DOI: 10.7860/JCDR/2021/48598.15047

Original Article

Paediatrics Section

An Analytical Study of Short-term Morbidities in Large for Gestational Age Infants- A Single Centre Experience from South India

KEERTHANA MENON[1], BHAVANI DEEPTHI PERUMALLA[2], VIGNESH KUMAR[3], GIRIDHAR SETHURAMAN[4]

ABSTRACT

Introduction: Globally, Large for Gestational Age (LGA) infants constitute a significant proportion of live births, with Gestational Diabetes Mellitus (GDM) being a primary contributor. Infants born to GDM mothers are more prone for morbidity and mortality and if born large, the incidence of morbidities could increase. The clinicodemographical profile of LGA infants has not been well analysed, especially in Lower Middle Income Countries (LMIC) like India, where gestational diabetes is very common.

Aim: To analyse the incidence, demographic profile and short-term neonatal outcomes of LGA births, stratified for GDM.

Materials and Methods: This was an analytical retrospective cohort study conducted in a tertiary care hospital in South India. Medical records of LGA infants ≥35 weeks born between December 2018 and May 2020 were reviewed (in December 2020 and January 2021), after Institutional Human Ethics committee approval (No:296/IHEC/JAN 2021). The LGA infants were grouped as GDM induced Large Infants born to gestational and pregestational Diabetes Mellitus mothers (LIDM) and large infants born to non gestational diabetes mellitus mothers (LnIDM). Case records with incomplete data were excluded. Demographic profile of the two groups at birth and their clinical morbidities during hospitalisation were recorded. The primary outcome was requirement of respiratory support in the two groups. The categorical outcomes were compared using Chi-square test/Fisher's exact test, while numerical variables were compared using Mann-Whitney U test. Odds ratio and their 95% Confidence Intervals (CI) were obtained as appropriate. Multivariate logistic regression, controlling for potential confounders, was done to derive the adjusted odds ratio. The p-value <0.05 was taken as significant. All analysis was performed using Statistical Package for the Social Sciences (SPSS) software version 22.0.

Results: Out of 2653 live births, 268 were LGA infants ≥35 weeks (9.72%). The LIDM were 126 (48.8%) and LnIDM were 132 (51.2%). Ten case records were excluded due to incomplete data hence, 258 infants were included in the final analysis. The median (Interquartile range) birth weight was significantly higher in the LIDM's {3.92 (3.86, 4.08) kg} compared to LnIDM's {3.89 (3.75, 3.96) kg}. The primary outcome of need for respiratory support was not significantly different between the two groups {Adjusted odd's ratio (aOR) 1.62; 95% CI 0.92 -2.83; p-value=0.08)}. Multivariate logistic regression, controlling for confounders, showed higher neonatal intensive care admission rates (aOR 2.15; 95% CI 1.17-4, p=0.01), neonatal hyperbilirubinemia (aOR 1.70; 95% CI: 1.01-2.84, p=0.04) and Persistent Pulmonary Hypertension (PPHN) (aOR 4.43; 95% CI: 1.41-13.82, p=0.004) in the LIDM infants.

Conclusion: GDM contributes significantly to LGA births in India, and is associated with higher Neonatal Intensive Care Unit (NICU) admissions, neonatal hyperbilirubinemia and PPHN, compared to non GDM causes.

Keywords: Macrosomia, Neonatal hyperbilirubinemia, Pulmonary hypertension

INTRODUCTION

A "big baby" is often regarded as a sign of good health. In statistical terms, these LGA infants have birth weight ≥ 90th percentile for a given gestational age [1]. The term "macrosomia" is also used interchangeably and implies growth beyond an absolute birth weight, historically 4,000 g or 4,500 g, regardless of the gestational age, according to the American College of Obstetrics and Gynaecology [1].

The incidence of LGA infants reported from various birth cohorts around the globe is between 7 to 10% [2-7]. The various antenatal risk factors for LGA births are Diabetes Mellitus (DM), maternal obesity, history of previous LGA births, increased maternal age and parity, excessive weight gain during pregnancy, post-dated births, genetic factors and geographic predisposition [8]. In High Income Countries (HIC's), the incidence of LGA births has been steadily rising [7], but there is hardly any data from LMIC's, where the focus has been more on low birth weight infants.

Contrary to the popular belief, being born "big" is not always better and studies from HIC's have clearly shown that LGA births are associated with significant maternal and neonatal morbidity [9-11]. Maternal DM constitutes to a significant public health problem, with rising prevalence, in many LMIC's including India [12]. The epidemiology of LGA births in LMIC's has not been clearly studied, but recent data seems to suggests that maternal diabetes is the main contributor [2].

