CHAPITRE 4 : ASSOCIATION ENTRE UNE EXPOSITION PRÉNATALE AU DIABÈTE GESTATIONNEL ET LA COMPOSITION CORPORELLE ET LA DISTRIBUTION DU TISSU ADIPEUX DES ENFANTS

Association of Prenatal Exposure to Gestational Diabetes with Offspring Body Composition and Regional Body Fat Distribution

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RÉSUMÉ

Le but de cette étude était de comparer la composition corporelle et la distribution du tissu adipeux de 56 enfants ayant été exposés (GDM+) et de 30 enfants n'ayant pas été exposés (GDM-) au DG *in utero* et d'étudier l'association entre ces variables et le profil glycémique des enfants. La grandeur, le poids et la circonférence de taille ont été mesurés. La composition corporelle du corps entier et de certaines régions spécifiques a été mesurée par DEXA. Les concentrations plasmatiques d'insuline et de glucose à jeun ainsi que de HbA1C ont été mesurées et l'indice HOMA-IR a été calculé. La circonférence de la taille, le pourcentage de gras, la masse grasse androïde, le pourcentage de gras androïde et le rapport entre les pourcentages de gras androïde et gynoïde étaient plus élevés chez les enfants GDM+. Les mesures d'adiposité de ces derniers étaient également positivement corrélées à leur HbA1C.

Association of prenatal exposure to gestational diabetes with offspring body composition and regional body fat distribution

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These results have been presented to the American Diabetes Association 77th scientific sessions (June 9-13, 2017, San Diego, California).

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Although body mass index (BMI) is frequently used to assess children adiposity, other anthropometric measures may be better indicators of cardiometabolic risk.
- Few studies investigated others adiposity measures in children exposed to gestational diabetes.

WHAT THIS STUDY ADDS

- In the current study, adiposity of children exposed to gestational diabetes is evaluated in a more complete and precise manner with assessment of body composition and fat distribution by dual-energy X-ray absorptiometry.
- This study also investigates the association of those adiposity measures with children glycaemic and insulin profile.

SUMMARY

The aim of this cohort study was to compare body composition and regional body fat distribution between children exposed (GDM+) or unexposed (GDM−) *in utero* to gestational diabetes mellitus (GDM) and to investigate the association with the glycaemic and the insulin profile. Data from 56 GDM+ and 30 GDM− were analysed. Height, weight and waist circumference were measured. Total and regional body composition was measured by dual-energy X-ray absorptiometry. Insulin, glucose and HbA1c were obtained from a fasting plasma sample, and the HOMA-IR index was calculated. ANOVA was performed to compare adiposity measures between GDM+ and GDM−. Associations between the glycaemic and insulin profile and adiposity measures were studied using partial Pearson correlations. Mean age was 6.6 ± 2.3 years. Waist circumference, fat mass percentage, android fat mass, android fat mass percentage and android-to-gynoid fat mass ratio were higher among GDM+, and lean mass percentage was lower ($P < 0.05$). Among GDM+ children, body mass index (BMI) z score, waist circumference, fat mass percentage, android fat mass percentage and android-to-gynoid fat mass ratio were all positively correlated with HbA1C ($r = 0.32–0.43$, $P < 0.05$). Prenatal exposure to GDM is associated with increased total and abdominal adiposity. This increased adiposity observed among GDM+ children is associated with an altered glycaemic profile. This study is registered in the Clinical Trials.gov registry (NCT01340924).

INTRODUCTION

Gestational diabetes mellitus (GDM) is a state of glucose intolerance that is first diagnosed during pregnancy (1). In addition to neonatal complications, such as macrosomia and hypoglycaemia at birth (2), growing evidence suggests that GDM is associated with long-term health risks in children exposed *in utero* (3). Results from a multi-ethnic case–control study comparing youth with and without a diagnosis of type 2 diabetes demonstrated an association between intrauterine exposure to maternal diabetes (including both GDM and pregestational diabetes) and type 2 diabetes in youth (4). In a recent multinational study, prenatal exposure to GDM was positively associated with obesity at 9–11 years of age (5). Accordingly, results from a cohort study of 7355 mothers and their children reported an increased risk of overweight and obesity in children exposed to GDM (6).

