Maternal body mass index, excess gestational weight gain and diabetes are positively associated with neonatal adiposity in the Pregnancy and Neonatal Diabetes Outcomes in Remote Australia (PANDORA) study.

Running title: Neonatal adiposity in the PANDORA study

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Abstract

Background

In-utero exposures likely influence the onset and severity of obesity in youth. With increasing rates of type 2 diabetes mellitus (T2DM) and maternal adiposity in pregnancy globally, it is important to assess the impact of these factors on neonatal adipose measures.

Objectives

To evaluate the contribution of maternal ethnicity, body mass index (BMI), gestational weight gain and hyperglycemia to neonatal adiposity.

Methods

PANDORA is a longitudinal cohort study of Australian mother and neonate pairs. In this analysis, Indigenous (n=519) and Europid (n=358) women were included, of whom 644 had hyperglycemia (type 2 diabetes (T2DM), diabetes in pregnancy (DIP) or gestational diabetes (GDM).Associations between maternal ethnicity, hyperglycemia, BMI and gestational weight gain and the neonatal outcomes of: length, head circumference, sum of skinfolds, total body fat and percentage body fat were examined. Models were adjusted for maternal age, smoking status, parity, education, neonatal gender and gestational age.

Results

Among those with hyperglycemia in pregnancy, Indigenous women had a higher proportion of T2DM and DIP (36%, 13%) compared to Europid women (4%, 3%). In multivariate analysis, maternal T2DM (compared to no hyperglycaemia), BMI during pregnancy, and excess compared to appropriate gestational weight gain, were significantly associated with greater neonatal measures. DIP was associated with greater sum of skinfolds, total body fat and percentage body fat. Indigenous ethnicity was associated with greater sum of skinfolds.

Conclusions

Maternal BMI, excess gestational weight gain and hyperglycemia operated as independent factors influencing neonatal adiposity. Interventions addressing these factors are needed to reduce neonatal adiposity.

Introduction

Indigenous populations, including Indigenous Australians, have very high rates and earlier onset of obesity and type 2 diabetes mellitus (T2DM) [1, 2]. Complex factors, including a history of rapid nutritional change, social disruption and poverty have potentially contributed to this. However, early life exposures (including *in-utero*) may influence the risk and timing of young people developing obesity and T2DM [3-5] and may represent an opportunity for intervention.

Neonatal anthropometric measures are sensitive tools to evaluate *in-utero* development [6], and may be influenced by maternal adiposity, placental health, *in-utero* exposure to excess fuels and genetic factors [7-10]. Ethnic-specific differences for neonatal body composition specifically for fat mass and fat free mass have been reported. Singh *et al.* [10] reported that African American infants had lower birth weights than Caucasian neonates, and that differences were due to lower lean body mass rather than reduced adiposity. South Asian neonates were found to have similar skinfold measures despite being significantly lighter than Caucasian neonates [11]. Paley *et al.* reported lower body fat percent in Caucasian neonates compared to African American, Hispanic and Asian neonates, with differences stronger in male neonates [12].

Indigenous Australian adults have higher fat mass for a given body mass index (BMI) compared to non-Indigenous Australians [13], similar to other populations that have experienced rapid nutritional change [14]. At birth, Indigenous Australian neonates are at risk of being small for gestational age [15, 16], due to maternal smoking and nutritional deficiency, but are also at risk of large for gestational age, due to high rates of hyperglycaemia in pregnancy[17]. However, prior to establishment of this cohort, detailed evaluation of body composition, beyond that of birth weight, in relation to maternal adiposity

and hyperglycaemia had not been undertaken in Indigenous compared to non-Indigenous Australian neonates.

In the context of hyperglycemia in pregnancy, studies have shown that neonates born to mothers with gestational diabetes mellitus (GDM) have significantly greater adiposity than neonates born to mothers with normal glucose tolerance [6, 18]. However, there is a lack of information regarding neonatal adiposity in those born to mothers with T2DM [19]. Assessing the impact of T2DM is important as prevailing hyperglycemia is more severe. The risk for earlier onset obesity and T2DM in offspring is potentially increased if maternal T2DM is associated with greater neonatal adiposity. As T2DM is a significant contributor to cardiovascular disease and renal disease, particularly in indigenous populations, earlier onset T2DM may have critical consequences[20].This study aims to evaluate maternal predictors of neonatal body composition and adiposity in Indigenous and Europid offspring of mothers with and without hyperglycemia in pregnancy, as part of the Pregnancy and Neonatal Diabetes Outcomes in Remote Australia (PANDORA) study, which was conducted in the Northern Territory (NT)..

