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GESTATIONAL-AGE-RELATED VARIATION IN PLACENTAL PATHOLOGY AMONG LOW-BIRTH-WEIGHT NEONATES: A COMPARATIVE ANALYSIS OF PRETERM AND TERM BIRTHS

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ABSTRACT **Background:** Placental abnormalities associated with low birth weight may vary with gestational maturity, yet direct comparisons between preterm and term low-birth-weight births remain limited. **Objective:** To compare placental morphometry and histopathological findings between preterm and term births among neonates enrolled in a low-birth-weight cohort. Methods: This prospective observational study examined 100 fresh placentas from inborn neonates at a tertiary-care centre in Central India between July 2024 and December 2025. Placentas underwent gross examination followed by haematoxylin-and-eosin histopathology. For the principal comparison, extremely preterm, very preterm and preterm births were combined as the preterm group (n=36) and compared with term births (n=61); three postterm births were excluded from this comparison. **Results:** Mean placental weight was lower in preterm than term births (267.78 ± 67.81 g versus 307.74 ± 79.62 g; p=0.010), as was mean birth weight (1.87 ± 0.44 kg versus 2.15 ± 0.32 kg; p=0.001). Villous vasculature differed between groups (p=0.016): absent vasculature was found in 16.7% of preterm placentas and 1.6% of term placentas. Excessive syncytial knots occurred in 25.0% and 14.8%, fibrinoid necrosis in 33.3% and 31.1%, villitis in 13.9% and 8.2%, and infarction in 16.7% and 4.9% of preterm and term placentas, respectively. Perivillous fibrin deposition was present in all placentas, while calcification occurred in 97.2% of preterm and 95.1% of term placentas. **Conclusion:** Within this low-birth-weight cohort, preterm births had lower placental and neonatal weights and a significantly different villous vascular distribution, characterised by a higher proportion of absent vasculature. Most other histopathological lesions were distributed similarly between the two groups.

KEYWORDS : Gestational Age; Low Birth Weight; Placenta; Preterm Birth; Placental Histopathology; Villous Vasculature

INTRODUCTION

Low birth weight, defined as a birth weight below 2500 g regardless of gestational age, arises chiefly from preterm birth, fetal growth restriction, or both [1]. The placenta is central to both pathways. It provides the structural interface for maternal-fetal exchange and regulates the transfer of oxygen, nutrients and metabolic substrates required for fetal growth [2,3]. Disturbance of placental development or perfusion can reduce exchange efficiency, restrict fetal growth and contribute to adverse perinatal outcomes [4].

Placental pathology in low-birth-weight births includes lesions reflecting maternal vascular malperfusion, altered villous development, inflammation and chronic tissue injury. Reported findings include infarction, fibrinoid necrosis, reduced villous vascularity, increased syncytial knots, stromal fibrosis, villitis and perivillous fibrin deposition [5]. Their interpretation is influenced by gestational age because the placenta undergoes continuous structural maturation, and the pathological processes associated with spontaneous and medically indicated preterm delivery are not identical [6]. Comparative observations have also suggested a greater burden of abnormal histology in preterm than term placentas [7], while placental inflammation and malperfusion in extremely premature births have been linked with adverse neonatal outcomes [8].

Most low-birth-weight placental studies have focused on comparisons with normal-birth-weight controls or have described lesions in term births. Fewer have examined how placental morphology and histopathology vary within a low-birth-weight population according to gestational maturity. A gestational-age-based comparison may help distinguish findings related to developmental immaturity from lesions that remain prominent at term. The objective of this study was therefore to compare placental weight and histopathological findings between preterm and term births among neonates in a low-birth-weight cohort.

MATERIALS AND METHODS

This prospective observational study was conducted in the Departments of Paediatrics at a tertiary care institute of central india. Recruitment took place over 18 months, from 1 July 2024 to 31 December 2025. The study included 100 fresh placentas from inborn neonates meeting the protocol's birth-weight criteria. Mothers were included only after providing written informed consent for placental examination.