Although body mass index (BMI) is frequently used to assess children's adiposity, other anthropometric measures may be better indicators of cardiometabolic risk (7). In order to improve our understanding of the relationship between GDM exposure and long-term health risk, there is a need for more studies investigating the adiposity of children born from a GDM pregnancy in a more precise manner (5, 8). As body composition and fat distribution may be predictive of cardiometabolic disease, their consideration would be of primary interest (7). Therefore, our study aims to compare body composition and regional body fat distribution between children who have been exposed or not exposed to GDM *in utero* and to investigate the association of adiposity measures with the glycaemic and insulin profile.

MATERIALS AND METHODS

Study population

Subjects were children aged between 3 and 12 years who participated in an ongoing cohort study that aims to evaluate the impact of GDM exposure during pregnancy and the influence of prenatal and postnatal lifestyle factors on offspring metabolic alterations predicting future risk of type 2 diabetes and obesity in childhood. This study started in 2012 and is taking place at the Institute of Nutrition and Functional Foods (INAF) at Laval University (Quebec City, Canada). Mothers who had a pregnancy complicated or not complicated by GDM between 2003 and 2013 were recruited, as well as their children. They were recruited through invitation letters sent to women with a diagnosis of GDM according to medical records of

the two major hospitals with a neonatal care unit in the metropolitan area of Quebec City (*Hôpital Saint-François d'Assise, Centre Hospitalier de l'Université Laval – CHUL*) or according to administrative data from the provincial health plan registry (*Régie de l'assurance maladie du Québec*) (9). Recruitment was also conducted by emails sent to Laval University community as well as posts on Facebook and healthcare websites. Children born from a pregnancy complicated by type 1 or type 2 diabetes were not eligible. The GDM status during pregnancy was obtained from medical records (53%) or from the provincial health plan registry (*Régie de l'assurance maladie du Québec*) databanks (39%). For the remaining participants (8%), GDM status was selfreported. Outcomes were measured during a 1 h visit that took place at the INAF clinical unit. Written consent was obtained from all participants. This project was approved by the Laval University Ethics Committee (2011–196-A-4 R-3) and the *Centre hospitalier universitaire de Québec - Université Laval* Ethics Committee (2015–2031) and is registered in the Clinical Trials.gov registry (NCT01340924).

Outcomes

Adiposity measures

Children's height was measured to the nearest millimetre with a stadiometer. Weight was measured to the nearest 0.1 kg with a calibrated balance (Tanita BC-418, Tanita Corporation of America Inc., Arlington Heights, IL, USA), and BMI was calculated (kg m−2). Weight and BMI *z* scores were obtained from the WHO AnthroPlus software (version 1.0.4, World Health Organization, Geneva, Switzerland). As weight-for-age cannot distinguish between height and body mass during the pubertal growth spurt, weight *z* score was available for children under 10 years only (10). Waist circumference was measured twice to the nearest millimetre at the umbilical level (11). The average of the two measures was considered for the analysis. Total body composition was measured with a dual-energy X-ray absorptiometry scanner (DXA, GE Lunar Prodigy Bone Densitometer, GE Healthcare Lunar, Madison, WI, USA) by trained professionals using the Lunar enCORE software version 13.40. Thereafter, the first step was to exclude subjects with blurred images. To do so, two trained professionals (MK and JP) independently examined all scans to identify subjects with blurred image (i.e., when a deformation of body outlines was observed, probably caused by children movements during the exam). Disagreements were resolved by a third investigator (JR), and seven subjects were finally excluded. All scans were subsequently examined by a unique trained

