Original Article

Effect of maternal anthropometry and metabolic parameters on fetal growth

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A B S T R A C T

Objective: The aim of this study was to determine the effect of maternal anthropometry and metabolic parameters on neonatal anthropometry. **Materials and Methods:** This observational cross-sectional study was conducted from January 2008 to June 2009 at a single tertiary care center. Maternal anthropometry and metabolic parameters like fasting serum insulin, lipid profile, and random blood glucose were estimated in 50 pregnant women at term. Detailed anthropometry of the neonates was performed. **Results:** Large for gestational age (LGA) babies had higher maternal body mass index (BMI), fasting serum insulin, and cord blood insulin levels, and lower maternal high density lipoprotein (HDL) compared to appropriate for gestational age (AGA) group ($P < 0.001$). Among the maternal parameters, BMI, gestational age, fasting serum insulin, and random blood sugar (RBS) had significant positive correlation, while HDL had negative correlation with birth weight ($P < 0.05$). However, only maternal BMI was the significant predictor of neonatal birth weight on multiple regression analysis (ß = 0.340, $P = 0.01$). **Conclusion:** The BMI of glucose-tolerant mother is more important than metabolic parameters in determining the birth weight of term babies.

Key words: Appropriate for gestational age, body mass index, large for gestational age, anthropometry

INTRODUCTION

Human fetal growth is characterized by sequential patterns of tissue and organ growth, differentiation, and maturation. In early gestation, the major determinant of fetal growth is the fetal genome. But in late pregnancy, environmental, nutritional, and hormonal influences become increasingly important.[1] Several maternal anthropometric and demographic variables like pregravid weight, height, body mass index, gestational weight gain, parity, and gestational age at delivery independently predict birth weight.[2] Among hormones, insulin plays an important role as an endocrine metabolic regulator of fetal growth and birth weight, principally due to its anabolic action.[3] Pregnancy *per se* is a state of hyperinsulinemia owing to the action of

insulin antagonists like placental estrogen, progesterone, human placental lactogen (hPL), cortisol, prolactin, human chorionic gonadotropin (hCG), etc. which increases with advancing gestation.

Our study aims to evaluate the effects of maternal anthropometry and metabolic parameters on neonatal anthropometry.

MATERIALS AND METHODS

The present study was undertaken in a tertiary care center from January 2008 to June 2009. All pregnant women at term, attending the antenatal clinic or getting admitted to the antenatal ward, were considered. Those having gestational diabetes, overt diabetes, polycystic ovarian syndrome (PCOS), or taking steroid were excluded as these conditions are associated with insulin resistance. Also, those with any medical or obstetric condition likely to affect birth weight were excluded, like hypertension, chronic renal disease, anemia, heart disease, multiple pregnancy, chronic infection, etc. After appropriate exclusion, 50 women were

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included as subjects. The study was approved by the ethical committee of the institute. Informed consent was obtained from all study participants.

A detailed history and physical examination including anthropometry was performed in each case. Gestational age was estimated by last menstrual period and confirmed by first trimester scan. Maternal fasting serum insulin, lipid profile, and random blood glucose levels were obtained. During delivery, cord blood was collected before placental separation. Detailed anthropometric measurements of the neonates were recorded within 24 h of birth and neonatal outcome was observed till discharge. Neonatal birth weight above 90th percentile of gestational age-adjusted birth weight curve was defined as large for gestational age (LGA); those having weight between 10th and 90th centile were appropriate for gestational age (AGA).

Blood glucose was measured by the oxidase method. Serum total cholesterol (TC), triglyceride (TG), and high density lipoprotein (HDL) were measured with enzymatic method; low density lipoprotein (LDL) and very low density lipoprotein (VLDL) were calculated using Friedewald formula. Serum insulin level was estimated by chemiluminescense assay. The sensitivity of the assay was 2 mIU/L. The intra-assay and inter-assay coefficient of variation were less than 5%.

Statistical analysis was done using SPSS software version 16. The continuous variables were expressed as mean ± SD. The Student's *t*-test was used for comparison of continuous variables and Chi-square test for proportions. Correlation between the variables was evaluated using Pearson's correlation coefficients. For multivariate regression analysis, neonatal birth weight was used as dependent variable. $P < 0.05$ was considered as statistically significant.

RESULTS

The maternal and neonatal parameters are shown in Tables 1 and 2.