As GDM is an independent risk factor for adverse neonatal outcomes, being born large, due to GDM, could be an added disadvantage [13]. Hence, this study was undertaken to describe the clinico-epidemiological profile of LGA births from India, and to compare the difference in the morbidities of GDM from non-GDM LGA infants.

MATERIALS AND METHODS

This was an analytical retrospective cohort study conducted in the Neonatology Department of Chettinad Hospital and Research Institute, Tamil Nadu, India. The study was approved by the Institutional Human Ethics committee (No: 296/IHEC/JAN 2021). Case records of LGA infants {birth weight more than 90th percentile as per World Health Organisation (WHO) growth standards [14]} born between December 2018 to May 2020 were retrospectively reviewed by the investigators from December 2020 to January 2021.

Inclusion and Exclusion criteria: The LGA infants <35 weeks of gestation and case records with incomplete data were excluded. LGA infants were further classified as large infants born to gestational and LIDM and LnIDM. GDM was diagnosed if blood sugar was ≥140 mg/dL, 2 hours after a 75 g oral glucose challenge test, typically done between 24-28 week of gestation based on the WHO guidelines [15].

Infants born to mothers with pregestational or early GDM (Glucose intolerance diagnosed before pregnancy or in the first trimester or early second trimester) were also included in this group [16]. The LGA infants born to mothers without a diagnosis of GDM during pregnancy were chosen as controls, irrespective of the cause of LGA.

Clinicodemographic profile of the two groups at birth was recorded including socio-economic status according to Modified Kuppusamy scale [17], mode of conception, period of gestation, any antenatal comorbidities, mode of delivery, gender, birth weight, resuscitation details and any other significant antenatal history was also recorded.

As per the hospital policy, all sick infants and macrosomic infants >4000 g were admitted to the NICU. Other non sick LGA infants were roomed in with mother and initiated on breast feeding at birth as per WHO guidelines [18] and baby friendly hospital initiative policy [19]. All LGA infants underwent the following investigations: capillary blood glucose monitoring using glucometer every 6 hours for 3 days, serum ionised calcium in neonates with symptoms of jitteriness, seizures, lethargy, stridor or cardiac dysfunction, haemoglobin and haematocrit at 6 hours of life, serum bilirubin at 72 hours of life, or earlier, if the neonate was found icteric during routine clinical examination or if discharge of neonate is being planned. Initiation and termination of phototherapy was done as per the American Academy of Paediatrics guidelines [20]. Other investigations were done based on the clinical condition of the infant, as deemed necessary by the treating physician.

The National Neonatology Forum of India definitions used to draft the National Neonatal Perinatal Database 2002-03, were utilised in the study [21]. The data from case records were then abstracted and the short-term morbidities of all LGA infants during hospital stay till discharge were recorded. These included need for respiratory support; respiratory morbidities like transient tachypnoea of newborn, respiratory distress syndrome, meconium aspiration syndrome; requirement for NICU admission; perinatal depression, hypoxic ischemic encephalopathy, seizures; significant hyperbilirubinemia requiring phototherapy, peak bilirubin, duration of phototherapy and need for exchange transfusion; polycythemia (haematocrit ≥65%) and thrombocytopenia (platelet count <1,50,000/c.mm); echocardiography confirmed PPHN; cardiac morbidities and malformations; hypoglycaemia (capillary blood glucose ≤45 mg/dL after 4 hours of life) and hyperinsulinemia (any detectable insulin in the presence of critical glucose value ≤45 mg/dL); hypocalcaemia (serum total calcium <7 mg/dL); birth injuries like erb's palsy, significant cephalhaematoma/subgaleal haemorrhage, fractures; acute kidney injury; and sepsis. Any other significant short-term morbidities were also recorded. All recorded data was stratified for GDM status in mother.

The primary outcome analysed was the need for respiratory support in LGA infants, stratified for GDM. Other outcomes studied were the incidence, demographic profile and other clinical morbidities. Previous data had shown that the rate of respiratory distress and requirement of respiratory support varied from 5-8% in LGA infants [9,22]. To determine an increase in respiratory distress and requirement for respiratory support from 5% in the LnIDM group to 15% in the LIDM group, with 80% power and an alpha error of 0.05, 120 subjects were required in each group (STATA IC, ver. 13).

