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ORIGINAL ARTICLE

Neonatal anthropometrics and correlation to childhood obesity—data from the Danish Children's Obesity Clinic

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Abstract Recent evidence has demonstrated the prenatal initiation of childhood obesity as epidemiological studies and animal studies have illustrated the effect of the intrauterine milieu for subsequent development of childhood obesity. This study investigates the relationship between severe childhood obesity and the preceding in utero conditions expressed by birth weight and birth length, birth-weight-for-gestational-age and neonatal ponderal index in a Danish cohort of 1,171 severely obese children (median age 11.48 years, range 3.13 to 17.98 years) with a mean body mass index-standard derivation score (BMI-SDS) of +2.96 (range +1.65 to +9.72) treated in our national referral centre. In a linear general regression model adjusted for socioeconomic status and breastfeeding duration, a significant linear correlation between BMI-SDS at time of enrolment and both birth weight (p, 3.8×10^{-6}) and birth length (p, 6.1×10^{-4}), birth-weight-for-gestational-age (p, 4.3×10^{-7}) and the neonatal ponderal index (p, 0.02) was demonstrated. Duration of breastfeeding, however, was not found to be significant for either the BMI-SDS/BW or the BMI-SDS/BL correlation. *Conclusion*: These results indicate that the prenatal period can be considered as a potential window of opportunity for prevention of childhood overweight and obesity and anthropological measurements may in theory be used to help identify neonates at high risk for developing childhood obesity.

Keywords Birth weight · Childhood obesity · Neonatal ponderal index · DOHaD (developmental origins of health and disease)

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Introduction

Childhood obesity is a growing public health problem that affects a considerable part of the world's population across gender and ethnic groups [38]. Obese children and adolescents are more likely to become obese adults [2, 11]. Consequently, the prevalence of obesity-related complications is expected to increase in adults in the future [8, 11]. Childhood obesity is accompanied by a wide array of complications comprising among others hypertension, hypercholesterolaemia, non-alcoholic fatty liver disease and type 2 diabetes mellitus [11, 13] yielding significant implications for future health and disease including a shortening in expected life span.

The aetiology of childhood obesity is complex and multifactorial, and has among others been linked to genetic [3] and metabolic factors [18], early feeding practices [18], activity level of the infant [19], socioeconomic disadvantage [36], temperament of the child [4], maternal depression and neglect [6], and prenatal factors. Intrauterine life is a time of rapid growth, cellular replication and differentiation, and functional maturation of organ systems. These processes are very sensitive to alterations in the intrauterine milieu [33] and it is becoming increasingly apparent that the in utero environment in which a foetus develops may have long-term effects on subsequent health and survival [10].

Accordingly, increasing circumstantial evidence for the prenatal initiation of childhood obesity has emerged [32]. Several epidemiological studies have shown relationship between birth weight (BW) and body mass index (BMI) in childhood and adult life [27, 28, 34, 38]. This association has been reported as linear [22, 30] and linear moving to U-shaped with increasing age [26, 29]. Also, in direct experimental animal studies, prenatal overfeeding cause permanent changes in the appetite regulatory system and lipocytes and induce modifications in chromatin structure, associated with increased triglycerides and body weight in foetuses and juveniles [1, 5, 21, 23, 24].

Birth weight is a frequently used indicator of in utero conditions [7]. However, birth weight depends largely on the duration of the pregnancy and should consequently be related to gestational age (GA) to assess the relative birth weight. Also, the relative neonatal thinness or fatness expresses as weight divided by length raised to the power of 3 and referred to as ponderal index (PI) may more accurately indicate the relative intrauterine nutritional excess or deprivation than birth weight alone [37]. As an example, neonatal PI rather than birth weight is associated to insulin resistance [16] and reduced glucose tolerance [17] in childhood.

The present study aims to further explore the relationship between childhood obesity and the preceding in utero conditions expressed by BW, body length (BL), birth-weight-for-gestational-age (BWfGA) and neonatal PI in a Danish cohort of severely obese children and adolescents treated at a national referral centre.

Material and methods

Subjects The study population were obese children treated at the Children's Obesity Clinic, Copenhagen University Hospital Holbaek, Denmark. This is a national referral centre using The Children's Obesity Clinics Treatment Protocol [12]. Inclusion criteria at enrolment were childhood obesity defined as a BMI above the 95th percentile for sex and age according to the Danish BMI charts [25] and age between 3 and 18 years. All participants and/or parents signed informed consent. The study was approved by the Danish Data Protection Agency and Scientific Ethics Committee (SJ-104) and registered at Clinical Trials NCT00928473.

Measurements Height and weight were measured at the time of enrolment by skilled research assistants yielding baseline height, weight, and BMI. BMI-standard derivation score (SDS) was calculated according to the Danish BMI charts [25]. Additional data on gender, age, birth weight and length, GA, breastfeeding, and socioeconomic status was secured through a family interview and hospital records. Thinness/fatness at birth was calculated as PI (weight/length^3). BWfGA was estimated by calculating the expected birth-weight-for-term using previously published data for a Scandinavian birth cohort [20]. Birth-weight-for-gestational-age was defined as small-for-GA (SGA) (below −2SDS), appropriate-for-GA (AGA) or heavy-for-GA (HGA) (above +2SD). The degree of baseline obesity is expressed in SDS in order to adjust for age-related variation in reference intervals. The 95th percentile of BMI is set at 1.64 SDS and the 99th percentile at 2.33 SDS yielding the following groups: obesity (SDS 1.64 to 2.32) and severe obesity (SDS ≥2.33).