Table 3 compares the above parameters among the 10 LGA and 40 AGA neonates. It is evident that the LGA neonates had significantly higher insulin levels in both maternal serum and cord blood, compared to AGA neonates ($P \leq 0.001$). There was no difference in maternal glycemic status though mothers of LGA babies had higher body mass index (BMI).

Table 4 shows the correlation between maternal clinical parameters and neonatal anthropometry. Birth weight had a significant correlation with gestational age at delivery ($r = 0.28$, $P = 0.02$), maternal weight ($r = 0.46$, $P = 0.0002$), and maternal BMI ($r = 0.52$, $P < 0.0001$).

Table 1: Maternal parameters

Parameters	Mean ± SD	Range
Age (years)	25.4 ± 3.35	19–36
Gestational age (weeks)	39.6 ± 1.14	37.1–41.3
Parity (one)	41 (82%)	
Weight (kg)	56.56 ± 7.19	43–75
BMI (kg/m^2)	24.33 ± 3.06	17.2–32.4
Maternal fasting insulin (mIU/ml)	18.66 ± 15.15	0.95–66.3
RBS (mg/dl)	88.03 ± 30.06	60–164
TC (mg/dl)	256.13 ± 60.65	138.5–420.8
TG (mg/dl)	197.82 ± 62.77	71.2–392.4
LDL (mg/dl)	115.76 ± 10.90	86–142
HDL (mg/dl)	59.72 ± 15.92	35–105
VLDL (mg/dl)	41.13 ± 13.48	15–78

*BMI: Body mass index, RBS: Random blood sugar, TC: Total cholesterol, TG: Triglyceride, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein

Table 2: Neonatal parameters

Parameters	Mean ± SD	Range
Cord blood insulin (mIU/ml)	13.53 ± 13.73	0.23–72.8
Birth weight (kg)	3.01 ± 0.47	2.5–4.2
Length (m)	0.48 ± 0.02	0.42–0.52
PI (kg/m^3)	27.65 ± 3.49	24.5–33.7
HC (cm)	33.68 ± 1.69	30.5–37.8
AC (cm)	30.45 ± 2.35	26.5–37.5
CC (cm)	32.79 ± 1.74	30–37.5

PI: Ponderal index, HC: Head circumference, AC: Abdominal circumference, CC: Chest circumference

Table 3: Comparison between appropriate for gestational age and large for gestational age neonates

Parameters	AGA (40)	LGA (10)	*P* value
Age (years)	25.27 ± 3.29	25.90 ± 3.75	0.60
Gestational age (weeks)	39.04 ± 1.14	39.64 ± 1.10	0.15
Parity (one)	33 (82%)	08 (80%)	$\chi^2 = 0.076$, $P > 0.05$
Weight (kg)	55.15 ± 6.44	62.2 ± 7.56	0.003
BMI (kg/m^2)	23.68 ± 2.71	26.98 ± 3.10	0.001
Maternal serum insulin (mIU/ml)	14.98 ± 13.21	33.39 ± 13.87	0
Maternal RBS (mg/dl)	82.72 ± 15.71	109.26 ± 56.78	0.07
TC (mg/dl)	260.97 ± 60.34	236.77 ± 61.05	0.13
TG (mg/dl)	189.82 ± 56.08	229.86 ± 77.72	0.40
LDL (mg/dl)	114.39 ± 9.73	121.22 ± 14.00	0.07
HDL (mg/dl)	62.34 ± 16.28	49.24 ± 8.89	0.0003
VLDL (mg/dl)	39.46 ± 12.26	47.80 ± 16.63	0.06
Male babies (%)	18 (45%)	08 (80%)	$\chi^2 = 2.69$, $P > 0.05$
Cord blood insulin (mIU/ml)	10.96 ± 13.28	23.77 ± 10.79	0.0007
Neonatal weight (kg)	2.80 ± 0.27	3.79 ± 0.21	0
Length (m)	0.47 ± 0.01	0.50 ± 0.01	0
PI (kg/m^3)	27.06 ± 3.56	30.00 ± 1.93	0.0002
HC (cm)	33.28 ± 1.52	35.26 ± 1.44	0
AC (cm)	29.76 ± 1.91	33.23 ± 1.91	0
CC (cm)	32.23 ± 1.28	35.05 ± 1.49	0