professional (MK) to ensure that lines automatically positioned by the software were correctly aligned with specific anatomic points and to manually adjust these lines when needed. This procedure ensures that all body parts, including the android and gynoid regions, were correctly framed in the regions of interest. As such, the head line and the caudal limit of the android region were exactly placed at the base of the chin and at the top of the iliac crest, respectively. The upper limit of the android region was then automatically set to a height corresponding to 20% of the distance between the caudal limit and the head line. The upper limit of the gynoid region was automatically set below the android region, at a distance of 1.5 times the height of the android region. The caudal limit of the gynoid region was automatically set to a distance of 2 times the height of the android region. Thereafter, all scans were transferred to the Lunar enCORE software version 14.1 to create the report of all body fat measures because this version includes the CoreScan option, which enables the estimation of visceral fat. Total fat mass, lean mass and their proportion were obtained. Fat mass and fat mass percentage in the android and the gynoid regions were assessed, and the android-to-gynoid fat mass ratio was calculated (android fat mass percentage/gynoid fat mass percentage). Furthermore, we obtained the visceral fat mass and the visceral fat volume in the android region, a method that has been previously validated in the paediatric population (11).

Glycaemic and insulin profile

Blood samples were collected after a 12-h fasting period. Plasma glucose was measured enzymatically by hexokinase (12), and plasma insulin was measured by electrochemiluminescence (Roche Diagnostics, Indianapolis, IN, USA). The glycated haemoglobin (HbA1c) level was measured using the Cobas Integra 800 analyser standardized to the National Glycated Haemoglobin Standardization Program (Integra Inc., Roche, Switzerland). The homeostasis model assessment for insulin resistance (HOMA-IR) index was calculated (fasting insulinemia (μU L−1)*fasting glycaemia (mmol L−1)/22.5) (13).

Other measurements

Information regarding pregnancy, breastfeeding and sociodemographic characteristics was obtained from the mother using self-administered questionnaires. Birth weight *z* score was calculated according to a population-based Canadian reference of birth weight for gestational

age (14). Pubertal status was assessed by a questionnaire based on the Marshall and Tanner method (15, 16). The questionnaire was filled by children or their mother, according to their age and their preference. Children who were at least at Tanner stage 2 for genital/breast development or for pubic hair development were considered to have reached puberty onset (17). Information about lifestyle habits was also collected. A first 24-h food recall was administered, in person, using the Automated Multiple Pass Method. The recall was administered to the mother if the children were younger than 10 years and to the children if they were older. In each case, both the mother and the child were present to add information, when needed. A second 24-h food recall was administered to the mother, by phone, within 7–10 days after the visit to the testing unit. Both recalls were analysed with the Nutrition Data System for Research software (NDSR version 2011, Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN, USA), and the average caloric intake was obtained. Mother's current waist circumference was measured twice, to the nearest millimetre, at the midpoint between the iliac crest and the lateral lowest limb, and the average of the two measures was calculated (18). Mother's fat mass percentage was obtained by bioelectrical impedance analysis (Tanita BC-418). Height, weight and calculation of BMI were obtained by following the same method used for children.

Statistical analyses

Participants' characteristics were compared between children exposed (GDM+) and unexposed (GDM−) to GDM *in utero* using Chi-square tests for categorical variables and student t-tests for continuous variables. ANOVA was used to compare adiposity measures and glycaemic and insulin profile between groups with adjustments for age and gender. The HPGENSELECT procedure, which uses maximum likelihood techniques and a stepwise selection method, was used to determine for which additional covariables it was relevant to adjust among the following: pubertal onset status (yes/no), breastfeeding (yes/no), total duration of breastfeeding (months), birth weight *z* score, daily energy intake, annual family income and the mother's current BMI. Subsequently, pubertal status, birth weight *z* score and the mother's current BMI were added in the model for adiposity measures variables. Variables were transformed according to Box-Cox analysis, when needed, to meet basic assumptions of the model. Partial Pearson correlation coefficients were calculated to study the association between adiposity measures and the fasting glycaemic and insulin profile

among GDM+ children, with adjustments for age and gender. Participants who had missing data for a variable were excluded from specific analyses that required this variable. Statistical significance was fixed to $P < 0.05$, and the SAS software (version 9.4, SAS Institute Inc.; Cary, NC, USA) was used for analyses.

