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Association of maternal risk factors with large for gestational age fetuses in Indian population

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Abstract: *Objective:* To estimate the risk of delivering large-for gestational age (LGA) fetuses associated with maternal obesity, excessive maternal weight gain, and gestational diabetes mellitus (GDM)- in Indian mothers. *Design:* Retrospective study. *Settings:* Fernandez Hospital Private Limited, Hyderabad, Andhra Pradesh, India; a tertiary perinatal centre. *Populations:* Pregnant singleton mothers with correct pregnancy dating. *Methods:* Estimated fetal weight (EFW) is determined using ultrasound variables [Biparietal diameter (BPD), Head Circumference (HC), Abdominal Circumference (AC), Femur Length (FL)]. This EFW is plotted on SONOCARE software [Medialogic solutions (P) Ltd, Chennai, India] to determine the type of antenatal fetal growth and a total of 192 LGA fetuses are selected. At birth newborn growth pattern are determined according to birth weight at the gestational age of delivery which divide the cohort into two groups: true LGA fetuses after delivery and true AGA fetuses after delivery. *Main outcome measures:* The association of maternal risk factors (body mass index, maternal weight gain and gestational diabetes mellitus) to the newborns between these two groups is evaluated. *Results:* Among the risk factors obesity and excess maternal weight gain among non-obese has highest risks for delivering LGA fetuses (relative risk 1.89 and 1.88; respectively); followed by excess maternal weight gain among obese (relative risk 1.5) and gestational diabetes mellitus (relative risk 1.4). *Conclusions:* Obesity, excessive maternal weight gain, and GDM all are associated with LGA. Decreasing the prevalence of obesity also reduce the prevalence of LGA fetuses apart from controlling excess maternal weight gain.

Keywords: Gestational diabetes mellitus, Obesity, Large for gestational age, ultrasonography, Maternal weight gain.

Introduction

Large for gestational age (LGA) describes a newborn fetus whose birth weight is more than 90th percentile from the mean for the gestational age. For the mother, delivering an LGA neonate increases the risk of prolonged labour, caesarean delivery, shoulder dystocia, and birth trauma. An LGA neonate is more likely to have fetal hypoxia and intrauterine death, neonatal hypoglycaemia, hyperbilirubinemia and to develop diabetes, obesity, metabolic syndrome, asthma, and cancer later in life [1].

Over the last two to three decades there has been a 15–25% increase in many countries in the number of women giving birth to large infants [2], which is only partly attributable to decreasing maternal smoking, increasing maternal, increases in maternal body mass index and increasing gestational diabetes [3]. Maternal obesity, maternal weight gain during pregnancy and gestational diabetes mellitus (GDM) are independent risk factors for delivering an LGA neonate and also there is complex interaction between these risk factors [4]. The objective of this article is to estimate the association of large for gestational age babies to known risk factors like pre-pregnancy BMI, maternal weight gain during pregnancy and GDM in Indian population.

Material and Methods

This is a retrospective study done at Fernandez Hospital Private Limited, Hyderabad, Andhra Pradesh, India, a tertiary, referral, and perinatal centre with about 5000 deliveries per year. The study population are pregnant mothers who has undergone routine antenatal visit and has diagnosed with having LGA fetus detected by fetal growth scan done between 26-36^{+6} weeks of gestational age.

Inclusion criteria:

1. Singleton pregnancy
2. Accurate pregnancy dating

Exclusion criteria:

1. Multiple pregnancy
2. No dating scan
3. Congenital anomaly
4. Referral cases

Definition used in study:

Antenatal:

1. Large for gestational age (LGA): Fetuses whose estimated fetal weight is greater than 90^{th} centile for the gestational age.
2. Average for gestational age (AGA): Fetuses whose estimated fetal weight is between 10^{th} and 90^{th} centile for gestational age.

Postnatal:

1. Large for gestational age - Newborns with birth weight above the 90^{th} percentile for the gestational age.
2. Average for gestational age - Newborns whose weight is between 10^{th} and 90^{th} percentile for gestational age.

All the ultrasound examinations are performed with Voluson 730 expert (GE Medical system), Voluson I (GE Medical system), Logiq P_3 (GE Medical system). All ultrasound measurements are done by trained obstetric sonologists in fetal medicine unit at Fernandez hospital. Estimated fetal weight (EFW) is calculated using ultrasound variables [Biparietal diameter (BPD), Head Circumference (HC), Abdominal Circumference (AC), Femur Length (FL)].

This EFW is plotted on population growth curves (SONOCARE software; Medialogic solutions (P) Ltd, Chennai, India) to determine the type of antenatal fetal growth. We select a total of 192 LGA fetuses whose EFW fall beyond the 90^{th} percentile in the SONOCARE software and followed them longitudinally till birth.

At birth newborn growth pattern are determined according to birth weight at the gestational age of delivery which divide the newborns into two groups: True LGA fetuses after delivery and true AGA fetuses after delivery.