All inborn neonates meeting the study birth-weight criteria and whose mothers consented were eligible. Outborn neonates, mothers unwilling to participate, neonates weighing below 500 g or above 2500 g, and infants born to serology-positive mothers were excluded. Maternal age, parity, obstetric history and relevant comorbidities were recorded. Neonatal information included sex, gestational age, birth weight, date of birth and 1-minute Apgar score.

Placentas were collected immediately after delivery and rinsed under running tap water to remove blood and clots. Gross examination included placental weight, shape, dimensions, thickness, cord insertion and other cord features, membranes, fetal and maternal surfaces, infarction, calcification and fibrin deposition. Placental weight was measured with an electronic weighing scale. Tissue samples were fixed in 10% formalin, processed routinely and stained with haematoxylin and eosin. Eight randomly selected microscopic sectors were examined, with assessment of 100 villi for syncytial knots, fibrinoid necrosis and vascular changes. Villitis, stromal fibrosis, basement-membrane status, vasculosyncytial-membrane status, placental infarction, perivillous fibrin deposition and calcification were also recorded.

Gestational age was obtained from the obstetric record and classified as extremely preterm, very preterm, preterm, term or postterm. For the principal preterm-term comparison, the first three categories were combined as preterm (n=36) and compared with term births (n=61). The three postterm births were retained in the descriptive gestational-age profile but excluded from the binary comparison.

Data were compiled in Microsoft Excel and analysed using IBM SPSS Statistics version 25. Categorical variables are presented as numbers and percentages, and continuous variables as mean ± standard deviation. The association between gestational-age category and birth-weight category was assessed using Pearson's chi-square test. Preterm and term means were compared using Welch's independent-samples t test. Binary histopathological variables were compared using Fisher's exact test, and variables with more than two categories using the Fisher-Freeman-Halton exact test. All tests were two-sided, and $p<0.05$ was considered statistically significant. Institutional Ethics Committee approval was obtained before study initiation, and participant confidentiality was maintained throughout.

RESULTS

One hundred placentas were evaluated. The gestational-age distribution comprised 1 (1.0%) extremely preterm, 3 (3.0%) very preterm, 32 (32.0%) preterm, 61 (61.0%) term and 3 (3.0%) postterm births. Mean placental and neonatal weights increased across the extremely preterm, very preterm, preterm and term categories; the corresponding descriptive values are shown in Table 1.

Table 1. Gestational-age Distribution and Placental and Neonatal Weight Parameters

Gestational-age category	n (%)	Placental weight (g) Mean ± SD	Birth weight (kg) Mean ± SD
Extremely preterm	1 (1.0)	150.00	0.50
Very preterm	3 (3.0)	223.33 ± 66.58	1.53 ± 0.56
Preterm	32 (32.0)	275.63 ± 64.83	1.94 ± 0.35
Term	61 (61.0)	307.74 ± 79.62	2.15 ± 0.32
Postterm	3 (3.0)	280.00 ± 17.32	2.05 ± 0.13
Total	100 (100.0)	292.52 ± 76.44	2.04 ± 0.38

SD was not estimable for the single extremely preterm observation.

For the direct comparison, the combined preterm group included 36 births and the term group 61 births. Mean placental weight was 267.78 ± 67.81 g in the preterm group and 307.74 ± 79.62 g in the term group (p=0.010). Mean birth weight was 1.87 ± 0.44 kg and 2.15 ± 0.32 kg, respectively (p=0.001). Birth-weight category was associated with gestational-age category (χ^2=45.543, df=12, p<0.001). The distribution of extremely low, very low, low and ≥2.5 kg birth weights across the five gestational-age categories is presented in Figure 1.

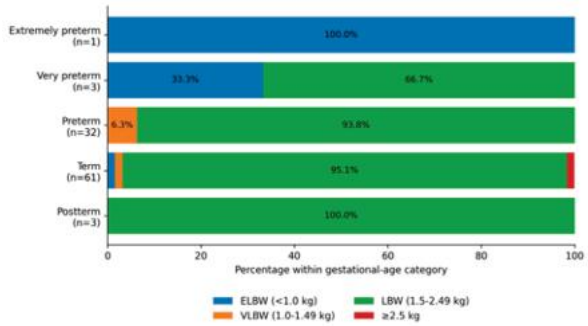

Figure 1. Distribution of Birth-weight Categories Across Gestational-age Groups

Percentages are calculated within each gestational-age category. ELBW: extremely low birth weight; VLBW: very low birth weight; LBW: low birth weight.