AGA: Appropriate for gestational age, LGA: Large for gestational age, TC: Total cholesterol, TG: Triglyceride, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, PI: Ponderal index, HC: Head circumference, AC: Abdominal circumference, CC: Chest circumference

Table 5 depicts the correlation between metabolic parameters and neonatal anthropometry. Maternal serum insulin had a significant correlation with birth weight ($r = 0.35$, $P < 0.01$) and chest circumference ($r = 0.35$, $P < 0.01$) but not with other anthropometric indices. On the contrary, cord blood insulin had significant correlation with all measurements except ponderal index (PI) and abdominal circumference. Maternal serum insulin levels were significantly higher than cord blood levels (18.66 ± 15.15 mIU/ml vs. 13.53 ± 13.73 mIU/ml, $P < 0.05$). Figure 1 illustrates the correlation between maternal serum insulin and cord blood insulin ($r = 0.41$, $P = 0.001$).

Among the other metabolic variables, maternal random blood glucose at term had significant positive correlation with birth weight ($r = 0.35$, $P < 0.01$) and chest circumference ($r = 0.36$, $P < 0.01$) only. Triglycerides had significant positive correlation only with neonatal length ($r = 0.34$, $P < 0.01$) and head circumference ($r = 0.29$, $P < 0.05$). The positive correlation of LDL-cholesterol with head, chest, and abdominal circumferences was significant ($P < 0.05$, $P < 0.05$, $P < 0.01$, respectively), but that with birth weight was nonsignificant. HDL-cholesterol negatively correlated with all anthropometric measurements, but reached statistical significance only for birth weight ($P < 0.01$), length ($P < 0.05$), and chest circumference ($P < 0.05$).

Multivariate regression analysis using parameters like gestational age, parity, maternal BMI at term, fasting insulin, lipid profile, and random blood glucose revealed that maternal BMI is the significant predictor of neonatal birth weight [Table 6].

DISCUSSION

Maternal weight and BMI, which are the indicators of maternal nutrition, have been consistently proved to be directly correlated with birth weight and length.[4,5] This was also evident from our study. Maternal BMI was significantly correlated with all neonatal anthropometric variables except PI. The fact that gestational age at delivery is an important determinant of birth weight,[6] was also corroborated in our study.

Our study reaffirmed the fact that insulin plays a central role in regulating fetal growth. There was a significant correlation of maternal serum insulin with birth weight and chest circumference, unlike the reports of Gruyter[7] and Wiznitzer.[8] This role of maternal insulin in regulating fetal growth, especially in the rapid phase of somatic growth in late gestation, has also been demonstrated by Clausen *et al*.[9]

Cord blood insulin showed significant correlation with most anthropometric measurements (except Pondreral Index and abdominal circumference). This positive correlation of cord blood insulin with birth weight has been reported earlier by various authors.[10-15] But few have refuted such an association.[8,16] While Ong *et al*.[11] had postulated that cord blood insulin is positively correlated particularly to PI, a marker of adiposity at birth, our study did not find a significant correlation of either maternal serum or cord blood
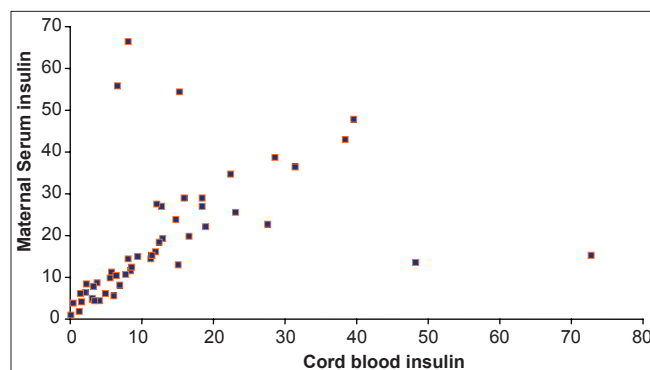

Figure 1: Correlation between maternal serum insulin and cord blood insulin

Table 4: Correlation between maternal clinical parameters and neonatal anthropometry

Maternal parameters	Weight	*P* value	Length	*P* value	PI	*P* value	HC	*P* value	CC	*P* value	AC	*P* value
Maternal age	0.19	0.08	0.14	0.16	0.08	0.28	0.44	0.0004	0.13	0.18	0.17	0.11
Gestational age	0.28	0.02	0.26	0.03	0.03	0.41	0.26	0.03	0.27	0.03	0.13	0.19
Maternal weight	0.46	0.0002	0.43	0.0005	0.09	0.27	0.39	0.002	0.35	0.005	0.43	0.0005
Maternal BMI	0.52	<0.0001	0.44	0.0003	0.14	0.16	0.36	0.003	0.40	0.001	0.46	0.0002