The association of maternal risk factors (pre-pregnancy body mass index, maternal weight gain and gestational diabetes mellitus) to these fetuses is evaluated retrospectively from the antenatal database. As pre-pregnancy BMI is not available to our database, we have calculated the BMI from antenatal database having height and weight data documented at 1^{st} booking visit and classified into two groups normal weight (<25) and obese (>25) according to the new obesity guidelines proposed by the Indian Ministry of Health and Family Welfare [5].

Gestational diabetes mellitus is diagnosed by 2 hour 75gm oral glucose tolerance test following International Association of Diabetes in Pregnancy Study Groups criteria (IADPSG)[Fasting > 92mg%; 2hr >153mg%] [6]. Maternal weight gain data is initially calculated by the Institute of Medicine (IOM) published revised pregnancy weight gain guidelines [Normal weight (18.5–24.9 kg/m^2): 11.5 to 16 kg; Overweight (25.0–29.9 kg/m^2): 7 to 11.5kg; Obese (≥ 30.0 kg/m^2): 5 to 9 kg] [7].

As we have taken new obesity guidelines proposed by the Indian Ministry of Health and Family Welfare; we have modified pregnancy weight gain data according to following criteria for this study:

For obese (BMI>25): Normal weight gain 5 to 11.5 kg; Excess weight gain >11.5kg

For non-obese (BMI<25): Normal weight gain 11.5 to 16 kg; Excess weight gain >16kg

To quantify the true risks, we have compared the association of known maternal risk factors with true LGA fetuses after delivery and true AGA fetuses after delivery. Thus we can nullify the effect of 10% inherent error associated with measurement of EFW by fetal growth scan; as all LGA fetus predicted at growth scan are not delivered as LGA, some of them delivered as AGA. The AGA group act as control group in this study.

Statistical analysis is analysed with chi-square test and $P < 0.05$ was taken as the level of significance.

Results

Total number of LGA predicted by ultrasonography is 192 during the 26-36^{+6} wks gestational age (N=192). After delivery 92 newborns is grouped as true LGA and 100 newborns are grouped as true AGA.

In this study, we have 42.7% mothers in 25-29 years age group, 23.9% mothers in 20-24 age group and 24.5% mothers in 30-35 years age group.

Obesity (BMI>25) has sensitivity of 75.95% (95% CI: 65.02% to 84.85%) for prediction of true LGA fetuses after delivery with a relative risk of 1.89 (95% CI: 1.29 to 2.79) (P 0.0012) than normal BMI women (BMI<25) [Table 1: BMI and the prediction of LGA fetuses after delivery].

Also gestational diabetes mellitus (GDM) has sensitivity of 51.09% for prediction of true LGA fetus after delivery with relative risk of 1.40 (95% CI: 1.04 to 1.87) than women with normal blood sugar (P 0.023) [Table 2: Maternal gestational diabetes mellitus and the prediction of LGA fetuses after delivery].

Table-1: BMI and the prediction of LGA fetuses after delivery

BMI	True LGA fetuses after delivery	True AGA fetuses after delivery
Obese (BMI >25)	71	52
Normal (BMI <25)	21	48
Sensitivity	**77.17%** (95% CI: 67.25% to 85.28%)	
Specificity	48% (95% CI: 37.9 % to 58.22 %)	
Positive predictive value	**57.72%** (95% CI: 48.49 % to 66.58 %)	
Negative predictive value	69.57% (95% CI: 57.31 % to 80.07 %)	
Relative risk	**1.89** (95% CI: 1.29 to 2.79)	
P value	**0.0012**	

Table-2: Maternal gestational diabetes mellitus and the prediction of LGA fetuses after delivery

Diabetes status	True LGA fetuses after delivery	True AGA fetuses after delivery
GDM	47	35
Normal	45	65
Sensitivity	**51.09%** (95% CI: 40.44 % to 61.66 %)	
Specificity	65% (95% CI: 54.81 % to 74.27 %)	
Positive predictive value	**57.32%** (95% CI: 45.91 % to 68.18 %)	
Negative predictive value	59.09 (95% CI: 49.31 % to 68.37 %)	
Relative risk	**1.40** (95% CI: 1.04 to 1.87)	
P value	**0.023**	

Excess maternal weight gain among obese women (>11.5 kg) has relative risk of 1.57 (95% CI: 1.09 to 2.24) for delivering true LGA fetuses with positive predictive value of 70%, although it has low sensitivity (23.33%) [Table 3: Maternal weight gain in obese (BMI>25) during pregnancy and the prediction of LGA fetuses after delivery]. Similarly, excess maternal weight gain among non-obese women (>16 kg) has relative risk of 1.88 (95% CI: 1.17 to 3.03) for delivering true LGA fetuses with positive predictive value of 68.13%. Sensitivity of excess maternal weight is more in non-obese (46.88%) than obese women (23.33%) for prediction of delivering LGA fetuses [Table 4: Maternal weight gain in non-obese (BMI<25) during pregnancy and the prediction of LGA fetuses after delivery].

