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Prevalence And Risk Factors Of Extra-Uterine Growth Restriction In Preterm Neonates: A Retrospective Study From A Tertiary Care Hospital

Sushma K[1], Tokpam Reshma Chanu[1*], Shagufa Irem[2], Arsala[2],B S Meghana[2]

[1]Department of Pediatrics, JSS Medical College, Mysuru, Karnataka, India.

[1,2]Department of Nutrition & [2]Dietetics, JSS Academy of Higher Education & Research, Mysuru, Karnataka, India

***Corresponding Author:**

Tokpam Reshma Chanu

Assistant Professor, Department of Nutrition & Dietetics, JSS Academy of Higher Education & Research, Mysuru, Karnataka, India

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ABSTRACT

Background: Extra-uterine growth restriction (EUGR) is a prevalent complication among very low birth weight (VLBW) preterm infants, associated with long-term adverse developmental outcomes.

Objectives: The study aimed to determine the prevalence of EUGR in preterm infants and identify associated clinical and maternal risk factors.

Methods: A retrospective analysis was conducted in the NICU at JSS Hospital, Mysuru, among 128 preterm infants with birth weight <1500 g, admitted between July 2022 and January 2024. Baseline characteristics and clinical data were analyzed using SPSS. Multivariate logistic regression identified independent predictors of EUGR.

Results: Of the 128 preterm infants, 95 (74%) were classified as EUGR. Males were more affected (55%) than females (45%). Significant factors associated with EUGR included lower gestational age ($p = 0.003$), lower birth weight ($p = 0.001$), lower discharge weight ($p < 0.0001$), and delayed achievement of full feeds ($p = 0.003$). Gestational diabetes mellitus (GDM) was a significant independent predictor (OR: 0.26, CI: 0.09–0.69, $p = 0.007$).
Conclusions: EUGR is prevalent among preterm infants in this setting, particularly in males and those with low gestational age and birth weight. GDM emerged as a key risk factor. Improved early nutritional strategies and maternal risk factor management may mitigate EUGR incidence.

Keywords: *EUGR, preterm infants, very low birth weight, growth restriction, gestational diabetes mellitus.*

1. INTRODUCTION

Extra-uterine growth restriction (EUGR) is a common problem and a known risk factor for poor development in very low-birth-weight (VLBW) new-borns. In recent years, there was an enormous increase in the survival rate of preterm infants, particularly those categorized as very-low-birth-weight (VLBW, with birth weight < 1500 g).[1] Very low birth weight (VLBW, <1500 g) infants continued with poor weight gain as the most common morbidity, although significant advances in the growth of hospitalized preterm infants during the past twenty years. Neurodevelopmental impairment is another typical problem seen in VLBW infants. VLBW infants show trouble in many of areas including cognitive, motor, language, and behavioral functioning. Children and their families suffer from these challenges, and the costs to society of early intervention and special education services are significant.[2] in very low birth weight (VLBW) and extremely low birth weight (ELBW) preterm infants, extra-uterine growth restriction (EUGR), frequently referred to as postnatal growth restriction, continuing to be a serious problem. In the previous research, the 10th percentile of expected growth value (weight, length, or head circumference) at discharge was taken to be less than or equal to EUGR. Since EUGR can occur in both small for gestational age infants at birth and appropriate gestational age infants, some experts have characterized EUGR as a z-score between birth and discharge >1 SD. Thus, adequate and vigorous diet modification in the first few days of birth to prevent growth failure in VLBW and ELBW have been widely recommended and emphasized in recent decades. Therefore, higher daily calorie intakes of 45–55 kcal/kg, higher protein intakes of 3–4 g/kg, higher glucose intakes of 7–10 g/kg, and higher lipid infusion levels of up to 1 g/kg have been recommended for VLBW and ELBW infants in their first few days of life.[3]

According to the definition and growth chart used, the incidence of EUGR may vary from 13% to 97%. There currently exist two types of growth charts that can be used to figure out the prevalence of EUGR: "standards" charts, which show "how growth has to be," and "reference" charts, which indicate "how growth actually is." While the reference charts can use data got without restrictions, the standard charts must be based on highly selected patients and restrictive criteria. [4]

In premature infants, Extra-Uterine Growth Restriction (EUGR) is a common and widely known condition. Other names used for it are poor in-hospital growth, postnatal growth retardation, postnatal growth failure, and postnatal growth limitations. Preterm infants with EUGR that are categorized to have a poor neurodevelopmental prognosis based on their weight, head circumference, or length. Longitudinal studies, that evaluate differences in growth between two points in time, usually begin at birth. four If an infant's birth weight is in the lowest decile on a birth weight curve specific to a given gestational age, it is considered growth restricted, or small for gestational age (SGA). Particularly in preterm infants, means, medians, and 10th centiles of birth weight distributions are lower compared to that of estimated fetal weight distributions. [5]

2. RESEARCH METHODOLOGY

Research Design: This study utilized a retrospective study survey design. This design was chosen because it allows for the collection of data from a large number of participants at a single point in time.

