^d	52.0 (42.0;68.0)	<0.001 ^d
Glucose (mmol/L)	4.44 (3.72;5.49)	4.58 (4.11;5.16)		1.000 ^d	4.47 (3.83;5.11)	1.000 ^d
Insulin (pmol/L)	48.6 (13.9;187.5)	55.6 (27.8;138.9)		0.833 ^e	20.8 (13.9;41.7)	<0.001 ^e
HOMA-IR	1.40 (0.40;5.40)	1.65 (0.70;4.50)		0.668 ^e	0.60 (0.30;1.30)	<0.001 ^e
HDL (mmol/L)	1.29 (0.72;2.04)	1.24 (0.90;1.73)		1.000 ^d	1.45 (1.01;2.09)	0.151 ^d

Triglycerides (mmol/L)	0.73 (0.36;3.75)	0.75 (0.38;1.86)	1.000 ^e	0.52 (0.25;1.34)	0.011 ^e
Apolipoprotein A-I (g/L)	1.22 (0.90;1.59)	1.18 (0.94;1.64)	1.000 ^d	1.37 (1.31;1.57)	0.046 ^d
Apolipoprotein B (g/L)	0.79 (0.5;1.16)	0.74 (0.42;0.96)	0.114 ^d	0.59 (0.43;0.89)	0.010 ^d
Leptin (ng/mL)	10.6 (1.4;24.7)	10.5 (2.5;40.2)	1.000 ^d	3.3 (0.7;10.2)	<0.001 ^d
Adiponectin (µg/mL)	25.7 (3.1;61.5)	23.0 (7.6;42.9)	1.000 ^d	15.7 (7.4;55.2)	0.190 ^d
Ghrelin (pg/mL)	1141.0 (497.4;3329.0)	857.9 (387.6;1404.2)	0.007 ^e	968.8 (673.6;1736.0)	0.372 ^e
CRP (mg/L)	0.16 (0.04;3.99)	0.20 (0.03;5.41)	0.502 ^e	0.12 (0.02;0.19)	0.030 ^e
Homocys (µmol/L)	5.3 (3.6;8.9)	6.2 (4.1;8.3)	0.235 ^d	4.3 (3.1;6.5)	<0.001 ^d

Data presented as n for gender and MS, and as median and range (min;max) for other variables. WC: waist circumference; BP: blood pressure; HOMA-IR: Homeostasis model assessment of insulin resistance; HDL: high density lipoprotein; CRP: C-reactive protein; Homocys: homocysteine. To convert glucose from mmol/L to mg/dL divide by 0.05551; insulin from pmol/L to µU/mL divide by 6.945; HDL from mmol/L to mg/dL divide by 0.02586; TG from mmol/L to mg/dL divide by 0.01129; Apolipoproteins A-I and B from g/L to mg/dL divide by 0.01.

^a: Significance level for the differences between overweight children at Tanner stage I and Tanner stage II; ^b: Significance level for the differences between overweight children at Tanner stage I and control children; n.a.: non applicable (due to small sample of children with MS)

Statistic tests with Bonferroni correction for multiple comparisons between groups: ^c Chi-square test; ^d t-Student; ^e Mann-Whitney.

Table 2 Correlations between insulin, adipokines (leptin, adiponectin) and ghrelin levels with variables related to metabolic syndrome and insulin resistance in overweight children, at baseline

	Insulin ^a	Leptin ^b	Adiponectin ^b	Ghrelin ^a
BMI	0.418***	0.602***	-0.027	-0.301*
Z-score BMI	0.347***	0.543***	0.025	-0.132
Waist circumference	0.461**	0.541***	-0.130	-0.214
Systolic BP	0.170	0.030	0.020	-0.105
Diastolic BP	0.072	-0.098	-0.137	-0.122
HDL	-0.163	-0.056	0.058	-0.032
TG	0.426***	0.260*	-0.115	-0.184
HOMA-IR	0.976***	0.425***	-0.064	-0.284*
Insulin	-	0.587^{a***}	0.009 ^a	-0.256*

Statistic tests: ^a Spearman's rho correlation; ^b Pearson correlation. *p<0.05; **p<0.005; ***p<0.001.

BP: Blood pressure; HOMA-IR: Homeostasis model assessment of insulin resistance; HDL: High density lipoprotein; TG: Triglycerides.

Table 3 Baseline and follow-up anthropometric, clinical and biochemical characteristics according to treatment assignment

	(n = 61)	Treat. type	Baseline	Follow-up 6-months	Follow-up 1-year	p*		
						t	T†t	T
zBMI		IT	1.98 (1.31;2.61)	1.84 (1.18;2.44)	1.76 (1.18;2.46)	<0.001	0.582	0.042
		GT	1.87 (1.54;2.37)	1.82 (0.94;2.36)	1.57 (1.01;2.27)			
WC (cm)		IT	72.8 (63.2;95.0)	73.3 (59.5;95.8)	74.4 (60.0;100.0)	0.081	0.803	0.079
		GT	71.2 (61.0;81.2)	71.0 (57.3;82.2)	73.2 (59.8;81.4)			
WCheight		IT	0.54 (0.47;0.65)	0.52 (0.46;0.65)	0.53 (0.46;0.66)	<0.001	0.760	0.042
		GT	0.53 (0.47;0.59)	0.52 (0.43;0.57)	0.51 (0.44;0.57)			
SBP (mmHg)		IT	115.5 (97.0;133.0)	1168.0 (99.0;140.0)	115.5 (93.0;130.0)	0.403	0.493	0.668
		GT	116.0 (101.0;128.0)	113.0 (81.0;125.0)	114.0 (92.0;130.0)			
DBP (mmHg)		IT	61.5 (42.0;88.0)	60.0 (46.0;78.0)	61.0 (43.0;75.0)	0.047	0.382	0.687
		GT	61.0 (52.0;100.0)	59.0 (45.0;68.0)	61.0 (51.0;74.0)			
Insulin (pmol/L)		IT	55.6 (13.9;187.5)	55.6 (13.9;243.1)	55.6 (13.9;250.0)	0.381	0.223	0.079
		GT	48.6 (34.7;90.3)	48.6 (20.8;138.9)	41.7 (20.8;83.3)			
HOMA-IR		IT	1.5 (0.4;5.4)	1.5 (0.4;7.4)	1.5 (0.3;7.6)	0.270	0.367	0.098

	GT	1.5 (0.9;2.5)	1.3 (0.5;4.3)	1.3 (0.5;3.1)		
	IT	1.22 (0.72;2.04)	1.25 (0.85;1.78)	1.27 (0.85;1.89)		
HDL (mmol/L)	GT	1.34 (0.80; 1.73)	1.24 (0.96;1.78)	1.50 (1.03;1.86)	0.019	0.235 0.042
	IT	0.74 (0.36;3.75)	0.79 (0.32;1.59)	0.76 (0.37;1.93)		
TG (mmol/L)	GT	0.76 (0.38;2.64)	0.67 (0.38;2.64)	0.72 (0.35;2.29)	0.009	0.482 0.158
	IT	10.9 (1.4;40.2)	8.0 (3.3;25.0)	8.9 (1.6;35.5)		
Leptin (ng/mL)	GT	10.4 (2.5;19.3)	9.2 (3.6;22.6)	8.6 (3.8;18.0)	0.199	0.341 0.148
	IT	26.0 (3.1;61.5)	19.8 (4.4;57.6)	19.1 (3.0;65.5)		
Adiponectin (µg/mL)	GT	24.6 (6.4;41.1)	20.0 (6.7;53.1)	27.9 (3.3;49.4)	0.505	0.114 0.602
	IT	1060.6 (387.6;3329.0)	984.4 (211.8;2686.3)	889.6 (369.4;3627.9)		
Ghrelin (pg/mL)	GT	1162.7 (511.5;1606.9)	963.6 (611.5;2317.9)	1373.6 (623.1;2355.0)	0.030	0.039 0.702

Data presented as median and range (min,max). Treat. = Treatment; IT: individual treatment (n=42); GT: group-based treatment (n=19); WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL: high density lipoprotein; TG: triglycerides. To convert insulin from pmol/L to µU/mL divide by 6.945; HDL from mmol/L to mg/dL divide by 0.02586; TG from mmol/L to mg/dL divide by 0.01129.

^a GLM repeated measures: *t* = time effect; *T* = treatment effect; *Tt* = treatment and time interaction.

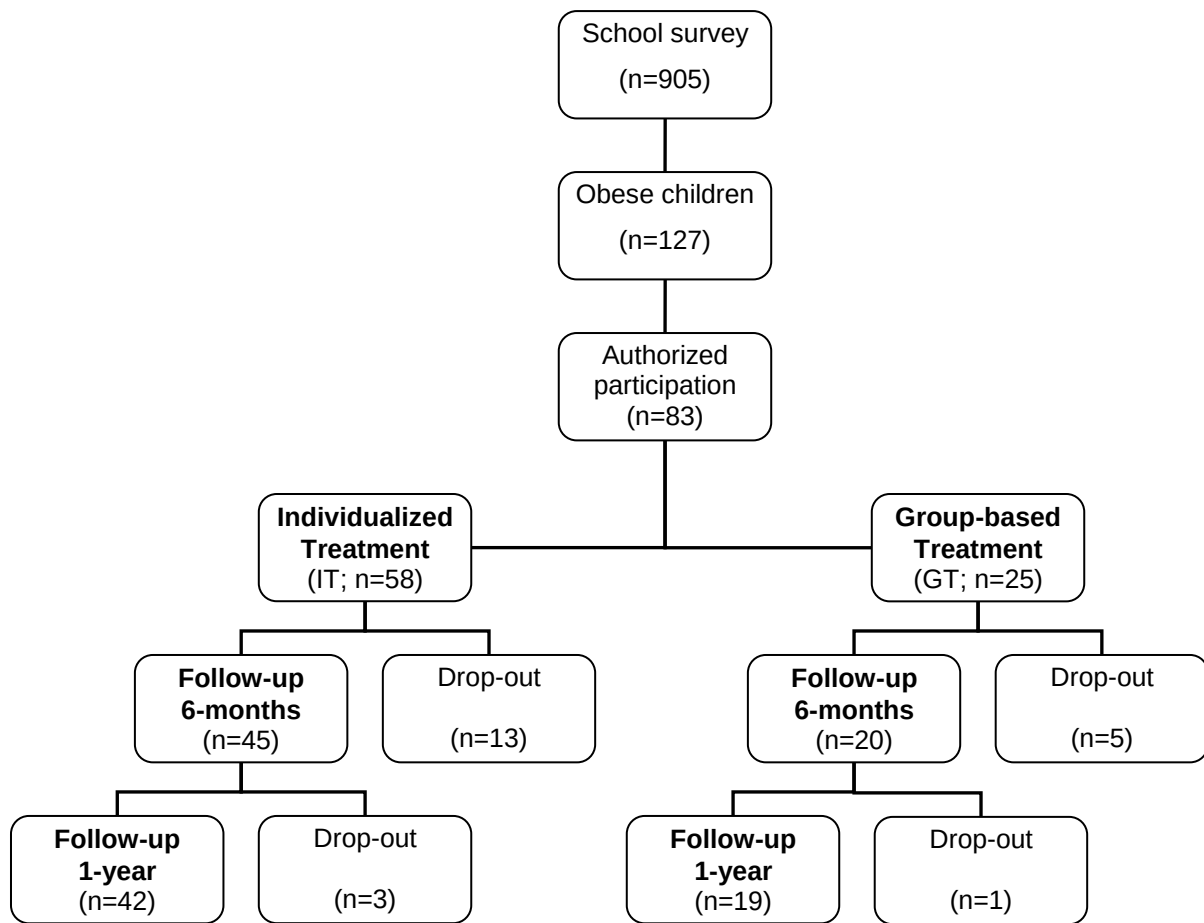
Table 4 Logistic regression showing the association between Metabolic Syndrome and several independent variables, at baseline

	OR (95% CI)	<i>p</i>
Tanner stage	0.029 (0.001-0.901)	0.043
	B ± SE	<i>p</i>
Apolipoprotein A-I	-0.117 ± 0.043	0.007
Insulin	0.180 ± 0.090	0.045
Leptin	0.138 ± 0.082	0.092

OR: Odds ratio; CI: Confidence intervals; B: Logistic regression coefficient; SE: Standard error.

Variables entered: gender, Tanner, age, zBMI, Apolipoprotein A-I, Apolipoprotein B, glucose, insulin, C-peptide, leptin, adiponectin and ghrelin.

Figure 1 Study design of the outpatient lifestyle intervention program



ARTIGO 5

DIET, PHYSICAL ACTIVITY AND METABOLIC SYNDROME IN OVERWEIGHT SCHOOLCHILDREN PARTICIPATING IN A LIFESTYLE INTERVENTION PROGRAM

Submetido para publicação

**DIET, PHYSICAL ACTIVITY AND METABOLIC SYNDROME IN OVERWEIGHT
SCHOOLCHILDREN PARTICIPATING IN A LIFESTYLE
INTERVENTION PROGRAM**

Running title: Lifestyle intervention program in overweight children

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ABSTRACT

Objective: To evaluate the dietary intake in overweight schoolchildren enrolled in a lifestyle intervention program and to estimate the association between diet, physical activity and metabolic syndrome (MS) components.