Methods

1. Data Collection

Women with hyperglycemia in pregnancy in the NT, Australia, are referred to the NT Diabetes in Pregnancy Clinical Register by a health professional. Women on this register who consented to be involved in further research were then invited to participate in the PANDORA study. From November 2011 to February 2017, PANDORA collected antenatal, peripartum and demographic information on 1170 neonates and mother pairs as previously described [21]. A convenience sample of women without hyperglycemia in pregnancy (with a normal oral glucose tolerance test (OGTT)) (n=235) were recruited through antenatal clinics specifically for the PANDORA study, and were representative of women who birthed in the

NT in terms of age and geographic location, compared to the NT Midwife Data Collection database (a population-based census of all NT births) in 2013. For this analysis we excluded neonates: (i) born to mothers with type 1 diabetes (n=19), (ii) from twin pregnancies (n=17), (iii) of intrauterine fetal deaths or stillbirth (n=7), and (iv) who were not Aboriginal or Europid (n=250).

2. Maternal measures

Maternal glycaemic status was determined from plasma glucose obtained during a 75g OGTT, HbA_{1c} performed in pregnancy, or from medical records to confirm previously diagnosed T2DM. Women were classified as having no hyperglycemia in pregnancy (OGTT results below the diagnostic criteria for GDM at the time of testing and no prior diagnosis of T2DM diabetes) or hyperglycemia in pregnancy. All women in the group without hyperglycemia in pregnancy had an OGTT. Median gestation at the time of the OGTT for those with no hyperglycemia in pregnancy was 28 weeks. Hyperglycemia in pregnancy was then further classified into GDM, diabetes in pregnancy (DIP) or T2DM. GDM was determined if a woman developed hyperglycemia during pregnancy, based on results of an OGTT, consistent with criteria used during recruitment: (i) the 1999 Australian Diabetes in Pregnancy Society guidelines and (ii) World Health Organization and International Association of the Diabetes and Pregnancy Study Groups guidelines [22]. The median gestation at the time of the OGTT in women with GDM was 27 weeks. DIP was determined if OGTT or HbA_{1c} results were consistent with a diagnosis of T2DM, (fasting glucose ≥7.0 mmol/L or 2 hour glucose ≥11.1 mmol/L, HbA_{1c} ≥6.5%), but not diagnosed prior to pregnancy. The median gestation at the time of the OGTT for those with DIP was 27 weeks. However 10% (n=17) had an OGTT prior to 20 weeks. Furthermore, another 19% (n=11) were diagnosed with DIP by HbA1c and the median gestation for these women at diagnosis

was 18 weeks. All women with DIP received intra-partum diabetes management from the time of the diagnosis of DIP, as if they had pre-existing T2DM. T2DM was determined if OGTT or HbA_{1c} (see above criteria) were diagnostic prior to pregnancy and confirmed on medical record.

In addition, the following maternal variables were also assessed: maternal ethnicity (Indigenous or Europid), location of residence (urban versus regional/remote), nulliparity, body mass index (BMI- from first measured weight and height adjusted for gestation), gestational weight gain (calculated as the difference between third trimester weight closest to delivery and gestation-adjusted first measured weight adjusted for BMI and then classified according to the Institute of Medicine guidelines as excess, within or below recommendations [23]), any smoking in pregnancy (yes/no), education attainment (completion of 12 years versus <12 years of school).

3. Neonatal outcomes and measures

Neonatal outcomes included: length, head circumference, sum of three skinfolds (flank, subscapular and triceps) (mm), total body fat (grams), percentage body fat, fat free mass (grams), mid-upper arm circumference, abdominal circumference and calf circumference (cm). Total body fat was determined from the fat mass calculation outlined below. Fat free mass was determined by subtraction of total body fat from birth weight.

Anthropometric measures were conducted by a team of clinicians within 72 hours of birth, except for 184 neonates (21%) that were measured between 72 and 120 hours after birth. Mean inter-observer coefficient of variations were 0.1% for weight, 0.1% for length, 0.6% for head circumference, 3.9% for triceps skinfold, 1.3% subscapular skinfold and 4.9% for flank skinfold, which were comparable to those reported in the Hyperglycemia Adverse Pregnancy Outcomes (HAPO) study [18]. All measurements were made on the left side, except for n=8