Participants: The study's target group consisted of patients with extra uterine growth restriction (EUGR) who were hospitalised between July 2022 and January 2024. The study was conducted on 128 preterm new-borns (95 EUGR and 33 NON EUGR) at the NICU, Department of Paediatrics, JSS Hospital, Mysuru.

Data collection: This study was approved by the Institutional Ethics Committee of JSS Medical College (JSSMC/IEC/070324/14 NCT/2024-25). Patients who were dead or against medical leave were excluded in the study. After availing the permission, the information was gathered and imported into the Microsoft excel for the further analysis. The data from the patient's medical record was collected in order to collect secondary data. Information on the patient' initial features, risk factors, delivery mode, etc., was documented. Fenton preterm growth chart was used to determine the growth factor by plotting the graph.

Data Analysis Methods: Data were analysed using SPSS software. Descriptive statistics were used to summarize the data, median interquartile range (IQR) was employed for the prevalence for EUGR and multivariate logistic regression was performed to identify the incidence and associated factors for EUGR with 95% confidence interval (CI) showing the statistical significance from the results.

3. RESULTS

From the present study total of 128 subjects born preterm were enrolled in the study out of which 71 male and 57 female preterm infants. The table 1 shows that the baseline characteristics which allowed us to determine that the median of the maternal age was 26 for EUGR and had an interquartile range (IQR) of 23–31, while the median age of NON EUGR median of the maternal age was 27 with an IQR of 23–30 and a P value of 0.84, which was less significant. Whereas the median of the gestational age for NON EUGR was 32 with an IQR of 30-33 and the p value was 0.003, the median of gestational age for EUGR was 33 with an IQR of 32-34.

Table 1: Baseline characteristics of Quantitative variables:

	EUGR	**NON EUGR**	
	Median (IQR)	**Median (IQR)**	**p value**
Maternal Age	26 (23-31)	27 (23-30)	0.84
Gestational Age (weeks)	33 (32-34)	32 (30-33)	0.003
Birth weight (grams)	1580 (1340-1800)	1900 (1480-2260)	0.001*
Discharged weight (grams)	1540 (1380-1690)	1800 (1600-2200)	0.0001*
Rate of weight gain/kg	-2.1 (-8.5-1.85)	-3.9 (-8-6.3)	0.6
Duration of stay	15 (10-22.5)	9 (3-12)	0.51
Days of respiratory support	3 (1-6.5)	2 (0-3)	0.676
Day full feed was achieved	7 (4-14)	4 (2-6)	0.003

The birth weight in grams was evaluated; and the p value was 0.001, which is highly significant; the median for EUGR was 1580 grams with an IQR of 1340-1800, whereas the median for NON EUGR was 1900 grams with an IQR of 1480-2260. The birth weight in grams was evaluated; the p value was 0.001, which is very significant.

Comparable to discharge weight in grams, for EUGR the median discharge weight was 1540 with an IQR of 1380-1690, whereas for NON EUGR it was 1800 with an IQR of 1600-2200, and a highly significant p value was determined to be 0.0001. While the weight gain per kg was calculated, it was proved that the median in EUGR was -2.1 with an IQR of -8.5-1.85, whereas the median in NON EUGR was -3.9 with an IQR of -8-6.3 and a p value of 0.6. As the median duration of stay for non-EUGR was reported as 9, with an IQR of 3–12 and a p value of 0.51, the median duration of stay for EUGR was observed to be 15, with an IQR of 10–22.5. For EUGR, the days of respiratory support were found to have a median of 3 with an IQR of 1-6.5, yet for NON-EUGR, the same information was estimated to have a median of 2, with an IQR of 0-3, and a p value of 0.676. Days the full feed achieved was the moment where lactation started; for EUGR, the median was 7 with an IQR of 4–14, and for NON EUGR, it was 4 with an IQR of 2–6 with a p value of 0.003. From the p values for birth weight and discharge weight (in grams), which are less than 0.05 and 0.001 and 0.0001, respectively, we might assume from the baseline characteristics shown in Table 1 that the growth of the infants is highly significant for both of those weights.