STATISTICAL ANALYSIS

Baseline clinicodemographical profile and outcome variables were presented as frequency and proportion for categorical variables. Distribution of numerical variables was assessed, using Shapiro wilk test, as skewed and hence, represented as median {Interquartile Range (IQR)}. The categorical outcomes between IGDM or non-IGDM groups were compared using Chi-square test/Fisher's exact test, while numerical variables were compared using Mann-Whitney U test. Odds ratio and their 95% CI was obtained as appropriate. Multivariate logistic regression, controlling for potential confounders, was done to derive the adjusted odds ratio. The p-value <0.05 was taken as significant. All analysis was performed using SPSS software version 22.0. (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp, California, USA).

RESULTS

During the duration of retrospective review of case records, between December 2018 to May 2020, 2653 infants were delivered in institution, out of which 268 were LGA infants ≥35 weeks (9.72%). Ten case records had incomplete data and were excluded. Hence, 258 infants were included in the final analysis.

The LIDM were 126 (48.8%) and LnIDM were 132 (51.2%). Among mothers of LIDM, 69 (54.76%) mothers had gestational diabetes controlled on diet, 15 (11.9%) were on oral hypoglycaemic agents, 30 (23.8%) were on insulin and overt pregestational diabetes were seen in 12 (9.53%). The clinico-demographic profile of both the groups of LGA infants at birth is shown in [Table/Fig-1].

Parameter	LIDM n=126	LnIDM n=132	p-value
Gender			
Male	66 (52.4)	75 (56.8)	0.532
Female	60 (47.6)	57 (43.2)	
Socio-economic class*			
I	20 (15.9)	10 (7.6)	
II	51 (40.5)	69 (52.3)	
III	47 (37.3)	46 (34.8)	0.11
IV	8 (6.3)	7 (5.3)	
V	-	-	
Mode of delivery			
Normal vaginal delivery	24 (19)	33 (25)	0.28
Instrumental vaginal delivery	9 (7.14)	6 (4.5)	
Elective c-section: (Indications)	27 (21.4)	36 (27.3)	
Previous LSCS	9 (33.3)	11 (30.5)	
Bad obstetric history	-	1 (2.7)	
Fetal macrosomia	15 (55.5)	23 (63.9)	
Maternal request	3 (11.1)	1 (2.7)	
Emergency c-section: (Indications)	66 (52.4)	57 (43.2)	
Cephalopelvic disproportion in labour	19 (28.8)	22 (38.6)	
Gestational hypertension	5 (7.6)	8 (14)	
Failed induction	18 (27.3)	13 (22.8)	
Malpresentation	7 (10.6)	3 (5.3)	
Non stress test- non reactive	17 (25.7)	11 (19.3)	
Antenatal co-morbidities			
Gestational hypertension	15 (11.9)	24 (18.2)	0.169
Hypothyroidism	36 (28.6)	9 (6.8)	0.000‡
Rh negative	6 (4.8)	9 (6.8)	0.598
Risk of sepsis (any from fever/urinary infection/preterm prelabour rupture of membranes/foul smelling vaginal discharge)	7 (5.6)	5 (3.8)	0.564
Gestational age in weeks			
Median (IQR)	37.93 (37-38.29)	37.57 (37-38)	0.071
35-36 6/7 Gestational age	9 (7.1)	8 (6.1)	0.805
Birth weight (kg) Median (IQR)	3.92 (3.86-4.08)	3.89 (3.75-3.96)	0.001‡
Macrosomia (>4000 g)	45 (35.7)	27 (20.5)	0.008‡

[Table/Fig-1]: Birth characteristics of the study groups.
*Categorical outcomes expressed as frequency (percentage) and compared using Chi-square test/Fisher's-exact test; †Numerical variables expressed as median {Interquartile range (IQR)} and compared using Mann-Whitney U test; ‡The p-value <0.05 was taken as significant; C-section: Caesarean section; CI: Confidence interval; *(Modified Kuppusamy scale) [17]