Methods: A total of 83 overweight children (7-9 years-old) were assigned to a 1-year individual (IT) or group-based treatment (GT), and 61 children (27 boys; 34 girls) completed the program. Anthropometric and biochemical parameters were assessed at baseline, at 6-months and at 1-year. Dietary intake was assessed by 3-day food records and 24-hour recalls. A physical activity questionnaire was applied. MS was defined by the NCEP/ATPIII criteria modified by Cook.

Results: At baseline, MS prevalence was 16.4%. Children consumed on average 46.6% of energy from carbohydrates, of which 19.4% from sugars; 31.8% from fat, of which 12.6% from saturated fatty acids (SFA); and 21.1% from proteins. MS-children presented a significantly higher energy, total carbohydrates and total sugars intake, while percentage of energy as SFA and extra-curricular exercise were lower. By logistic regression analysis, total fat intake was a positive predictor of MS ($p=0.031$). SFA ($p=0.025$), sleeping hours ($p=0.033$) and extra-curricular exercise ($p=0.031$) were negative predictors. Dietary intake and physical activity did not change significantly over time. A significant improvement of zBMI ($p<0.001$) was observed, more pronounced in GT subjects (-0.18 and -0.25 in IT and GT, respectively). MS prevalence decreased to 14.8%.

Conclusions: Dietary components and physical activity are associated with MS. Both treatments led to an improvement in the degree of obesity and MS components, however without significant changes in dietary intake.

Keywords: children, dietary intake, obesity, Metabolic Syndrome, lifestyle intervention.

INTRODUCTION

Worldwide, the prevalence of childhood obesity has been increasing at a dramatic rate (1). In Europe, 31.8% of schoolchildren were estimated to be overweight, including 7.9% estimated to be obese (2,3). In Portugal, the prevalence of excess weight in 7-9 year-old children is 31.5% (4), similar to what we found (28%) in a previous local study in Aveiro (5).

Obesity is a multifactorial condition that results of an imbalance between energy intake and expenditure. Indeed, environmental factors, particularly the ones related to sedentary lifestyles and consumption of energy-dense foods, play a major role in the aetiology of obesity (6,7). This disease is associated to an increased risk of other chronic diseases, including dyslipidemia, diabetes and cardiovascular diseases (7). Metabolic syndrome (MS), a clustering of symptoms as obesity, hyperinsulinemia, glucose intolerance, hypertension, high plasma levels of triglycerides (TG) and decreased levels of high density lipoprotein (HDL) cholesterol, is rapidly increasing in prevalence with rising in childhood obesity (8). Approximately one-third of overweight children and one half of overweight adolescents remain obese as adults, and the cardiometabolic risk factors tend to track into adulthood (9, 10). Therefore, there is a need for effective intervention strategies to control childhood obesity and its consequences. These include a better understanding of eating and physical activity patterns of obese children. However, to date, longitudinal studies in children have not found clear causal associations between energy intake or diet composition and overweight development (11, 12). Indeed, eating is a complex exposure variable, composed of several behaviours that act in combination and even synergistically. These complex links may explain why straightforward associations between dietary habits and measures of overweight are not always identified (13). Besides, diet studies in children are difficult since dietary assessment techniques are time consuming and methodologically limited and usually rely on a child or parent's recall of food intake (14).

The aims of our study were to evaluate food intake in overweight Portuguese schoolchildren enrolled in a 1-year outpatient lifestyle intervention program and to estimate the association between diet and MS components.

METHODS

Study Population

From a previous population-based study (5) involving 905 schoolchildren between 7-9 year-old, we identified 125 children as obese ($\geq 95^{\text{th}}$ BMI percentile) according to the US Centers for Disease Control and Prevention (CDC) (15) and invited them to participate in the study. Eighty-three accepted the invitation and 61 (27 boys, 34 girls) concluded the 1-year study protocol. Between the assessment at school and the first visit, 10 children initially classified as obese became overweight (90-95th BMI percentile). These were also included in the study. None of the children had diagnosed primary dyslipidemia, hypertension, diabetes or glucose intolerance, secondary obesity, or were receiving pharmacological treatment.

Each parent gave written informed consent and children agreed to participate. Assessments were done at the Department of Endocrinology, Diabetes and Nutrition of the Hospital Infante D. Pedro. The study was approved by the Hospital Ethics Committee.

Study Protocol

The children were randomly assigned to one of the two interventions: an individual conventional treatment (IT) or a group-based treatment (GT). Since GT implied more visits to the Department and due to staff and space limitations, GT was assigned with probability 1/3 and IT with probability 2/3. The main objective of both interventions was to promote lifestyle changes in obese children and their families, and consequently to stop weight gain. In IT, a healthy eating plan meeting nutrient needs according to recommendations was prescribed and explained to children and their parents. It included a reduction of refined carbohydrates, sweetened beverages and saturated fats, and an increase in vegetables and fruits consumption. Additionally, physical activity was encouraged and sedentary behaviours were discouraged. In GT, children and their parents participated in a group-based (4 children per group) nutrition education program, which consisted of 4 consecutive sessions conducted by a nutritionist, each of 60 minutes duration. These sessions covered several topics regarding childhood obesity and comorbidities, healthy eating habits, healthy cooking methods, portion size control, food labelling and physical activity promotion. The acquired knowledge was reinforced at each session and whenever necessary at follow-up visits. Both in IT and GT, follow-up visits were held at

3-months, 6-months and 1-year after the first visit. Forty-two children at the IT intervention and 19 at the GT completed the 1-year follow-up visit.

Anthropometric Measures

Weight, height and waist circumference were measured according to standardized procedures (16). Weight was measured to the nearest 0.1 kg using an electronic column scale (SECA-780); height was measured to the nearest 0.1 cm using a stadiometer (SECA-220); waist circumference (WC) was measured at the mid-point between the iliac crest and the lower edge of the ribs at the end of a normal expiration. BMI was calculated with measured height and weight and was standardised (zBMI) by using age- and gender-normative data from the CDC (15, 17). The term overweight includes the obese children. Abdominal obesity was defined using the sex and age-specific 90th waist circumference percentile by McCarthy *et al* (18). All measurements were repeated at each follow-up visit.

Dietary Intake

Dietary intake was measured at five different occasions. At baseline and at 1-year follow-up visits, parents were asked to complete a 3-day food diary (3dFD), with two weekdays and one weekend day. These days were chosen in order to obtain an accurate insight into the children food intake. Parents were instructed to record all food, drink and portion sizes, brand-name foods and cooking methods, with as much detail as possible. All food diaries were reviewed after collection by a nutritionist and missing or incomplete information was obtained whenever possible. At follow-up visits (3-months, 6-months and 1-year), three complete 24-hour dietary recalls (24HR) were obtained. The questionnaires were administered by a nutritionist to the child, in the presence of at least one parent. In order to estimate volumes and portion sizes, household measures and photographs of food portions (19) were used. All participants were asked if they considered the day intake to be usual. The energy and nutrient composition of the foods consumed were calculated using the dietary analysis program MicroDiet Plus (version 1.1, 2000, Downlee Systems Limited, High Peak, UK), based in the McCance and Widdowson's food composition table (20) and the supplements to the tables. Nutrient composition of items not included in the database was entered manually either from the manufacturer's information or from the Portuguese food composition table (21).

Energy and nutrient data were averaged across the days of each 3dFD to obtain a mean daily energy and nutrient intake, in each time point. In order to identify misreporting in food intake, the difference between each day and the three days averaged intake, for each child, was computed. The days that did not differ from the mean intake more than 1.96 SD (522 kcal) were considered. Maffei's equations (22) were used to calculate resting metabolic rate (RMR) at each time point. As an external validation of the nutritional data (23, 24), the Goldberg's criteria (24) was used, assuming a light activity level equal to 1.2. The calculated threshold to define underreporting, and consequent exclusion from further analysis, was $\text{energy intake/RMR} \times 1.2 \leq 0.89$. The Acceptable Macronutrient Distribution Range (AMDRs) from the Institute of Medicine's (25) was used for comparison of the actual intake to the recommendations for the respective age.

Clinical and Biochemical Measures

A physical examination was performed and puberty status was assessed according to Tanner stages (26). Blood pressure (BP) was measured on the right arm with the patient seated, after rest, using a digital sphygmomanometer (OMRON M6) and appropriate sized cuff. After three measurements, the lowest blood pressure value was recorded. Children were classified according to sex, height and age-specific charts (27). Baseline blood samples were collected in the morning (8:00 to 9:00) after an overnight fast (10 to 12 hours) and after a local application of a topical anaesthetic patch (EMLA). Blood glucose levels were determined by the glucose oxidase method (Siemens Healthcare Diagnostics Inc., Newark, DE, USA). HDL-cholesterol (HDL) and triglycerides (TG) levels were measured by enzymatic colorimetric methods (Siemens Healthcare Diagnostics Inc.). Plasma and serum were frozen until further analysis of insulin by luminescence immunometric assay (Siemens Healthcare Diagnostics Inc.), at an external laboratory (ENDOCLAB, Porto, Portugal). Insulin resistance was determined by the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) calculated as the product of the fasting plasma insulin level ($\mu\text{UI/ml}$) and the fasting plasma glucose level (mmol/l), divided by 22.5 (28). Outcome measures were obtained at follow-up visits at 6-months and 1-year.

Physical activity

A questionnaire concerning children activities was applied at baseline and at 1-year follow-up visit. The children were asked about the time spent at school, watching TV, playing computer/video games and sleeping. The frequency and duration of physical activities performed at school and/or extra-curricular were also quantified.

Family History

Parents were asked about the presence of overweight/obesity. Weight and height were not measured.

Definition of MS

MS was defined according to the National Cholesterol Education Program Adult Treatment Panel III criteria modified by Cook (29), with adjustment for fasting glucose according to the recent American Diabetes Association definition for impaired fasting glucose (30). MS was considered if three or more of the following criteria were present: 1) abdominal obesity (WC $\geq 90^{\text{th}}$ percentile for age and sex) (18); 2) fasting triglycerides ≥ 110 mg/dl; 3) HDL ≤ 40 mg/dl; 4) systolic/diastolic BP $\geq 90^{\text{th}}$ percentile for age, sex and height (27); 5) fasting glucose ≥ 100 mg/dl (30).

Statistical Analysis

Descriptive statistics were executed. Pearson (R) and Spearman (ρ) correlation coefficients were used. Partial correlation was computed controlling for gender, age and Tanner stage. Chi-square test was used in nominal categorical variables. Independent samples t test was performed in continuous variables with Normal distribution and Mann-Whitney test in those without Normal distribution. Normal distribution was assessed using the Kolmogorov-Smirnov test. Logistic regression analysis was used to assess the impact of dietary and physical activity factors at baseline on the likelihood of the presence of MS, considering the confounding effects of gender and age. A reduced model was obtained by backward stepwise (using the likelihood ratio criteria). We considered a significance level of 0.05. Statistical analysis was performed using SPSS (version 17.0, 2008).

RESULTS

Of the 83 overweight children evaluated at first visit, 73.5% (n=61) completed the program. The retention rate was similar in both interventions (72.4% in IT; 76.0% in GT). The main reason referred

to drop-out of the study was the lack of time due to school/work schedules. No significant differences were observed in the evaluated parameters between dropouts (n=22) and those who finished the study. The dropouts were excluded from the subsequent analysis. Also, there were no significant differences in all parameters measured at baseline between IT and GT subjects.

Baseline Characteristics

The anthropometric characteristics and MS criteria of the 61 overweight (51 obese, 10 overweight) children are shown in Table 1. There were no statistical differences between genders. The prevalence of MS was 16.4% and none of the children presented the five criteria of the MS. The number of components of MS was higher in children with higher zBMI ($\rho=0.418$, $p<0.001$). At baseline, most children were prepubertal. Insulin resistance (HOMA-IR >2.5) was found in 8% of the subjects.

Daily intakes of energy and nutrients by gender and by status of MS are shown in Table 2. Participants consumed on average 46.6% of energy from carbohydrates, of which 19.4% from sugars; 31.8% from fat, of which 12.6% from saturated fatty acids (SFA); and 21.1% from proteins. There were no significant differences between genders. MS-children presented a significantly higher energy intake ($p=0.030$), higher total carbohydrates ($p=0.050$) and total sugars ($p=0.028$), while percentage of energy as SFA was lower ($p=0.005$). MS-children consumed less meals per day ($p=0.018$).

Girls spent more time watching TV ($p=0.012$), while boys spent more time playing computer ($p=0.001$) and in extra-curricular physical activities ($p=0.005$) (Table 3). MS children spent fewer hours in extra-curricular exercise ($p=0.004$) than children without MS.