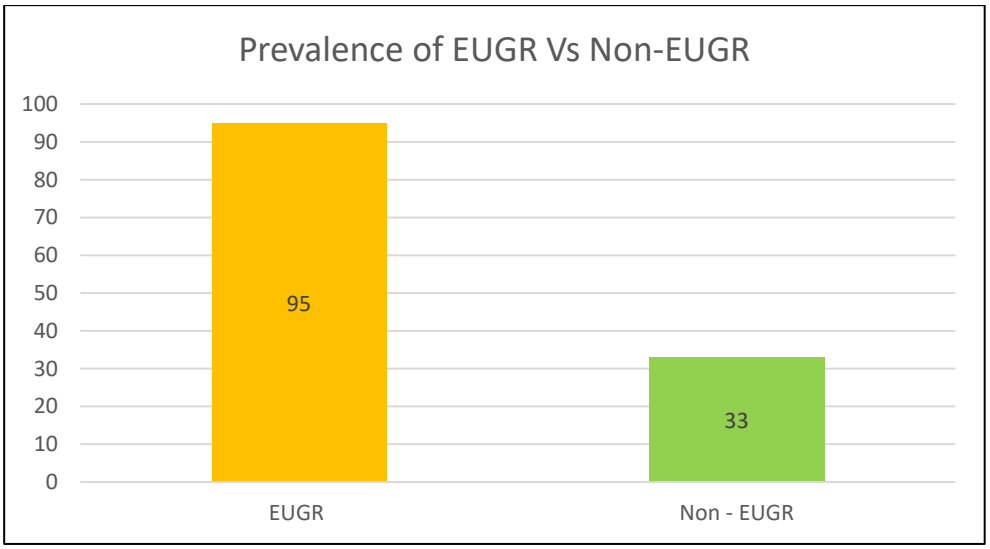

Figure 1: Prevalence of EUGR vs. Non EUGR

Figure 1 shows that there is a significant prevalence of both preterm infants, with a higher proportion in the EUGR than from NON EUGR. The EUGR group is defined as those with growth parameters (weight, length, and cranial circumference) ≤ 10th percentile for post-menstrual age (PMA) at discharge and preterm babies born more than 30 weeks gestational age.

Table 2 shows the predominance of EUGR and NON EUGR. Males (55%) and females (45%) were found to be impacted by EUGR among the preterm babies when factors such as NON EUGR and EUGR were taken into account. Male (58%) and female (42%) were impacted by NON EUGR. This led us to the conclusion that male were more prone to EUGR than female category.

Table 2: Distribution of qualitative variables through gender wise

	Male	Female
EUGR	55%	45%
NON EUGR	58%	42%

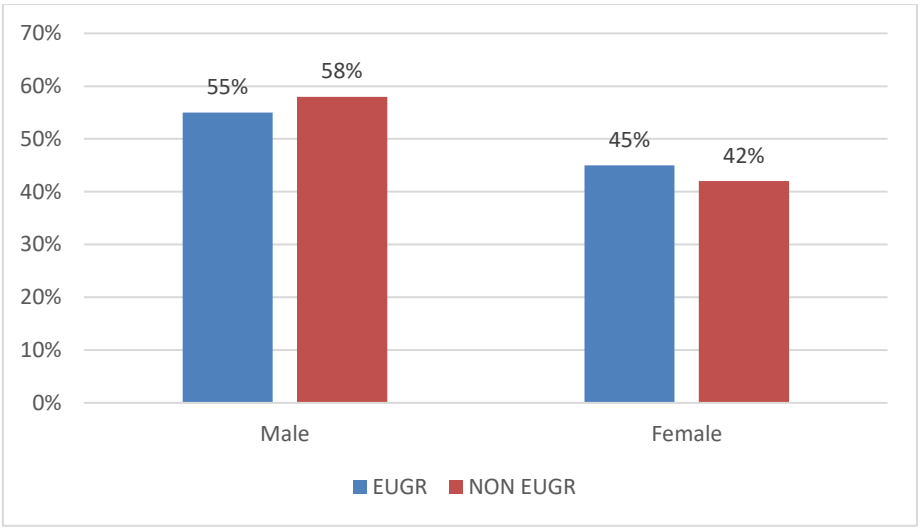

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Figure 2: Distribution of qualitative variables through gender wise

From the Figure 2, the percentage of preterm births by gender in the population is shown. With 55% of EUGR and 58% of NON EUGR, the male population is larger than the female population, which is between 45% and 42% of EUGR and NON EUGR, respectively.