Outcome	LIDM n=126	LnIDM n=132	Crude odd's ratio (95% CI)	Adjusted odd's ratio (95% CI)	p-value
Need for respiratory support (Invasive/Non invasive ventilation)	42 (33.3)	30 (22.7)	1.700 (0.98-2.95)	1.62 (0.92-2.83)	0.08
Respiratory morbidities					
Transient tachypnoea of newborn	36 (28.6)	27 (20.5)	1.55 (0.87-2.75)	1.46 (0.81-2.62)	0.2
Meconium aspiration syndrome	6 (4.8)	3 (2.3)	2.15 (0.52-8.78)	2.28 (0.56-9.38)	0.23
Need for NICU admission	100 (79.4)	89 (67.4)	1.85 (1.06- 3.26)	2.15 (1.17-4)	0.01‡
Perinatal depression	18 (14.30	12 (9.10)	1.66 (0.76-3.61)	1.43 (0.62-3.21)	0.33
Hypoxic ischemic encephalopathy	4 (3.17)	1 (0.75)	4.29 (0.47-39)	3.44 (0.33-32.1)	0.23
Seizures	1 (0.8)	1 (0.75)	1.04 (0.06-16.93)	0.87 (0.05-14.64)	0.9
Neonatal hyperbilirubinemia	79 (62.7)	66 (50)	1.68 (1.02-2.76)	1.70 (1.01 -2.84)	0.04‡
Peak bilirubin mg/dL, median (IQR)†	16 (15.2,16.5)	16 (15.6, 16.72)			0.55
Duration of phototherapy hours, median (IQR)†	24 (24-40)	24 (20-25.5)			0.11
Exchange transfusion (Indications)	4 (3.2)	2 (1.5)	2.13 (0.38-11.84)	1.60 (0.27-9.41)	0.6
Polycythemia	1 (0.8)	2 (1.5)			
Neonatal hyperbilirubinemia	3 (2.4)				
Haematocrit median (IQR)†	51 (48, 60.5)	52 (49.6, 59)			0.53
Polycythaemia	10 (7.9)	3 (2.3)	3.7 (0.99-13.79)	3.73 (0.98-14.22)	0.053
Thrombocytopenia	9 (7.14)	2 (1.5)	5 (1.06-23.7)	4.2 (0.86 -20.3)	0.08
Persistent Pulmonary Artery Hypertension (PPHN)	18 (14.3)	4 (3.03)	5.33 (1.75-16.23)	4.43 (1.41 -13.82)	0.004‡
Ventricle hypertrophy	5 (4)	1 (0.75)	5.41 (0.62-46.99)	4.2 (0.43-41.25)	0.17
Patent ductus arteriosus	7 (5.5)	2 (1.5)	3.82 (0.78-18.8)	3.21 (0.626-16.53)	0.13
Ventricular septal defect	3 (2.4)	1 (0.75)	3.19 (0.32-31.12)	1.89 (0.18-19.71)	0.58
Hypoglycaemia	15 (11.9)	6 (4.5)	2.83 (1.06-7.56)	2.26 (0.82-6.2)	0.11
Hypocalcaemia	3 (2.38)	1 (0.75)	3.19 (0.32-31.12)	0.63 (0.02-16.8)	0.78
Birth injuries:					
Clavicle fracture	4 (3.17)	2 (1.5)	2.13 (0.38-11.84)	2.45 (0.44-13.68)	0.29
Extracranial bleeds (cephalohaematoma/subgaleal bleed)	3 (2.4)	6 (4.5)	0.51 (0.12-2.09)	0.353 (0.08-1.53)	0.15
Shoulder dystocia/Erb's palsy	4 (3.17)	2 (1.5)	2.13 (0.38-11.84)	1.80 (0.32-10.28)	0.50
Acute kidney injury	5 (3.97%)	2 (1.51%)	2.686 (0.51-14.10)	2.5 (0.47-13.17)	0.26
Sepsis	16 (12.69%)	10 (7.57%)	1.77 (0.77-4.07)	1.85 (0.79-4.3)	0.14

[Table/Fig-2]: Comparison of clinical outcomes of study groups.
*Categorical outcomes expressed as frequency (percentage) and compared using Chi-square test/Fisher's exact test; †Numerical variables expressed as median {Interquartile Range (IQR)} and compared using Mann-Whitney U test; ‡p value <0.05 statistically significant; CI: Confidence interval

The LIDM's weighed higher (p=0.001) and were more macrosomic (p=0.008) compared to LnIDM's [Table/Fig-1]. The clinical outcomes of the two study groups and their comparison are shown in [Table/Fig-2].

On univariate analysis, the primary outcome of need for respiratory support was not significantly different between the two groups (aOR 1.62; 95% CI 0.92 -2.83; p=0.08), but NICU admission rates {100 (79.4) vs 89 (67.4)}, neonatal hyperbilirubinemia {79 (62.7) vs 66 (50)}, thrombocytopenia {9 (7.14) vs 2 (1.5)} and PPHN {18 (14.3) vs 4 (3.03)} n(%) were significantly higher in the LIDM's compared to the LnIDM's. On multivariate logistic regression, controlling for covariates like gestational age, birthweight, gestational hypertension and polycythaemia; NICU admission rates (aOR 2.15; 95% CI 1.17-4; p=0.01), neonatal hyperbilirubinemia (aOR 1.70; 95% CI 1.01-2.84; p=0.04) and PPHN (aOR 4.43; 95% CI: 1.41 -13.82; p=0.004) were still significantly higher in the LIDM's. None of the other morbidities were different between the study groups.