RESULTS

In total, 161 children participated in the study, but 86 of them (56 GDM+ children and 30 GDM−) were included in these analyses as they had complete measures of body composition and fat distribution. Participants' characteristics according to GDM exposure status are presented in Table 1. GDM+ children tended to be younger ($P = 0.091$). Birth weight was similar between groups. Although gestational age at birth was lower among GDM+ children ($P = 0.024$), birth weight for gestational age *z* score was also similar. Energy intake and the proportion of breastfed children tended to be lower among GDM+ children ($P = 0.077$ and 0.090, respectively). Furthermore, current BMI, waist circumference and fat mass percentage were higher among mothers of GDM+ children (P = 0.015, 0.003 and 0.011, respectively).

Associations between GDM exposure status and the various adiposity measures are shown in Table 2. Weight *z* score, BMI *z* score and total lean mass were similar between groups ($P = 0.508$, 0.224 and 0.959, respectively). Nevertheless, GDM+ children tended to have increased total fat mass ($P = 0.098$), and they had a significantly higher fat mass percentage and lower lean mass percentage compared to GDM− children ($P = 0.022$ and 0.025, respectively). GDM+ children also presented a higher total and relative amount of fat in the android region ($P = 0.048$ and 0.025, respectively), a larger waist circumference ($P = 0.034$) and a higher android-to-gynoid fat mass ratio ($P = 0.019$). The total and relative amount of fat in the gynoid region tended to be higher among GDM+ children, although this difference did not reach statistical significance ($P = 0.062$ and 0.051, respectively). The estimated volume of visceral adipose tissue in the android region was not associated with GDM exposure status. Adjustment for birth weight *z* score did not substantially change these results. On the other hand, additional adjustment for mother's BMI attenuated the associations in a more important manner as none of the outcomes remained significantly higher. Adjustment for the mother's waist circumference or fat mass percentage attenuated the associations in a similar manner (data not shown). Regarding the fasting glycaemic and

insulin profile, none of the four biochemical markers was associated with GDM exposure status (Table 3).

As shown in Table 4, among GDM+ children, BMI *z* score, waist circumference, fat mass percentage, android fat mass percentage and android-to-gynoid fat mass ratio were all positively correlated with HbA1C (r = 0.32–0.43, $P < 0.05$). In addition, BMI *z* score and waist circumference tended to be positively correlated with fasting glycaemia (r = 0.26 and 0.25, respectively, $P < 0.10$). None of the adiposity measures were correlated with fasting insulinemia and HOMA-IR.

DISCUSSION

In this cohort study, being born from a mother with a pregnancy complicated by GDM was associated with alterations in fat mass proportion and distribution. Indeed, *in utero* exposure to GDM was associated with a higher fat mass proportion and with indicators of abdominal fat deposition. Moreover, these alterations were associated with a less favourable glycaemic profile.

Results from this study showed that GDM+ children presented increased fat mass percentage compared to GDM− children. This is in agreement with results from a multinational cohort study conducted by Zhao *et al.*, where the body fat *z* score was also higher among children aged 9–11 years who have been exposed to GDM *in utero* compared to children who have not been exposed (5). However, this study also reported an increased BMI *z* score among children exposed to GDM, which was not observed in the current study (5). In contrast, Wright *et al.* observed an association between GDM exposure and children's adiposity measured by the sum of skinfolds, but not by BMI *z* score at 3 years old (19). Moreover, in a study including overweight and normal-weight children who had been exposed or not to GDM, a main effect of GDM exposure status on fat mass percentage was observed irrespective of weight status (20). Those results combined with results obtained in the current study suggest that there might be body composition alterations in GDM+ children even in the absence of apparent increased weight. BMI is a less precise marker of adiposity compared to fat mass, suggesting that subtle changes in body composition may not be reflected by measured weight (7, 19). Considering that our cohort includes a majority of young children

(57% are 6 years old or younger), we can hypothesize that current alterations in fat mass are subtle and that alterations in BMI may not be fully apparent before a certain age (8, 19).