Table 3: Distribution of qualitative data through Mode of delivery

	LSCS	Vaginal
EUGR	86%	14%
NON EUGR	73%	27%

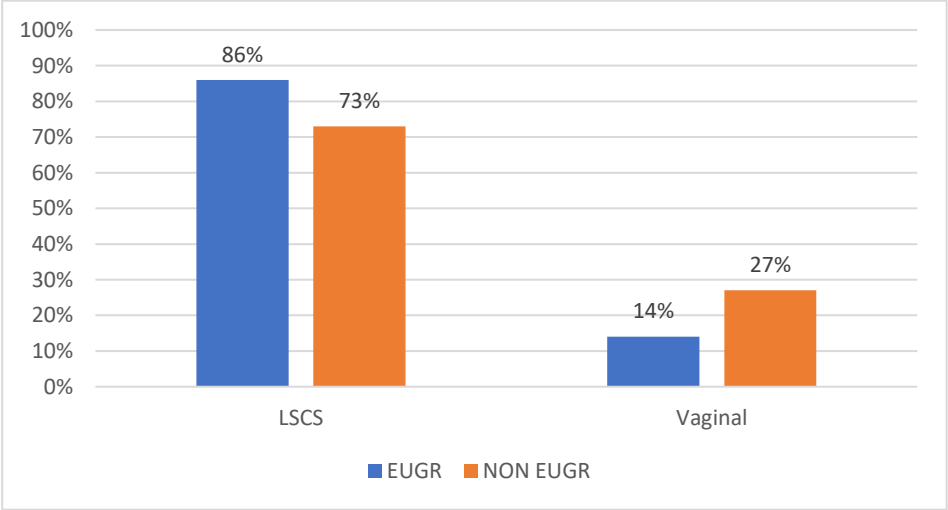

Figure 3: Distribution of qualitative data through mode of delivery

From the Figure 3**,** it shows that LSCS between 70-90% were more prone to cause the reasons of delivering as preterm (EUGR) while vaginal delivery was less between 10-15% in EUGR.

Table 4: Distribution of qualitative data based on parity:

	Primi	Multi
EUGR	**55%**	**45%**
NON EUGR	**61%**	**39%**

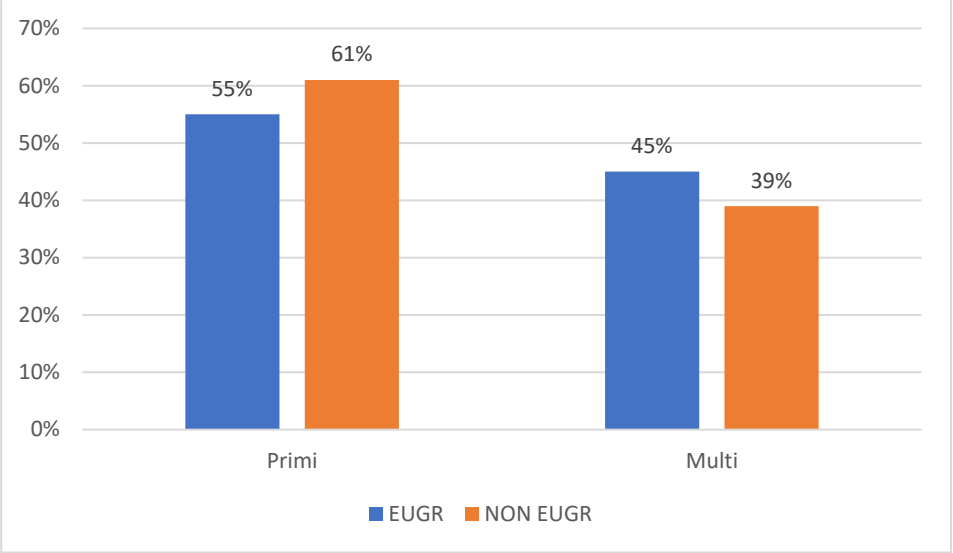

Figure 4: Distribution of qualitative data based on parity

According to Figure 4, out of 128 preterm babies, 45% of the mothers gave birth more than once, and 55% of the mothers gave birth to their first child (primi). This leads us to the conclusion that primi parity was higher in EUGR and NON EUGR, whereas multi parity was lower in both.