DISCUSSION

The LGA infants constitute a significant proportion of live births but this population has not been well studied, at least in LMIC's like India, where GDM is widely prevalent and is a major cause of LGA births [2]. In present study, the LGA incidence was 9.72% and GDM contributed to 48.8% of LGA births. LIDM's required more neonatal admission (aOR 2.15; 95% CI 1.17-4; p=0.01*), and had significantly higher neonatal hyperbilirubinemia (aOR 1.70; 95% CI 1.01-2.84; p=0.04*) and PPHN (aOR4.43; 95% CI: 1.41-13.82, p=0.004*), compared to LnIDM's, after adjusting for confounding factors.

The LGA incidence of 9.72% reported in this study was close to another single centre study from South India where Jeyaseelan L et al., had reported an LGA incidence of 9.4% in their analysis of 35,718 deliveries over a 15-year period [2]. But Malik M et al., in a community based study of a rural population from North India, had reported a LGA prevalence of 1.3% [23]. The difference in rates could be explained by the differing patient characteristics, demographic factors and heterogeneity in screening criteria used. A prevalence ranging from 2.3% to 19.1% has been reported from other LMIC's [13,24-27].

In our study, GDM contributed to 48.8% of all LGA births, which was higher than previous studies (10.3%-18.7%) [9,22,28,29]. The GDM is a known risk factor for LGA births and GDM has a high prevalence among pregnant women in India [13,30-33]. Hence, it is not surprising that a higher proportion of LGA births are related to GDM. Nevertheless, in current study, the pre-pregnancy weight and weight gain during pregnancy were not documented in all case records and hence, the role of maternal obesity and excessive weight gain during pregnancy as an additional contributor to LGA births in GDM mothers cannot be ruled out.

In present study, LIDM's had a significantly higher median birth weight (3.92 kg vs. 3.89 kg, p=0.001**) and were more likely to be macrosomic (35.7% vs. 20.5%, p=0.008*), compared to LnIDM's. Other similar studies had also reported a higher birth weight in the GDM group compared to the non-GDM [9,28,34]. But, unlike

these studies, which reported a higher rate of caesarean section (78-87.7%) in the LIDM's, compared to LnIDM's (38-68.5%), in this study, the caesarean section rates were similar in both the groups (73.8% vs. 70.5%, p=0.28). This finding was not surprising, as the need for caesarean section is determined by various obstetric and patient driven factors, and not necessarily by standard indications [35].

In this study, LIDM's had a higher need for NICU admission which was also shown in previous studies [9,22,29]. As most clinical morbidities were higher in LIDM's compared to the LnIDM's, it is only expected that the NICU admission rates in this group is higher. Also, LIDM infants had a significantly higher risk of neonatal hyperbilirubinemia in this study, consistent with previous reports [22,34,36]. Both LGA births and GDM are associated with greater risk of neonatal hyperbilirubinemia [37] and as GDM contributed significantly to LGA births in this study, the risk of neonatal hyperbilirubinemia was higher in the LIDM group.

The PPHN is an important cause of hypoxemic respiratory failure and mortality in term infants. In a California birth cohort, Steurer MA et al., found a significant higher prevalence of PPHN in LGA infants (aOR 1.8, 95% CI 1.6-2.0) and infants with maternal diabetes (14.2 vs 8.4%) [38]. Also, a recent meta-analysis showed a significant association between maternal DM and pulmonary hypertension (risk ratio-1.37; 95% C.I. 1.23-1.51) [39]. In our study, the LIDM's had 4.43 times higher odds of developing PPHN, compared to LnIDM's, after adjusting for confounding co-variates (p=0.004). Other studies, similar to ours, have not reported on PPHN [9,22, 28,29,34]. As both LGA and GDM are independent risk factor for PPHN [38,39], GDM induced LGA is a double whammy and this could explain the higher odds of PPHN obtained in the study. In this study, a higher but non significant proportion of infants required respiratory support (aOR1.62; 95% CI 0.92-2.83; p=0.08), whereas respiratory morbidities like transient tachypnoea of newborn and meconium aspiration syndrome were not different between groups. Higher need for respiratory support was also seen in other similar studies [9,29].