Table 5: Correlation between metabolic parameters and neonatal anthropometry

Metabolic parameter	Birth weight	*P* value	Length	*P* value	PI	*P* value	HC	*P* value	CC	*P* value	AC	*P* value
RBS	0.35	0.004	0.22	0.05	0.16	0.14	0.23	0.05	0.36	0.003	0.46	0.11
TG	0.16	0.13	0.34	0.006	0.19	0.09	0.29	0.02	0.13	0.18	0.11	0.23
LDL	0.22	0.22	0.09	0.27	0.15	0.15	0.25	0.03	0.27	0.02	0.32	0.009
HDL	−0.36	0.004	−0.29	0.02	−0.12	0.20	−0.22	0.06	−0.25	0.04	−0.23	0.05
VLDL	0.16	0.13	0.34	0.005	0.20	0.08	0.32	0.01	0.16	0.14	0.17	0.17
Maternal serum insulin	0.35	0.004	0.22	0.05	0.16	0.17	0.2	0.08	0.35	0.004	0.18	0.10
Cord blood insulin	0.4	0.001	0.4	0.001	0.04	0.40	0.41	0.0001	0.28	0.02	0.22	0.06

RBS: Random blood sugar, TG: Triglyceride, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein

Table 6: Multiple regression analysis results

Maternal parameters	β	*P* value
BMI	0.340	0.01
Gestational age	0.148	0.25
Parity	0.139	0.29
Fasting serum insulin	0.138	0.30
RBS	0.102	0.45
Triglyceride	0.012	0.92
LDL	0.173	0.18
HDL	−0.202	0.11

BMI: Body mass index, RBS: Random blood sugar, LDL: Low density lipoprotein, HDL: High density lipoprotein

insulin levels with the PI.

As in other studies,[17-20] maternal blood glucose exhibited a positive correlation with birth weight. Whether it is attributable to fasting or postprandial glycemia and early or late pregnancy, is still debatable. Most studies have concluded that postprandial glucose levels in late pregnancy predict fetal growth.[21-24] Few authors[25-27] have reported fasting glucose to be a significant predictor of birth weight, while one study[28] found both fasting and postprandial glucose to be poorly predictive.

Maternal triglycerides and non–HDL-cholesterol in the first half of pregnancy have been shown to be positively correlated with birth weight, whereas there is a negative correlation for HDL-cholesterol.[9,29] Some studies have found high triglycerides in late pregnancy to be a predictor of macrosomia.[30,31] Our findings partly agree with the above because, we found that HDL-cholesterol had significant negative correlation with birth weight, length, and chest circumference, whereas triglycerides and LDL-cholesterol had positive correlation with various other anthropometrics, but not birth weight. Mothers of LGA babies had also lower HDL-cholesterol compared to mothers of AGA group (P = 0.0003). Increased fetal weight gain associated with dyslipidemia is either due to increased nutrient transfer across the placenta or associated hyperinsulinemia, the marker of insulin resistance.

While maternal BMI, gestational age, and metabolic parameters like insulin, glucose and HDL correlated with birth weight, multiple linear regressions analysis found only maternal BMI to be a significant predictor of birth weight. This emphasizes the importance of maternal obesity as a risk factor for macrosomia, which is itself a strong determinant for metabolic syndrome in the offspring.

As with every study, our study too had few limitations. Firstly, the various factors affecting neonatal birth weight like maternal nutrition, pre-pregnancy weight, and weight gain during pregnancy were not considered in this study.

Secondly, calculation of maternal insulin sensitivity was not possible because of non-availability of fasting blood glucose level. Finally, being a cross-sectional study with small sample size, it has its own drawbacks. Larger randomized control trials (RCTs) are required to revalidate our findings.

CONCLUSION

This cross-sectional study revealed that maternal anthropometry is more important than metabolic parameters in determining birth weight. It also reaffirmed the fact that glucose-tolerant mothers are not protected from having large for gestational age babies. So, prevention and control of maternal obesity before and during pregnancy will help in controlling the epidemic of childhood obesity and associated cardiovascular complications in adulthood.

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