We also observed that GDM+ offspring presented higher measures of waist circumference, android fat mass, android fat mass percentage and android-to-gynoid fat mass ratio compared to GDM− children. Other studies reported increased waist circumference among children exposed to GDM or pre-existing diabetes (5, 8). In addition, 82 children aged 6–13 years exposed to maternal GDM from the retrospective EPOCH cohort study presented an increased subscapular-to-triceps skinfold thickness ratio, another indicator of central fat deposition, and a larger quantity of subcutaneous fat in the abdominal area, measured by magnetic resonance imaging (8). Chandler-Laney also reported an increased trunk fat mass measured by DXA among 24 children aged 5–10 years who were exposed to maternal GDM (20). These results are consistent with results obtained in the current study and suggest that children born from a pregnancy complicated by GDM are predisposed to a more centralized fat pattern, which may influence the risk of cardiovascular disease (7). Similar to the EPOCH study, we did not observe a significant increased quantity of visceral adipose tissue in the abdominal area (8). Considering that the majority of children's abdominal fat is subcutaneous and that visceral fat deposition generally increases with age, we can hypothesize that it was too early to detect increased visceral adipose tissue (8, 21, 22).

Mechanisms explaining the association between GDM exposure and alterations in fat proportion and distribution are not fully understood. Existing, albeit limited, sibling studies suggest that the association between maternal GDM or pregestational diabetes and offspring's long-term health cannot be entirely explained by genetic inheritance (23, 24). It has been proposed that maternal hyperglycaemia creates an altered *in utero* environment, which leads to foetal hyperinsulinemia (2). This may result in increased foetal growth or, more specifically, in increased fat mass at birth that could persist in childhood (2, 25–27). However, in the current study and others, the association between GDM exposure and adiposity measures remained significant after adjustment for birth weight, suggesting that the association observed cannot completely be explained by foetal overgrowth (8). One possibility is that birth weight is probably not the most precise indicator of foetal overgrowth (25). Indeed, Catalano *et al.* observed that normal weight neonates of GDM pregnancies still

present increased fat mass (27). Another explanation is that the altered *in utero* environment associated with GDM may predispose to later body composition and fat distribution alterations through epigenetic mechanisms (2, 28). In the present report, as well as in other studies (5, 8), results were attenuated when adjustments for maternal BMI or other adiposity measures were performed. Indeed, obesity is a risk factor for GDM and is associated with insulin resistance (1, 25). This physiological state, in addition to, contributing to hyperglycaemia, is also associated with increased free fatty acids and triglyceride levels, which may possibly promote foetal growth (25). Thus, maternal adiposity may contribute to the altered *in utero* environment to which the foetus is exposed in GDM pregnancies (25).

This study has some limitations. Reliable information about mothers' blood glucose levels during pregnancy was unavailable. It has been previously shown that outcomes in children born from diabetic pregnancies may be dependent on the degree of hyperglycaemia to which they were exposed *in utero* (29). Consequently, the degree of GDM severity and the glycaemic control of the recruited mothers may have modulated the association that we have observed. For the same reason, an accurate value for mothers' pre-pregnancy BMI was not available, and current BMI was used in the present study. Nevertheless, other authors noted that current BMI strongly correlates with pre-pregnancy BMI, suggesting that it is a reliable estimate (5, 30). Finally, family income was relatively high in our cohort, which may limit the generalizability of our results. This study also has many strengths. Among those, various adiposity measures of body composition and body fat distribution were investigated, while most studies reported results on children's BMI only. Moreover, adiposity measures were obtained with a DXA scan, which is considered a precise and accurate method in the paediatric population (31). Finally, only exposure to maternal GDM (not other types of diabetes) was investigated, and GDM status was medically confirmed for the majority of the participants.