In present study, other neonatal morbidities which were nearing statistical significance were polycythaemia (aOR3.73; 95% CI 0.98-14.22; p 0.053) and thrombocytopenia (aOR4.2; 95% CI 0.86-20.3; p 0.08). The risk of polycythaemia is high in GDM due to relative foetal hypoxia induced erythropoiesis, but whether this risk is increased in GDM induced LGA infants compared to non-GDM LGA infants is unknown [40]. Cordero L et al., and Onal EE et al., observed a higher risk of polycythaemia in LGA neonates of GDM mothers [9,28], but the same was not observed in other similar studies [22,34]. Polycythaemia increases the risk of neonatal thrombocytopenia and hyperbilirubinemia [40,41] and both have been reported in a higher proportion of LIDM's in our study. Further large studies with a bigger sample size, are required to determine the association between polycythaemia and LGA births, and this could help in re-evaluating the policy of routine haematocrit estimation in all LGA irrespective of cause.

Previous studies have reported that neonatal outcomes like hypoglycaemia and birth injuries were more common in LIDM's compared to LnIDM's [9,34,42], but this was not seen in this study. A higher proportion of LIDM's developed hypoglycaemia (aOR2.26; 95% CI 0.82-6.2; p=0.11), but statistical significance could not be obtained due to the small sample size. The lower rate of birth injuries in current study, could be explained by the lower proportion of vaginal births and macrosomia [43].

Limitation(s)

The retrospective study design and small sample size were potential limitations of the study. Present study was a single centre experience, which could limit its generalisability and external validity. Also, we could not access more antenatal data on known risk factors of LGA births like pre-pregnancy weight and weight gain during pregnancy. Thus, the exact burden of non-GDM induced LGA could not be ascertained. Also, certain significant outcomes reported in our study, like neonatal hyperbilirubinemia, had wide CI, and the long-term morbidities of LGA infants were not analysed. Lastly, as with any observational study, confounding bias is a problem, as all confounding covariates could not have been accounted for.

CONCLUSION(S)

This study which analysed and compared LIDM {126 (48.8%)} and LnIDM {132 (51.2%)} clearly showed that GDM contributes significantly to LGA births, and is associated with further increase in short term morbidities, compared to non-GDM causes. These infants are more likely to require NICU admission and paediatricians caring for these infants, should recognise the need for respiratory support and echocardiography, in addition to screening for hyperbilirubinemia, hypoglycaemia and polycythaemia.

Further, large population-based studies are required to refine our knowledge about LGA infants and the influence of GDM. Also, a longer follow-up period is needed to capture any additional morbidities like abnormal anthropometry and cardiometabolic parameters.

REFERENCES

[1] Macrosomia: ACOG Practice Bulletin, Number 216. Obstet Gynecol. 2020;135:e18-35.
[2] Jeyaseelan L, Yadav B, Silambarasan V, Vijayaselvi R, Jose R. Large for gestational age births among south indian women: Temporal trend and risk factors from 1996 to 2010. J Obstet Gynaecol India. 2016;66(Suppl 1):42-50.
[3] Li G, Kong L, Li Z, Zhang L, Fan L, Zou L, et al. Prevalence of macrosomia and its risk factors in china: A multicentre survey based on birth data involving 101,723 singleton term infants. Paediatr Perinat Epidemiol. 2014;28(4):345-50.
[4] Koyanagi A, Zhang J, Dagvadorj A, Hirayama F, Shibuya K, Souza JP, et al. Macrosomia in 23 developing countries: An analysis of a multicountry, facility-based, cross-sectional survey. Lancet. 2013;381(9865):476-83.
[5] Vinturache AE, Chaput KH, Tough SC. Pre-pregnancy body mass index (BMI) and macrosomia in a Canadian birth cohort. J Matern-Fetal Neonatal Med. 2017;30:109-16.
[6] Salihu HM, Dongarwar D, King LM, Yusuf KK, Ibrahimi S, Salinas-Miranda AA. Trends in the incidence of fetal macrosomia and its phenotypes in the United States, 1971-2017. Arch Gynecol Obstet. 2020;301(2):415-26.
[7] Henriksen T. The macrosomic fetus: A challenge in current obstetrics. Acta Obstet Gynecol Scand. 2008;87(2):134-45.
[8] Jolly MC, Sebire NJ, Harris JP, Regan L, Robinson S. Risk factors for macrosomia and its clinical consequences: A study of 350,311 pregnancies. Eur J Obstet Gynecol Reprod Biol. 2003;111(1):09-14.
[9] Cordero L, Paetow P, Landon MB, Nankervis CA. Neonatal outcomes of macrosomic infants of diabetic and non-diabetic mothers. J Neonatal Perinatal Med. 2015;8(2):105-12.
[10] Ng SK, Olog A, Spinks AB, Cameron CM, Searle J, McClure RJ. Risk factors and obstetric complications of large for gestational age births with adjustments for community effects: Results from a new cohort study. BMC Public Health. 2010;10:460.
[11] Chauhan SP, Rice MM, Grobman WA, Bailit J, Reddy UM, Wapner RJ, et al. MSCE, for the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units (MFMU) Network. neonatal morbidity of small- and large-for-gestational-age neonates born at term in uncomplicated pregnancies. Obstet Gynecol. 2017;130(3):511-19.
[12] Seshiah V, Balaji V, Balaji MS, Sanjeevi CB, Green A. Gestational diabetes mellitus in India. J Assoc Physicians India. 2004;52:707-11.
[13] Mallouli M, Derbel M, Ingrid A, Sahli J, Zedini C, Ajmi T, et al. Associated outcomes to fetal macrosomia: Effect of maternal diabetes. Tunis Med. 2017;95(2):120-25.
[14] WHO. WHO Child Growth Standards: Methods and development: Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age. WHO; Geneva: 2006.
[15] Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy: A World Health Organisation Guideline. Diabetes Res Clin Pract. 2014;103(3):341-63.
[16] American College of Obstetricians and Gynecologists' Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 201: Pregestational Diabetes Mellitus. Obstet Gynecol. 2018;132(6):e228-48.
[17] Wani RT. Socioeconomic status scales-modified Kuppuswamy and UdaiPareekh's scale updated for 2019. J Family Med Prim Care. 2019;8(6):1846-49.
[18] WHO: Protecting, promoting and supporting breastfeeding in facilities providing maternity and newborn services. Available from https://www.who.int/nutrition/publications/guidelines/breastfeeding-facilities-maternity-newborn/en/#.X89q7phad-I.google (Accessed on Jan 4, 2021).