HDL levels correlated significantly with percentage of energy as protein ($R=0.317$; $p=0.028$) and total sugars ($R=-0.305$; $p=0.039$). TG presented a significant correlation with total sugars ($R=0.297$; $p=0.045$). Insulin correlated negatively with total carbohydrates ($\rho=-0.303$, $p=0.036$) and as percentage of energy ($\rho=-0.322$, $p=0.026$). Fibre intake correlated significantly with zBMI ($R=-0.300$; $p=0.043$), TV viewing ($R=-0.369$; $p=0.012$), extra-curricular ($R=0.330$; $p=0.025$) and total physical activity ($R=0.294$; $p=0.047$). When adjusted for age, gender and Tanner, the effects described by the partial correlations are clearer. TG showed a negative correlation with percentage of energy as protein ($R=-0.313$; $p=0.041$) and weight correlated positively with percentage of energy as sugars ($R=0.320$; $p=0.036$).

Diet and physical activity presented an influence on MS by logistic regression (Table 4), considering the confounding effects of gender and age. Model 1 contained dietary intake variables (total protein,

total carbohydrates, total fat, total sugars, SFA and fibre) and Model 2 contained physical activity variables (sleeping hours, watching TV, playing computer/videogames, curricular and extra-curricular exercise). Only two independent variables made a significant contribution both to Model 1 and to Model 2. Total fat intake was a positive predictor of MS ($p=0.031$), while SFA, sleeping hours and extra-curricular exercise were negative predictors of MS ($p=0.025$; $p=0.033$; $p=0.031$, respectively). Energy-adjusted nutrient intake (as percentage of energy) was also tested, but no significant results were obtained (data not shown).

Overweight/obesity was present in 42.6% of the mothers, 37.7% of the fathers and 14.8% of both parents of these overweight children (65.6% had at least one of their parents with overweight).

Dietary intake and MS components along the study period

Table 5 reports the mean daily energy and nutrient intake at baseline and at 3-month, 6-month and 1-year follow-up visits. Total energy intake and nutrient composition did not change significantly over time. There were no significant differences between genders or between IT and GT children. In subjects with MS, total energy intake was lower at 1-y follow-up visit according to 3dFD (MS: 1412.6 ± 144.0 Kcal vs. non-MS: 1668.6 ± 199.2 Kcal; $p=0.037$). The same was observed for total carbohydrates (MS: 159.3 ± 32.1 g vs. non-MS: 201.4 ± 26.5 g; $p=0.005$), total fat (MS: 46.5 ± 7.3 g vs. non-MS: 60.9 ± 11.9 g; $p=0.023$) and fibre intake (MS: 11.7 ± 5.5 g vs. non-MS: 16.5 ± 3.2 g; $p=0.021$). Time spent in extra-curricular exercise did not change significantly over time (14.8 ± 15.3 min/day at baseline vs. 15.6 ± 14.6 min/day at 1-y). A significant improvement of zBMI was observed from baseline to 1-y follow-up (1.93 ± 0.28 vs. 1.73 ± 0.34 ; $p<0.001$), more pronounced in the GT subjects (-0.18 and -0.25 in IT and GT, respectively; $p=0.042$). The MS prevalence decreased to 14.8%, mainly in boys ($p=0.030$). BP levels $\geq 90^{\text{th}}$ percentile decreased by 23% after 1-y ($p=0.063$) and IR decreased to 6.6%. There were no significant differences between IT and GT children. Obesity ($\geq 95^{\text{th}}$ BMI percentile) decreased from 83.6% ($n=51$) at baseline to 59.0% ($n=36$) at 1-year, and one child presented a $\text{BMI} \leq 85^{\text{th}}$ percentile.

According to the 24HRs, significant positive correlations ($p<0.05$) were found at 3-m between energy and macronutrient intake and weight, BMI and WC. At 6-m, energy and carbohydrates intake correlated negatively with HDL levels ($R=-0.310$; $p=0.029$ and $R=-0.350$; $p=0.013$, respectively). At 1-y, fibre correlated with zBMI ($R=-0.362$; $p=0.011$), insulin ($\rho=-0.350$; $p=0.014$) and HOMA-IR ($\rho=-0.341$; $p=0.017$). Sugars consumption correlated with HOMA-IR ($\rho=0.292$; $p=0.042$) and

extra-curricular exercise ($R=-0.308$; $p=0.031$). When adjusted for age, gender and Tanner, total carbohydrates showed a partial correlation with diastolic BP ($R=0.380$; $p=0.009$). According to the 3dFD at 1-y, energy intake correlated significantly with total physical activity ($R=-0.338$; $p=0.036$). When adjusted, total sugar consumption improved its correlation with extra-curricular exercise ($R=-0.349$; $p=0.047$).

DISCUSSION

In this study we describe the dietary intake of overweight schoolchildren participating in a lifestyle intervention protocol and its associations with MS and its components.

Our children presented a high prevalence of MS (16.4%), similar to the one found in other European countries (31, 32), and the number of components of MS increased in parallel to the increasing severity of obesity. Indeed, increases in BMI centiles during early childhood may be related to the development and acceleration of adverse cardiovascular and metabolic risk factors (7). We found a greater prevalence of elevated BP levels, almost 2/3 of the children, when compared to other studies (32, 33). This may be due to distinct dietary habits in our population, namely sodium intake. Furthermore, we used a digital sphygmomanometer which may overestimate BP levels. None of our children showed impaired fasting glucose levels. However, abnormalities of glucose homeostasis are already seen, since we found a high frequency of IR (8%) in this age group.

The dietary intake of children has an important impact on their future risk for obesity, diabetes, cardiovascular disease, and other chronic diseases (34). Although excess intake of energy is thought to be the main cause of overweight, both in children and adults, it has been difficult to prove it (35, 36). One reason for this is the difficulty inherent to an accurate measure of dietary intake, especially in children. Several studies have suggested that the various assessment methods in children, particularly in overweight, may not reflect the usual diet. Children such as adults tend to underestimate dietary intakes (24), more commonly in overweight subjects (23, 36). In order to minimize this, we excluded data from children who reported energy intakes below estimated minimal needs. We used two 3dFD and three 24HRs to obtain dietary information. The 3dFD has been recognized as a valid nutritional tool to measure dietary intake, and combining 24HRs and a food diary provides a good overview of a child's habitual diet (37, 38). Besides, children as young as 8 years-old are recognized to reliably report food intake (37), and parents were responsible for complete the 3dFD and were able to assist children in the 24HR.

It is known that modern diets, which often include processed foods containing simple carbohydrates, refined sugars and saturated fats, have a detrimental effect on body composition and metabolism (39). The macronutrient profile observed in our children was in accordance to the AMRDs (25), however the percentage of energy as carbohydrates was near the minimum limit range of 45%. Besides, we found a high intake of total sugars when compared to recommendations (<18% of energy intake), which implies a lower consumption of complex carbohydrates. Sugars intake is associated with increased cardiometabolic risk factors (40) and consequently with a higher prevalence of MS (41), as observed by the higher intake in MS-children and by the trend to be a predictor of this syndrome. As verified by us, a high carbohydrate diet, particularly sugars, elicits a reduction in fatty acid oxidation that results in a greater TG concentration (42), which in turn is associated with decreases in HDL (43), both criteria of MS. This is consistent with the American Heart Association statement that high intake of added sugars in the setting of the pandemic of obesity and CVD has heightened concerns about their adverse effects (44).

Dietary components influence many of the individual criteria of MS (39). In our study, a significant greater energy intake in MS-children was observed, in addition to carbohydrates and total sugars intake. However, only total fat and SFA intake were showed as significant predictors of MS. The assessment of fat intake appears to be less accurate than of proteins or carbohydrates (45), namely when reporting fat incorporated in cooking, which may lead to an under-reporting of fat and could affect the association between dietary factors and MS. Surprisingly, higher intake of SFA was a predictor of a lower risk of MS. This higher intake may be associated to the consumption of dairy products by children. Nevertheless, most studies support the concept that in order to prevent MS it may be appropriate to implement a reduction in consumption of foods rich in SFA in favour of those rich in unsaturated fat, for their influence on insulin sensitivity and some of the related metabolic abnormalities (46).

Although we were expecting significant changes in dietary intake over time, they did not occur. Only an increase in fibre intake was observed with 3dFD at 1-y, not confirmed with 24HR. Fibre intake was associated with lower zBMI, and despite no significance it was lower in MS-children, as showed by others (47). An inverse correlation with insulin and HOMA-IR was also observed, which may contribute to the positive effects of fibre in glucose homeostasis (48). A trend to a lower energy intake (kcal/kg) was verified with both assessment methods. Moreover, metabolic positive outcomes were observed and the degree of obesity decreased, independently of the intervention applied (IT and GT). This

allows us to argue that the small positive changes in the diet may have contributed to the observed improvement in BMI and consequently in MS components. However, the moderate severity of obesity in our children ($zBMI: 1.93 \pm 0.28$) may have limited the ability to show more substantial changes.

In addition to diet, physical activity seems to be also an important modifier of risk. The number of hours spent watching TV or playing videogames is described as an important risk factor for the development of excess body fat during childhood (49). Our overweight and MS-children spent around 2 hours per day in sedentary activities, while only about 15 minutes in extra-curricular exercise. Indeed, extra-curricular physical activity showed to be a predictor of MS in these children, such as the number of sleeping hours. According to Ara et al (50), participation in extra-curricular sports is associated with a lower fat mass and a healthier distribution of body fat, which may have beneficial effects in metabolic outcomes. Also, it seems to be associated with healthier food choices, as observed by a positive correlation with fibre intake and an inverse with energy and sugars intake. The association of short sleep duration and obesity as been described in children (51), and seems to be associated to an increased sympathetic activity, elevated cortisol, decreased leptin levels and insulin resistance (52), which may increase the risk of development of metabolic abnormalities. Short time available, lack of appropriate infrastructures and insecurity in outdoor activities were some of the reasons pointed out by parents for not improving time devoted to exercise.

Although data were obtained by self-report, excess weight was reported in about 2/3 of the family members of our children. Actually, a family environment that promotes obesity and comorbidities in one family member may be more likely to promote it in others (53).

Our study presents some limitations. First, the sample size, which may contribute to decrease the detection of significant associations between diet and MS. Second, potential contributors to measurement errors, which include the children's age, the use of 24HRs, and the possible underreporting at which overweight children and parents are prone. Third, dietary intake of overweight children was not compared to normalweight ones, which would allow for a better categorization. Fourth, physical activity assessment was obtained by self-report, which may limit the validity of these measures.

In conclusion, our results showed a significant prevalence of MS in Portuguese overweight schoolchildren. Dietary intake was in accordance to recommendations, although total sugars were highly consumed. MS-children presented a significantly higher degree of obesity, a higher dietary intake and a lower physical activity level. Total fat and SFA intake, sleeping hours and extra-curricular

exercise were predictors of MS. No significant changes were observed in diet composition along the study, although weight loss and a moderate improvement of MS components were showed. The modest magnitude of the benefits observed argues for a longer-term and more intensive intervention. Also, an evaluation of dietary patterns will be relevant to a better understanding of the links between diet and childhood obesity.

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Table 1 Anthropometric characteristics and Metabolic Syndrome criteria of overweight children, according to gender, at baseline.

	Total (n = 61)	Boys (n = 27)	Girls (n = 34)
Age (y)	8.6 ± 0.7	8.7 ± 0.8	8.6 ± 0.3
Weight (kg)	42.0 ± 6.6	43.1 ± 7.0	41.1 ± 6.3
Height (cm)	134.9 ± 6.1	136.2 ± 6.4	134.0 ± 5.8
BMI (kg/m ²)	22.9 ± 2.3	23.2 ± 2.4	22.8 ± 2.2
Z-score BMI	1.93 ± 0.28	1.88 ± 0.32	1.97 ± 0.25
Waist circumference (cm)	72.8 ± 6.4	74.2 ± 6.3	71.6 ± 6.4
Insulin (μUI/ml)	8.4 ± 4.2	8.2 ± 4.3	8.5 ± 4.1
HOMA-IR	1.68 ± 0.87	1.65 ± 0.88	1.70 ± 0.88
Metabolic Syndrome	16.4%	20.5%	11.1%
WC Percentile ≥90 th	100%	100%	100%
BP percentile ≥90 th	63.9%	62.9%	64.7%
Fasting glucose ≥100 mg/dl	0%	0%	0%
HDL ≤40 mg/dl	13.1%	7.4%	17.6%
Triglycerides ≥110 mg/dl	13.1%	11.1%	14.7%
Tanner stage (I / II)	(70.5% / 29.5%)	(77.8% / 22.2%)	(64.7% / 35.3%)

Data presented as mean ± SD for all variables, except for Metabolic Syndrome and Tanner stage presented as percentage (%). HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; WC: waist circumference BP: blood pressure; HDL: high density lipoprotein.

No significant differences were found at baseline.