(0.9%), and for most measurements, the mean of two measures was used. If two measures differed by more than a pre-specified amount (0.5cm for length, head circumference and abdominal circumference, 0.5mm for skinfold measures), a third measure was taken. The mean of the two closest measures was taken when two of the three measures differed by less than the pre-specified amount, or the mean of all three measures was used when differences were greater than the pre-specified amount. Length (cm) was measured from the crown of the head (against a headboard) to a footboard held against the plantar surface of the feet, on a standardized length board (Seca, Hamburg, Germany). Skinfold measures using Holtain calipers (Holtain Ltd, Crosswell, Pembrokeshire, UK) were taken: (i) triceps - midway between the acromion and olecranon, (ii) subscapular - lower angle of the scapula, and (iii) flank - mid-axillary line above crest of the ilium. In a subset of neonates born to mothers with hyperglycemia in pregnancy, the following measures were added: (i) thigh skinfold (n=194) - measured midway between the crural fold and the large semilunar crease above the patella with the leg extended, and (ii) circumference measures (n=199) of the abdomen at the level of the umbilicus, and of the limbs at the midpoint of the upper and lower extremities. The sum of skinfolds outcome was determined from the triceps, subscapular and flank fold in all neonates.

Body fat mass was determined according to the following validated equation: Fat mass = 1000 (0.39055 (birth weight (grams)/1000) + 0.0453 (flank skinfold (mm) - 0.03237 (length (cm)) + 0.54657 [18, 24-26]. Four neonates had negative fat mass according to the equation, and a fat mass of zero grams was substituted. Percentage body fat was determined by calculating total body fat as a percentage of birth weight.

Neonatal ethnicity was determined by maternal ethnicity (84% of neonates born to an Indigenous Australian mother reported paternal Indigenous ethnicity).

4. Statistical Methods

Statistical analysis was performed using Stata version 14 (Stata Corporation, College Station, TX). Differences in maternal and neonatal characteristics by maternal glycemia in pregnancy status (hyperglycemia in pregnancy vs. no hyperglycemia in pregnancy) and ethnicity (Indigenous vs. Europid Australians) were assessed. Continuous variables were analysed using two-unpaired sample t-tests for normally distributed data and the Wilcoxon rank sum test for non-normally distributed data. Pearson's χ squared test was used for categorical variables. Linear regression models were developed to assess whether maternal hyperglycemia, BMI, gestational weight gain and ethnicity were significant predictors of each neonatal outcome. Covariates included in each multivariate models were maternal age, parity, smoking, gestational age and sex of the infant. Additional variables were selected for inclusion in the models if they demonstrated an association on bivariate analysis ($p < 0.1$).

Sensitivity analyses were performed with respect to timing of neonatal measures (<72 hrs and 72-120hrs) and gestational weight gain. As a number of women did not have weight measured in the third trimester, (n=130), multivariable models were repeated by replacing maternal BMI with gestational weight gain.

Results

Maternal characteristics according to maternal glycemia and ethnicity

Indigenous women were younger than Europid women, but Indigenous women with hyperglycemia in pregnancy were older than Indigenous women without hyperglycemia in pregnancy (Table 1). Among Indigenous women, 51% had GDM, 36% had T2DM and 13% had DIP, whereas, for Europid women most hyperglycemia in pregnancy was accounted for by GDM. Indigenous women, irrespective of hyperglycemia in pregnancy status, were more

likely to smoke in pregnancy, were less likely to live in an urban centre and were less likely to have achieved 12 years of education than Europid women. Among Indigenous women, those with hyperglycemia in pregnancy had lower rates of nulliparity compared to those without hyperglycemia in pregnancy. Among Indigenous and Europid women, BMI was higher in those with hyperglycemia in pregnancy compared to those without hyperglycemia in pregnancy. However, those with hyperglycemia in pregnancy had lower gestational weight gain than those without hyperglycemia in pregnancy.

Neonatal outcomes according to maternal glycemia and ethnicity

On unadjusted comparisons, among those born to mothers with hyperglycemia in pregnancy, Indigenous neonates were born a week earlier (38 vs 39 weeks) and were 5mm shorter than those born to Europid mothers, however, there were no ethnic differences with regards to birth weight or circumference anthropometrics, except for calf circumference which was smaller in Indigenous neonates. Indigenous neonates had greater individual and summed skinfold measures than Europid neonates (Table 2).

Among those born to mothers without hyperglycemia in pregnancy, anthropometric patterns were similar for Indigenous and Europid neonates except that Indigenous neonates had a significantly smaller head circumference, and greater flank skinfold measures. Other skin fold measures were also greater for Indigenous compared to Europid neonates, but differences did not reach statistical significance (Table 2).

