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Frequency of Neonatal Morbidity and Mortality in Intrauterine Growth-Restricted Term Pregnancies in Karachi: A Hospital-Based Cross-Sectional Study

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ABSTRACT

Intrauterine growth restriction (IUGR) is a major cause of illness and death in neonates. Growth-restricted term neonates are susceptible to hypoglycemia, respiratory distress, and perinatal mortality. **Objective:** To determine the frequency of neonatal morbidity and mortality among intrauterine growth-restricted (IUGR) term pregnancies. **Methods:** A hospital-based cross-sectional study was performed at the Department of Obstetrics and Gynecology, Liaquat National Hospital, Karachi, from June to November 2024. A total of 143 women with singleton term pregnancies (≥ 37 weeks diagnosed with intrauterine growth restriction (IUGR) due to estimated fetal weight below the 10th percentile were enrolled through consecutive sampling. Neonatal outcomes were documented. Categorical variables were presented as frequency and percentage. A p-value of ≤ 0.005 was deemed statistically significant. **Results:** The median maternal age was 29 years, with a 30.8% having a history of IUGR and 37.8% experiencing intrauterine death; 53.1% delivered vaginally and 46.9% through a cesarean section. Meconium aspiration occurred on 31.5%, low birth weight in 9.1%, and NICU admission in 35.0%, with hypoglycemia (2.1%) and perinatal mortality (4.9%) being uncommon. Lower maternal age was associated with low birth weight and hypoglycemia, adverse Apgar scores with adverse neonatal outcomes, and increased NICU admission after cesarean delivery. **Conclusions:** Intrauterine growth-restricted term pregnancies are strongly associated with adverse perinatal outcomes, including respiratory compromise, metabolic instability, and increased risk of mortality.

INTRODUCTION

Intrauterine growth restriction (IUGR) is a condition in which the fetus fails to reach its genetically set growth potential. It is usually characterized as an estimated fetal weight less than the 10% for gestational age. It significantly contributes to poor perinatal outcomes, including increased risks of neonatal morbidity and mortality [1, 2]. IUGR can cause short- and long-term problems that increase mortality and morbidity in neonates. About 7%-9% of neonates have preterm IUGR, which is associated with 50% of unexplained stillbirths [3]. It affects 10-15% of births worldwide, with higher prevalence in low- and middle-income countries (LMICs) like Pakistan, where it can approach 25% [4, 5]. Although the substantial decline in perinatal morbidity and death over the past thirty years, IUGR remains the second most prevalent cause of perinatal mortality [6]. Birth weight under the 10th percentile for the gestational period affects 30 million neonates worldwide, primarily in LMICs [7, 8]. In Pakistan, IUGR accounts for around 20-24% of live births, acting as a major contributor to newborn problems and mortality [7]. Maternal factors such as pregnancy-induced hypertension (HTN) and thyroid dysfunction have been studied [9]. These risk

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factors increase the likelihood of intrauterine growth restriction and expose affected neonates to long-term health issues such as neurodevelopmental and metabolic issues [10]. Inácio *et al.* concluded that intrauterine growth restriction is associated with adverse perinatal outcomes. It increases the risk of respiratory distress and the need for neonatal resuscitation in neonates [11]. Pregnancies with undetected IUGR have an over eightfold heightened incidence of stillbirth relative to pregnancies without intrauterine growth restrictions (19.8 versus 2.4 per 1000 births)[12].

Previous studies have examined intrauterine growth restriction, but few have examined newborn outcomes in term pregnancies in local settings, underscoring the requirement for context-specific research. This study aimed to determine the frequency of neonatal morbidity and mortality among intrauterine growth-restricted (IUGR) term pregnancies.