Table 2 Dietary intake of overweight children, according to gender and the diagnose of metabolic syndrome, at baseline

	Boys	Girls	MS	Non-MS
Dietary intake (3dFD)	(n = 19)	(n = 28)	(n = 6)	(n = 41)
Energy intake (Kcal)	1649.9 ± 207.0	1634.2 ± 269.5	1840.6 ± 337.9	1610.4 ± 217.5*
Energy intake (Kcal/Kg BW)	40.5 ± 6.0	41.19 ± 7.9	45.0 ± 10.8	40.2 ± 6.4
Total protein (g)	86.7 ± 14.39	85.7 ± 15.5	90.5 ± 16.6	85.5 ± 14.8
% energy as protein	21.3 ± 3.3	21.0 ± 2.9	19.6 ± 1.3	21.3 ± 3.2
Total carbohydrates (g)	200.8 ± 34.4	203.8 ± 34.1	227.8 ± 27.8	199.0 ± 33.3*
% energy as carbohydrates	45.9 ± 4.5	47.1 ± 3.8	49.2 ± 4.5	46.3 ± 3.9
Total sugars (g)	89.0 ± 17.8	83.2 ± 23.7	103.3 ± 25.3	82.8 ± 19.9*
% energy as sugars	20.1 ± 3.3	18.9 ± 3.6	21.1 ± 4.2	19.1 ± 3.4
Total fat (g)	59.0 ± 10.8	57.6 ± 12.2	63.1 ± 13.8	57.4 ± 11.3
% energy as fat	32.3 ± 3.6	31.5 ± 4.2	30.6 ± 4.1	32.0 ± 3.9
SFA (g)	23.6 ± 4.6	24.7 ± 17.0	19.6 ± 4.6	24.9 ± 14.3
% energy as SFA	12.8 ± 1.8	12.4 ± 3.3	9.7 ± 2.1	13.0 ± 2.6*
Fiber (g)	15.2 ± 3.9	14.6 ± 3.6	14.1 ± 5.2	15.0 ± 3.5
Fiber (g) / 1000 kcal	9.2 ± 2.1	9.1 ± 2.3	7.7 ± 2.5	9.3 ± 2.1
<i>Number of meals per day</i>	5.6 ± 1.0	5.7 ± 0.7	5.0 ± 1.0	5.8 ± 0.8*

Data presented as mean±SD. MS: children with metabolic syndrome; non-MS: children without metabolic syndrome; 3dFD: 3-day food diary; BW: body weight; SFA: saturated fatty acid.

*p<0.05 (t-student test for significant differences between MS and non-MS children); No significant differences were found between genders.

Table 3 Sedentary and extra-curricular physical activities of overweight children, according to gender and the diagnose of metabolic syndrome, at baseline

	Boys	Girls	MS	Non-MS
	(n = 27)	(n = 34)	(n = 10)	(n = 51)
Sedentary activities				
School (h/day)	7.3 ± 2.2	7.4 ± 1.7	7.6 ± 1.7	7.2 ± 2.0
Sleeping (h/day)	9.4 ± 0.5	9.6 ± 0.8	9.1 ± 0.7	9.6 ± 0.6
Watching TV (h/day)	1.4 ± 0.6	2.0 ± 1.0 [‡]	2.3 ± 0.7	1.6 ± 0.7
Playing computer / videogames (h/day)	0.8 ± 0.5	0.4 ± 0.4 ^{‡‡}	0.3 ± 0.4	0.6 ± 0.5
Physical activities				
At school (min/day)	7.3 ± 7.8	11.6 ± 8.7 [‡]	11.6 ± 9.0	9.3 ± 8.5
Extra-curricular (min/day)	21.7 ± 17.0	9.4 ± 11.4 ^{‡‡}	3.0 ± 6.4	17.2 ± 15.5 ^{**}

Data presented as mean±SD. MS: children with metabolic syndrome; non-MS: children without metabolic syndrome.

[‡]p<0.05; ^{‡‡}p<0.005 (Mann-Whitney test for significant differences between genders); ^{**}p<0.005 (Mann-Whitney test for significant differences between MS and non-MS children).

Table 4 Logistic regression models of dietary intake variables (3dFD) and physical activity on Metabolic Syndrome, at baseline

Presence of MS at baseline			
	B ± SE	p	95.0%CI
Model 1			
Age (y)	-1.863 ± 1.141	0.102	[0.017;1.452]
Total sugars (g)	0.059 ± 0.034	0.081	[0.993;1.134]
Total fat (g)	0.214 ± 0.099	0.031	[1.019;1.505]
SFA (g)	-0.526 ± 0.234	0.025	[0.373;0.935]
Model 2			
Age (y)	-1.140 ± 0.648	0.079	[0.090;1.139]
Sleeping (h/day)	-1.405 ± 0.658	0.033	[0.068;0.890]
Extra-curricular physical activities (min/day)	-0.124 ± 0.058	0.031	[0.789;0.989]

B: Logistic regression coefficient; SE: Standard error; CI: Confidence interval; SFA: Saturated fatty acids.

All models were adjusted for age and gender.

Excluded variables in Model 1: total protein, total carbohydrates, fibre. Excluded variables in Model 2: watching TV, playing computer/videogames, curricular physical activities.

Table 5 Dietary intake of overweight children measured at baseline and at follow-up visits at 3-month, 6-month and 1-year

	3-day food diary			24-hour recall	
	Baseline visit (n = 48)	Follow-up 1-Year (n = 39)	Follow-up 3-month (n = 48)	Follow-up 6-month (n = 52)	Follow-up 1-Year (n = 49)
Energy intake (Kcal)	1640.4 ± 244.6	1673.5 ± 194.1	1700.1 ± 316.3	1691.0 ± 330.8	1646.7 ± 271.4
Energy intake (Kcal/Kg BW)	40.8 ± 7.2	38.5 ± 7.7	40.1 ± 7.18	40.3 ± 9.7	36.8 ± 8.6
Total protein (g)	86.1 ± 14.9	90.1 ± 13.9	89.0 ± 21.4	88.6 ± 18.9	85.5 ± 23.3
Total carbohydrates (g)	202.6 ± 33.9	199.3 ± 29.2	207.6 ± 40.4	206.2 ± 43.5	203.1 ± 38.9
Total sugars (g)	85.4 ± 21.6	82.3 ± 16.8	90.0 ± 23.2	88.6 ± 24.9	87.7 ± 24.9
Total fat (g)	58.2 ± 11.6	60.4 ± 12.3	62.9 ± 16.0	63.0 ± 19.4	60.3 ± 17.2
SFA (g)	24.3 ± 13.5	23.3 ± 5.1	24.3 ± 7.9	24.4 ± 7.6	23.1 ± 7.0
Fiber (g)	14.8 ± 3.7	16.0 ± 3.6	15.9 ± 5.5	15.6 ± 3.4	14.6 ± 4.9

Data presented as mean ± SD. BW: body weight.

No significant differences are found in dietary intake along the study protocol.

DISCUSSÃO E CONCLUSÕES

Este trabalho representa o primeiro estudo acerca da prevalência de excesso de peso e obesidade em crianças do concelho de Aveiro. Dos poucos trabalhos realizados a nível nacional ^(37, 287), nenhum havia reportado a dimensão deste problema em Aveiro, o quinto distrito de maior densidade populacional em Portugal ⁽²⁸⁸⁾. A faixa etária seleccionada, entre os 7 e os 9 anos, corresponde geralmente ao período que antecede a puberdade ⁽²⁸⁹⁾. Além disso, a presença de obesidade nesta idade está relacionada com a sua manutenção na idade adulta ⁽¹¹⁵⁾. Assim, assumindo a componente preventiva deste trabalho, o diagnóstico precoce da situação resulta numa oportunidade de limitar o ganho de peso e promover a sua correcção ⁽²⁹⁰⁾ previamente à fase da adolescência, esta última fortemente associada à manutenção da situação no adulto ^(115, 291).

A prevalência de excesso de peso e obesidade verificada, segundo as curvas de $Perc_{IMC}$ do CDC ⁽²⁶⁾ e descritas no Boletim de Saúde Infantil de acordo com normativa da Direcção Geral de Saúde ⁽³⁰⁾, traduz-se numa relação de 1 para cada cerca de 3 crianças com $Perc_{IMC}$ superior a 85, consistindo numa das prevalências mais elevadas da União Europeia ^(292, 293), contudo ainda inferior à verificada nos EUA ⁽²⁹⁴⁾. Segundo os critérios de Cole, recomendados pela IOTF para comparações internacionais ^(7, 27), a prevalência documentada de excesso de peso e obesidade (20,0% e 8,1%, respectivamente) vai de encontro à descrita por Padez e col. em 5511 crianças de cinco distritos portugueses (Porto, Vila Real, Coimbra, Lisboa, Évora) ⁽³⁷⁾. Estes dados confirmam Portugal nos lugares cimeiros de prevalência de excesso de peso em idade pediátrica na Europa ^(295, 296). Recentemente, a OMS constituiu o primeiro Sistema Europeu de Vigilância Nutricional Infantil – *WHO European Childhood Obesity Surveillance Initiative* – em crianças dos 6 aos 10 anos de idade ⁽²⁹⁷⁾. Em Portugal, no primeiro ano de avaliação (2008/2009), este estudo (*COSI – Portugal*) abrangeu 3847 crianças de 185 escolas. Segundo este e de acordo com os critérios do CDC, os autores verificaram uma prevalência de excesso de peso em 32% da amostra ⁽³⁸⁾, o que corrobora os constatados no concelho de Aveiro.

Tal como descrito por outros autores ^(293, 297-299), a prevalência de obesidade é maior segundo os critérios do CDC, o que se deve aos diferentes pontos de corte aplicados, em populações diferentes, e em anos diferentes, justificando as distintas prevalências encontradas. Apesar das diferenças no desenvolvimento de ambos os critérios, o valor de IMC correspondente ao ponto de corte de 25 kg/m² da IOTF e ao Perc_{IMC} 85 do CDC, é semelhante entre os 6 e os 17 anos de idade. Relativamente ao ponto de corte de 30 kg/m² da IOTF, este é superior ao Perc_{IMC} 95 do CDC, correspondendo aproximadamente ao percentil 97 em crianças com idade compreendida entre os 6 e os 12 anos ^(17, 298). Este facto associa-se a uma menor sensibilidade dos pontos de corte da IOTF para o diagnóstico de obesidade, comparativamente com os do CDC ^(300, 301), o que explica as diferenças na prevalência de excesso de peso e obesidade encontradas, nomeadamente a existência de quase o dobro dos casos de obesidade de acordo com os critérios do CDC. Assim, pode-se afirmar que a definição de obesidade segundo os critérios da IOTF tende a ser mais cautelosa ^(293, 302). Atendendo à perspectiva de prevenção das complicações associadas ao excesso de peso, a aplicação dos critérios do CDC torna-se mais abrangente, permitindo chegar a maior número de crianças e intervir nestas e respectivas famílias, mesmo com o risco de criar falsos positivos. Ambas as definições apresentam elevada especificidade e baixa sensibilidade na previsão das comorbilidades na idade adulta ^(16, 302, 304).

Geralmente não se observam diferenças significativas na prevalência de excesso de peso entre os sexos ^(294, 296, 305, 306), não havendo predomínio consistente dos rapazes ou das raparigas em determinada faixa etária ^(128, 307). A maior prevalência de sobrecarga ponderal encontrada no sexo feminino pode estar associada a uma tradicionalmente menor prática de actividade física pelas raparigas ^(307, 308). Esta variável não foi avaliada quando do rastreio, porém foi possível constatar posteriormente este facto no grupo de crianças que participaram do programa de intervenção.

A presença de um maior número de casos de obesidade nas crianças mais jovens, tal como relatado por outros ^(292, 309), alerta-nos para o provável início de ganho de peso em idades mais precoces, o que poderá vir a influenciar negativamente a prevalência de obesidade quer na adolescência, quer na idade adulta nos anos vindouros. Neste sentido, é importante a detecção precoce e atempada do excesso de peso na infância, e respectiva intervenção, de modo a prevenir a persistência do mesmo e consequentes complicações.