Multivariable results for the neonatal outcomes of length, head circumference, sum of skinfolds, total body fat, percentage body fat, and fat free mass are presented in Figure 1. Maternal BMI (Figure 1) was associated with an increase in all outcomes. Compared to no hyperglycemia in pregnancy, maternal T2DM and DIP, but not GDM, tended to be associated with increased neonatal outcomes. Maternal BMI and DIP or T2DM operated independently, and were positively associated with all neonatal outcomes, independent of maternal age,

neonatal gender, gestational age, smoking, nulliparity. With respect to percentage body fat, maternal BMI was positively associated with percentage body fat (0.36% per 2kg/m^2). DIP (vs no hyperglycemia) was significantly positively associated with neonatal percentage body fat (1.83%) as was T2DM (vs no hyperglycemia)(1.35%). The associations with DIP and T2DM remained when adjusting for gestational weight gain instead of maternal BMI in sensitivity analyses (Figure S1). Weight gain in pregnancy that exceeded the recommendation (n=142) (compared to weight gain within recommendation (n=208)) was associated with a significant increase in sum of skin folds, total body fat, fat free mass and percentage body fat (see Figure S1). Weight gain in pregnancy below recommendation (n=360) (compared to weight gain within recommendation) was associated with a decrease in all neonatal anthropometric outcomes except length. There was a positive association between excess weight gain in pregnancy and percentage body fat. Compared to those with appropriate weight gain, excess weight gain in pregnancy was significantly associated with a 1.46% increase in neonatal percentage body fat (Figure S1), in multivariate models. Indigenous ethnicity was significantly associated with higher sum of skinfolds (Figure 1.3). Smoking was associated with a decrease in all anthropometric measurements.. Nulliparity was associated with lower sum of skinfolds,total body fat and percentage body fat. Male gender was associated with higher length, head circumference and fat free mass and a lower sum of skinfolds. Timing of measurement (<72hrs or 72-120hrs) did not impact results (data not shown). Further analysis was performed to evaluate neonates born to mothers with GDM vs no hyperglycemia in pregnancy. GDM was associated with sum of skinfolds on linear regression adjusted for maternal age, gender and gestational age of neonate (0.64mm p=0.02, n=554), but no significant associations were observed between GDM and the other neonatal outcomes. Step-wise regression modelling revealed that the inclusion of BMI in the model, but not other covariates, attenuated the association between GDM and sum of skinfolds.

Discussion

Our study is the first to report on neonatal adiposity and anthropometrics in Australian Indigenous and Europid neonates in relation to maternal hyperglycaemia, BMI and gestational weight gain. Firstly, we showed that there was a significant positive association between maternal BMI and excess gestational weight gain and neonatal adiposity. Secondly, compared to neonates born to women without hyperglycemia in pregnancy, maternal T2DM and DIP, but not GDM, were associated with an increase in neonatal anthropometric measures and adiposity. Maternal T2DM and BMI were independently associated with neonatal adipose measures in this analysis. Thirdly, among women with hyperglycemia in pregnancy, Indigenous neonates had significantly higher skinfold measures compared to Europid neonates. In multivariate analysis, Indigenous ethnicity was significantly associated with neonatal sum of skinfolds, and this was independent of maternal diabetes, maternal BMI, gestational weight gain, nulliparity and smoking in pregnancy.

Our findings, that maternal BMI and excess gestational weight gain were positively associated with neonatal anthropometric measures and adiposity, are consistent with findings from other groups [27-29]. The HAPO study showed that in neonates born to women with hyperglycemia in pregnancy, excess maternal gestational weight gain was associated with increased neonatal sum of skinfolds and percentage body fat [7]. In an ethnically diverse cohort from North America without hyperglycemia in pregnancy, a continuous association was reported of maternal BMI, and gestational weight gain with neonatal adiposity (as measured with fat free mass and total body fat) [30]. The association between maternal and neonatal adiposity is thought to be due to excess nutrient fuels, including lipids, amino acids and adipokines from maternal adipose tissue [31, 32]. We have shown that maternal DIP and T2DM, together with BMI and excess gestational weight gain operate as independent risk factors for neonatal adiposity, and thus each represent important areas for intervention.

There are few studies evaluating the impact of T2DM on neonatal adiposity. Studies of neonates born to women with T2DM have reported higher rates of macrosomia or large for gestational age compared to neonates of women with GDM or no hyperglycemia in pregnancy [33]. The findings from PANDORA are novel as they provide detail about the nature of this weight discrepancy. Our findings indicate that with increased severity of type of diabetes (DIP and T2DM), neonatal adiposity increases. The HAPO study demonstrated a graded relationship between increasing glycaemia and neonatal adiposity [25]; however, this study excluded participants with more severe hyperglycemia in pregnancy, including T2DM. We now show that compared to no hyperglycemia in pregnancy, associations for T2DM and DIP with neonatal adiposity were stronger than those observed for GDM. The duration of fetal exposure to hyperglycemia is likely longer in women with T2DM and DIP and this may contribute to greater neonatal adiposity.