Table 5: Multivariate Logistic Regression:

Variable	Odds Ratio (95%CI)	p value
Gender	0.73 (0.30-1.75)	0.48
Order of delivery	0.99 (0.41-2.32)	0.98
PIH	1.98 (0.69-5.7)	0.2
GDM	0.26 (0.09-0.69)	0.007*
MOD	1.99 (0.69-5.7)	0.20
RDS	0.56 (0.22 – 1.44)	0.231
Sepsis	2.3 (0.82-6.4)	0.111
NEC	1.03 (0.17 – 6.06)	0.976

*p value (0.05) highly significant

From the Table 5, it represents that 95% confidence interval (CI) showing the statistical significance of which the p value is less than 0.05. In a similar way for both vaginal and LSCS delivery orders, the chances ratio 95% CI was found to be 0.99 (0.41-2.32) with a p value of 0.98, showing that the outcome is not significant. Examining pregnancy-induced hypertension (PIH), another result indicated an odds ratio of 1.98 with a 95% confidence interval of 0.69-5.7 and a non-significant value of 0.2. The outcome of this multivariable logistic regression led us to conclude that there is a significant chance that a newborn will suffer from gestational diabetes mellitus (GDM), which is demonstrated by the p value of 0.007 (< 0.05). An odds ratio of 1.99 with a 95% confidence interval of 0.69-5.7 and a not significant p value of 0.20 was identified when multiple organ dysfunction was evaluated. When it placed next to respiratory distress syndrome (RDS), it also gave an odds ratio of 0.56 with a 95%CI of (0.22-1.44) and a p value of 0.231, which is not significant. The sepsis odds ratio, that was 2.3 with a 95% confidence interval of (0.82-6.4) were p value of 0.111, was not significant. Necrotizing enterocolitis (NEC) odds ratio was 1.03, with a 95% CI of (0.17-6.06) were p value of 0.976, showing no statistical significance.

4. DISCUSSION

Based on the findings, it was determined a prevalence of 95 infants, Males (55%) and females (45%) preterm infants as EUGR and 33 Males (58%) and females (42%) preterm infants as NON EUGR with a gestational age <32 weeks and birth weight <1500grams. Netsanet Workneh Gidi et al, Pedro C. Marques et al, CAO wei et al, Kukreja B et al, Ioanna Kakatsaki et al, analyzed significantly in different populations. In particular, Netsanet Workneh Gidi et al. reported 436 preterm infants

in which, 223 (51%) were male, 224 (51.4%) were very low birth weight (VLBW), and 185 (42.4%) were small for gestational age (SGA), 86.2% had EUGR, Pedro C. Marques et al. reported of the 101 VLBW neonates examined, 35 (34.7%) exhibited EUGR, CAO Wei et al. reported that 284 (40.9%) of the 694 infants showed EUGR at discharge. Kukreja B et al reported 45.2% were EUGR.[6]

Ioanna Kakatsaki et al, reported that 17.5% of infants were born greatly preterm (< 28 weeks), having a mean (±SD) gestational age of 29.6 (±1.7) weeks. At a mean body weight of 1341.5 (±363.3) grams, 55.8% of newborns were male. [7] Mala Kumar et al, observed in the study that of the 111 neonates included, the gestational age and birth weight varied between 28 and 36 weeks (median 33) and 880-2460 g (median 1580 g). At discharge, 72 (64.8%) had a EUGR. Whereas from the present study we observed that the median of the maternal age was 26 for EUGR and had an interquartile range (IQR) of 23–3 with p value 0.84, the median of gestational age for EUGR was 33 with an IQR of 32-34 with p value 0.003.[8]