Neste trabalho, procedeu-se também à medição do perímetro da cintura, parâmetro este habitualmente não avaliado nos rastreios. Devido à ausência de percentis de perímetro da cintura para a população portuguesa, seleccionaram-se os percentis descritos por McCarthy e col. ⁽³¹⁰⁾, avaliados no ponto médio entre a crista ilíaca e o bordo inferior da última costela. Os pontos anatómicos descritos para a medição do perímetro da cintura são vários, contudo o descrito por McCarthy apresenta uma elevada correlação com a percentagem de massa gorda avaliada por bioimpedância ⁽³¹¹⁾, tendo sido recentemente considerado um forte factor preditivo do risco metabólico em crianças e adolescentes com excesso ponderal ⁽³¹²⁾. De acrescentar que segundo a definição de Cook e col. para o diagnóstico da SM na idade pediátrica, e utilizada neste estudo, a obesidade abdominal é definida como o percentil de perímetro da cintura acima do percentil 90 medido neste mesmo ponto anatómico ⁽²³⁴⁾. Assim, a obesidade abdominal foi observada na maior parte das crianças com excesso ponderal e obesidade, embora cerca de 15% das crianças classificadas como obesas apresentassem um perímetro da cintura inferior ao percentil 90. Segundo Freedman e col. ⁽³¹³⁾, quando comparado com o perímetro da cintura, o IMC é um teste de rastreio adequado para a identificação das crianças com necessidade de intervenção, mas não é um diagnóstico do nível de adiposidade, particularmente em crianças com $Perc_{IMC}$ inferior a 95. A forte associação entre o perímetro da cintura e o tecido adiposo visceral, e consequentemente entre os diversos factores de risco metabólico e cardiovascular, tem favorecido a sua utilização na prática clínica ^(172, 270, 314), podendo permitir uma melhor distinção das crianças a intervir com maior urgência.

O nível socioeconómico das famílias não foi avaliado neste estudo, no entanto estamos cientes da associação, ainda que inconclusiva, entre esta variável e o risco de desenvolvimento de excesso ponderal ⁽³¹⁵⁾. O ambiente em que a escola se insere, classificado como rural ou urbano, poderá ser um indicador indirecto do nível socioeconómico das famílias. Na realidade, os habitantes das zonas mais rurais geralmente apresentam um nível educacional e socioeconómico mais baixo, com maior risco de excesso de peso, influenciando também a dieta e estilo de vida das suas famílias ⁽³¹⁶⁻³¹⁸⁾. Além disso, um nível socioeconómico inferior está também relacionado com a diminuição da actividade física em crianças e adolescentes, o que aumenta o risco de obesidade ^(319, 320). Porém, e ao contrário de outros trabalhos que mostram uma maior prevalência de obesidade em crianças e adolescentes que vivem num ambiente rural ^(320, 322), no nosso estudo não se verificou qualquer distinção entre o tipo de ambiente em que a escola se insere e a presença de excesso de peso. Este facto pode estar associado à dimensão do concelho de Aveiro, diminuindo a fronteira entre o rural e o urbano.

A prevalência observada de SM, 1 em cada cerca de 5 crianças com $\text{Perc}_{\text{IMC}} \geq 95$, é deveras preocupante, principalmente atendendo ao facto da amostra ter sido obtida na população escolar, em que o grau de severidade de obesidade não é tão elevado como nos estudos de cariz clínico. Nas crianças com $\text{Perc}_{\text{IMC}} < 95$, a SM esteve ausente. Esta associação entre a presença de obesidade, a sua severidade avaliada pelo z-IMC e a presença da SM tem sido também relatada por outros autores ^(210, 246, 323). De facto, constatou-se uma correlação significativa entre o número de critérios da SM e o z-IMC. O aumento do grau de severidade da obesidade resulta também no aumento da gravidade desta síndrome, como descrito por Bell e col. em crianças e adolescentes entre os 6 e os 13 anos de idade, ao longo de um largo intervalo de z-score ⁽³²⁴⁾.

A ausência de consenso relativamente à definição da SM na idade pediátrica dificulta a comparação entre os estudos. Diversos trabalhos têm sido publicados referentes

à prevalência da SM, quer em crianças quer em adolescentes com excesso ponderal, encontrando-se valores desde 18% a cerca de 45% segundo a definição de Cook ^(239, 245, 246, 325-327). As diferentes faixas etárias, graus de excesso de peso, etnias, a variação geográfica e factores epigenéticos poderão explicar esta amplitude ⁽²³⁹⁾. Recentemente, numa população de adolescentes portugueses (10-20 anos de idade) maioritariamente obesos, os autores verificaram uma prevalência de SM de 15,6% ⁽³²⁸⁾, muito próxima à constatada neste estudo. Porém, além da faixa etária ser superior, estes jovens foram observados em contexto clínico para tratamento da sua obesidade, o que pressupõe um grau de excesso de peso superior. Esta semelhança entre a nossa prevalência e a descrita nos adolescentes é algo preocupante, uma vez que estes apresentam alguns anos adicionais para o desenvolvimento dos diversos componentes da SM, sendo de esperar uma prevalência inferior nas crianças.

Todas as 82 crianças com excesso de peso apresentaram pelo menos 1 critério da SM, enquanto 2, 3 e 4 critérios foram apresentados respectivamente em 50%, 11% e 4,9% das mesmas, o que nos alerta para o facto de o agrupamento de factores de risco metabólicos e cardiovasculares se iniciar já na infância. Além disso, as crianças com esta síndrome apresentaram na maior parte dos parâmetros avaliados neste trabalho, valores significativamente superiores quando comparadas com crianças sem diagnóstico de SM.

No que respeita aos diferentes critérios da SM, a totalidade das crianças com excesso de peso apresentou obesidade abdominal. Esta medida antropométrica correlaciona-se significativamente com o tecido adiposo visceral ^(268, 270, 271), sendo útil na determinação do risco associado à obesidade. Na realidade, diversos autores têm demonstrado a associação do perímetro da cintura com o risco metabólico e cardiovascular na idade pediátrica, sendo considerado um forte factor preditivo da SM ^(268-270, 314, 329).

A presença de níveis tensionais superiores ao percentil 90 ⁽³³⁰⁾ em cerca de 2/3 das crianças com excesso de peso, contrariamente aos 14% nas normoponderais, traduz uma elevada e inquietante prevalência tendo em conta a faixa etária em análise.

Comparativamente com a literatura ^(183, 239, 245, 246, 323, 326, 328), a prevalência por nós descrita é bastante superior, sendo raros os trabalhos com dados semelhantes, apesar da obesidade por si só ser actualmente o principal factor de risco para a hipertensão arterial em idade pediátrica ^(331, 332). A metodologia utilizada, com recurso a um esfigmomanómetro digital, pode sobrestimar os níveis tensionais ^(333, 334), apesar do instrumento empregue estar validado de acordo com o protocolo internacional ⁽³³⁵⁾. Este facto poderá justificar parcialmente os valores mais elevados, porém e uma vez que das três medições realizadas apenas foi considerada aquela de menor valor, esta sobrestimação poderá estar minimizada. É de acrescentar que as discrepâncias observadas relativamente a outras populações podem também ser devidas a uma maior ingestão de sal pela nossa população. Apesar de se ter procedido à avaliação da ingestão alimentar, a quantificação do teor de sal não foi objecto de estudo, pelo que não é possível a confirmação desta hipótese. Numa meta-análise recente, He e col. demonstraram que uma redução modesta na ingestão de sal reduz a pressão arterial de crianças e adolescentes, e a manter-se pode muito bem diminuir o subsequente aumento da mesma com a idade ⁽¹²⁶⁾. Considerando os estudos realizados na população adulta portuguesa verifica-se um consumo excessivo de sal, quase o dobro do recomendado pela OMS ⁽³³⁶⁾, além de que o problema da hipertensão arterial apresenta uma magnitude superior à descrita em outras populações ⁽³³⁷⁾. Uma vez que a pressão arterial na idade adulta se relaciona directamente com a da infância e da adolescência ^(187, 338, 339), é plausível que os valores encontrados sejam superiores aos de outras populações onde a prevalência de hipertensão arterial é inferior. Num estudo realizado em adolescentes da cidade do Porto, Ramos e col. descreveram uma prevalência idêntica de cerca de 42% de hipertensão arterial e cerca de 15 a 20% de pré-hipertensão, de acordo com o sexo ⁽³⁴⁰⁾.

Apesar de menos prevalente, a dislipidemia ocorreu entre os 11% e os 19,5% das crianças com excesso de peso, consoante o componente da fracção lipídica em causa, e em apenas 4,5% das crianças normoponderais. Esta relação entre obesidade e

dislipidemia, além de observada nos adultos, tem sido também documentada por outros autores em crianças e adolescentes ^(171, 179, 185, 341). Dados do *Bogalusa Heart Study* demonstraram que as crianças com excesso ponderal têm concentrações significativamente mais elevadas de colesterol total, LDL e triglicerídeos e significativamente inferiores de HDL ⁽¹⁷⁰⁾, correspondentes a um perfil lipídico aterogénico. Assim, nas crianças ainda jovens podemos já constatar a presença de factores de risco cardiovascular, sendo o início e o tempo de duração da obesidade um factor importante no desenvolvimento da patologia ^(161, 195). Um importante aspecto epidemiológico é que embora possa existir uma variabilidade no que concerne ao perfil lipídico ao longo do crescimento e maturação ⁽³⁴²⁾, os níveis de lípidos plasmáticos em idade pediátrica apresentam um forte poder preditivo dos mesmos em idade adulta ^(174, 175, 343), para além de que estão associados a um aumento da espessura da íntima-média carotídea, traduzindo um risco aumentado de aterosclerose e DCV no adulto ^(178, 189-192, 196). De acordo com o descrito na literatura ⁽³⁴⁴⁻³⁴⁷⁾, verificou-se uma associação entre a resistência à insulina, a obesidade e os níveis de lípidos plasmáticos. Na realidade, o hiperinsulinismo e a resistência à acção da insulina constituem factores de risco, além da obesidade, para o desenrolar destas alterações lipídicas ^(180, 185, 345), conforme inicialmente explanado.

Um outro componente da SM é a alteração da glicose em jejum, cujo limite recentemente corrigido se define por uma glicemia superior a 100 mg/dl ⁽³⁴⁸⁾. Nenhuma das crianças avaliadas apresentava este critério, descrito como pouco frequente na idade pediátrica ^(202, 210), embora outras alterações do metabolismo glicídico e da insulina, nomeadamente hiperinsulinismo, resistência à insulina (segundo o *Homeostasis Model Assessment of Insulin Resistance* - HOMA-IR) e acantose *nigricans* tenham sido observadas.

A acantose *nigricans* corresponde ao espessamento da camada córnea da epiderme e sua pigmentação, precedendo geralmente a resistência à insulina indicada pela prova de tolerância oral à glicose (PTGO), o que denuncia um subgrupo de indivíduos com

risco aumentado de desenvolver DM2 ^(349, 350). Constatou-se a presença desta lesão em cerca de um quinto das crianças avaliadas, valor superior à prevalência de hiperinsulinismo e de resistência à insulina medida pelo HOMA-IR. Este facto, além de preocupante pelo risco implícito e precoce atendendo à faixa etária considerada, alerta-nos também para a importância da realização de um exame físico adequado nas crianças de grupos de risco, nomeadamente nas obesas. Nas crianças com resistência à insulina, os índices antropométricos mostraram-se mais elevados, bem como as concentrações de lípidos plasmáticos, enzimas hepáticas e de leptina, corroborando as associações descritas por outros autores entre a obesidade, esta resistência e os componentes da SM ^(210, 257, 264, 346, 351). O HOMA-IR procura demonstrar a relação entre a capacidade das células β pancreáticas de produzirem insulina e a capacidade desta hormona em manter uma glicemia adequada ⁽³⁵²⁾, sendo um método simples mas igualmente preciso como indicador de diminuição da sensibilidade à insulina ⁽³⁵³⁾. Nas crianças e adolescentes obesos, a presença de resistência à insulina é um forte factor preditivo de diminuição da tolerância à glicose e, futuramente, de DM2 ^(202, 212, 216). Assim, é razoável supor que a diminuição da tolerância à glicose na criança obesa representa uma fase de transição em que se observa uma ligeira diminuição na sensibilidade da resposta das células β pancreáticas na primeira fase de secreção de insulina, enquanto a segunda fase se mantém preservada. Por seu lado, na DM2 observa-se a quase ausência de resposta das células β na primeira fase e um defeito na segunda fase de secreção de insulina ^(265, 350, 354). Esta associação entre a obesidade e a resistência à acção da insulina está também relacionada com a distribuição de gordura abdominal ^(173, 355, 356), nomeadamente as crianças com um perímetro da cintura superior ao percentil 90 parecem ter um risco particular para o desenvolvimento desta resistência ⁽³⁵⁵⁾. Se considerarmos que o perímetro da cintura está associado à gordura visceral e esta por sua vez se encontra associada à secreção de moléculas pró-inflamatórias, pró-aterogénicas e pró-diabetogénicas ^(173, 257, 264, 357), então compreendemos a relação existente entre este parâmetro antropométrico e a resistência à insulina, bem

como entre esta e os vários componentes da SM. Recentemente Maffeis e col. demonstraram a existência de correlação entre a sensibilidade à insulina e o tecido adiposo visceral subcutâneo, medido através de ressonância magnética, não tendo conseguido confirmar a mesma relativamente ao tecido adiposo visceral ⁽³⁵⁸⁾. Uma das razões apontadas pelos autores para esta discrepância relaciona-se com a deposição preferencial de gordura na região subcutânea em crianças pré-púberes.

