

## Original Research Article

# Maternal clinical profile and immediate neonatal outcome in term large for gestational age neonates

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## ABSTRACT

**Background:** The objective of the study was to know the maternal clinical profile and short term outcome of term large-for-gestational-age (LGA) neonates.

**Methods:** The study was a prospective observational study conducted in the tertiary neonatal unit, Odisha, during the study period February to November 2018. All inborn term neonates with birth weight above 90th percentile for gestational age excluding neonates with major congenital anomalies were included. Maternal clinical profile data from the antenatal records, neonatal demographic profile and co-morbidities over time were recorded using a checklist. The analysis of data was done using SPSS 21.0. Univariate summary statistics and bivariate Fischer's exact test were used to analyse the data.

**Results:** The prevalence of delivery of LGA and macrosomic neonate in our institution was 2.5%, and 1.1% respectively. Ninety one percent of LGA neonates were born before 39 weeks and 80% babies delivered by cesarean section. Majority 39 (86.7%) of LGA babies were born to non-diabetic mother, four (8.9%) neonates born to GDM mother, two (4.4%) were born to mother with pre pregnancy diabetes mellitus. Sixteen (35.5%) neonates were admitted to NICU for different comorbidities like neonatal jaundice (37.8%), polycythemia (24.4%), transient tachypnea of new-born (20%), hypoglycemia (15.6%), hypocalcaemia (15.6%), and seizure (4.4%). The comorbidities like hypoglycaemia, hypocalcemia, respiratory distress were more in LGA babies with diabetic mother compared to non-diabetic mother.

**Conclusions:** About nine in ten LGA neonates were born to non-diabetic mothers, however, LGA infants of diabetic mothers are at higher risk of metabolic complications like hypoglycemia, hypocalcemia compared to non-diabetic mother.

**Keywords:** LGA neonate, Macrosomia, Comorbidities

## INTRODUCTION

Birth weight more than 4000 gm, irrespective of gestational age is called macrosomia and birth weight lies above 90<sup>th</sup> percentile of that gestational age, is called large for gestational age (LGA). Over last decades, there is parallel increase of macrocosmic birth and maternal complication like diabetes and obesity in developing

countries. The prevalence of macrosomia in India is around 0.5%, however in developed countries it is between 5%-20%.<sup>1,2</sup> Macrosomia is a well-known cause of perinatal morbidity and neonatal adverse outcomes, including hypoglycaemia, hypocalcaemia, unexplained hyperbilirubinemia, polycythaemia, respiratory distress, cardiac disorders and neurologic impairment and birth traumas. In long-term, LGA neonates are high risk for

type 2 diabetes and obesity.<sup>3,4</sup> The modifiable risk factor of macrosomia like pre-gestational maternal anthropometric characteristics, gestational weight gain, maternal nutrition intake, maternal glucose metabolism can prevent macrosomia.<sup>5</sup> Due to paucity of literature regarding maternal clinical profile and morbidities of LGA babies in a hospital based setting, particularly in eastern India in recent years, this study was conducted.

## METHODS

The study was conducted as a prospective observational study in the tertiary neonatal care unit of Odisha, for a period of 10 months from February 2018 to November 2018. All inborn term neonates with birth weight above 90th percentile for that gestational ages based on Fenton growth chart were included. Term new-born with birth weight above 90<sup>th</sup> percentile for that gestational age with major congenital anomalies and left against medical advice before completion of treatment.

The parents were informed regarding the study and written consent was obtained from the parents in the local language i.e. Odia. Maternal data were extracted from the antenatal records of the mother like maternal age, parity, gestational age, pre-gestational weight, height, history of diabetes and third trimester HbA1C. Neonatal demographic profile like birth weight, sex, gestational age, Apgar score at 1 and 5 min, requirement of admission in neonatal intensive care unit (NICU) were recorded. The expected co-morbidities like hospital length of stay, hypoglycaemia, hypocalcaemia, unexplained hyperbilirubinemia, seizure, polycythaemia, birth injuries, respiratory distress were recorded. Last menstrual period, available first trimester ultrasound scan or New Ballard scoring system was used for gestational age calculation. Birth weight was measured within one hour of delivery by the trained nurses using electronic weighing scales and the revised Fenton growth charts used for diagnosis of LGA. Macrosomia was estimated when the birth weight exceeding 4000 gm irrespective of gestational age.

