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Original Research Article

Impact of placental histopathology and maternal risk factors on neonatal morbidity in late preterm infants

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ABSTRACT

Background: Maternal and placental risk factors are critical determinants of neonatal outcomes in preterm infants. This study aims to evaluate the impact of placental histopathological findings and maternal risk factors on neonatal morbidity and mortality among late preterm infants.
Methods: This prospective study was conducted between January and July 2018 at Başkent University Faculty of Medicine. A total of 62 late preterm infants, born via cesarean section between 34^0⁄7 and 36^6⁄7 weeks of gestation, were included. Neonatal morbidities were assessed in relation to placental histopathological features and maternal risk factors. Placental examinations included both gross and microscopic evaluations, focusing on maternal vascular malperfusion, chronic inflammation, placentomegaly, placental hematomas, and fetal obliterative vasculopathy.
Results: Placental histopathological abnormalities and maternal risk factors were significantly associated with adverse neonatal outcomes. Maternal vascular malperfusion correlated with an increased risk of hyperbilirubinemia and intracranial hemorrhage. Chronic placental inflammation was linked to polycythemia and feeding intolerance. Placentomegaly was associated with early-onset neonatal sepsis and feeding difficulties. Additionally, maternal conditions such as preeclampsia, thrombophilia, oligohydramnios, and maternal infections were found to influence neonatal morbidity.
Conclusions: Placental histopathological findings particularly maternal malperfusion, chronic inflammation, and placentomegaly appear to contribute significantly to neonatal morbidity in late preterm infants. The combined assessment of placental pathology and maternal risk factors may enhance early prediction of neonatal complications and guide postnatal clinical management.

Keywords: Late preterm, Late preterm morbidity, Maternal risk factors, Placenta, Placental pathology

INTRODUCTION

Prematurity remains the leading cause of neonatal morbidity and mortality, with late preterm infants those born between 34⁰⁄₇ and 36⁶⁄₇ weeks of gestation accounting for approximately 65-70% of all preterm births.[1] These infants experience significantly higher rates of complications, with morbidity and mortality risks increased by 3.5-fold and 4.6-fold, respectively, compared to term infants.[2-4] Maternal risk factors play a pivotal role in shaping neonatal outcomes among late preterm infants.[5]

For instance, the presence of preterm premature rupture of membranes (PPROM) has been shown to elevate the risk of neonatal sepsis and respiratory distress syndrome (RDS) in this population.[6,7] Additionally, infants born to mothers with preeclampsia are more likely to develop RDS and be classified as small for gestational age (SGA).[8] Effective monitoring and management of gestational diabetes mellitus (GDM) during pregnancy are known to mitigate the risk of adverse neonatal outcomes. Nevertheless, RDS, metabolic disturbances, and polycythemia are commonly observed among infants of mothers with GDM.[9,10]

Awareness and early identification of these maternal risk factors are crucial for timely intervention and improving neonatal prognosis. Beyond these established associations, recent studies underline how underlying placental changes function as mediators of neonatal risk. For example, in adverse obstetric scenarios (preterm labor, FGR, preeclampsia), inflammatory lesions and fetal thrombotic vasculopathy are frequently observed, highlighting placenta's central role in adverse outcomes.[11] Additionally, conditions like PPROM and GDM often co-occur with placental histopathological abnormalities such as maternal vascular malperfusion, exacerbating neonatal morbidity.[12]

The placenta plays a fundamental role in fetal development by mediating nutrient and oxygen exchange, waste elimination, and acting as an endocrine organ throughout gestation.[13] Birth weight has been shown to closely correlate with placental weight and villous surface area, underscoring the functional significance of placental morphology.[13] In recent years, growing evidence has linked specific placental histopathological findings with increased neonatal morbidity and mortality.[14-16]