A desregulação associada à obesidade da secreção de adipocinas pelo tecido adiposo parece constituir uma potencial justificação para algumas das alterações verificadas no decorrer da SM ^(58, 274, 359). O papel das adipocinas na génese desta síndrome na infância é ainda pouco estudado, pelo que nesta investigação se avaliou a concentração plasmática de leptina e adiponectina e a sua relação com a obesidade e a SM nas crianças.

A leptina, tal como a insulina, é secretada em maior quantidade durante períodos de balanço energético positivo ^(61, 64), que ocorrem geralmente na obesidade, pelo que a sua concentração plasmática se correlaciona significativamente com o IMC quer em adultos, quer em crianças ^(277, 360-362). Em consonância, além da associação entre esta hormona e os parâmetros antropométricos avaliados, verificou-se uma concentração plasmática nas crianças obesas cerca de três vezes superior às normoponderais. Paralelamente a insulina, HOMA-IR, perfil lipídico (colesterol total, LDL, triglicerídeos, Apo B), provas hepáticas e proteína C reactiva, correlacionaram-se positivamente com a leptina, o que evidencia o papel desta na etiopatogenia da SM, quer directamente pelos seus efeitos sobre o metabolismo ^(63, 64, 208, 363), quer indirectamente pela interacção com a insulina e regulação da sensibilidade a esta hormona ^(275, 364, 365). Outros autores têm relatado resultados semelhantes ^(275, 277, 366), principalmente a relação existente entre a leptina, a insulina e a resistência a esta, mas nem sempre os resultados são consistentes no que respeita aos restantes parâmetros. Estas pequenas diferenças podem dever-se às características da população estudada, nomeadamente no que respeita à idade, grau de puberdade e severidade da obesidade ^(65, 275, 367). A relação entre leptina e insulina tem sido descrita de

acordo com o eixo adipo-insular, uma ansa bidireccional de *feed-back* existente entre estas duas hormonas ⁽³⁶⁸⁾, em que a leptina suprime a secreção de insulina pelas células β pancreáticas, enquanto a insulina aumenta a secreção de leptina. A resistência à leptina que se manifesta na obesidade poderá conduzir à interrupção deste eixo, com agravamento do hiperinsulinismo eventualmente presente ^(67, 367). Segundo Chu e col., as crianças com valores plasmáticos de leptina no último quartil de distribuição possuem um perfil cardiovascular mais adverso ⁽²⁷⁷⁾.

A adiponectina, descrita como uma adipocina “protectora” devido ao seu papel anti-aterogénico, anti-inflamatório e insulino-sensibilizador ^(76, 369-371), tem sido proposta em vários trabalhos como um possível marcador da SM, resistência à insulina e risco cardiovascular ^(76, 280, 281, 372, 373). Surpreendentemente, os resultados por nós descritos parecem em desacordo com a literatura ^(278, 279, 374), verificando-se uma concentração de adiponectina superior nas crianças com excesso de peso e obesidade comparativamente com as normoponderais, ainda que sem significado estatístico. De realçar que a concentração média de adiponectina determinada na totalidade das crianças é superior à geralmente descrita em outros estudos ^(281, 375), situando-se entre o percentil 75 e 97,5, segundo os percentis específicos para a idade e sexo descritos no *EarlyBird 15 Study* ⁽³⁷⁶⁾ obtidos de uma coorte de 307 crianças britânicas aparentemente saudáveis. Este facto poderá estar associado a uma característica genética específica da população por nós avaliada. Num trabalho em crianças e adolescentes do distrito do Porto, a concentração média desta adipocina mostrou-se inferior ⁽³⁷⁷⁾, mediante a aplicação de uma metodologia distinta para a sua determinação. Neste sentido, as diferenças existentes entre as metodologias e outros procedimentos podem explicar os diferentes resultados obtidos. Todavia, os procedimentos aplicados são padronizados e as determinações foram realizadas em laboratório acreditado.

A adiponectina de alto peso molecular (HMW) tem sido reportada como a isoforma activa desta adipocina ⁽³⁶⁹⁾, de tal modo que a HMW bem como a razão adiponectina

HMW/total, estão associadas a efeitos metabólicos favoráveis tais como sensibilidade à insulina e melhoria do perfil lipídico ^(76, 378-380). Contudo, o método analítico empregue mede apenas a concentração de adiponectina total. Porém, podemos especular a possível presença de níveis mais elevados de adiponectina HMW ou de um aumento da razão adiponectina HMW/total nas crianças normoponderais, enquanto nas crianças com excesso de peso a concentração de adiponectina HMW seria inferior, apesar da concentração de adiponectina total ser superior. Isto foi confirmado por Martos-Moreno e col. em crianças pré-púberes ⁽³⁸¹⁾, tendo justificado a concentração superior de adiponectina total nas crianças obesas pelo facto de nestas o aumento da gordura corporal se fazer inicialmente à custa de um aumento do número de adipócitos e não da sua hipertrofia.

As correlações descritas entre a adiponectina e os parâmetros associados à definição da SM não foram confirmadas. De acordo com os valores de HOMA-IR, observa-se uma tendência para concentrações inferiores desta adipocina nas crianças com resistência à insulina, inclusive quando comparadas com as crianças normoponderais. Segundo Weiss e col., os efeitos moduladores da adiponectina sobre a sensibilidade à insulina devem-se em parte ao seu papel na diminuição do conteúdo intramiocelular lipídico ^(261, 263). Segundo alguns trabalhos, a adiponectina mostra-se mais associada com a resistência à insulina do que propriamente com a adiposidade ^(278, 382, 383), apesar de nem todos os autores corroborarem estes factos ^(279, 374, 384, 385). A influência da idade, sexo e grau de puberdade na concentração de adiponectina ^(384, 386, 387), pode justificar as diferenças encontradas em alguns estudos. O ambiente genético também pode influenciar fortemente os níveis de adiponectina ⁽³⁸⁸⁾.

Em relação à grelina, e segundo a literatura, este peptídeo orexígeno encontra-se aumentado no jejum e antes das refeições, induzindo a ingestão alimentar ^(78, 389, 390). Este efeito conduziu à hipótese inicial de que a sua concentração se encontraria aumentada nos obesos contribuindo para a patogénese da doença, contudo vários autores têm verificado o oposto ^(81, 391, 392). De acrescentar que o efeito orexigénico da grelina após a refeição é

retomado mais cedo nos obesos comparativamente com os indivíduos normoponderais ^(392, 393), o que em parte pode explicar a rápida recuperação do apetite observada nos primeiros. Segundo Tschöp e col. ⁽⁸¹⁾, a concentração plasmática de grelina no obeso representa uma adaptação fisiológica a um balanço energético positivo, o que parece traduzir uma *downregulation* da grelina na obesidade, porventura consequência da hiperinsulinemia e da hiperleptinemia que ocorrem nesta situação. De acordo com outros autores ^(394, 395), não se verificou qualquer associação significativa entre este peptídeo e a leptina, porém observou-se uma correlação negativa entre este e os níveis de insulina e HOMA-IR. Não obstante o papel da grelina na obesidade infantil ainda não ser totalmente compreendido ^(391, 392, 395), a interacção entre este peptídeo e a sensibilidade à insulina tem sido descrita como independente da adiposidade ^(84, 392). Além do efeito supressor da insulina sobre os níveis de grelina ^(391, 396, 397), estudos recentes reforçam a opinião de que a grelina endógena funciona também como um regulador fisiológico da insulinemia e glicemia ^(395, 398), o que traduz a bidireccionalidade das relações existentes entre as várias moléculas envolvidas.

Todas as crianças com SM apresentavam obesidade, mas nem todas as crianças obesas apresentavam SM. Na realidade, a razão pela qual algumas crianças obesas desenvolvem critérios desta síndrome enquanto outras não, ainda não é totalmente compreendida ^(211, 219, 246). A presença de resistência à insulina em cerca de um quarto das crianças com SM sugere um papel fisiopatológico importante no desenrolar dos eventos que culminam nesta síndrome ^(211, 219, 346). Assim, podemos pressupor que nas crianças obesas se gera um ambiente favorável ao desenvolvimento da resistência à acção da insulina, acompanhado de alterações na secreção de outros mediadores, reflectindo-se esta complexa interacção nas diversas complicações associadas à SM. Na realidade, a existência de correlações entre a insulina, a leptina e alguns parâmetros da SM, nomeadamente com o perímetro da cintura e a concentração de triglicéridos, foram documentadas. A concentração de insulina evidenciou-se como um factor preditivo desta

síndrome, reforçando o seu papel como elo de ligação entre a obesidade e os factores de risco cardiovasculares e metabólicos ^(351, 399, 400). Para além desta hormona, a apolipoproteína A-I (Apo A-I) e o estágio pubertário destacaram-se como determinantes da presença de SM nestas crianças. A Apo A-I, principal proteína das HDL, apresentou-se como factor preditivo negativo da SM, o que pode estar associado ao seu papel como mediador do transporte reverso de colesterol exercendo um efeito anti-aterogénico ^(401, 402). Além disso, a Apo A-I estimula a utilização da glicose e melhora a resistência à insulina nos tecidos periféricos, desempenhando assim um importante efeito protector ⁽⁴⁰³⁾. A puberdade tem sido reconhecida como uma fase propícia ao desenvolvimento de resistência à insulina devido às alterações hormonais e da composição corporal decorrentes da maturação ^(21, 22, 404, 405), porém através da regressão logística esta associação não foi confirmada. Este facto pode dever-se ao reduzido número de crianças em estágio 2 de Tanner no início do estudo, o que pode ter constituído um efeito confundidor.

De entre as moléculas secretadas pelo tecido adiposo, apenas a leptina se manteve no modelo final de regressão logística como determinante da presença da SM, embora sem significância estatística. Esta associação entre a leptina e a SM tem sido relatada e encontra-se relacionada fundamentalmente com o desenvolvimento da resistência à insulina e intolerância à glicose promovida pela leptina ^(275, 364). Relativamente à adiponectina não se confirmou o papel descrito como marcador clínico da SM ^(280, 281).

Nenhum dos parâmetros antropométricos relacionados com a adiposidade se mostrou como preditivo da SM, nomeadamente o perímetro da cintura. Na realidade, em todas as crianças avaliadas este perímetro apresentou-se superior ao percentil 90, o que explica a baixa capacidade preditiva desta variável na nossa amostra. Este aspecto reforça também a hipótese da contribuição de outros factores além da gordura corporal na resistência à insulina e na SM ^(261, 406).

Uma vantagem da definição da SM em crianças obesas é a identificação daquelas em maior risco de doença futura e que mais irão beneficiar da participação em programas de intervenção específicos, no âmbito da promoção de estilos de vida saudáveis e perda de peso. Isto torna-se importante uma vez que os recursos, quer humanos quer materiais, na saúde são muitas vezes limitados, e a intervenção generalizada na população raramente é uma possibilidade realista ⁽²²⁹⁾. Para além disso, o facto de a agregação dos vários factores de risco cardiovasculares e metabólicos durante a infância prever o desenvolvimento da SM, DM2 e DCV na idade adulta ^(250-253, 407), realça a importância de uma intervenção atempada nas crianças em risco.

Neste sentido, foi também objectivo deste trabalho avaliar a resposta a dois tipos de tratamento: o tratamento individual (TrI) e o tratamento em grupo (TrG), ambos baseados na educação alimentar (plano alimentar estruturado ou sessões de educação alimentar, respectivamente) e promoção da actividade física.

A maior parte do conhecimento sobre o tratamento da obesidade em idade pediátrica é proveniente de estudos em crianças com obesidade grave, recrutadas em centros clínicos ^(285, 286, 408, 409). Deste modo, as alterações no peso e no z-IMC em resposta à intervenção realizada nestes centros são geralmente surpreendentes, pois estas crianças podem atingir maiores perdas de peso, quando comparadas com crianças com z-IMC menores ^(168, 410). O grau de obesidade nas nossas crianças é relativamente moderado, o que se reflecte não só nos modestos transtornos observados, bem como na progressão menos evidente ao longo do período de um ano de estudo. Apesar desta limitação, o z-IMC diminuiu em ambos os grupos de estudo, de modo mais pronunciado no TrG. Esta diminuição não se fez acompanhar por uma diminuição do peso, porém convém não esquecer que o peso e a estatura aumentam com o processo de desenvolvimento ^(21, 22), pelo que o melhor parâmetro de avaliação da evolução ponderal será o z-IMC. No final do estudo, cerca de 60% das 61 crianças mantinham-se ainda acima do Perc_{IMC} 95. Segundo Ford e col., a diminuição mínima no z-IMC necessária para se verificar melhorias na

composição corporal e no risco cardiometabólico é da ordem de 0,25 ⁽⁴¹¹⁾, valor este obtido na variação média das crianças submetidas ao TrG, enquanto que para obter efeitos benéficos mais significativos a diminuição deverá ser de 0,5 ^(411, 412).