This study suggests that despite a normal BMI, children born from a pregnancy complicated by GDM may present alterations in body fat proportion and distribution that are associated with a less favourable glycaemic profile. These results highlight the importance of expanding anthropometric evaluation in this population to other measurements than BMI alone, both in

research and clinical settings. Future research is needed to identify how to prevent these alterations during the prenatal period or during infancy and childhood.

CONFLICT OF INTEREST STATEMENT

Dr. Tchernof reports grants from Johnson & Johnson Medical Companies, outside the submitted work. Other authors declared no conflicts of interest.

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AUTHOR CONTRIBUTION

IM, SJW, AT and JR participated in the conception and the design of the study. MK and JP made a substantial contribution to data acquisition. MK, JP and JR participated in data analysis and interpretation. The first draft of the manuscript was written by MK, and all authors revised it critically for important intellectual content and approved the final version. JR is responsible of the integrity of the study.

Table 1. Participants' characteristics according to GDM exposure status

	GDM+ n=56	**GDM-** n=30	***p***
Age (years)	6.3 ± 2.4	7.0 ± 2.1	0.091
3-6 years	35 (62.5)	14 (46.7)	0.313
7-9 years	14 (25.0)	12 (40.0)	
10-12 years	7 (12.5)	4 (13.3)	
Gender			
Boys	29 (51.8)	14 (46.7)	0.651
Pubertal status[a]			
Puberty onset	12 (22.2)	4 (13.3)	0.320
Gestational age[b]	38.8 ± 1.4	39.5 ± 1.2	**0.024**
Birth weight (g)[c]	3346 ± 442	3267 ± 558	0.479
Birth weight > 4000 g	1 (1.9)	2 (6.9)	0.284
Birth weight *z* score[d]	0.03 ± 0.85	-0.39 ± 1.18	0.102
Birth order[a]			
1st	26 (48.1)	17 (56.7)	0.722
2nd	18 (33.3)	9 (30.0)	
≥3rd	10 (18.5)	4 (13.3)	
Breastfed children[b]	46 (83.6)	29 (96.7)	0.090
Energy intake (kcal/day)	1611 ± 339	1787 ± 473	0.077
Maternal characteristics			
GDM treatment			
Diet[e]	51 (94.4)	-	-
Insulin[f]	33 (62.3)		
Other medication[f]	1 (1.9)		
Annual family income ($ CA)[g]			
0 – 39 999	8 (18.2)	6 (25.0)	0.768
40 000 – 79 999	10 (22.7)	7 (29.2)	
80 000 – 99 999	9 (20.4)	3 (12.5)	
≥ 100 000	17 (38.6)	8 (33.3)	
Current BMI (kg/m^2)	27.2 ± 7.2	23.6 ± 4.4	**0.015**
Current waist circumference (cm)	89.4 ± 16.8	79.9 ± 8.9	**0.003**
Current fat mass percentage	33.8 ± 8.9	28.8 ± 7.7	**0.011**

