Introduction

Diabetes is a metabolic disorder characterized by hyperglycaemic resulting from insulin resistance, inadequate insulin secretion, or both. Type 1 diabetes is characterized by little or no endogenous insulin secretory capacity depending totally on exogenous insulin therapy for survival[1]. It accounts for 5 to 10% of all diagnosed cases of diabetes[1;2], being the predominant type in younger ages[3]. On type 2 diabetes, insulin secretion is normal or even excessive, but it is insufficient to compensate for insulin resistance. It is responsible for 90 to 95 % of all diagnosed cases of diabetes[4] and is usually associated with older age, obesity, familiar history of diabetes, history of gestational diabetes, impaired glucose metabolism, race/ethnicity[2;3;5], physical inactivity[6] and socioeconomic status[7;8]. The mean age of patients with type 2 diabetes is rising due to the large proportion of elderly people affected by the disease. In addition, since type 2 diabetes is increasing in the younger, it is expected that the serious complications of diabetes appears sooner in life[4], which will increase the economic burden of this disease in the society[3;8;9].

Estimates and projections of incidence and prevalence of diabetes require revision as new and better epidemiologic information becomes available. An increase in prevalence may be due to a true increase in diabetes prevalence, but also to a better ascertainment of cases, improved or early diagnosis, improved survival of patients or a combination of these factors. Nevertheless, it is expected that the worldwide prevalence of diabetes increases 35% until the year 2025 (from 4.0 in 1995 to 5.4% in 2025) and that the number of adults with diabetes will be increased by 122% (from 135 million in 1995 to 300 million in 2025)[5]. If no urgent action takes place, diabetes death will increase by more than 50% in the next 10 years[1].

Glycated haemoglobin (HbA1c) is the measure of glycaemia that correlates best with the risk of complications and has been used as the metabolic target for therapy[10]. However, although guidelines exist, there is a large discrepancy between treatment targets and clinical results; almost 73% of type 2 diabetic patients do not reach targets for HbA1c and 58% of the patients have blood pressure levels higher than the national guidelines of 140/85 mmHg[11]. This emphasises the need for more aggressive blood pressure treatment, especially if microalbuminuria and diabetic nephropathy are present, as 76-86% of patients in this group are treated with anti-hypertensive agents.

Much of the increased mortality and morbidity saw in diabetic patients' results from complications that develop with increasing duration of the disease. This is of special concern since by the time the symptoms of severe hyperglycaemia (polydepsia, polyuria, and fatigue) appear and patients are diagnosed with the disease, about 30%[8] have vascular complications already[12]. The EDC study[9] showed that after 20 years' duration of diabetes, the risk for complication increases two- to threefold.

Hypertension and ischemic heart disease are the major macrovascular complications of diabetes. Heart disease and stroke are responsible for more than 65% of deaths in people with diabetes[2]. Though, control of blood pressure is now considered to be as important as glycaemic control in type 2 patients. When both conditions are present, they should be vigorously treated, as reductions in micro- and macrovascular outcomes can be additive[4;8]. Results from the UKPDS shows that tight blood pressure control (<150mmHg), significantly reduce the risk of cardiovascular and microvascular outcomes, with risk reduction in the range of 24 to 56%[4].

Diabetes is the leading cause of new cases of blindness among adults aged 20-74 years with diabetic retinopathy causing 12,000 to 24,000 new cases of blindness each year[2]. Intensive drug regimens may prevent microvascular complications. In general, every percent point reduction in A1C blood test results (e.g. from 8.0 to 7.0%) reduces the risk of microvascular complications (eye, kidney, and nerve diseases) by 40%[2;4].

Nephropathic changes associated with microvascular disease develop in up to 30% of patients with type 1 diabetes and in up to 40% of those with type 2 disease. The most important approach to slowing the progression of diabetic nephropathy is an aggressive antihypertensive control[13]. Lowering blood pressure can reduce the decline in kidney function by 30 to 70%[2;9;13].

Insulin plays an important role in lipid metabolism. Deficient insulin action promotes hypertriglyceridaemia and a blood-lipid profile associated with an increased risk of atherosclerosis, and hence of macrovascular complications. Where drug therapy is needed, statins are the lipid-lowering drugs of choice for both secondary and primary prevention of cardiovascular events in type 2 diabetic patients. Reduction in relative risk with statin treatment has at least similar benefits on both diabetic and nondiabetic patients with CAD[14].