[19] World Health Organisation (WHO). Baby-friendly hospital initiative: Revised, updated and expanded for Integrated care Preface for the 2009 BFHI materials: Revised, updated and expanded for Integrated care. Available from www.ncbi.nlm.nih.gov/books/NBK153495/ (Accessed on Jan 4, 2021).
[20] American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004;114:297.
[21] Network NN. National neonatal-perinatal database (report 2002-2003). New Delhi, India: Department of Pediatrics, All India Institute of Medical Sciences. 2005.
[22] Lloreda-García JM, Sevilla-Denia S, Rodríguez-Sánchez A, Muñoz-Martínez P, Díaz-Ruiz M. Perinatal outcome of macrosomic infants born to diabetic versus non-diabetic mothers. Endocrinol Nutr. 2016;63(8):409-13.
[23] Malik M, Khanna P, Verma R. The association of maternal risk factors to macrosomia in rural areas of Haryana, India: A community based study. International Journal of Community Medicine and Public Health. 2018;5(9):3842-46.
[24] Pereda J, Bove I, Pineyro MM. Excessive maternal weight and diabetes are risk factors for macrosomia: A cross-sectional study of 42,663 pregnancies in Uruguay. Front Endocrinol (Lausanne). 2020;11:588443.
[25] Said AS, Manji KP. Risk factors and outcomes of fetal macrosomia in a tertiary centre in Tanzania: A case-control study. BMC Pregnancy Childbirth. 2016;16:243.
[26] Tela FG, Bezabih AM, Adhanu AK, Tekola KB. Fetal macrosomia and its associated factors among singleton live-births in private clinics in Mekelle city, Tigray, Ethiopia. BMC Pregnancy Childbirth. 2019;19:219.
[27] Najafian M, Cheraghi M. Occurrence of fetal macrosomia rate and its maternal and neonatal complications: A 5-year cohort study. ISRN Obstet Gynecol. 2012;2012:353791.
[28] Onal EE, Hirfanoglu IM, Beken S, Altuntas N, Turkyilmaz C, Duyan Camurdan A, et al. Are the neonatal outcomes similar in large-for-gestational age infants delivered by women with or without gestational diabetes mellitus? World J Pediatr. 2012;8:136-39.
[29] Das S, Irigoyen M, Patterson MB, Salvador A, Schutzman DL. Neonatal outcomes of macrosomic births in diabetic and non-diabetic women. Arch Dis Child Fetal Neonatal Ed. 2009;94(6):F419-22.
[30] Arora GP, Thaman RG, Prasad RB, Almgren P, Brøns C, Groop LC, et al. Prevalence and risk factors of gestational diabetes in Punjab, North India: Results from a population screening program. Eur J Endocrinol. 2015;173(2):257-67.
[31] Gopalakrishnan V, Singh R, Pradeep Y, Kapoor D, Rani AK, Pradhan S, et al. Evaluation of the prevalence of gestational diabetes mellitus in North Indians using the International Association of Diabetes and Pregnancy Study groups (IADPSG) criteria. J Postgrad Med. 2015;61(3):155-58.
[32] Raja MW, Baba TA, Hanga AJ, Bilquees S, Rasheed S, Haq IU, et al. A study to estimate the prevalence of gestational diabetes mellitus in an urban block of Kashmir valley (North India). Int J Med Sci Public Health. 2014;3:191-95.
[33] Bhatt AA, Dhore PB, Purandare VB, Sayyad MG, Mandal MK, Unnikrishnan AG. Gestational diabetes mellitus in rural population of Western India- Results of a community survey. Indian J Endocrinol Metab. 2015;19:507-10.
[34] Opati P, Zheng R, Wang J, Xin Y, Zhao H, Bi D. Comparison of neonatal outcomes in macrosomic infants of diabetic and non-diabetic mothers. J Neonatal Perinatal Med. 2015 Mar 10.
[35] da Silva Charvalho P, Hansson Bittár M, Vladic Stjernholm Y. Indications for increase in caesarean delivery. Reprod Health. 2019;16(1):72.
[36] Norman M, Åberg K, Holmsten K, Weibel V, Ekéus C. Predicting non hemolytic neonatal hyperbilirubinemia. Pediatrics. 2015;136(6):1087-94.
[37] Karmon A, Levy A, Holcberg G, Wiznitzer A, Mazor M, Sheiner E. Decreased perinatal mortality among women with diet-controlled gestational diabetes mellitus. Int J Gynaecol Obstet. 2009;104(3):199-202.
[38] Steurer MA, Jelliffe-Pawlowski LL, Baer RJ, Partridge JC, Rogers EE, Keller RL. Persistent pulmonary hypertension of the newborn in late preterm and term infants in California. Pediatrics. 2017;139(1):e20161165.
[39] Shu LP, Zhang RH, Cai YH, Zhou JB, Yang JK, Qi L. Maternal diabetes mellitus and persistent pulmonary hypertension of the newborn: Accumulated evidence from observational studies. Can J Diabetes. 2020;44(4):327-34.e3.
[40] Jones CW. Gestational diabetes and its impact on the neonate. Neonatal Netw. 2001;20(6):17-23.
[41] Vlug RD, Lopriore E, Janssen M, Middeldorp JM, Rath ME, Smits-Wintjens VE. Thrombocytopenia in neonates with polycythemia: Incidence, risk factors and clinical outcome. Expert Rev Hematol. 2015;8(1):123-29.
[42] Esakoff TF, Cheng YW, Sparks TN, Caughey AB. The association between birthweight 4000 g or greater and perinatal outcomes in patients with and without gestational diabetes mellitus. Am J Obstet Gynecol. 2009;200(6):672.e1-4.
[43] Linder N, Linder I, Fridman E, Kouadio F, Lubin D, Merlob P, et al. Birth trauma-risk factors and short-term neonatal outcome. J Matern Fetal Neonatal Med. 2013;26(15):1491-95.