Placental histopathological findings in the preterm and term groups are shown in Table 2. Villous vasculature differed significantly between groups (p=0.016). Adequate vasculature was present in 25 (69.4%) preterm and 54 (88.5%) term placentas, whereas absent vasculature was observed in 6 (16.7%) and 1 (1.6%), respectively. Excessive syncytial knots were identified in 9 (25.0%) preterm and 9 (14.8%) term placentas (p=0.169). Fibrinoid necrosis was present in 12 (33.3%) and 19 (31.1%) placentas (p=0.826), and villitis in 5 (13.9%) and 5 (8.2%) placentas (p=0.492).

Stromal fibrosis occurred in 5 (13.9%) preterm and 8 (13.1%) term placentas (p=1.000). Placental infarction was present in 6 (16.7%) preterm and 3 (4.9%) term placentas (p=0.073). Basement and vasculosyncytial membranes were normal in every placenta in both groups. Perivillous fibrin deposition was present in all placentas, and calcification was observed in 35 (97.2%) preterm and 58 (95.1%) term placentas (p=1.000).

Table 2. Placental Histopathological Findings in Preterm and Term Births

Histopathological parameter	Category	Preterm (n=36) n (%)	Term (n=61) n (%)	p value
Syncytial knots	Few	26 (72.2)	52 (85.2)	0.169
	Excessive	9 (25.0)	9 (14.8)	
	Absent	1 (2.8)	0 (0.0)	
Fibrinoid necrosis	Present	12 (33.3)	19 (31.1)	0.826
	Absent	24 (66.7)	42 (68.9)	
Villous vasculature	Adequate	25 (69.4)	54 (88.5)	0.016
	Decreased	5 (13.9)	6 (9.8)	
	Absent	6 (16.7)	1 (1.6)	
Cytotrophoblast	Normal	31 (86.1)	56 (91.8)	0.492
	Villitis present	5 (13.9)	5 (8.2)	
Basement membrane	Normal	36 (100.0)	61 (100.0)	NA
	Abnormal	0 (0.0)	0 (0.0)	
Vasculosyncytial membrane	Normal	36 (100.0)	61 (100.0)	NA
	Abnormal	0 (0.0)	0 (0.0)	
Stromal fibrosis	Present	5 (13.9)	8 (13.1)	1.000
	Absent	31 (86.1)	53 (86.9)	
Placental infarction	Present	6 (16.7)	3 (4.9)	0.073
	Absent	30 (83.3)	58 (95.1)	
Perivillous fibrin deposition	Present	36 (100.0)	61 (100.0)	NA
	Absent	0 (0.0)	0 (0.0)	
Calcification	Present	35 (97.2)	58 (95.1)	1.000
	Absent	1 (2.8)	3 (4.9)	

Preterm includes extremely preterm, very preterm and preterm births; postterm births (n=3) were excluded. P values are two-sided Fisher exact tests for binary variables and Fisher-Freeman-Halton exact tests for variables with more than two categories. NA: not applicable because there was no between-group variation.

DISCUSSION

The principal finding was a gestational-age-related difference in placental size and villous vascularity within the low-birth-weight cohort. Preterm births had lower mean placental and neonatal weights than term births. Among the histopathological variables, villous vasculature was the only parameter showing a statistically significant between-group difference, driven chiefly by the greater frequency of absent vasculature in preterm placentas. Placental infarction was numerically more frequent in preterm births, although the difference did not reach statistical significance. Fibrinoid necrosis, villitis, stromal fibrosis, perivillous fibrin deposition and calcification showed broadly similar distributions.