Meng Sun et al, reported that the data analysis identified 43 children where gestational age was below 32 weeks, 61 children whose gestational age was within 32 and 35 weeks, and 28 children where gestational age were over 35 weeks. In 48 (36.36%) preterm babies in the group of no more than 32 weeks, 55 (41.67%) infants in the group of 32–35 weeks, and 29 (21.97%) infants in the group of over 35 weeks, EUGR was determined according to weight, length, and head circumference. In short, a significant relationship was observed between the weight, length, and head circumference of preterm infants of different birth ages and the incidence of EUGR (p value <0.05).[9] We observed that the birth weight in grams was evaluated; and the p value was 0.001, which is highly significant; the median for EUGR was 1580 grams with an IQR of 1340-1800, similarly in a review article 132 infants in the study, Meng Sun et al reported that 16 had a birth weight of under 1500 g, 93 had a birth weight that was between 1500 and 2500 g, and 23 had a birth weight of over 2500 g. The weight, body length, and head circumference of infants who had different weights at birth had a significant association to their EUGR (P<0.05). The results of Kyoung Eun Joung's et al. study, the median birth weight was 865 (740, 1040) g, and the median gestational age was 29.4 (28.4, 30.9) weeks.[9,10] Comparable to discharge weight in grams, for EUGR the median discharge weight was 1540 with an IQR of 1380-1690, and a highly significant p value was determined to be 0.0001. While the weight gain per kg was calculated, it was proved that the median in EUGR was -2.1 with an IQR of -8.5-1.85, p value of 0.6. p value of 0.51, the median duration of stay for EUGR was observed to be 15, with an IQR of 10–22.5. For EUGR, the days of respiratory support were found to have a median of 3 with an IQR of 1-6.5, and a p value of 0.676. Days the full feed achieved was the moment where lactation started; for EUGR, the median was 7 with an IQR of 4–14, p value of 0.003. Based on the baseline parameters presented in Table 1, we can infer that the infants' growth is highly significant for both birth weight and discharge weight (in grams), as indicated by the p values for those weights being less than 0.05, or 0.001 and 0.0001, respectively. The findings of the multivariate logistic regression showed that the odds ratios for the male and female genders were 0.73 (0.30-1.75) and 0.48, respectively, with a 95% confidence interval (CI) indicating the statistical significance of the results. Similarly, for both vaginal and LSCS delivery orders, the results indicate that the outcome is not significant, with the chances ratio 95% CI being found to be 0.99 (0.41-2.32) and a p value of 0.98. Another result on pregnancy-induced hypertension (PIH) showed an odds ratio of 1.98 with a non-significant value of 0.2 and a 95% confidence interval of 0.69-5.7. The odds ratio of gestational diabetes mellitus (GDM) was determined to be 0.26 in our study, with a very significant p value of 0.007 (< 0.05) and a 95% confidence interval of 0.09-0.69. When multiple organ dysfunction was assessed, an odds ratio of 1.99 with a 95% confidence interval of 0.69-5.7 and a not significant p value of 0.20 was found. It also showed a non-significant odds ratio of 0.56 with a 95% confidence interval of (0.22-1.44) and a p value of 0.231 when positioned next to respiratory distress syndrome (RDS). Again, not significant was the sepsis odds ratio, which was 2.3 with a 95% confidence interval of (0.82-6.4) and a p value of 0.111. With a p value of 0.976 and an odds ratio of 1.03 with a 95% confidence interval of 0.17–6.06, necrotizing enterocolitis was not statistically significant. Based on the study by CAO Wei et al, there existed a significant variation (P<0.05) in the incidences of respiratory distress syndrome, apnea, necrotizing enterocolitis, and septicemia among the EUGR and non-EUGR group. The independent risk factors for EUGR, according to the logistic regression analysis, were birth weight, gestational age at birth, and IUGR.[11] Based on the results of this multivariable logistic regression, we were able to determine that a newborn has a considerable risk of developing gestational diabetes mellitus (GDM), as indicated by the p value of 0.007 (< 0.05).

5. CONCLUSION

In newborns whose postnatal growth declines, EUGR is an additional crucial metric to monitor. It has been associated with a number of causes, the most important of which is insufficient nutrition. One of the main issues facing neonatologists is the prevention of EUGR in premature newborns. In a neonatal facility, the absence of evidence-based and standardised nutritional procedures is the most common and adjustable risk factors that cause EUGR. Further essential study on EUGR will be helpful for both immediate identification of faltering genuine growth and the execution of remedial measures. The most frequent reasons are inconsistent and diverse nutritional habits. Throughout the NICU stay, nutritional assessments should be performed at least once a week to enable prompt diagnosis and treatment of EUGR. More research is needed to determine the optimal and suggested dietary intakes than to just optimise and comprehend the variance in body compositions of these preterm newborns, which impacts the postnatal growth.

6. ACKNOWLEDGEMENT

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