METHODS

This hospital-based cross-sectional study was conducted in the Department of Obstetrics and Gynaecology, Liaquat National Hospital, from June 1, 2024, to November 1, 2024, after the approval of the synopsis by the institutional review board (IRB No. 1036-2024-LNH-ERC). A hospital-based cross-sectional study was conducted to assess morbidity and mortality in term IUGR pregnancies. The employed sampling technique was non-probability consecutive sampling. The sample size was determined using a single proportion formula based on a previously reported prevalence of neonatal hypoglycemia (24%) [13], with a 95% CI and a 7% margin of error. In the absence of comprehensive local data on composite neonatal morbidity in intrauterine growth restriction (IUGR) pregnancies, hypoglycemia was utilized as a representative indicator of neonatal morbidity to estimate sample size. The final computed sample size was 143. All patients fulfilling the inclusion criteria were enrolled after receiving informed consent. Study participants were enrolled in a study at delivery, and previous antenatal records from 20 weeks onward were reviewed to confirm the diagnosis. Patients were excluded if they had oligohydramnios or polyhydramnios, renal or hepatic dysfunction, premature rupture of membranes, or if neonates presented with congenital anomalies, chromosomal abnormalities, or syndromic conditions affecting growth. IUGR was considered positive as an estimated fetal weight below the 10th percentile for gestational age and sex, according to World Health Organization growth standards. Intrauterine growth restriction was considered positive as an estimated weight below the tenth percentile for gestational age and sex, based on WHO standards. Estimated fetal weight using ultrasound biometry (Hadlock formula), and diagnosis was supported by Doppler assessment, where available. Morbidity was assessed in terms of intrauterine death, meconium aspiration syndrome, Apgar score, hypoglycemia, low birth weight, and admission to the neonatal intensive care unit (NICU) within 24 hours of birth. Neonatal morbidity included meconium aspiration syndrome, low birth weight (<2500 g), hypoglycemia, poor Apgar score (<7 at 5 minutes), and neonatal intensive care unit stay. Neonatal mortality was defined as intrauterine fetal death (stillbirth) or premature neonatal death within 7 days of birth. Birth weight <2500 g after 37 weeks of gestation was considered low birth weight, which was measured using a calibrated digital weighing machine with appropriate adjustments for blankets or diapers. Apgar scores were recorded at 1 and 5 minutes post-delivery, based on standardized criteria. Meconium aspiration syndrome was diagnosed clinically in neonates with respiratory distress and meconium-stained amniotic fluid. Perinatal mortality was calculated as the number of stillbirths and neonatal deaths among births ≥37 weeks and ≥1500 g. Hypoglycemia was considered if blood glucose was <47 mg/dL within the first 24 hours of life, measured using a point-of-care glucometer.

Data were analyzed using IBM SPSS version 27.0. Data analysis was conducted to assess the association between maternal and clinical factors and neonatal outcomes within the intrauterine growth-restriction group. The Mann-Whitney U test was used for non-normally distributed continuous variables, such as birth weight and Apgar scores. Continuous variables were presented as median (IQR), whereas categorical variables were reported as frequency (%). The Mann-Whitney U test and the Chi-square test were used when applicable. A p-value of ≤ 0.005 was considered a significant value.

RESULTS

The median maternal age was 29 (IQR 22-34), and the median number of children was 2. Healthy neonates had median Apgar scores of 7 at 1 minute (IQR 4-7) and 9 at 5 minutes (IQR 5-9). The median birth weight was 2.1 kg (IQR 1.2-2.9) and blood sugar 130 mg/dL (Table 1).

Table 1: Baseline Clinical and Laboratory Characteristics of Study Participants

Variables	Median (IQR; min–max)
Mother's Age (years)	29.0 (6.0; 22.0–34.0)
Parity	2.0 (2.0; 1.0–5.0)
APGAR Score at 1 min	7.0 (3.0; 4.0–7.0)
APGAR Score at 5 min	9.0 (0.0; 5.0–9.0)
Birth Weight (kg)	2.1 (0.8; 1.2–2.9)
Blood Sugar Level	130.0 (31.0; 65.0–153.0)

The study shows the distribution of major clinical characteristics and neonatal outcomes across the study

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participants. 30.8% of patients had a history of IUGR, and 37.8% had intrauterine death (IUD). In terms of delivery mode, 53.1% of study participants had vaginal deliveries, while 46.9% underwent caesarean sections. Meconium aspiration occurred in 31.5% of neonates, as did low birth weight in 9.1%. Furthermore, 35.0% of neonates required NICU admission, although hypoglycemia and perinatal death were quite uncommon, occurring in 2.1% and 4.9% of cases, respectively (Table 2).