Latent class analysis-a novel, evidence-based approach has revealed that in late preterm births, distinct clusters such as maternal vascular malperfusion, acute inflammation, and fetal vascular thrombosis are strongly predictive of neonatal morbidity.[17] In fetal growth restriction (FGR), particularly when accompanied by reduced fetal movements, placental insufficiency appears to contribute to worse neonatal outcomes.[18] Moreover, placental pathology exhibits gestational age dependent variation: late-term and post-term births show higher rates of inflammation and fibrin deposition compared to early-term births.[19] Studies focusing on placental dysfunction such as maternal vascular malperfusion and infection/inflammation further demonstrate their strong association with neonatal complications including RDS and lower birth weights.[20]

Furthermore, placental lesions such as maternal VUE (villitis of unknown etiology) and perivillous fibrin deposits have been increasingly recognized as contributors to FGR and adverse neonatal outcomes, particularly when recurrent or exaggerated.[21] In FGR cases with or without reduced fetal movements placental maldevelopment and insufficiency remain central etiological factors.[22]

Advanced placental features have even been linked with long-term neurodevelopment; for example, certain histopathological patterns in the placenta are associated with neurodevelopmental outcomes up to 40 months of age.[23]

Emerging methodologies like artificial intelligence promise to further enhance the diagnostic accuracy and consistency of placental pathology, potentially enriching perinatal risk stratification.[24] These multidisciplinary insights underscore the importance of integrating both maternal risk factors and placental pathology into neonatal risk assessment.

In this context, the present study aims to investigate the impact of maternal risk factors and placental histopathology on neonatal morbidity and mortality in late preterm infants, with a particular focus on identifying complications during the early neonatal period.

METHODS

This prospective study was conducted between January and July 2018 at Başkent University Faculty of Medicine. A total of 62 infants born between 34⁶⁄₇ and 36⁶⁄₇ weeks of gestation were enrolled. The study protocol was approved by the Institutional Review Board of Başkent University Faculty of Medicine (Approval No: KA18/79). All late preterm infants with gestational ages confirmed by maternal dating and antenatal ultrasonography were included. Exclusion criteria comprised term infants, those born before 34 weeks, and infants with major congenital anomalies.

For each infant, birth weight (BW), gestational age (GA), sex, mode of delivery, maternal risk factors, and placental histopathological findings were recorded using standardized data collection forms. Clinical characteristics were documented, including duration of respiratory support, presence of feeding intolerance, hypoglycemia, sepsis, hyperbilirubinemia, polycythemia, intraventricular hemorrhage, and necrotizing enterocolitis. Maternal risk factors assessed included maternal age, placenta previa, placental abruption (ablatio placenta), preeclampsia, gestational diabetes mellitus (GDM), polyhydramnios, oligohydramnios, intrauterine infection, thrombophilia, and premature rupture of membranes (PPROM).

Placental histopathological evaluation was conducted in accordance with the classification system described by Stanford University (USA) in 2016, categorizing findings into the following groups: (1) Amniotic fluid infection sequence, (2) Maternal uterine malperfusion, (3) Full-thickness perivillous fibrin deposition, (4) Chronic inflammation, (5) Fetal obliterative vasculopathy, (6) Placentomegaly, (7) Hematoma, (8) Normal, and (9) Other. Subcategories and related pathological features were also assessed in detail (Table 1).[25]

Table 1: Histopathological evaluation of placenta.[25]

1-Amniotic fluid infection sequence	
Fetal inflammatory response	≥2 chorionic plate vessels with vasculitis
	Umbilical arteritis
Maternal inflammatory response	Acute subchorionitis with abscess formation
	Subacute or necrotizing acute chorioamnionitis
2-Maternal uterin malperfusion	Size ≤10th percentile
	Distal villous hypoplasia
	≥2 Infarcts
	Maternal decidual vasculopathy, severe
3-Full thickness perivillous fibrin	
4-Chronic inflammation	Chronic chorionitis and basal chronic villitis
	Parenchymal chronic villitis
5-Fetal vascular obstruction	Large vessel thrombi
	Villous damage from fetal ischemia
6-Placentomegaly	Size ≥90th percentile
	Villous edema
7-Placental hematoma	Intraplasental, subcorionic, full thickness, retroplacental, secondary to biopsy
8- Normal	Normal (morphology compatible with gestational week)
9- Others	Marginal or velamentous cord insertion
	Subcorionic cyst
	Single artery anomaly
	Koranjiosis
	Koranjioma
	Delay in maturation Large vessel anastomosis