Body mass index (BMI) was calculated from the weight and height of mother just before conception [weight (kg)/height (m)<sup>2</sup>]. Women with a BMI less than 18.5 kg/m<sup>2</sup> - underweight, BMI of 18.5–24.9 kg/m<sup>2</sup> normal weight, BMI of 25–29.9 kg/m<sup>2</sup> - over weight and obese for BMI more than 30 kg/m<sup>2</sup>. Maternal diabetic status was determined from antenatal records of two-hour glucose challenge test in accordance with protocol. When maternal third trimester HbA1C data is not available, HbA1C was done within 24 hours of delivery. Blood glucose <40 mg/dl at any period during the hospital stay was classified as hypoglycaemia. Any serum bilirubin needed phototherapy as per AAP chart was defined as unexplained hyperbilirubinemia. Polycythaemia was defined as peripheral venous haematocrit 65%. Hypocalcaemia was defined as serum calcium <8 mg/dl. Diagnosis of sepsis was based on clinical symptoms, supported by sepsis screen and blood culture positivity.

Respiratory distress syndrome was based on clinical finding distress and radiological finding on chest X-ray. Babies with birth asphyxia were considered based on NNPD network definition. The data was analysed using SPSS 21.0. Statistical estimates such as frequency and percentages were used to describe the data. Chi-square or Fischer's exact test were used to assess association between various categorical variables. For statistical significance, a p value less than 0.05 was taken into account.

## RESULTS

Out of 1800 inborn deliveries during the study period, 48 (2.5%) babies were LGA and 19 (1.1%) were macrosomia. Three patients were excluded as per exclusion criteria so 45 patients constituted the study population. In our study, 26 (57.8%) neonates had birth weight ≤4000 g and 19 (42.2%) were macrosomia (>4000 gm), 29 (64.4%) were male and 16 (35.6%) babies were delivered by caesarean section. Out of 45 LGA babies, 41 (91.9%) were early term, 8.9% babies were full term (Table 1). Majority 39 (86.7%) of LGA babies were born to non-diabetic mother, four (8.9%) neonates born to GDM mother, two (4.4%) were born to mother with pre-pregnancy DM (Table 2).

**Table 1: Demographic profile of the study population (n=45).**

Clinical characteristics	Number	%
<b>Birth weight (in gram)</b>	≤4000	26
	>4000	19
<b>Gender</b>	Male	29
	Female	16
<b>Mode of delivery</b>	Vaginal delivery	9
	LSCS	36
<b>Gestational age (in weeks)</b>	Early term	41
	Late term	4

**Table 2: Distribution of cases according to maternal diabetic status (n=45).**

Maternal diabetes status	Number	%
<b>Pre-pregnancy diabetes</b>	2	4.4
<b>Gestational diabetes</b>	4	8.9
<b>Non diabetic</b>	39	86.7

**Table 3: Comparison of maternal factors with gestational outcome (n=45).**

Variables	LGA	%
<b>Pre-pregnancy BMI</b>	18.5-24.9	19
	>25	26
<b>HbA1c</b>	<5.7	21
	>5.7	24

Out of 45 LGA neonate, 26 (57.8%) babies were born to mother with pre pregnancy higher BMI and 19 (42.2%) were born to mother with normal BMI. Similarly, 24 (53.4%) babies were born to mother with higher HbA1c during third trimester (Table 3). Out of 45 LGA babies, 17 (37.8%) babies had jaundice, 11 (24.4%) neonates had polycythemia, nine (20%) neonates developed respiratory distress. The metabolic complication like hypoglycaemia found in seven (15.6%) neonates and hypocalcaemia in seven (15.6%) babies. The neurological complication like birth asphyxia and seizure were found in three (8.9%) and two (4.4%) babies respectively. For the above comorbidities, 16/45 (35.5%) babies required NICU admission (Table 4). LGA babies born to diabetic mother had more complications of hypoglycaemia and

hypocalcemia compared to neonates of non-diabetic mother (Table 5).

**Table 4: Different type of comorbidities in LGA neonates (n=45).**

Co-morbidities	Number	%
<b>Jaundice</b>	17	37.8
<b>Polycythemia</b>	11	24.4
<b>Respiratory distress</b>	9	20
<b>Hypoglycemia</b>	7	15.6
<b>Hypocalcemia</b>	7	15.6
<b>Birth asphyxia</b>	4	8.9
<b>Seizure</b>	2	4.4
<b>NICU stay</b>	16	35.5

**Table 5: Neonatal outcome in association with maternal diabetic status.**

Neonatal complication	LGA from diabetic mother (n=6)	LGA from non-diabetic mother (n=39)	P value
	N (%)	N (%)	
<b>Hypocalcemia</b>	4 (66.7)	3 (7.6)	0.003
<b>Hypoglycemia</b>	4 (66.7)	3 (7.6)	0.003
<b>Respiratory distress</b>	2 (33.3)	7 (17.95)	0.583
<b>Jaundice</b>	4 (66.7)	13 (33.33)	0.179
<b>Polycythemia</b>	3 (50)	8 (20.5)	0.146
<b>Birth asphyxia</b>	0 (0)	4 (10.2)	0.71
<b>Seizure</b>	1 (16.7)	1 (2.5)	0.251