Statistical analyses Data were analysed by generalised linear model (GLM) for correlation between BMI-SDS at inclusion and BW, BL, BWfGA and PI at birth. Furthermore, adjustments for breastfeeding and socioeconomic status were performed to examine independent association of these variables. Data were logarithmical transformed when appropriate. In order to evaluate for linear or non-linear regression relationship between BW, BWfGA, PI and subsequent degree of childhood obesity at enrolment, data were grouped in deciles and best-fitted linear and non-linear curves were calculated and compared (Fig. 1). Nonparametric Wilcoxon rank test were used to relate each parameter to baseline BMI. Statistical modelling was performed using the R software version 2.10.2.

Results

The study included 1,171 children found to be obese (n=117) or severely obese (n=1,054). Baseline characteristics are given in Table 1.

In a GLM adjusted for socioeconomic status and breastfeeding duration, a significant correlation between BMI-SDS at time of enrolment and both birth weight (p, 7.8×10^{-6}) (Fig. 1a) and birth length (p, 6.1×10^{-4}) was found. Socioeconomic status was significantly correlated to both the BMI-SDS/BW correlation (p, 1.1×10^{-3}) and the BMI-SDS/BL correlation (p, 1.2×10^{-3}). Duration of breastfeeding, however, was not found to be significant for either the BMI-SDS/BW correlation (p, 0.4) or the BMI-SDS/BL correlation (p, 0.5).

Equally, we found that BMI-SDS at time of enrolment correlates to both the BWfGA (p, 4.3×10^{-7}) and the PI index (p, 0.020) when analysed in a GLM adjusted for socioeconomic status and breastfeeding duration. Once again, the socioeconomic status was significantly correlated to the BMI-SDS/BWfGA and BMI-SDS/PI correlation (p, 5.8×10^{-4} and p, 50×10^{-3}, respectively), whereas the duration of breastfeeding was not (p, 0.39 and p, 0.46, respectively). Further adjustment for duration of any breastfeeding

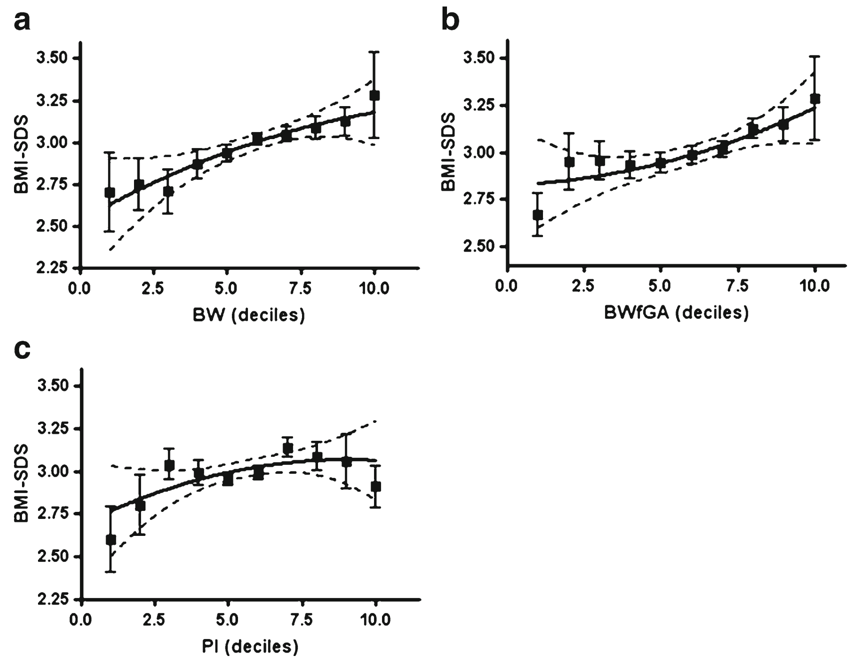

Fig. 1 Best-fitted curves of BMI-SDS as a function of BW (**a**), BWfGA (**b**) and PI (**c**). *Dashed lines* are 95 % intervals. See text for details

up to 9 months of age in analyses including birth weight or neonatal ponderal index did not alter the results (data not shown).

Pre- or post-mature birth did not predict childhood obesity as no association between duration of pregnancy and degree of childhood obesity was demonstrated (p, 0.46). In nonparametric Wilcoxon rank test, BMI-SDS was found to associate with BW, BL, PI, BWfGA and breastfeeding ($p<0.001$), however, not with socioeconomic status (p, 0.79).Comparing the SGA, AGA and HGA groups did not demonstrate an increased risk of end of the BWfGA spectrum (Kruskal–Wallis, p, 0.236).