Table 2. Association between *in utero* GDM exposure and adiposity measures

	GDM+ n=56	**GDM-** n=30	**Cohen's d**	***P*[1]**	***P*[2]**	***P*[3]**
Weight (kg)	25.2 ± 10.9	24.9 ± 6.9	0.03	0.395	0.807	0.629
Weight *z* score[a]	0.27 ± 0.86	0.08 ± 0.71	0.24	0.508	0.771	0.727
BMI (kg/m^2)	16.6 ± 2.9	16.0 ± 1.7	0.25	0.109	0.151	0.618
BMI *z* score	0.33 ± 1.02	0.03 ± 0.81	0.33	0.224	0.376	0.918
Waist circumference (cm)	56.8 ± 8.1	55.3 ± 5.8	0.21	**0.034**	**0.040**	0.255
Fat mass (g)	7182 ± 5273	6205 ± 2323	0.49	0.098	0.157	0.997
Fat mass percentage	27.0 ± 6.4	24.7 ± 4.0	0.43	**0.022**	**0.023**	0.381
Lean mass (g)	16 988 ± 5762	17 707 ± 4676	0.14	0.959	0.649	0.411
Lean mass percentage	69.3 ± 6.2	71.5 ± 3.9	0.42	**0.025**	**0.025**	0.401
Android fat mass (g)	355.8 ± 365.8	257.4 ± 152.2	0.35	**0.048**	0.055	0.571
Android fat mass percentage	20.3 ± 9.4	16.7 ± 6.0	0.46	**0.025**	**0.023**	0.359
Gynoid fat mass (g)	1157 ± 890	1005 ± 435	0.22	0.062	0.101	0.806
Gynoid fat mass percentage	32.1 ± 7.1	29.5 ± 4.8	0.43	0.051	**0.048**	0.519
Android-to-gynoid fat mass ratio	0.61 ± 0.17	0.56 ± 0.13	0.33	**0.019**	**0.019**	0.251
Android visceral adipose tissue mass (g)	82.6 ± 131.8	53.7 ± 42.8	0.29	0.191	0.224	0.599
Android visceral adipose tissue volume (cm^3)	87.6 ± 139.6	56.9 ± 45.4	0.30	0.193	0.228	0.605

Table 3. Association between *in utero* GDM exposure and glycaemic and insulin profile

	GDM+ n=52	**GDM-** n=26	**Cohen's d**	***P*[1]**
Glycaemia[a]	5.09 ± 0.40	5.07 ± 0.40	0.05	0.528
Insulinemia[a]	59.2 ± 25.9	55.2 ± 17.4	0.18	0.204
HbA_{1c}	0.053 ± 0.003	0.052 ± 0.002	0.39	0.107
HOMA-IR[b]	1.97 ± 1.02	1.80 ± 0.66	0.20	0.155

Table 4. Association between adiposity measures and fasting glycaemic and insulin profile among GDM+ children

	Glycaemia[a]	Insulinemia[a]	HbA_{1c}[a]	HOMA-IR[a]
BMI *z* score	0.26*	0.14	**0.37****	0.17
Waist circumference	0.25*	0.19	**0.37****	0.21
Fat mass percentage	0.17	0.21	**0.43****	0.22
Android fat mass percentage	0.21	0.08	**0.41****	0.11
Android-to-gynoid fat mass ratio	0.22	0.01	**0.32****	0.05

Table Legends

Table 1: Results are expressed as raw means ± standard deviations or n (%). *P* values in bold are below 0.05. GDM: gestational diabetes mellitus, GDM+: exposed to gestational diabetes *in utero*, GDM-: unexposed to gestational diabetes *in utero*, [a]n=84 [b]n=85 [c]n=82 [d]n=81 [e]n=54 [f]n=53 [g]n=68

Table 2: Results are expressed as raw means ± standard deviations. *P* values in bold are below 0.05. BMI: body mass index, GDM: gestational diabetes mellitus, GDM+: exposed to gestational diabetes *in utero*, GDM-: unexposed to gestational diabetes *in utero* [1]Adjusted for age and sex (except for *z* scores) and puberty onset (yes/no) [2]Adjusted for age and sex (except for *z* scores), puberty onset (yes/no) and birthweight *z* score [3]Adjusted for age and sex (except for *z* scores) puberty onset (yes/no), birthweight *z* score and actual maternal BMI, [a]n=75

Table 3: Results are expressed as raw means ± standard deviations. GDM+: exposed to gestational diabetes *in utero*, GDM-: unexposed to gestational diabetes *in utero,* HOMA-IR: Homeostasis model assessment for insulin resistance, [1]Adjusted for age and sex, [a]n=25 for GDM- children, [b]n=24 for GDM- children

Table 4: Results are expressed as partial Pearson's correlation coefficients (r) with adjustments for age and sex. Coefficients in bold represent a significant correlation ($P < 0.05$). BMI: body mass index, GDM+: exposed to gestational diabetes *in utero*, HbA_{1c}: glycated hemoglobin, HOMA-IR: Homeostasis model assessment for insulin resistance, [a]n=52, [*]p<0.10, [**]p<0.05