Type 2 diabetes mellitus is a complex and progressive disorder which is difficult to treat effectively in the long term. Selection of initial monotherapy is based on clinical and biochemical patients' assessments followed by safety considerations of medicines[15]. Recent studies have shown that if insulin is combined at early stages with sulphonylureas, glycaemic control does not deteriorate. Also, aggressive insulin treatment in type 2 diabetes has been found to improve metabolic prognosis in patients with ischemic heart disease[11].

Although controversial, pharmacological therapy for type 2 diabetes has been suggested to increase the risk for heart failure. A retrospective cohort study[16] with data from 25,690 patients registered in the U.K. General Practice Research Database between 1998-1999, showed a 4.75-fold higher risk for heart failure in patients with antidiabetic use than those without it. However, the risk did not persist beyond the first year after diagnosis of diabetes nor with type of antidiabetic used, which may indicate that the severity of diabetes or the preclinical duration of diabetes and the need for drug therapy, may be an explanation for heart failure in type 2 diabetic patients.

Material and Methods

Data on the prevalence of diabetes was obtained as part of an ongoing cross-sectional health and nutrition survey of adults living in Porto, Portugal, during 2001-2004. Recruitment and interview methods have been published elsewhere[17;18]. Trained interviewers collected data for 1,289 participants, using structured questionnaires. Data included information on demographic, social and medical characteristics. Education was recorded as completed years of schooling and divided in three broad categories: less then 5, 5-12 and more then 13 years. Socio-economic status was classified according to the registrar-general's (RG's)[19] occupational classification into five groups: I- Professional occupations, II- Intermediate occupations, III_N- Nonmanual skilled occupations and III_M- Manual skilled occupations, IV- Partly skilled occupations and V- Unskilled occupations. Two more groups were created with VI- Retired and Handicap and VII- Housewives and Unemployed. Socio-economic status was further simplified in three more board categories: Employed, Retired and Handicap, and Housewives and Unemployed.

Subjects who scored less then 24 in the MMSE were classified as inadequate to provide reliable information, leading to the exclusion of 49 individuals, remaining for the analysis 1,240 (762 women and 478 men) participants. Drug exposures were assessed by the question "Over the last 12 months have you been taken any medicine in a chronic continuous way?". All drugs were recorded by trade name and classified according to the Anatomical Therapeutic Chemical (ATC) classification system[20]. Diagnosed diseases by a physician were assessed by the question: "*Have your physician ever diagnosed …?*". For diabetes, questions about the time since diagnosis, type of diabetes and current and initial treatment were also asked. In eight (8) cases information about the type of diabetes was missing but it was possible to achieve through date since diagnose and therapy.

Statistical analysis was performed using the statistical software packages SPSS (version 12.0). The routines used were frequency distribution and bivariate associations by cross-tabulation using chi-squared (χ^2) test for categorical variables.

Results

During the study period 1,240 patients were interviewed and a prevalence of 5.6% (n=70) self-reported diabetes was found. Almost ninety percent (88.6%) were type 2 diabetics. Table 1 describes the characteristics of study participants by diabetes status. Diabetic patients were older and have low educational level (60% *vs* 31.2% with less than 4 completed years of school) than non-diabetic participants, with more subjects reporting being retired or handicapped (60% *vs* 25.8%) and less on current employment status (25.7% *vs* 53.8%). No statistical difference existed among sex. Diabetic patients were twice as likely to have hypertension (61.4% *vs* 31.6%) and dyslipidemia (52.9% *vs* 24.4%) than non-diabetics. Risk of hypertension was almost three times higher in diabetic women than in diabetic man (70.3% *vs* 29.7%) and only females had depression. No other significant difference was found between genders.

Distribution of reported drugs is presented on Table 2. Eighty (80) percent of diabetic patients were using antidiabetic drugs. Cardiovascular system drugs were being used by 67.1% of the patients. Drugs acting on the renin-angiotensin system (45.7%) were the most frequently reported followed by diuretics (18.6%) and calcium channel blockers (18.6%). Thirty (32.9%) percent of diabetic patients were using lipid modifying drugs and almost 16% where on psycholeptics.

Table 3 illustrates the currently and the initial therapy reported by diabetic patients. Initial treatment was essentially made of oral therapy. Fifty percent (51.4%) mentioned oral therapy only and almost 20% were on both oral therapy and diet. Seven patients (11.4%) referred that no treatment was given at the time. In 2 patients', insulin was the first therapy.