Table 2: Distribution of Clinical Characteristics and Outcomes

Variables	Category	n (%)
Previous History Of IUGR	Yes	44 (30.8%)
	No	99 (69.2%)
IUD	Yes	54 (37.8%)
	No	89 (62.2%)
Mode of Delivery	Vaginal	76 (53.1%)
	Caesarean	67 (46.9%)
Meconium Aspiration	Yes	45 (31.5%)
	No	98 (68.5%)
Low Birth Weight	Yes	13 (9.1%)
	No	130 (90.9%)
Admission to NICU	Yes	50 (35.0%)
	No	91 (63.6%)
Hypoglycemia	Yes	3 (2.1%)
	No	140 (97.9%)
Perinatal Death	Yes	7 (4.9%)
	No	136 (95.1%)

The results show strong associations between clinical parameters and adverse findings. Maternal age was lower in neonates with low birth weight (31 versus 28 years, p-value=0.005) and hypoglycemia (33.5 versus 28.5 years, with a p-value of 0.005). Parity was associated with meconium aspiration (2 vs 1, p=0.009), low birth weight (1 vs 2, p=0.046), and hypoglycemia (4 vs 2, p=0.047). Low birth weight, neonatal intensive care unit admission, and perinatal death were significantly associated with lower 1-minute and 5-minute Apgar scores (p<0.001). Low blood sugar levels were found in neonates with meconium aspiration, low birth weight, NICU hospitalization, and hypoglycemia (p<0.029) (Table 3).

Table 3: Comparison of Clinical Parameters by Neonatal Outcomes

Parameters	Meconium Aspiration (Yes/No)	Low Birth Weight (Yes/No)	NICU Admission (Yes/No)	Hypoglycemia (Yes/No)	Perinatal Death (Yes/No)
Mother's Age					
Median	27 / 29	31 / 28	29 / 29	33.5 / 28.5	30 / 28
p-value	0.426	0.005*	0.401	0.005*	0.055
Parity					
Median	2 / 1	1 / 2	2 / 2	4 / 2	2 / 2
p-value	0.009*	0.046*	0.733	0.047*	0.796
APGAR 1 min					
Median	7 / 7	5 / 7	6 / 7	7 / 7	6 / 7
p-value	0.071	<0.001*	<0.001*	0.353	<0.001*
APGAR 5 min					
Median	9 / 9	7 / 9	8 / 9	9 / 9	8 / 9
p-value	0.071	<0.001*	<0.001*	0.353	<0.001*
Birth Weight					
Median	2.225 / 2.125	1.5 / 2.15	2.04 / 2.55	1.525 / 2.15	1.98 / 2.15
p-value	0.178	<0.001*	<0.001*	0.051	<0.001*
Blood Sugar					
Median	121.5 / 130	104 / 130	128.5 / 139	101 / 130	127 / 130
p-value	0.023*	0.021*	0.029*	0.051*	0.690

A history of IUGR was not significantly associated with outcomes, although meconium aspiration (36/63 vs 9/35, p=0.003) and Neonatal Intensive Care Unit (NICU) admission (31/66 vs 19/25, p=0.013) were statistically significant, while low LBW (11/88 vs 2/42, p=0.221), hypoglycemia (2/97 vs 1/43, p-value<0.001), and perinatal death (5/94 vs 2/42, p<0.001) were not statistically significant. IUD was significantly associated with meconium aspiration (24/30 vs 21/68, p<0.001), but not with LBW (3/51 vs 10/79, p=0.209), neonatal intensive care unit admission (17/54 vs 33/87, p=0.436), or hypoglycemia (2/54 vs 1/87, p-value=0.558); however, it demonstrated a borderline significant association with perinatal death (0/54 vs 7/89, p-value=0.045). Mode of delivery (MOD) did not significantly influence meconium aspiration (26/50 vs 19/48, p-value=0.218), LBW (7/70 vs 6/61, p-value=0.975), hypoglycemia (2/74 vs 1/66, p-value = 1.000), or perinatal death (2/76 vs 5/62, p-value=0.243). However, neonatal intensive care unit (NICU) admission was significantly higher in cesarean sections compared to vaginal deliveries (22/64 vs 28/48, p-value=0.012) (Table 4).