To asses for non-linear associations, the best-fitted U-shaped, i.e. second-order polynomials, curves for BMI-SDS as a function of deciles of either BW, BWfGA or PI were calculated (Fig. 1). The curves were not significantly different from linear models (p, 0.40; p, 0.64 and p, 0.36, respectively); thus, no statistical evidence for non-linear association was found.

Discussion

Our findings demonstrate that neonatal anthropometrics relate to subsequent childhood obesity, and consequently, these findings indicate that intrauterine environment plays an important role in the later development of obesity.

Birth weight was found to be a predictor of severe childhood obesity in this study. Our data do not support the previously reported U-shaped relationship between birth weight and childhood obesity but rather support a linear association. More importantly, both birth-weight-for-gestational-age and PI were found to be correlated to the degree of childhood obesity when adjusted for socioeconomic

Table 1 Baseline characteristics of subjects at infancy and at inclusion. Figures are medians and ranges

	All patients (n=1,171)	Boys (n=545)	Girls (n=626)
Infancy			
GA (week + days)	40+3 [24+3; 44+0]	40+3 [26+4; 44+0]	40+3 [24+3; 44+0]
BW (g)	3,550 [740; 5,904]	3,600 [740; 5,904]*	3,540 [831; 5,210]
BL (cm)	52 [32–62]	52 [32; 60]*	52 [35; 62]
BWfGA (SDS)	−0.15 [−6.95; +3.05]	−0.22 [−6.95; +2.91]*	−0.70 [−5.94; +3.06]
PI (kg/m^3)	2.50 [1.29; 5.63]	2.48 [1.29; 3.62]*	2.52 [1.43; 5.63]
At the inclusion			
Age (years)	11.48 [3.13; 17.98]	11.72 [3.22; 17.98]	11.29 [3.13; 17.91]
BMI-SDS	2.96 [1.65; 9.72]	3.21 [1.69; 9.72]*	2.79 [1.65; 5.76]
Social class	3 [1; 5]	3 [1; 5]	3 [1; 5]
Breastfeeding (months)	4.0 [0; 60]	4.0 [0; 60]	4.0 [0; 60]

Values are medians and range

GA gestational age, *BW* birth weight, *BL* birth length, *BWfGA* BW for GA, *PI* ponderal index, *BMI-SDS* body mass index-standard derivation score

*$p<0.05$, statistically different from girls (Wilcoxon–Mann–Whitney test)

status and breastfeeding duration. Interestingly, birth weight was found to be a better predictor of subsequent childhood obesity than PI. This is in concordance with earlier finding by Haggarty et al. [9] indicating that birth weight is a better anthropometric measurement for body fatness in term neonates than PI.

Intrauterine life is characterised by rapid growth, cellular replication and differentiation and functional maturation of organ systems and these processes are very sensitive to alterations of the nutritional milieu [32]. Substrate excess has profound effect on the foetal–placental–maternal hormonal and metabolic interactions. As an example, high birth weight can indicate excessive conditions in utero and is often seen in children born by diabetic mothers [14, 15]. It has been hypothesised that a foetus exposed to gestational diabetes in utero is more prone to foetal hyperglycaemia and hyperinsulinaemia. Hyperinsulinaemia has been proposed to have anabolic properties leading to increased BW, insulin resistance and subsequent lipocyte proliferation thereby initiating an increased risk of excess weight gain when subsequently exposed to an obesogenic environment [15].

The data on the association between neonatal anthropological measurement and subsequent childhood obesity presented in this retrospective observational cohort study are derived from severely obese Danish children treated at our national referral centre. The strength of the present study is the number of included children and the accuracy of clinical data. Methodological studies have demonstrated that overweight individuals tend to underestimate their weight relative to their height [35] making the many interview or questionnaire-based studies on overweight subjects prone to bias. Our data can be considered valid in terms of two major potential biases in obesity studies on this subject: the degree of childhood obesity (i.e. height and weight) and birth weight and birth length. The duration of breast feeding and the socioeconomic status of the families were self-reported and are subject to well-known potential bias. However, it is less likely that any systematised bias has influenced the data.

Treating childhood obesity and the associated complications is an increasing public health problem. It is apparent that public attention towards prevention could help slowing and maybe even revert the increasing prevalence; however, this is partly hampered by a not fully understood aetiology. Our results adds to the growing evidence for the association between childhood obesity and the intrauterine nutritional environment influencing neonatal anthropological measurements, exemplified by birth weight, birth-weight-for-gestational-age and neonatal PI.

National data from Denmark indicate a yearly increase in BW of ~5 g from 1973 to 2003 [31] and this trend may to some extent underlie the increasing childhood obesity incidence. The prenatal period can be considered as a potential window of opportunity for prevention of childhood overweight and obesity and anthropometrics could in theory be used to help identify neonates at high risk for developing childhood obesity. However, further knowledge about aetiopathogenic mechanisms underlying the association is warranted before any future primary prenatal prevention strategies for childhood obesity and obesity-related diseases can be developed.

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Conflict of interest The authors declare that they have no personal financial relationship with the sponsoring organisations or other potential conflicts of interest.

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