Fifty (50) percent of diabetics were currently on oral drugs and 7.1% on insulin therapy; 4.3% were on an association of oral and insulin therapy. Diet was mentioned in 28.6% of the cases.

Discussion

Besides glycaemic treatment goals considerations have to be made regarding concomitant conditions and its management. Ignoring such an issue, may lead to an ineffective control of diabetes-specific risk factors and may deteriorate patients' functioning, quality of life and mortality risk. This study aims to describe the diabetes reality on a Portuguese urban population.

In the former study, we found a prevalence of diabetes of 5.6%, which is a little lower than the prevalence found in the last National Health Survey, where diabetes was present in 6.5% of the population inquired[21]. It is worth mentioned that this survey represents the total of the resident Portuguese population, whereas our study was restricted to a confined area of an urban area in the north of Portugal. In agreement with the published literature[1;2] we found a prevalence of type 2 diabetes in 88.6% of the inquired and type 1 diabetes in 11.4% of the cases.

Sixty (60) percent of diabetic patients reported being retired or handicapped and only 25.7% said that they were currently employed. This is of special importance if we consider that almost 60% of these patients are on active working ages (35-65 years). This may be a consequence of diabetes complications and/or comorbidities which are known to cause higher disability in these patients as well as an increased economic burden for the society[3].

Hypertension is twice as common in diabetic patients that on nondiabetic population, and is both associated with macrovascular complications and microvascular disease, specially with nephropathy[12]. More than fifty-percent of our diabetics were diagnosed with hypertension while only 20% of the non-diabetics reported having it. This number was also found in the Portuguese National Health Survey[21]. Drug treatment thresholds and treatment goals are lower in diabetic that of nondiabetic patients. Cardiovascular outcomes are improved by renin-angiotensin system blockers and can increase fasting glucose by as much as 28mg/dl and HbA1c by as much as 1%[12]. In our study, renin-angiotensin inhibitors were being used by more than 40% of the cases, followed by diuretics and β-blockers. Differences in response to specific therapeutic agents may be different among men and women. In women, ACE inhibitors and β-blockers use in the treatment of asymptomatic left ventricular systolic dysfunction, seems that doesn't confer a mortality benefit as it does in men[12]. However, no such difference was observed in our study.

Primary prevention of cardiovascular disease with lipid-lowering drugs is an important part in the management of high-risk patients. Improved control of cholesterol or blood lipids can reduce cardiovascular complications by 20-50%[2;8]. However, despite the evidence that patients with diabetes and CAD are at high risk for cardiovascular events, diabetic patients seems 17% less likely to receive lipid-lowering drugs that nondiabetic patients[14]. Although more than 60% of

our diabetics reported dyslipidemia less than 35% were on lipid lowering drugs, which is much lower than previous studies[22].

Although diabetic patients usually have double the odds of depression of the general population[7;23], the inverse was found in our study. Also, only women have mentioned having depression which can be a biased information. In addition, psycholeptic drugs were consumed by both sexes, with no significant difference found among them. Depression may influence communication with health care providers, self-management behaviours and metabolic control. It may affect the ability to maintain medication vigilance, good diet, and other lifestyle factors, such as smoking and exercise, which have an additive effect[23] on the overall quality of life of these patients. Nevertheless, since some psychopharmacologic medications (e.g. tricyclic antidepressants) may impair glycemic control, careful monitoring of glycemia should be taken while on this drugs[12].

Dietary and weight loss interventions are usually the first line of diabetes management. Nevertheless, only a minority of our patients reported such a non-pharmacological treatment. This can be due to low importance rates of physical activity by study subjects.

Treatment that lowers glucose blood levels also reduces the risk of diabetic retinopathy, nephropathy, and neuropathy. This is particularly notorious in type 1 diabetes where the risk reduction as already proven to range between 35 to 75%[4]. In general, as disease progresses, the majority of patients need multiple therapies to control hyperglycaemia and associated risk factors of hypertension and hyperlipidaemia, as none of the oral pharmacological monotherapies are capable to maintain intensive treatment goals[4;15]. In our study, only 4% of diabetic patients were on dual therapy of insulin and oral agents, which is similar to other Portuguese study[24], but much lower than others[25]. In the U.S., among adults with diagnosed diabetes, 16% took insulin only, 12% took both insulin and oral medications, 57% take oral medication only, and 15% do not take either medication[2]. These discrepancies between studies may be a consequence of patients' beliefs, drug use assessment or time since diagnosis. It is known that a higher proportion of patients remain on dual therapy of metformin plus sulfonylurea even after HbA1c≥8.0%, which suggests that there are important barriers to start insulin or a more complex regimen of multiple oral agents when treatment goals are not achieved[26]. Since good glycemic control is essential in preventing diabetes complications, educational programs in order to start earlier and more aggressive treatment to glycemic targets is essential.