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Compared to European Australian adults, Aboriginal Australian adults have higher skinfold measures, particularly on the trunk, at similar BMI values [13], and BMI reference ranges underestimate overweight and obesity [34]. Differences in skinfold measures between Indigenous and Europid neonates in this cohort are not fully explained by differences in maternal factors such as diabetes and obesity. Skinfold measures may be useful to evaluate adiposity, particularly in Indigenous neonates, however further research will be needed to assess whether neonatal skinfold measures are accurate in predicting future risk of obesity.

This is the largest prospective observational study to present a detailed evaluation of the impact of maternal adiposity and hyperglycaemia on neonatal anthropometrics and adiposity in Indigenous Australians. Importantly, the impact of T2DM and DIP in addition to GDM on neonatal anthropometrics was assessed. The anthropometric measures used in this study have been shown to be valid, and were performed by a small number of skilled clinicians.

However, our study has some limitations. Firstly, it was not feasible to use air displacement plethysmography, the gold standard for determining fat mass in neonates[35], as neonates were born in a number of remote centres. Secondly, the equation used in this study to determine percentage body fat was based on neonates in the United States, and even though it has been validated in other populations, it has not been validated in Indigenous Australian neonates. In our study, birth weight did not differ by ethnicity however, Indigenous babies were significantly shorter and were born significantly earlier. Therefore this equation may have led to underestimation of body fat in Indigenous neonates. Thirdly, maternal glycemia in pregnancy was assessed as a categorical factor, using a range of clinical measures which prevented the assessment of glycemia as a continuous variable. This may have obscured an association between a higher glycemic sub-group of GDM, and outcomes. Treatment for hyperglycemia and duration of T2DM were not evaluated and may have influenced outcomes, however, our study design precludes us drawing any conclusions on whether improved management of hyperglycemia in pregnancy has any impact on neonatal adiposity. Fourthly, paternal anthropometrics and ethnicity have not been evaluated and are likely to influence neonatal adiposity. Finally, longer term follow up will elucidate whether the statistical differences in skin fold measures between Indigenous and Europid neonates translate to clinically relevant outcomes.

In conclusion, maternal BMI, excess gestational weight gain, and more severe hyperglycemia in pregnancy (DIP and T2DM) operated as independent risk factors for neonatal adiposity for both Indigenous and Europid neonates. Indigenous neonates had higher skinfold measures and Indigenous ethnicity was independently associated with sum of skinfolds. However, longitudinal assessment of childhood adiposity will be important to assess whether neonatal anthropometrics measures can predict future risk of obesity and its complications.

Tables and Figures

Table 1. Maternal characteristics by ethnicity and glycemia status[1].

1. Results presented as n(%), mean(SD), median (25-75IQR)

Table 2. Neonatal outcomes including anthropometry stratified by ethnicity and maternal hyperglycemia in pregnancy[1].

1. Results presented as n(%), mean(SD), median (25-75IQR)

Figure 1. Multivariate regression models for select anthropometric outcomes[1].

1. Coefficient values based on full model

Figure 1.1 Length (cm)

Figure 1.2 Head circumference (cm)

Figure 1.3 Sum of skinfolds (mm)

Figure 1.4 Total body fat (grams)

Figure 1.5 Percentage body fat (%)

Figure 1.6 Fat free mass (grams)

Supplementary figure. Figure 2. Multivariate regression models for select anthropometric outcomes with gestational weight gain in model[1].

1. Coefficient values based on full model

Figure 2.1 Length (cm)

Figure 2.2 Head circumference (cm)

Figure 2.3 Sum of skinfolds (mm)

Figure 2.4 Total body fat (grams)

Figure 2.5 Percentage body fat (%)

Figure 2.6 Fat free mass (grams)

Author contributions

DKL was involved in study design, literature search, data analysis, data interpretation, writing of the manuscript. ELMB was involved in interpreting the data and writing of the manuscript. FB was involved in data analysis, data interpretation and writing of the manuscript. IL, MK, CW, VH, SG, PVD completed neonatal measurements. IL, KOD, AB, JO, HDM, JES, PC were involved in study design and writing of the manuscript. LMB was involved in study design, supervision of data collection, data interpretation and writing of the manuscript. All authors approved the final manuscript.