All 62 placentas underwent comprehensive macroscopic and microscopic histopathological analysis at the Department of Pathology. Standard sampling included sections from the umbilical cord, membrane rolls, and three full-thickness placental parenchyma sections. In multiple gestations with fused placentas, placental weights were halved to calculate the placental weight-to-birth weight ratio.

The classification of the amniotic fluid infection sequence was based on two fetal and two maternal criteria. Fetal indicators included umbilical arteritis and vasculitis in ≥2 chorionic plate vessels. Maternal indicators included acute subchorionitis with abscess formation and subacute or necrotizing chorioamnionitis. Maternal uterine malperfusion was defined by the presence of at least two of the following: placental weight ≤10th percentile for gestational age, distal villous hypoplasia, severe decidual vasculopathy (fibrinoid necrosis and/or atheromatous changes), and ≥2 infarcts (Figure 1).

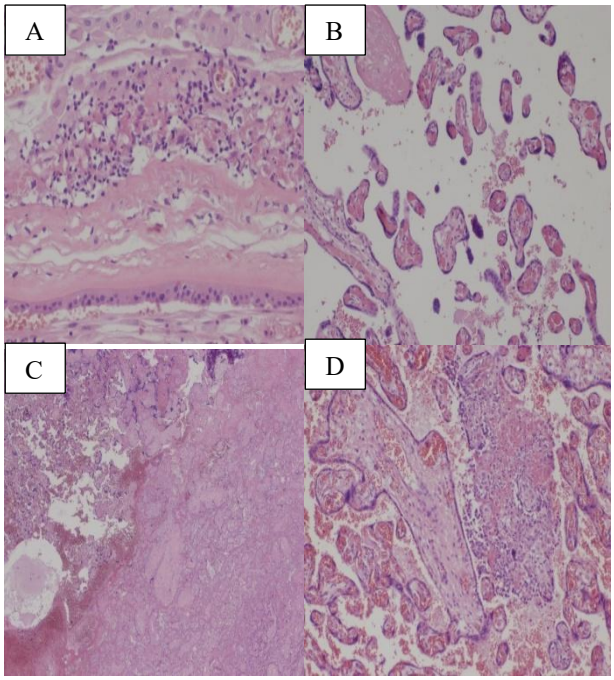

Figure 1: Placental histology. (A) Mononuclear inflammatory cell infiltration in placental membrane (H & E, x200); (B) Maternal malperfusion, distal villous hypoplasia (H & E, x200); (C) Maternal malperfusion, panoramic histopathological appearance consistent with infarction (H & E, x40); (D) Presence of chronic inflammation destructing the terminal chorionic villus compatible with chronic villitis (H & E, x200).

Chronic inflammation was characterized by either chronic chorionitis and basal villitis or parenchymal villitis, reflecting an aberrant maternal immune response (Figure 1). Chronic chorionitis was defined by mononuclear band-like infiltrates associated with membranous cytotrophoblast dropout and/or lymphohistiocytic inflammation of the basal chorionic plate visible at low magnification. Parenchymal villitis was diagnosed as villitis of unknown etiology, defined by >10 villi per focus on multiple slides (i.e., high-grade villitis).

Fetal vascular obstruction included large vessel thrombi and villous injury indicative of fetal ischemia. Placentomegaly was defined as placental weight ≥90th percentile with villous edema. This structured classification enabled detailed evaluation of maternal-fetal immune responses and pathologic correlates of neonatal outcomes.