PARTICULARS OF CONTRIBUTORS:
1. Paediatric Resident, Department of Neonatology, Chettinad Hospital and Research Institute, Rajiv Gandhi IT Highway, Kelambakkam, Chengalpattu, Tamil Nadu, India.
2. Resident, Department of Neonatology, Chettinad Hospital and Research Institute, Rajiv Gandhi IT Highway, Kelambakkam, Chengalpattu, Tamil Nadu, India.
3. Assistant Professor, Department of Neonatology, Chettinad Hospital and Research Institute, Rajiv Gandhi IT Highway, Kelambakkam, Chengalpattu, Tamil Nadu, India.
4. Professor, Department of Neonatology, Chettinad Hospital and Research Institute, Rajiv Gandhi IT Highway, Kelambakkam, Chengalpattu, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Giridhar Sethuraman,
Department of Neonatology, Chettinad Hospital and Research Institute,
Chettinad Health City, Rajiv Gandhi IT Highway, Kelambakkam,
Chengalpattu District-603103, Tamil Nadu, India.
E-mail: giridharsethu@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jan 20, 2021
- Manual Googling: Apr 09, 2021
- iThenticate Software: Apr 30, 2021 (6%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jan 19, 2021**
Date of Peer Review: **Mar 17, 2021**
Date of Acceptance: **Apr 19, 2021**
Date of Publishing: **Jun 01, 2021**