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Table 1. Neonatal outcomes including anthropometry stratified by ethnicity and maternal hyperglycemia in pregnancy[1]

	Maternal hyperglycemia			No maternal hyperglycemia			I vs I	E vs E
Descriptive variable	**Indigenous (I) *n=404***	**Europid (E) *n=240***	**p**	**Indigenous *n=115***	**Europid *n=118***	**p**		
Gender (male)	211 (52%)[1]	122 (51%)	0.73	62 (54%)	68 (58%)	0.57	0.75	0.23
Gestational age (weeks)	38 (37-38.9)	39 (38.3-39.7)	<0.001	39.7 (38.9-40.6)	40 (39-40.4)	0.24	<0.001	<0.001
Birth weight (g)	*n=318* 3241 (610)	*n=203* 3273 (438)	0.51	*n=91* 3317 (550)	*n=92*3413 (493)	0.21	0.28	0.01
Length (cm)	*n=317* 49.1 (2.8)	*n=204* 49.6 (2.4)	0.03	*n=91* 49.7 (2.4)	*n=97* 50.1 (2.1)	0.18	0.07	0.07
Ponderal index	*n=314* 2.72 (0.41)	*n=200* 2.69 (0.52)	0.42	*n=91* 2.69 (0.26)	*n=95* 2.69 (0.26)	0.94	0.44	0.99
Extremity lengths								
Upper arm	7.6 (0.9) *n-140*	7.8 (0.9) *n=57*	0.16	N/A	N/A			
Forearm	6.8 (0.9) *n-140*	6.9 (0.7) *n=57*	0.41	N/A	N/A			
Thigh	8.8 (1.2) *n-140*	9.0 (1.4) *n=57*	0.29	N/A	N/A			
Lower leg	8.2 (0.9) *n-140*	8.3 (0.8) *n=57*	0.40	N/A	N/A			
Circumferences								
Head	34.5 (1.6) *n=323*	34.7 (1.3) *n=208*	0.10	34.6 (1.5) *n=91*	35.2 (1.3)*n=98*	0.002	0.66	0.002
Umbilicus	31.4 (3.3) *n=140*	31.7 (2.5) *n=59*	0.52	N/A	N/A			
Mid-upper arm	11.2 (1.4) *n=140*	11.2 (1.1) *n=59*	0.81	N/A	N/A			
Forearm	10.0 (1.4) *n=140*	10.1 (1.0) *n=59*	0.46	N/A	N/A			
Thigh	15.6 (2.3) *n=140*	15.9 (1.9) *n=58*	0.36	N/A	N/A			
Calf	11.0 (1.5) *n=140*	11.4 (1.2) *n=58*	0.03	N/A	N/A			
Skinfolds								
Flank	3.9 (1.1) *n=322*	3.5 (0.9) *n=207*	<0.001	3.7 (0.8) *n=90*	3.4 (0.8) *n=95*	0.03	0.04	0.33
Subscapular	4.9 (1.4) *n=319*	4.3 (1.4) *n=206*	<0.001	4.1 (0.9) *n=91*	4.1 (0.9) *n=98*	0.66	<0.001	0.17
Triceps	5.2 (1.8) *n=321*	4.2 (1.3) *n=207*	<0.001	4.3 (0.9) *n=91*	4.0 (0.8) *n=98*	0.06	<0.001	0.14
Thigh	7.4 (2.2) *n=139*	6.2 (2.1) *n=55*	<0.001	N/A	N/A			
Sum of skinfolds	13.9 (3.6) *n=319*	12.0 (3.1) *n=206*	<0.001	12.0 (2.1) *n=90*	11.4 (2.0)*n=95*	0.07	<0.001	0.11
Total body fat	398 (212) *n=314*	376 (163) *n=199*	0.21	398 (178) *n=90*	408 (170)*n=92*	0.69	0.97	0.13
Percent body fat	11.6 (4.5) *n=314*	11.1 (3.6) *n=199*	0.20	11.5 (3.7) *n=90*	11.5 (3.5) *n=92*	0.97	0.85	0.35
Fat free mass	2841 (422) *n=314*	2901 (307) *n=199*	0.08	2917 (393) *n=90*	3008 (344) *n=92*	0.10	0.13	0.008

1.Results presented as n (%), mean (SD), median (25-75IQR)

Table 1. Maternal characteristics by ethnicity and glycemia status[1]