Statistical analysis

Power analysis indicated that a sample of 61 infants would yield 80.7% power to detect large effect sizes. Analyses were performed using SPSS 25.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used for demographics. Mauchly's and Box's M tests evaluated sphericity and homogeneity of variance. When assumptions were

violated, Greenhouse-Geisser or Huynh-Feldt corrections were applied. Bonferroni adjustment was used for post hoc comparisons. Categorical variables were analyzed using Chi-square, Fisher's exact, or Cochran's Q tests. A p value <0.05 was considered statistically significant.

RESULTS

The study included 62 late preterm infants with a mean birth weight of 2400.7±421.8 g (range: 1555-3820 g). Gestational age distribution comprised 13 infants at 34 weeks, 13 at 35 weeks, and 36 at 36 weeks, with mean birth weights of 1965 g, 2300 g, and 2535 g, respectively. Among these, 24 pregnancies were spontaneous, and 38 were achieved via in vitro fertilization, resulting in 32 males and 30 females. Multiple gestations accounted for 72.5% of pregnancies. Growth status was categorized as small for gestational age (SGA) in 38.7%, appropriate for gestational age (AGA) in 58.1%, and large for gestational age (LGA) in 3.2%. Of the 49 births, 17 were singletons, 21 twins, and 1 triplet. The average hospitalization duration was 5.9±5.0 days (range: 1-21 days), with 12.9% rehospitalization. Placental histopathology revealed abnormalities in 64.5% (n=40) of cases. No mortality was recorded.

Table 2: Demographic and clinical characteristics of the study cohort (n=62).

Characteristic	Value
Gestational age (weeks), N (%)	34: 13 (21.0); 35: 13 (21.0); 36: 36 (58.1)
Birth weight (g), mean±SD	2400.7±421.8
Sex, N (%)	Male: 32 (51.6); Female: 30 (48.4)
Mode of conception, N (%)	Spontaneous: 24 (38.7); IVF: 38 (61.3)
Plurality (pregnancy level)	Singleton: 17; Twin: 21; Triplet: 1
Multiple gestation (infant level), N (%)	45 (72.6)
Growth status, N (%)	SGA: 24 (38.7); AGA: 36 (58.1); LGA: 2 (3.2)
Length of hospital stay (days), mean±SD	5.9±5.0
Re-hospitalization, N (%)	8 (12.9)
Mortality, N (%)	0 (0)

Values are N (%) unless otherwise indicated

Neonatal morbidities by gestational age

Significant differences across gestational ages were found in hyperbilirubinemia (p=0.011), polycythemia (p=0.026), intracranial hemorrhage (p=0.016), feeding intolerance (p<0.001), and time to full enteral feeding (p<0.001). Infants born at 34 weeks had the highest incidences: hyperbilirubinemia (84.6%), polycythemia (30.8%), intracranial hemorrhage (15.4%), and universal feeding intolerance (100%). They also exhibited longer hospital stays (p=0.001) and greater rehospitalization rates, indicating this group's heightened vulnerability.

Table 3: Neonatal morbidities observed in the cohort (n=62).

Outcome	Number	Percent
Apnea	2	3.2
RDS	4	6.5
TTN	10	16.1
Pneumothorax	1	1.6
Hyperbilirubinemia	31	50.0
Early sepsis	1	1.6
Late sepsis	4	6.5
Hypoglycemia	20	32.3
Polycythemia	6	9.7
Intracranial hemorrhage	2	3.2
NEC	2	3.2
Feeding intolerance	35	56.5
Recurrent hospitalization	8	12.9

Maternal risk factors and placental pathologies

Gestational diabetes mellitus (GDM) was the most common maternal risk factor (22.6%), followed by oligohydramnios (17.7%) and thrombophilia (14.5%)-including factor V Leiden deficiency (50%), antiphospholipid syndrome (33%), and prothrombin mutation (16%). Other conditions included preeclampsia, PPROM, maternal infection, polyhydramnios, placenta previa, placental abruption, and chorioamnionitis. Placental pathologies were categorized into seven groups, with chronic inflammation (19.3%), placentomegaly (16.1%), and hematoma (11.2%) being the most frequent. Additional findings included maternal uterine malperfusion, full-thickness perivillous fibrin deposition, fetal obliterative vasculopathy, and amniotic fluid infection sequence.