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Table 4: Association of Maternal and Clinical Factors with Outcomes

Variables	Meconium Aspiration (Yes/No)	p-value	Low Birth Weight (Yes/No)	p-value	NICU Admission (Yes/No)	p-value	Hypoglycaemia (Yes/No)	p-value	Perinatal Death (Yes/No)	p-value
Previous History of IUGR										
Yes	9/35	0.003	2/42	0.221	19/25	0.013	1/43	<0.001	2/42	<0.001
No	36/63		11/88		31/66		2/97		5/94	
IUD										
Yes	24/30	<0.001	3/51	0.209	17/54	0.436	2/54	0.558	0/54	0.045
No	21/68		10/79		33/87		1/87		7/89	
Mode of Delivery										
Vaginal	26/50	–	7/70	–	28/48	–	2/74	–	2/76	–

DISCUSSION

Perinatal morbidity and death are associated with IUGR, which is a frequently observed situation in obstetrics [14]. Negative neonatal findings caused by intrauterine restrictive growth include hypoxia, poor neurodevelopment, and metabolic disorders in later life [15]. This study shows that intrauterine growth restriction in term pregnancies corresponds with a significant risk of negative neonatal outcomes. This study had a 4.9% perinatal mortality rate, and it's significant to consider that 37.8% of these deaths occurred within the uterus. These findings underscore the significant effects of affected fetal growth, even at term. The higher mortality observed in this study aligns with the findings of a study by Reibel *et al.* who found a substantially higher mortality rate among neonates with intrauterine growth restriction compared to appropriate-for-gestational-age extremely preterm infants (36.7% versus 7.1%, p<0.001) [16]. This study found that neonates with low birth weight showed markedly reduced Apgar scores, indicating the diminished physiological reserve typical of growth-restricted infants. A study conducted by Uniyal *et al.* found that neonates with IUGR had lower 5th-minute Apgar scores than controls [17]. The median birth weight difference of over 500g between neonates requiring admission to a neonatal intensive care unit (NICU) and those not requiring it underscores that even small reductions in birth weight have significant clinical implications. The NICU admission rate (35%) in the current study is higher than reported by Hubbard and Hay, suggesting higher disease severity in the current study participants [18]. The 31.5% prevalence of meconium aspiration in this study shows the significant fetal distress commonly associated with IUGR pregnancies. A study by Hubbard and Hay indicated that IUGR increases the risk of hypoglycemia due to reduced glycogen reserves and impaired glucose synthesis. The significant association between meconium aspiration and hypoglycemia shows that both arise from a common fetal problem [18]. Child hypoglycemia is a life-threatening disease with a complicated etiology and challenging diagnosis that requires early identification and comprehensive examination to prevent serious neurological complications [19]. In another study, most IUGR cases were found in women aged 21-25 years [20]. In a study, 22 of 120 IUGR cases (18.3%) died in the hospital, while 81.7% were discharged. Among the discharged infants, 66.3% were discharged in good condition, while 15.5% had abnormal neurological examinations. The morbidity and mortality patterns of complications indicated that hypoglycemia occurred in 63.3% of cases, while prenatal asphyxia was present in 45.0%, making them the most prevalent complications observed in the study [21]. The study confirms that IUGR infants are at significant risk of adverse outcomes. Our study revealed low hypoglycemia prevalence but high overall morbidity and mortality, suggesting population-specific variances or under-detection. Guidelines emphasize hypoglycemia as a serious concern. The use of a single diagnostic threshold and point-of-care testing shows the lack of universal criteria and practice variability, indicating the global need for standardized diagnostic and treatment protocols [22].

This study has some limitations. The findings may not generalize to other demographics or healthcare settings because this study was conducted at a single tertiary care hospital. The cross-sectional study design association, but not causal associations, between IUGR and neonatal outcomes. The outcomes may have been affected by maternal nutritional status, socioeconomic status, and prenatal care quality, which were not examined. Furthermore, the sample size was calculated based on a single neonatal measure finding (hypoglycemia) rather than a composite measure of morbidity and mortality, which may limit the generalizability of overall finding estimates.

CONCLUSIONS

This study illustrates that intrauterine growth restriction in term pregnancies is strongly linked to a high rate of neonatal morbidity and mortality, particularly neonatal intensive care unit admissions and respiratory issues. Early detection and optimized perinatal care are essential to improve outcomes.

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Authors' Contribution

Conceptualization: YA
Methodology: YA, ZN
Formal analysis: ZN, YQK
Writing and Drafting: ZN, YQK
Review and Editing: YA, ZN, YQK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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