Table-3: Maternal weight gain in obese (BMI>25) during pregnancy and the prediction of LGA fetuses after delivery		
Weight gain	**True LGA fetuses after delivery**	**True AGA fetuses after delivery**
Excess weight gain (>11.5kg)	14	6
Normal (5-11.5kg)	46	57
Sensitivity	**23.33%** (95% CI: 13.39% to 36.04%)	
Specificity	90.48% (95% CI: 80.4% % to 96.4 %)	
Positive predictive value	**70%** (95% CI: 45.73 % to 88.03 %)	
Negative predictive value	55.34% (95% CI: 45.22 % to 65.14 %)	
Relative risk	**1.57** (95% CI: 1.09 to 2.24)	
P value	**0.014**	

Table-4: Maternal weight gain in non-obese (BMI<25) during pregnancy and the prediction of LGA fetuses after delivery		
Weight gain	**True LGA fetuses after delivery**	**True AGA fetuses after delivery**
Excess weight gain (>16kg)	15	7
Normal (11.5-16kg)	17	30
Sensitivity	**46.88%** (95% CI: 29.11% to 65.25%)	
Specificity	81.1%% (95% CI: 64.84% % to 92 %)	
Positive predictive value	**68.18%** (95% CI: 45.13 % to 86.08 %)	
Negative predictive value	63.83% (95% CI: 48.52 % to 77.32 %)	
Relative risk	**1.88** (95% CI: 1.17 to 3.03)	
P value	**0.009**	

On the other hand, obesity and GDM is related. In our study; prevalence of GDM among obese mothers (BMI >25) is more than non-obese mothers (BMI< 25) [46.34% vs 30.51%; P <0.037] with relative risk of GDM among obese is 1.23 (95% CI 1.0127 to 1.4991); which is statistically significant.

Discussion

Main findings: Large for gestational age fetus can be predicted by presence of maternal risk factors like obesity, maternal weight gain and gestational diabetes mellitus. Among these risk factors obesity itself (RR 1.89) and excess maternal weight gain among both obese and non-obese has highest relative risk for delivering LGA fetuses (RR 1.57 and RR 1.88; respectively). GDM also has almost 1.5 times relative risks of delivering LGA fetuses (RR 1.40).

Strengths and limitations: Strength of our study was we have used serial fetal biometry to detect the LGA fetuses; which have made possible accurate case selection. One of the weaknesses of our study is that New ICMR criteria has classified women with BMI between 23-24.9 as overweight; however in this study this group is included in normal BMI group. Further study is needed to clarify the risks of overweight group in delivering LGA fetuses. Another weakness of our study is that, we have calculated BMI according to booking maternal weight because prepregnancy weight was not documented in our database because of retrospective nature of the study. Obesity is increasing because of the diet and life style of Indians; which is the predisposing factor for both diabetes and hypertension. But in this study incidence of hypertension were not included. Sometimes, LGA babies are also associated with congenital anomalies but this was excluded in the study.

Interpretations: New guideline by Indian council for Medical Research (ICMR) guideline for obesity for Indian population has lowered the cut-off of obesity form existing WHO category of obesity (From BMI>30 of

WHO guideline to BMI>25 in ICMR guideline) [8]. Lowering the cut-off value means; the prevalence of obesity in pregnant women will be increased along with consequent increased cost of antenatal and perinatal care. But it is evident in our study that using new ICMR criteria of obesity (BMI >25); also has the relative risk for delivering LGA fetuses increases almost 2 times than non-obese (BMI <25) women. In previously published data BMI >30 has an adjusted odds ratio of 1.6 for risks of delivery of LGA fetuses [9]; we have similar relative risk even if we lowered the cut-off of obesity according to new guideline; which justifies its applicability. GDM has independent risk for delivering LGA fetuses (RR 1.4); although obesity and GDM has statistically significant association. So reducing the prevalence of obesity also reduces the prevalence of LGA fetuses.

Conclusion

The obesity and excess weight gain, both the risk factors for LGA fetuses are amenable to intervention. Obese patients should be encouraged for weight-reduction before attempting pregnancy. During pregnancy optimum weight gain should be monitored by consultation with Nutritionist. Because obesity often proceeds to GDM, decreasing the prevalence of obesity also reduce the prevalence of GDM. In women with GDM, controlling the excess weight gain helps to reduce prevalence of LGA fetuses, apart from good glycaemic control. Furthermore, preventing excessive gestational weight gain will also aid in reducing postpartum weight retention, which in turn may contribute to the development of obesity while entering into the next pregnancy [10]. Further prospective study will be needed to estimate the risk factors of LGA fetuses overcoming the pitfalls of this study.

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