## DISCUSSION

Genetic, sociodemographic, geographical and racial variation and maternal clinical profile determines neonatal birth weight. The prevalence of LGA in our institutional delivery was 2.5% and 1.1% babies were macrosomia. The prevalence of macrosomia in India was around 0.5% by WHO survey.<sup>2</sup> In our study, 91.1% neonates were delivered before 39-week gestation (early term LGA) and 80% of the neonates were born by caesarean section. The high rate of caesarean section was reported in the larger birth weight babies by Linder et al and Mardani et al.<sup>6,7</sup> In our study, majority of LGA 86.7% were born to non-diabetic mother, 4.4% were born to diabetic mother, 8.9% were born to mother with GDM. Similar maternal clinical profile found in south Arabian study by Fahad et al, 89.9% of macrosomic babies were delivered to non-diabetic mother, 7.8% delivered to gestational diabetic mother and 2.3% babies delivered to diabetic mothers.<sup>8</sup> Aknabi et al found increased level of c peptide in cord blood of macrosomic infant of non-diabetic mother, suggestive of chronic hyperinsulinemia.<sup>9</sup> In our study, 26 (57.8%) babies were born to mother with higher pre pregnancy BMI and 24 (53.4%) babies were born to mother with high HbA1c during third trimester.

Around one third LGA neonates required NICU admission. Seventeen (37.8%) neonates had unconjugated hyperbilirubinemia requiring phototherapy, eleven (24.4%) neonates had polycythemia and

respiratory distress (transient tachypnea of newborn) in nine (20%) neonates. Earlier Metzger et al, had observed a weak association between maternal blood glucose levels and hyperbilirubinemia.<sup>10</sup> Polycythemia and poor liver conjugations are likely causes of increased neonatal jaundice. The possible mechanisms of polycythemia in infant of diabetic mother could be fetal hypoxia and increased levels of fetal erythropoietin. Increased insulin and IGFs levels can also increase erythropoiesis. The correlation between maternal  $\beta$ -hydroxybutyrate levels and polycythemia was strong and positive as observed by Cetin et al.<sup>11</sup> A state of relative surfactant deficiency in infant of diabetic mother, early term delivery and caesarean section increases the respiratory morbidities like transient tachypnea of new-born due to delayed clearance of lung fluid.

Among LGA babies, metabolic complication like hypoglycaemia found in seven (15.6%) neonates and hypocalcaemia in seven (15.6%) babies. The hypoglycaemic complication among LGA neonate with non-diabetic mother was 3/39 (7.6%) and babies with diabetic mother was 4/6 (66%). The incidence of hypoglycemia among infant of diabetic mother was 54% in Syeda et al.<sup>12</sup> Linder and Araz described the rate of hypoglycaemia in LGA neonate of non-diabetic mother was 1.2% and 16.7% respectively.<sup>6,13</sup> In our study neonatal complications like hypocalcemia, hypoglycaemia were more in LGA neonates with diabetic maternal profile than non-diabetic mother. Increased

placental transfer of glucose leads to hyperplasia of islets of Langerhans in the foetus of diabetic mother. Due to presence of excess insulin secretion, blood glucose reduces during the first few hours of life in infant of diabetic mother. The hypocalcaemia complication among LGA neonate with non-diabetic mother was 3/39 (7.6%) and babies with diabetic mother was 4/6 (66%) in our study. The prevalence of hypocalcemia was 43% among infant of diabetic mother in Kausar et al.<sup>12</sup> Higher maternal calcium level in diabetic mother causes increased concentrations of serum ionized calcium in utero and suppression of fetal parathyroid glands. The functional hypoparathyroidism leads to hypocalcemia in infant of diabetic mother.

Maternal diabetes and gestational diabetes are the strongest risk factor of macrosomia and its related complications, is a well-known science. Increased awareness regarding well controlled glycaemic monitoring during peri-conceptional and conceptual period might have decreased the incidences of diabetes-related macrosomia. In our study 86% of LGA babies were born to non-diabetic mother and 57.8% neonates were born to mother with high pre pregnancy BMI (>25 kg/m<sup>2</sup>). Further studies are necessary to identify a significant pool of non-diabetic mother, both during preconception and conception period for abnormal metabolic milieu to reduce large for gestational age neonatal complications.

## CONCLUSION

Majority of LGA neonates were born to non-diabetic mothers, however, LGA infants of diabetic mothers are at an increased risk of metabolic complications like hypoglycemia, hypocalcemia compared to non-diabetic mother.

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