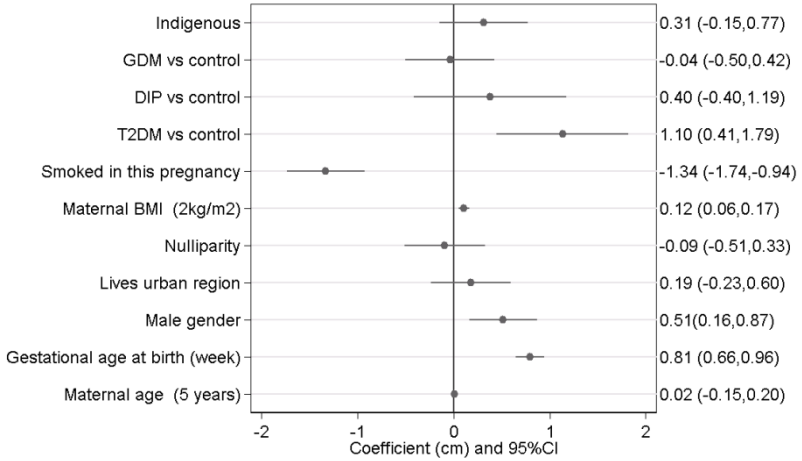
	Maternal hyperglycemia			No maternal hyperglycemia			I vs I	E vs E
	Indigenous n=404	**Europid n=240**	**p value**	**Indigenous n=115**	**Europid n=118**	**p value**	**p value**	**p value**
Maternal age (yrs)	30.0 (6.0)[1]	31.3 (5.6)	0.007	25.1 (4.7)	30.4 (5.0)	<0.001	<0.001	0.16
Glycaemia								
- GDM	209 (51%)	225 (94%)	<0.001	N/A	N/A			
- DIP	51 (13%)	6 (3%)	<0.001					
- T2DM	144 (36%)	9 (4%)	<0.001					
Smoked in pregnancy	179 (43%)	34 (15%)	<0.001	44 (38%)	20 (17%)	<0.001	0.39	0.58
Location (urban)	119 (29%)	170 (71%)	<0.001	22 (19%)	97 (82%)	<0.001	0.11	<0.001
Completed 12 years education	*n=388* 85 (22)	*n=234* 170 (73)	<0.001	41 (36)	88 (75)	<0.001	0.002	0.70
Nulliparity	74 (18%)	107 (45%)	<0.001	49 (43%)	61 (52%)	0.17	<0.001	0.21
BMI	29.6 (25.6-33.5)	29.4 (23.9-34.4)	0.92	23.9 (20.4-28.4)	24.9 (22.6-28.2)	0.06	<0.001	<0.001
Gestational weight gain (kg)	*n=344* 6.9 (5.3)	*n=184* 7.8 (5.9)	0.07	*n=95* 10.2 (5.6)	*n=92* 11.4 (4.6)	0.11	<0.001	<0.001
IOM guidelines[2]								
Excess	60 (17%)	37 (20%)	0.45	17 (18%)	28 (30%)	0.05	0.92	0.06
Within	95 (28%)	49 (27%)	0.80	31 (33%)	33 (36%)	0.64	0.34	0.11
Low	188 (55%)	97 (53%)	0.67	45 (47%)	30 (33%)	0.04	0.21	0.002

1.Results presented as n (%), mean (SD), median (25-75IQR)

2. Gestational weight gain, taking into account maternal BMI, as classified by IOM guidelines[23].

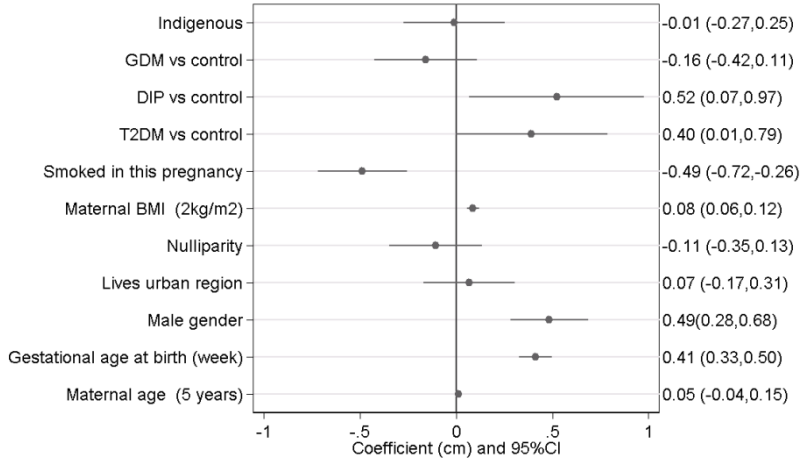
Figure 1 Multivariate regression models for select anthropometric outcomes[1]

Figure 1.1 Length (cm)



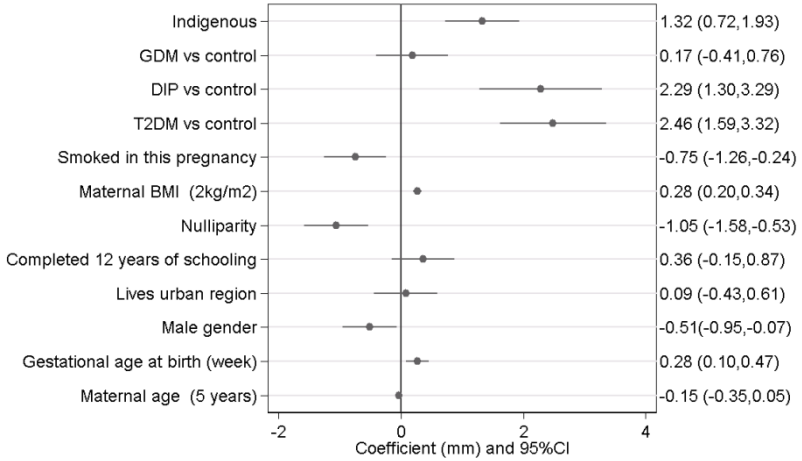
n=656 R^2 = 25%

Figure 1.2 Head circumference (cm)