Paralelamente à diminuição do z-IMC, também a razão perímetro da cintura/estatura diminuiu significativamente. Este índice tem-se mostrado vantajoso visto ser fácil de aplicar e ser independente do sexo e da idade ^(413, 414). Além disso, a razão perímetro da cintura/estatura tem sido descrita como um indicador, entre crianças obesas, da maior probabilidade de apresentarem risco metabólico e cardiovascular aumentado ^(414, 415). Assim, a sua melhoria poder-se-á reflectir na diminuição deste mesmo risco.

Neste sentido, podemos constatar que apesar da pequena diminuição no grau de obesidade, esta se fez acompanhar de uma melhoria dos factores de risco associados, nomeadamente na pressão arterial e no perfil lipídico, salientando uma melhor resposta no TrG. A insulina, HOMA-IR, leptina, adiponectina e grelina apresentaram uma evolução distinta de acordo com o tratamento instituído, sendo que os resultados mais favoráveis se verificaram também no TrG. O início da puberdade em algumas crianças poderá eventualmente ter condicionado esta evolução, tal como observado por Reinehr e col. cujo trabalho lhe permitiu concluir que os factores de risco cardiovasculares agravam com a puberdade, acompanhados de um aumento da resistência à insulina, associada a modificações na concentração das hormonas sexuais e das adipocinas ⁽⁴¹⁶⁾. Não obstante, é de salientar que considerando a necessária diminuição mínima de 0,25 no z-IMC, não é de surpreender que os resultados mais benéficos tenham sido alcançados com o TrG, onde esta meta foi cumprida.

Apesar de os valores de insulina e de HOMA-IR não terem acompanhado a diminuição do z-IMC, possivelmente resultado do desenvolvimento destas crianças ⁽⁴¹⁷⁾, verificou-se uma diminuição na prevalência da resistência à insulina e na acantose *nigricans*, denunciando as modificações positivas no metabolismo da insulina.

Segundo uma revisão recentemente publicada, a diminuição de apenas 1% no peso corporal é suficiente para promover uma diminuição na concentração de leptina, existindo poucas dúvidas no que respeita ao efeito da perda de peso na concentração de leptina ^(68, 418, 419). O mesmo já não se verifica relativamente à adiponectina, uma vez que os seus níveis não parecem ser tão sensíveis ao efeito da intervenção ⁽⁴¹⁹⁾, comportando-se de modo diferente entre os grupos. No entanto, tem sido relatado um aumento dos níveis de adiponectina após perda ponderal ^(381, 420). A variação na concentração de grelina apresentou sentidos opostos consoante o tipo de tratamento instituído, sendo que no grupo de maior perda ponderal - o TrG - este peptídeo aumentou, tal como descrito ^(421, 422). Este aumento tem sido inclusive sugerido como um obstáculo à manutenção da perda de peso devido ao efeito orexigénico da grelina ⁽³⁹⁰⁾.

A prevalência da SM diminuiu ligeiramente no decurso deste trabalho. Das crianças diagnosticadas inicialmente com esta síndrome, metade não a apresentavam no final do estudo, porém em contrapartida foram diagnosticados quatro novos casos. Estes últimos surgiram em crianças cujo IMC aumentou, enquanto nas outras este parâmetro diminuiu correspondendo a uma perda ponderal mais significativa. Nas crianças do sexo feminino e no estágio de Tanner 2, a prevalência da SM aumentou. Este dado contradiz a regressão logística inicial. Na realidade, verifica-se a existência de cerca de metade das crianças neste estágio no final do estudo, o que nos alerta para o possível efeito confundidor desta variável. No entanto, o resultado obtido poderá estar associado ao descrito efeito da puberdade sobre o perfil hormonal e metabólico ^(65, 386, 405, 404).

Diversos trabalhos em crianças obesas sujeitas a programas de intervenção têm sido recentemente publicados, e os resultados obtidos confirmam a melhoria dos factores de risco cardiovasculares e metabólicos associados à obesidade e à SM durante a infância e adolescência ^(285, 286, 408, 423, 424), sendo que quanto maior a perda ponderal obtida, menor a prevalência desta síndrome ⁽²⁸⁵⁾. Contudo, é de salientar que em alguns destes trabalhos a prescrição dietética aplicada às crianças e adolescentes é deveras restritiva, na ordem das

1000 a 1200 kcal⁽⁴²³⁻⁴²⁵⁾. Segundo as recomendações para o tratamento da obesidade em idade pediátrica, deve-se atingir o objectivo de diminuição do IMC, porém mantendo o crescimento e desenvolvimento normais^(103, 219, 426). Assim, embora os resultados obtidos neste trabalho sejam à partida menos evidentes, a melhoria verificada poderá ser mantida com uma intervenção mais prolongada que permita a aquisição sólida de hábitos saudáveis.

Conforme discutido, o modelo de tratamento com que se obteve os melhores resultados, ainda que modestos, foi o TrG. Esta metodologia tem sido aplicada com sucesso por outros autores^(285, 286, 408, 427-430), permitindo às crianças e suas famílias serem capazes de lidar com o problema da obesidade de forma consciente e independente, conduzindo a resultados mais consistentes do que aqueles obtidos com a terapêutica dietética convencional⁽⁴²⁸⁻⁴³⁰⁾. Para além disso, permite partilhar experiências e conhecimentos, facilitar a resolução dos problemas e reforçar a motivação pessoal^(427, 428, 430), envolvendo os intervenientes no tratamento. Em contrapartida, o TrI adopta uma abordagem prescritiva, mais rigorosa, que poderá ser entendida como uma substituição ou diminuição do papel dos pais na adopção de novas práticas e das suas responsabilidades na saúde da criança⁽⁴³⁰⁾, e que podem acabar por conduzir a uma diminuição da motivação, quer desta quer dos pais, no seu tratamento. Cerca de um quarto das crianças inicialmente avaliadas abandonou o estudo, reportando como principal entrave à participação a indisponibilidade de horário, quer por parte das crianças, quer por parte da família. Assim, este factor deve ser ponderado quando da implementação de programas de intervenção mais exaustivos. A resposta obtida ao tipo de tratamento instituído foi distinta consoante os sexos, o que nos alerta também para a necessidade de ajustar adequadamente o modelo terapêutico ao sexo e à idade da criança, de modo a obter melhores resultados.

Neste seguimento, o envolvimento da família no tratamento da criança é fundamental para a obtenção do sucesso, não só pelo papel facilitador na modificação dos hábitos e pelo apoio à criança^(431, 432), bem como muitas das vezes pela própria correcção

do excesso de peso em outros membros da família, funcionando assim como um exemplo a seguir pela criança ^(431, 433). Isto é particularmente importante em crianças mais jovens, em que a influência dos pais nos hábitos alimentares e de actividade física é maior do que na adolescência ⁽⁴³¹⁻⁴³³⁾. No nosso trabalho verificou-se uma elevada prevalência de excesso de peso na família, quer nos pais quer nos avós. Em cerca de dois terços das crianças com sobrecarga ponderal pelo menos um dos seus progenitores apresentava excesso de peso, comparativamente com cerca de 5% nas crianças normoponderais, com maior destaque para as mães. Porém, uma vez que este dado foi auto-reportado, sem medição do peso e estatura, esta prevalência poderá estar enviesada ⁽⁴³⁴⁾. De qualquer modo, a obesidade familiar tem sido descrita como preditiva do excesso de peso na criança ⁽⁹³⁻⁹⁶⁾, em particular a obesidade materna ^(94, 99), que poderá não só estar associada a factores genéticos e ambientais ^(93, 95, 98), bem como a factores intra-uterinos ^(99, 100). A presença de diversas comorbilidades associadas, tais como hipertensão arterial, dislipidemia, outras DCV e diabetes, também se constatou. Assim, a existência de um ambiente familiar favorecedor da obesidade e de suas complicações num dos membros da família torna mais provável a sua ocorrência nos restantes membros ⁽⁴³⁵⁾.

No presente trabalho foi observada a flutuação em alguns dos parâmetros avaliados, nomeadamente uma melhoria entre o início do estudo e a avaliação realizada aos 6 meses, seguida de um ligeiro agravamento entre esta e o final do estudo. Este facto pode ser devido ao maior número de consultas realizado durante o primeiro semestre, de acordo com o desenho do estudo, o que possivelmente permitiu uma maior aproximação entre a criança, a sua família e a equipa. Isto reforça a necessidade de um maior e mais prolongado acompanhamento das crianças com obesidade, com vista ao sucesso no seu tratamento, conforme descrito por outros autores ^(436, 437).

Através da análise dos componentes principais, verificou-se a existência de dois factores independentes de variação, nomeadamente o componente antropométrico (PC1) e o componente lipídico e hepático (PC2). As variações no tempo capturadas por estas

componentes principais mostraram-se diferentes entre os sexos para cada tipo de tratamento, o que reforça a importância em delinear abordagens adequadas. Contudo, a existência deste tipo de interações nem sempre é confirmada, tal como descrito por Kamath e col. numa revisão recente ⁽²⁸³⁾.

A ingestão alimentar desempenha um papel fundamental sobre o risco de desenvolvimento de obesidade, DM2, DCV, entre outras comorbilidades ^(3, 116). Contudo tem sido difícil demonstrar a associação entre esta ingestão e o desenvolvimento da doença ^(117, 118, 121, 128, 131).

A avaliação inicial da ingestão alimentar das crianças com excesso de peso mostrou que esta se enquadra nas recomendações relativas à distribuição de macronutrientes na dieta, nomeadamente entre 45 a 65% de hidratos de carbono (HC), 25 a 35% de lípidos e 10 a 30% de proteínas, de acordo com o *Institute of Medicine* ⁽⁴³⁸⁾. Em relação à ingestão de açúcares totais (adicionados e naturalmente presentes nos alimentos) e de ácidos gordos saturados (AGS) esta verificou-se superior às recomendações, enquanto o consumo de fibra alimentar se mostrou inferior à recomendação de 25g/dia ⁽⁴³⁸⁾. Todavia, se considerarmos as recomendações da OMS ⁽¹¹⁶⁾, as crianças avaliadas apresentam uma ingestão elevada de lípidos e de proteínas, e deficitária de HC. Estes resultados são semelhantes aos descritos em dois estudos levados a cabo em crianças portuguesas, apesar de nestes se ter observado uma ingestão energética superior, acompanhada de maior ingestão de HC totais e de açúcares em particular, ao contrário da ingestão proteica que se apresentou inferior à verificada ^(439, 440), diferenças estas que podem estar relacionadas com as diferentes metodologias empregues na avaliação da ingestão alimentar. Não obstante, estes trabalhos foram desenvolvidos na população infantil em geral e não especificamente em crianças com excesso de peso, sendo interessante notar que a ingestão alimentar nestas últimas é similar à da generalidade das crianças, tal como referido por outros autores ^(121, 441, 442). Em contrapartida, outros trabalhos constataam uma

maior ingestão de lípidos e menor de HC entre as crianças com excesso de peso e as normoponderais ^(132, 443, 444), o que realça o papel dos HC como nutrientes promotores de saciedade e reguladores do peso corporal, ao contrário dos lípidos ⁽⁴⁴⁵⁾. Estudos longitudinais na idade pediátrica não conseguiram estabelecer a existência de causalidade entre a ingestão energética, a composição da dieta e o desenvolvimento do excesso de peso ^(118, 126, 135, 446). Este facto pode dever-se à complexidade das diversas variáveis envolvidas, sendo muitas vezes difícil de distinguir os efeitos independentes dos nutrientes, alimentos e até de padrões alimentares no peso corporal ⁽¹¹⁸⁾. Além disso, a tendência descrita para a subestimação da ingestão por parte dos indivíduos com excesso de peso também pode contribuir para esta dificuldade ^(130, 447, 448).

De modo semelhante, permanece por explicar se a dieta como um todo ou os seus componentes individuais podem afectar independentemente o desenvolvimento da SM ⁽⁴⁴⁹⁾. Ao comparar as crianças com diagnóstico da SM com as crianças sem SM, constatou-se uma ingestão energética significativamente superior nas primeiras, acompanhada de maior consumo de HC e açúcares totais. Em contrapartida, o consumo de AGS apresentou-se inferior, bem como o número de refeições diárias. Através de regressão logística, apenas a ingestão total de lípidos e a de AGS se mostraram como factores preditivos da SM nestas crianças, porém em sentidos opostos. Assim, surpreendentemente o maior consumo de AGS relacionou-se a um menor risco de SM. Este resultado contraria o descrito e recomendado na maior parte dos estudos, que apontam como medida necessária para a diminuição no risco de desenvolvimento de obesidade e suas comorbilidades, uma diminuição da ingestão de AGS ⁽⁴⁵⁰⁻⁴⁵²⁾. Em diversos estudos observacionais uma ingestão elevada de AGS está associada a menor sensibilidade à insulina, a hiperinsulinemia e hiperglicemia ^(450, 453, 454), com maior risco de tolerância anormal à glicose e DM2 ^(116, 455). Paralelamente, alguns trabalhos também mostram uma associação, ainda que inconclusiva, entre uma elevada ingestão lipídica total e uma menor sensibilidade à insulina ^(450, 455, 456), factor importante no desenvolvimento da SM. Contudo, é de realçar que a avaliação da

ingestão de lípidos é geralmente menos precisa, sendo mais susceptível à subestimação do que a das proteínas ou dos HC ^(144, 457). Este aspecto pode dever-se à maior dificuldade na quantificação da gordura de adição na culinária, facto este que poderá ter contribuído para o resultado verificado. Além disso, embora sem significado estatístico, a ingestão proteica foi mais elevada nas crianças com SM, o que considerando como principal fonte as proteínas de origem animal, poderá contribuir hipoteticamente para uma maior ingestão de AGS. Royo-Bordonada e col. verificaram que as crianças com menor ingestão de AGS eram aquelas que apresentavam também menor ingestão de lacticínios, apresentando-se este grupo como o principal fornecedor de AGS na dieta ⁽⁴⁵⁸⁾. Relativamente à ingestão de açúcares totais, esta mostrou tendência para ser um dos factores preditivos da SM nestas crianças, o que corrobora a associação geralmente descrita entre estes e os factores de risco cardiovasculares e metabólicos ^(459, 460).