The lower placental weight among preterm births is consistent with the progressive increase in placental mass over gestation. Placental weight alone, however, does not measure functional capacity; its interpretation depends on fetal size, gestational age and adaptive efficiency [9]. In this cohort, both placental and birth weights increased through the term category, and gestational age was strongly associated with birth-weight category. The study population was predominantly term, whereas Shrestha et al. reported 56% preterm and 44% term births among 100 low-birth-weight cases [10]. Such differences in gestational composition are important when comparing lesion frequencies across studies.

The significant difference in villous vasculature was the most distinctive histological result. Adequate vascularity was less frequent in preterm placentas, and complete absence of villous vasculature was substantially more frequent in preterm than term births. Jadhav et al. reported hypovascular villi in 44% of low-birth-weight placentas [11], a higher frequency than the decreased-vascularity category in this cohort. Direct comparison is limited by differences in case mix and grading criteria, but both observations support careful assessment of the villous vascular compartment in growth-restricted and premature births. Reduced or absent villous vessels can diminish the effective fetal capillary bed and may reflect developmental immaturity or vascular compromise [4,5].

Placental infarction was found in 16.7% of preterm and 4.9% of term placentas. Although the p value of 0.073 does not establish a statistically significant difference, the direction of the finding is consistent with the comparative study by Nagesh et al., in which infarction, villitis and chorioamnionitis were more frequent in preterm placentas [7]. Shrestha et al. reported infarction in 8% of low-birth-weight placentas [10], close to the overall frequency in this cohort, whereas Jadhav et al. and Choudhary et al. reported substantially higher frequencies of 56% and 31%, respectively [11,12]. Nigam et al. also found infarction to be concentrated in low-birth-weight placentas compared with controls [13]. Variation in hypertensive disease, fetal growth restriction, gestational profile and diagnostic thresholds may account for the wide range.

Fibrinoid necrosis occurred in approximately one-third of both groups, indicating that this lesion was not confined to prematurity. Villitis was

more frequent numerically in preterm births, but the difference was not significant. Shrestha et al. observed villitis in 12% of low-birth-weight placentas [10], similar to the overall frequency recorded here. In term low-birth-weight neonates, Nkwabong et al. identified chronic villitis and placental infarction as independent predictors of low birth weight [14], while Budal et al. linked inflammatory placental lesions with serious morbidity among extremely premature neonates [8]. These findings emphasise the clinical importance of inflammatory lesions, while also showing that their prevalence and consequences depend on the population being examined.

Stromal fibrosis was nearly identical in preterm and term births. Higher frequencies have been reported by Jadhav et al. and Kumar et al. [11,15], possibly reflecting cohorts with a greater burden of placental insufficiency or different histological thresholds. Jha et al. found maternal vascular malperfusion to be the most frequent placental abnormality in fetal growth restriction, followed by inflammatory and fetal vascular malperfusion lesions [16]. The combination of impaired villous vascularity and a higher numerical frequency of infarction in preterm placentas in the current cohort is compatible with a vascular component, but the observational design does not permit causal attribution.

Perivillous fibrin deposition was recorded in every placenta and calcification in more than 95% of both groups. Their near-universal occurrence limited their value for discriminating preterm from term births. The high frequency of fibrin deposition may partly reflect the recording of even minimal deposits as present, whereas other studies have used threshold-based definitions. Accordingly, these findings should not be equated with massive perivillous fibrin deposition. More broadly, placental histology should be interpreted alongside gestational age, maternal disease, fetal growth and the extent of individual lesions rather than as an isolated binary finding.

Limitations

The extremely preterm and very preterm subgroups were small, requiring aggregation into a single preterm category and limiting assessment of variation within prematurity. Three postterm births were excluded from the principal comparison. These factors limit generalisability and prevent correlation of placental lesions with longer-term neonatal outcomes.

CONCLUSION

Among neonates in this low-birth-weight cohort, preterm births had lower placental and birth weights and a significantly different villous vascular distribution, characterised by more frequent absence of villous vasculature, than term births. Placental infarction was more frequent in preterm births but did not reach statistical significance, while most other lesions were similarly distributed. Gestational age should therefore be considered when interpreting placental histopathology in low-birth-weight deliveries.

Declarations

Ethical Approval: Institutional Ethics Committee approval was obtained before initiation of this prospective observational study.
Conflict of Interest: Nil.
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