Like all other chronic diseases, adherence to antidiabetics and its implication on glycaemic goals, is of concern. Several studies show that the overall rate of adherence to antidiabetics was 36-93% and that monotherapy regimens had higher adherence than polytherapy regimens (49 *vs* 36%)[27]. It should have been important to assess dose changes or account for patient's adherence to prescribed drug therapy.

References

1. World Health Organization. Fact sheet n.º 312, September. 2006.

2. Centers for Disease Control and Prevention. National diabetes fact sheet: general information and national estimates on diabetes in the United States, 2005. Atlanta, GA U. S. Department of Health and Human Services Centers for Disease Control and Prevention. 2005.

3. Gasby R. Epidemiology of diabetes. *Adv.Drug Deliv.Rev.* 2002;**54**:1165-72.

4. Genuth S, Eastman R, Kahn R, Klein R, Lachin J, Lebovitz H *et al*. Implications of the United kingdom prospective diabetes study. *Diabetes Care* 2003;**26 Suppl 1**:S28-S32.

5. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. *Diabetes Care* 1998;**21**:1414-31.

6. Petrella RJ, Lattanzio CN, Demeray A, Varallo V, Blore R. Can adoption of regular exercise later in life prevent metabolic risk for cardiovascular disease? *Diabetes Care* 2005;**28**:694-701.

7. Brown AF, Ettner SL, Piette J, Weinberger M, Gregg E, Shapiro MF *et al*. Socioeconomic position and health among persons with diabetes mellitus: a conceptual framework and review of the literature. *Epidemiol.Rev.* 2004;**26**:63-77.

8. Passa P. Diabetes trends in Europe. *Diabetes Metab Res.Rev.* 2002;**18 Suppl 3**:S3-S8.

9. Pambianco G, Costacou T, Ellis D, Becker DJ, Klein R, Orchard TJ. The 30-year natural history of type 1 diabetes complications: the Pittsburgh Epidemiology of Diabetes Complications Study experience. *Diabetes* 2006;**55**:1463-9.

10. World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: report of a WHO/IDF consultation. World Health Organization. 2006.

11. Eliasson B, Cederholm J, Nilsson P, Gudbjornsdottir S. The gap between guidelines and reality: Type 2 diabetes in a National Diabetes Register 1996-2003. *Diabet.Med.* 2005;**22**:1420-6.

12. Legato MJ, Gelzer A, Goland R, Ebner SA, Rajan S, Villagra V *et al*. Gender-specific care of the patient with diabetes: review and recommendations. *Gend.Med.* 2006;**3**:131-58.

13. Nosadini R,.Tonolo G. Cardiovascular and renal protection in type 2 diabetes mellitus: the role of calcium channel blockers. *J.Am.Soc.Nephrol.* 2002;**13 Suppl 3**:S216-S223.

14. Massing MW, Foley KA, Sueta CA, Chowdhury M, Biggs DP, Alexander CM *et al*. Trends in lipid management among patients with coronary artery disease: has diabetes received the attention it deserves? *Diabetes Care* 2003;**26**:991-7.

15. Krentz AJ,.Bailey CJ. Oral antidiabetic agents: current role in type 2 diabetes mellitus. *Drugs* 2005;**65**:385-411.

16. Maru S, Koch GG, Stender M, Clark D, Gibowski L, Petri H *et al*. Antidiabetic drugs and heart failure risk in patients with type 2 diabetes in the U.K. primary care setting. *Diabetes Care* 2005;**28**:20-6.

17. Ramos E, Lopes C, Barros H. Investigating the effect of nonparticipation using a population-based case-control study on myocardial infarction. *Ann Epidemiol.* 2004;**14**:437-41.

18. Santos AC,.Barros H. Smoking patterns in a community sample of Portuguese adults, 1999-2000. *Prev.Med* 2004;**38**:114-9.

19. John M.Last. A Dictionary of Epidemiology. Oxford University Press, 2001.

20. WHO Collaborating Centre for Drug Statistics Methodology, Oslo, Norway. Guidelines for ATC classification and DDD assignment. 2001.