Diversas correlações entre os constituintes da dieta e os componentes individuais da SM têm sido observadas em crianças e adolescentes ⁽⁴⁶¹⁻⁴⁶⁴⁾, porém nem sempre consistentes, o que pode estar associado à validade dos dados obtidos através da avaliação da ingestão alimentar ⁽⁴⁶⁵⁾. De destacar a associação entre a ingestão de açúcares, o peso corporal e um perfil lipídico menos favorável, enquanto a ingestão de fibra se correlacionou de forma inversa com o IMC, a insulina e o HOMA-IR. Como descrito por outros autores ^(462, 466), uma alimentação rica em HC, particularmente em açúcares, induz uma redução na oxidação de ácidos gordos resultando num aumento da concentração de triglicerídeos, além de reduzir a actividade da lipoproteína lipase ^(467, 468), o que por sua vez está associado à diminuição da concentração de HDL ⁽⁴⁶⁹⁾. O papel dos açúcares na promoção da obesidade tem vindo a ser debatido e não está ainda totalmente esclarecido ⁽⁴⁷⁰⁾, sendo que alguns estudos têm sugerido uma possível relação entre a ingestão de bebidas açucaradas e o peso corporal em crianças e adolescentes ^(471, 472). De acordo com o estudo europeu *Pro Children*, as crianças geralmente não consomem as porções recomendadas de frutas e hortícolas, embora Portugal tenha apresentado das maiores

taxas de ingestão deste grupo de alimentos ⁽⁴⁷³⁾. Este baixo consumo faz-se acompanhar de uma menor ingestão de fibra e de um aumento da densidade energética da dieta ⁽⁴⁷⁴⁾. Steffen e col. mostraram que o consumo de cereais integrais, ricos em fibras, está associado a maior sensibilidade à insulina e menor IMC em adolescentes, particularmente nos obesos ⁽⁴⁷⁵⁾. Assim, apesar de a eficácia da fibra alimentar diferir de acordo com as suas fontes alimentares, o seu consumo pode contribuir para a modulação de alguns parâmetros associados à SM ^(463, 476).

No decurso do estudo, nomeadamente aos 3 e 6 meses e ao 1 ano, não se observaram alterações significativas na ingestão alimentar e na distribuição dos macronutrientes, ao contrário do que seria esperado em resposta ao tratamento implementado ⁽⁴⁷⁷⁾. Porém, atendendo ao crescimento das crianças durante este período, verificou-se uma diminuição da ingestão energética por quilograma de peso corporal, ainda que sem significado. Esta diminuição pode traduzir uma modesta correcção dos hábitos alimentares na população em estudo, associada a uma melhoria do z-IMC e de alguns parâmetros bioquímicos. Segundo uma revisão recente, as intervenções em crianças que incluem modificações na dieta mostram-se eficazes na obtenção de respostas positivas no que respeita aos resultados relacionados com o peso ⁽⁴⁷⁸⁾.

De salientar que a avaliação da ingestão alimentar, especialmente em crianças, apresenta diversas limitações nomeadamente a capacidade de memória, de estimação das quantidades e porções ingeridas, e a subestimação do consumo ^(129, 479). De modo a minimizar o efeito inerente a estas limitações foram empregues dois métodos diferentes de avaliação da ingestão, bem como um manual de quantificação de alimentos permitindo a visualização e selecção das porções ingeridas. Além disso, os pais participaram na recolha da informação e os inquéritos que reportavam uma ingestão alimentar inferior às necessidades energéticas basais foram excluídos.

Numa revisão recentemente publicada, Janssen e LeBlanc concluíram que as crianças devem despende pelo menos 60 minutos de actividade física moderada a vigorosa por dia, a fim de promoverem melhorias na sua saúde, sendo que alguns desses benefícios podem já ser atingidos com pelo menos 30 minutos de actividade diária ⁽⁴⁸⁰⁾. Contudo, de modo a prevenir a resistência à acção da insulina, bem como outros componentes da SM, Andersen e col. recomendam uma duração de pelo menos 90 minutos por dia ⁽⁴⁸¹⁾. Comparativamente, e tendo em conta apenas os valores de actividade física extra-curricular, as crianças avaliadas ficaram bastante aquém do recomendado. Uma vez que o exercício físico desenvolvido na escola é dependente dos currículos e geralmente é de participação obrigatória, sem a directa responsabilidade da família ou da criança, este não foi considerado aquando do incentivo ao aumento da actividade física pelas crianças. Assim, considerando apenas a actividade física desenvolvida fora do horário escolar, as crianças com sobrepeso e do sexo feminino apresentaram um menor tempo despendido quando comparadas com as normoponderais e os rapazes, respectivamente. Estes dados estão de acordo com a literatura ^(148, 153, 308, 482), apesar das diferenças no tempo despendido para a actividade física diária, o que se deve possivelmente às diferentes faixas etárias, populações e metodologia utilizada nos diferentes estudos. Atendendo à metodologia empregue neste trabalho, com aplicação de um inquérito para a determinação do tempo despendido diariamente nas actividades desportivas e sedentárias, estes resultados poderão estar enviesados ⁽⁴⁸³⁾. Contudo, a actividade extra-curricular revelou-se um importante factor preditivo do desenvolvimento da SM nestas crianças, correlacionando-se negativamente com a concentração de leptina. Na realidade, a participação em actividades desportivas extra-curriculares está associada a menor percentagem de massa gorda e a uma melhor distribuição da mesma, o que se pode traduzir em efeitos benéficos em termos metabólicos ⁽⁴⁸⁴⁾.

A conjugação do aumento da actividade física com a correcção alimentar têm-se mostrado como benéfica na redução do excesso de peso e na melhoria dos factores de

risco cardiovasculares e metabólicos em crianças e adolescentes sujeitos a programas de intervenção nos estilos de vida ^(157, 284-286, 424, 409). Na realidade, as crianças com maior actividade desportiva apresentaram uma ingestão energética e de açúcares totais inferior, além de uma ingestão de fibras superior. Estas associações parecem demonstrar, por parte de algumas crianças e famílias, uma maior consciencialização da problemática da obesidade e das medidas a seguir para a sua correcção. Porém, o tempo destinado à prática do exercício extra-curricular manteve-se constante durante o decurso do estudo, facto este justificado pela menor disponibilidade de tempo, falta de infra-estruturas para prática de desporto e pela insegurança nas actividades realizadas ao ar livre, o que poderá ter contribuído para a menor resposta observada, quer em termos antropométricos quer metabólicos. As limitações relatadas pelos progenitores são factores importantes a ter em conta aquando da implementação de programas de intervenção.

As actividades sedentárias, tais como ver televisão e jogar computador, foram também avaliadas verificando-se um maior tempo dedicado a estas actividades nas crianças com sobrepeso. Na maior parte dos trabalhos, o tempo despendido a ver televisão tem sido descrito como um importante factor promotor da obesidade infantil ⁽⁴⁸⁵⁻⁴⁸⁷⁾, contudo nem sempre esta associação se mostrou clinicamente relevante ⁽⁴⁸⁵⁾. De salientar que em estudos longitudinais se tem verificado uma associação entre o tempo a ver televisão durante a infância e a presença de excesso de peso na adolescência ⁽¹⁵⁵⁾ e idade adulta ⁽⁴⁸⁸⁾, bem como com o risco de desenvolvimento da SM ⁽¹⁵⁰⁾. A relação estabelecida entre obesidade e televisão pode justificar-se pela substituição de tempo destinado à actividade física, pela ingestão de alimentos de maior densidade energética nesse período e pela diminuição do metabolismo basal ⁽¹⁵¹⁾.

Os hábitos de sono têm sido também descritos como associados à obesidade infantil ⁽⁴⁸⁹⁻⁴⁹²⁾, facto confirmado pelo significativo menor número de horas de sono nas crianças com excesso de peso. Esta relação paradoxal, visto dormir ser a actividade mais sedentária, é ainda pouco clara parecendo dever-se à ocorrência de alterações metabólicas

e hormonais, tais como um aumento da actividade simpática, diminuição da concentração de leptina, aumento dos níveis de cortisol e grelina, e diminuição da tolerância à glicose ^(492, 493). Verificou-se que o número de horas de sono constitui um factor preditivo do desenvolvimento da SM, o que se pode justificar com as modificações acima descritas. De acrescentar que a menor duração do sono pode promover uma diminuição da actividade física devido a maior cansaço, bem como pode fornecer uma oportunidade para a ingestão de alimentos de maior densidade energética no número superior de horas disponível ^(489, 490, 494). Assim, é recomendada uma duração do sono superior a 10 horas na prevenção da obesidade ⁽⁴⁸⁹⁾.

Da discussão desta dissertação podemos concluir as seguintes observações:

- 1) A prevalência de excesso de peso e obesidade verificada nas crianças entre os 7 e os 9 anos de idade residentes no concelho de Aveiro é semelhante à verificada em estudos com representatividade nacional, encontrando-se entre as mais elevadas da Europa.
- 2) As crianças com obesidade apresentaram uma prevalência elevada de SM, que se verificou estar ausente nas crianças com percentil de IMC inferior a 95. A obesidade abdominal e a hipertensão arterial destacaram-se como os principais critérios desta síndrome na nossa amostra.
- 3) As crianças com SM exibiram parâmetros antropométricos mais elevados do que as restantes, bem como modificações nos parâmetros bioquímicos, nomeadamente com perfil lipídico menos favorável, maior frequência de resistência à insulina e níveis de leptina mais elevados.

- 4) A concentração de insulina verificou-se como o único factor preditivo positivo da SM, enquanto a concentração de apolipoproteína A-I e o estágio pubertário se mostraram como factores preditivos negativos.
- 5) A avaliação da ingestão alimentar mostrou que esta se enquadra nas recomendações relativas à distribuição de macronutrientes para esta faixa etária, com excepção dos ácidos gordos saturados e dos açúcares totais que se apresentaram acima do recomendado, enquanto o consumo de fibra se situou abaixo das recomendações.
 - a) O consumo total de gordura constitui um factor preditivo positivo da SM, ao contrário dos ácidos gordos saturados que constituíram um factor preditivo negativo desta síndrome.
- 6) O tempo despendido na prática da actividade física diária verificou-se estar abaixo do recomendado, facto este mais marcante nas crianças do sexo feminino e nas crianças com SM.
 - a) Destacaram-se como factores preditivos negativos da SM o tempo despendido na actividade física extra-curricular e as horas de sono.
- 7) A intervenção dirigida à correcção dos hábitos alimentares e promoção da actividade física conduziu a resultados significativos, ainda que moderados, na perda ponderal e na regressão de alguns parâmetros associados à SM, contudo não se verificaram alterações significativas quer na ingestão alimentar quer na actividade física ao final de um ano de estudo.
 - a) As crianças inicialmente diagnosticadas com SM e que deixaram de cumprir com esses critérios no final do período de estudo, foram aquelas que apresentaram melhor resposta na regressão da sua obesidade, enquanto as crianças

diagnosticadas com esta síndrome no final do mesmo período aumentaram ou mantiveram o seu grau de obesidade.

- b) As crianças sujeitas ao tratamento em grupo, comparativamente com as sujeitas ao tratamento individual, apresentaram uma evolução mais favorável dos diversos parâmetros antropométricos e bioquímicos.

Para finalizar, é importante salientar que no actual ambiente *obesogénico* os componentes da SM são cada vez mais prevalentes em crianças, nomeadamente nas obesas. Assim, é razoável sugerir que a intervenção precoce destinada a controlar a obesidade possa reduzir o risco de desenvolvimento desta síndrome e de outras comorbilidades associadas, quer no presente, quer no futuro quando adultos. Esta intervenção deve assentar na modificação dos hábitos alimentares e no aumento da actividade física como principais medidas quer para a prevenção, quer para o tratamento da obesidade e suas complicações nas crianças, promovendo a aquisição de hábitos de vida saudáveis.

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