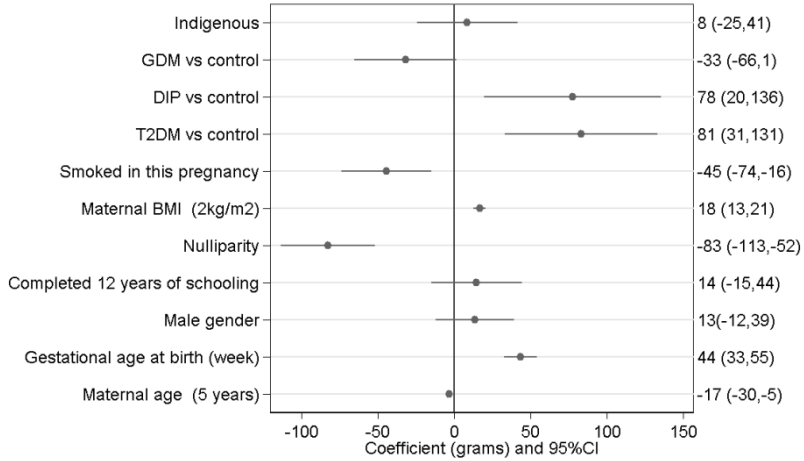
n=664 R^2 = 23%

Figure 1.3 Sum of skinfolds (mm)



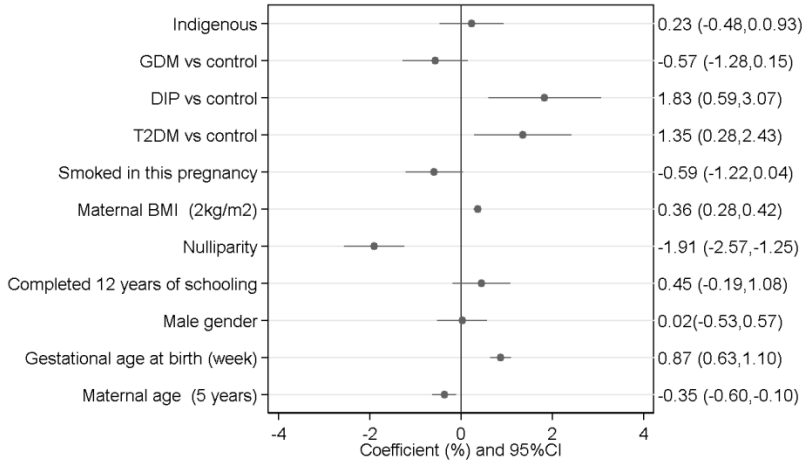
n=648 R^2 = 28%

Figure 1.4 Total body fat (grams)



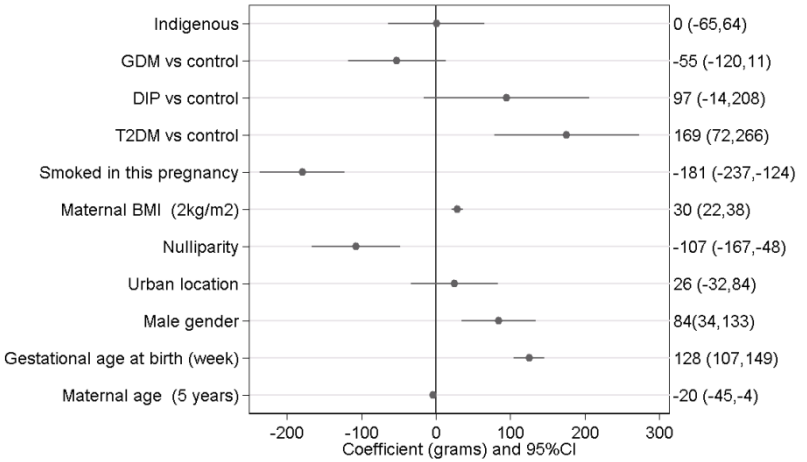
n=660 R^2 = 24%

Figure 1.5 Percentage body fat (%)



n=660 R^2=21%

Figure 1.6 Fat free mass (grams)



n=643 R^2=33%

1. Coefficient values based on full model