Maternal risk factors and neonatal morbidities

No significant association was found between GDM and neonatal morbidities (p>0.05). However, preeclampsia correlated with increased hyperbilirubinemia (p=0.023) and feeding intolerance (p=0.008). Thrombophilia was linked to feeding intolerance (p=0.025), hyperbilirubinemia (p=0.012), and early neonatal sepsis (p=0.014). Oligohydramnios was associated with hyperbilirubinemia (p=0.020) and feeding intolerance (p=0.005). Maternal infection significantly correlated with early neonatal sepsis (p=0.001) and rehospitalization (p=0.022).

Placental histopathology and neonatal morbidities

Chronic inflammation, placentomegaly, and maternal uterine malperfusion showed significant associations with neonatal outcomes (Table 4). Maternal uterine

malperfusion correlated with hyperbilirubinemia (p=0.043) and intracranial hemorrhage (p=0.035). Chronic inflammation was linked to polycythemia (p=0.046), feeding intolerance (p=0.015), and recurrent hospitalizations (p=0.035). Placentomegaly was associated with early neonatal sepsis (p=0.005) and feeding intolerance (p=0.011). Fetal obliterative vasculopathy was significantly related to polycythemia (p=0.049).

Table 4: The relationship between placental histopathological findings and neonatal morbidities, n (%).

	N (%)	Apnea	RDS	TTN	Pneum-othorax	Hyperb-ilirubinemia	ES	LS	Hypog-lycemia	Polycyt-hemia	ICH	NEC	FI	RH
Total, N (%)	62	2/62 (3.2)	4/62 (6.5)	10/62 (16.1)	1/62 (1.6)	31/62 (50)	1/62 (1.6)	4/62 (6.5)	20/62 (32.3)	6/62 (9.7)	2/62 (3.2)	2/62 (3.2)	35/62 (56.5)	8/62 (12.9)
Amniotic fluid infection sequence, N (%)	1/62 (1.6)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)
Maternal malperfu-sio, N (%)	6/62 (9.6)	0/6 (0)	1/6 (16.7)	2/6 (33.3)	0/6 (0)	5/6 (83.3)*	0/6 (0)	0/6 (0)	3/6 (50)	1/6 (16.7)	2/6 (33.3)*	1/6 (16.7)	6/6 (100)	2/6 (33.3)
Full thickness perivillous fibrin, N (%)	2/62 (3.2)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	1 /2 (50)	0/2 (0)	0/2 (0)	1 / 2 (50)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)
Chronic inflam-mation, N (%)	12/62 (19.3)	1/12 (8.3)	1/12 (8.3)	3/12 (25)	0/12 (0)	7/12 (58.3)	0/12 (0)	0/12 (0)	2/12 (16.6)	2/12 (16.6)*	0/12 (0)	0/12 (0)	11/12 (91.6)*	3/12 (25)*
Fetal vascular obstruct-ion, N (%)	2/62 (3.2)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	2/2 (100)	0/2 (0)	0/2 (0)	1 / 2 (50)	1 / 2 (50)*	0/2 (0)	0/2 (0)	2/2 (100)	0/2 (0)
Placentomegaly, N (%)	10/62 (16.1)	1/10 (10)	1/10 (10)	0/10 (0)	0/10 (0)	4/10 (40)	1/10 (10)*	2/10 (20)	5/10 (50)	0/10 (0)	0/10 (0)	0/10 (0)	2/10 (20)*	2/10 (20)
Placental hematoma, N (%)	7/62 (11.2)	0/7 (0)	1/7 (14.3)	1/7 (14.3)	1/7 (14.3)*	4/7 (57.1)	0/7 (0)	0/7 (0)	2/7 (28.6)	0/7 (0)	0/7 (0)	0/7 (0)	3/7 (42.9)	1/7 (14.3)

