Abstract

Nowadays, it is recognized that intrauterine and early postnatal growth play a role in the development of metabolic and cardiovascular diseases. The first 1 000 days from conception are claimed to be the growth period with major impact on later disease risk. However, nothing is known about the role of growth in the period of newborn weight loss – the first 2 to 3 days of life – on later disease risk. This is a period of huge adaptations to extra uterine conditions, including the adaptation of energy intake and expenditure. So, in the present thesis, it was hypothesized that newborn weight change (NWC) during this period may affect the development of metabolic and cardiovascular disease in childhood. The effect of early growth on metabolic and cardiovascular diseases in childhood is less consistently shown than in adulthood. The prevalence of precursors of such diseases, as well as the prevalence of unhealthy dietary intake, have been increasing among children and are now at an epidemic level, which boosts the dimension of the problem.

Programming and tracking are two mechanisms by which early growth can impact on later health. These two mechanisms should be explored using a life course approach, ideally using a birth cohort, where participants are followed from birth to adulthood. In order to study the determinants of NWC during the very first days of life and its effect on child health outcomes and dietary intake, data from a Portuguese birth cohort – Generation XXI – whose participants were evaluated at birth, and at 4 and 7 years of age, was used.

The first specific objective was to estimate weight change during the first 96 hours of life and its reference intervals and time (in hours) of nadir (Paper I). A percentile chart for NWC up to 96 hours of life was constructed, where it can be observed that, after birth, newborns began to lose weight and at 6, 12, 24, 36, and 48 hours of life the mean weight ratio [weight/ birth weight (BW)] and 10th–90th percentiles were 0.978 (0.968-0.988), 0.968 (0.953-0.983), 0.951 (0.928-0.974), 0.939 (0.909-0.969), and 0.933 (0.898-0.969), respectively. The curve inflection point (nadir) was achieved at 52.3 hours of life, corresponding to a weight ratio of 0.933, i.e. 6.7% loss of BW, and a loss of 218g. After 52.3 hours of life, newborns started to gain weight.

After having described the NWC, the objective was to identify its determinants (Papers II and III). In paper II, it was found that an excessive weight loss was positively associated with maternal age ≥40 years (OR=3.32, 95% CI 1.19, 9.25), maternal education (OR=1.04, 95% CI 1.00, 1.09), caesarean delivery (OR=2.42, 95% CI 1.12, 5.23), and phototherapy-treated jaundice (OR=1.69, 95% CI 1.00, 2.87). On the opposite, an insufficient weight loss was positively associated with low BW (OR=2.68, 95% CI 1.13, 6.33), and formula/mixed feeding (OR=1.74, 95% CI 1.13, 2.66). In paper III, the role of umbilical cord leptin, adiponectin and resistin on NWC, as well as on intrauterine growth, was explored. It was found that low leptin levels were associated with lower BW (β=-137.3g, 95% CI -268.6g, -6.1g) and high leptin levels were associated with higher BW (β=276.3g 95% CI 145.8g, 406.8g) and higher NWC (β=1.10%, 95% CI 0.29%, 1.92%).

Afterwards, the effect of NWC, as well as of BW, on childhood health outcomes was explored (Papers IV and V). The specific objectives were to evaluate the association of both BW and NWC with body composition and metabolic risk (MR) measures, namely
body mass, fat mass, and fat-free mass indexes, waist circumference, waist-to-height ratio, glucose, high density lipoprotein cholesterol (HDL-C), triglycerides, and systolic and diastolic blood pressure, assessed at age 4 and 7; and to explore whether the potential effect of BW and NWC on these measures at age 7 was direct or mediated by the same measure at age 4. It was concluded that NWC had no effect on body composition or on MR during childhood, but BW was an important factor for its development. BW had a direct effect on all body composition measures and on HDL-C at age 4. For each 100g increase in BW, there was an increase of 0.048 (95% CI 0.029, 0.068) on body mass index (BMI), 0.033 (95% CI 0.014, 0.051) on fat mass index, 0.022 (95% CI 0.004, 0.040) on fat-free mass index, 0.049 (95% CI 0.031, 0.066) on waist circumference, and 0.022 (95% CI 0.004, 0.040) on waist-to-height ratio z-scores, and a decrease of 0.044 (95% CI -0.074, -0.014) on HDL-C z-score. Regarding the effects at age 7, the higher the BW, the higher the BMI, fat mass index, fat-free mass index, and waist circumference and the lower the HDL-C, which means that there was a total effect of BW on the previous variables. However, for body composition measures, the total effect was explained by the indirect effect, which means that the effect of BW on these variables at age 7 was mediated by the same body composition measure at age 4. Conversely, regarding HDL-C, BW exerts a total, indirect and direct effect at age 7. A high tracking was found between ages 4 and 7 for all the variables studied.

One of the mechanisms by which early growth plays a role on later health could be by programming of appetite. Accordingly, the following specific objective was to evaluate the associations of BW, NWC and weight trajectories during childhood with dietary intake at age 4 (Paper VI). Children with higher BW were less frequently in the dietary pattern rich in high energy dense food (EDF) and dairy products (OR=0.94, 95% CI 0.89, 0.98, for 100g increase in BW) and children with higher NWC had lower odds of ingesting fruit ≥3/day (OR=0.93, 95% CI 0.87, 0.99, for 1% increase in NWC). Children that were heavier during all childhood had higher odds of being in the dietary pattern rich in EDF and dairy products (OR=1.90, 95% CI 1.04, 3.47) and lower odds of ingesting vegetable soup ≥2/day (OR=0.56, 95% CI 0.34, 0.91) while children that suffered catch-up growth in the first year of life had higher odds of ingesting dairy products ≥3/day (OR=3.76, 95% CI 1.31, 10.80).

In conclusion, the present thesis provided a NWC percentile chart, which will be particularly important for newborns of older mothers that were born by caesarean delivery and that had the need of phototherapy treatment for jaundice and, also, for low BW newborns that were fed formula, because these two clusters of characteristics are associated with excessive and insufficient weight loss, respectively. Regarding the long-term effects of NWC, apparently NWC had no effect on body composition or MR in childhood, but some effect on dietary intake at age 4 was found, which could have some implications for later disease risk. On the other hand, intrauterine growth seems to exert long-term effects on body composition, MR and dietary intake. In a public health perspective, the present thesis provided a useful tool for health professionals and parents to monitor the newborn growth, which is important since it has implications in the neonatal period, but also demonstrated that NWC will not have major effects on later metabolic and cardiovascular disease. Instead, focus should be in the intrauterine growth and, specifically, concerning high BW.