21. Statistics Portugal. 4th National Health Survey. 2007.

22. Grant RW, Devita NG, Singer DE, Meigs JB. Polypharmacy and medication adherence in patients with type 2 diabetes. *Diabetes Care* 2003;**26**:1408-12.

23. Goldney RD, Phillips PJ, Fisher LJ, Wilson DH. Diabetes, depression, and quality of life: a population study. *Diabetes Care* 2004;**27**:1066-70.

24. Duarte-Ramos F,.Cabrita J. Using a pharmaco-epidemiological approach to estimate diabetes type 2 prevalence in Portugal. *Pharmacoepidemiol.Drug Saf* 2006;**15**:269-74.

25. Gudbjornsdottir S, Cederholm J, Nilsson PM, Eliasson B. The National Diabetes Register in Sweden: an implementation of the St. Vincent Declaration for Quality Improvement in Diabetes Care. *Diabetes Care* 2003;**26**:1270-6.

26. Cook MN, Girman CJ, Stein PP, Alexander CM, Holman RR. Glycemic control continues to deteriorate after sulfonylureas are added to metformin among patients with type 2 diabetes. *Diabetes Care* 2005;**28**:995-1000.

27. Cramer JA. A systematic review of adherence with medications for diabetes. *Diabetes Care* 2004;**27**:1218-24.

Table 1. Descriptive statistics of study participants (n=1,240)

	Diabetic nr (%)	*Non diabetic nr (%)*
Total	70 (100)	1,170 (100)
Sex		
Female	41 (58.6)	721 (61.6)
Male	29 (41.4)	449 (38.4)
*Age (years)**		
≤ 34	0 (0)	249 (21.3)
35-65	44 (62.9)	702 (60.0)
≥ 66	26 (37.1)	219 (18.7)
*Education (years)**		
≤4	42 (60.0)	365 (31.2)
5-12	21 (30.0)	445 (38.0)
≥13	7 (10.0)	360 (30.8)
*Socio-economic status**		
Employed	18 (25.7)	629 (53.8)
Retired or handicap	42 (60.0)	302 (25.8)
Housewife or unemployed	10 (14.3)	239 (20.4)
Disease Conditions		
Circulatory system	47 (67.1)	418 (35.7)
Myocardial infraction*	5 (7.1)	23 (2.0)
Angina*	6 (8.6)	42 (3.6)
Ischemic heart disease	2 (2.9)	25 (2.1)
Cardiac arrhythmia	5 (7.1)	101 (8.6)
Hypertension*	37 (52.9)	286 (24.4)
Endocrine, Nutrition and Metabolism	70 (100)	378 (32.3)
Dyslipidemia*	43 (61.4)	370 (31.6)
Mental and behavioural	7 (4.9)	136 (11.6)
Depression	7 (4.9)	136 (11.6)

*p<0.0001 for differences between diabetic and non diabetic patients

Table 2. Prevalence of drug use among diabetic patients (n=70)

ATC Group	*Nr (%)*
Alimentary tract and Metabolism	*57 (81.4)*
a02 – drugs for acid-related disorders	6 (8.6)
a10 – drugs used in diabetes	56 (80)
Cardiovascular system	*50 (71.4)*
c01 - cardiac therapy	8 (11.4)
c03 – diuretics	13 (18.6)
c04 – peripheral vasodilators	6 (8.6)
c05 - vasoprotectives	6 (8.6)
c07 - beta blocking agents	6 (8.6)
c08 - calcium channel blockers	13 (18.6)
c09 - agents acting on the rennin-angiotensin system	32 (45.7)
c10 – lipid modifying agents	23 (32.9)
Nervous system	*18 (25.7)*
n02 - analgesics	5 (7.1)
n05 - psycholeptics	11 (15.7)
n06 – psychoanaleptics	7 (10.0)

Table 3. Current and initial antidiabetic treatment

Treatment	*Current therapy nr (%)*	*Initial therapy nr (%)*
None	6 (8.6)	8 (11.4)
Diet	20 (28.6)	7 (10.0)
Physical activity	-	-
Diet and physical activity	1 (1.4)	-
Oral therapy	35 (50.0)	36 (51.4)
Insulin	5 (7.1)	2 (2.9)
Oral therapy and insulin	3 (4.3)	2 (2.9)
Diet and oral therapy	-	13 (18.6)
Diet, physical activity and oral therapy	-	2 (2.9)