ES= Early sepsis; LS= Late sepsis; Feeding intolerance; Recurr-ent hospitalization; *-significant

DISCUSSION

The placenta serves a dual function by facilitating the transfer of nutrients and oxygen between the mother and fetus, while also acting as a vital endocrine organ. Maternal risk factors and placental pathologies play a crucial role in neonatal morbidity and mortality.[13] Recent studies further emphasize the role of placental histopathology as a biomarker for predicting neonatal complications, especially in late preterm infants.[18,19]

Placenta previa, as well as membranous and ring-shaped placentas, may contribute to maternal antepartum hemorrhage, thereby increasing the risk of stillbirth and neonatal mortality.[26,27] In our study, placenta previa was rarely observed (3.2%), yet it was significantly associated with serious neonatal complications. Consistent with the literature, we identified a significant association between placenta previa and respiratory distress syndrome (RDS) (p = 0.011). Lin et al reported an incidence of RDS in 37% of 40 infants with placenta previa, while Bekku et al found RDS in 29.3% of 99 such infants.[26,27] Placenta previa may elevate the risk of RDS by causing antenatal bleeding, which can lead to fetal hypoxia and anemia.[27] Additionally, we observed a significant relationship between placenta previa and intracranial hemorrhage (p = 0.001). Conversely, Yoshimoto et al reported a significant association between intracranial hemorrhage and placental abruption in a cohort of 98 premature infants.[28] More recent evidence also suggests that abnormal placentation, including previa and accreta spectrum disorders, predisposes neonates to higher risks of hypoxic and hemorrhagic complications.[11]

In the literature, infants born to mothers with thrombophilia often exhibit respiratory-related morbidities and neonatal sepsis. Boffa et al documented increased risks of hydrops fetalis, intrauterine growth retardation, and neonatal sepsis in infants of mothers with thrombophilia.[29] Similarly, in our study, thrombophilia was a frequently observed maternal risk factor and was associated with early neonatal sepsis (p = 0.014). Moreover, infants born to mothers with thrombophilia demonstrated a higher

incidence of hyperbilirubinemia (p = 0.012) and feeding intolerance (p = 0.025). Thrombophilia may contribute to neonatal morbidities by causing placental insufficiency.[29] Recent meta-analyses confirmed that inherited and acquired thrombophilias significantly increase the risk of placental vascular lesions, leading to fetal growth restriction and neonatal complications.[12]

Our study revealed that early neonatal sepsis (p=0.001) and recurrent hospitalization (p=0.022) were more common among infants born to mothers who experienced urinary tract infections during pregnancy. The significant association between maternal infection and early neonatal sepsis is consistent with numerous reports in the literature. Marahatta et al described a high incidence of early neonatal sepsis in infants born to mothers with pyelonephritis in a study including 600 pregnant women.[30] Additionally, a meta-analysis encompassing 4,712 studies published between 1960 and 2013 demonstrated a strong correlation between maternal infection and neonatal colonization within the first week of life.[31] Newer cohort studies further support the contribution of maternal urinary and intrauterine infections to systemic neonatal inflammation and sepsis risk, even in late preterm infants.[17]

Preeclampsia, a prominent maternal risk factor in our study, was associated with increased neonatal morbidities, specifically feeding intolerance (p=0.008) and hyperbilirubinemia (p=0.023). Suhonen et al reported a higher frequency of hyperbilirubinemia in infants born to preeclamptic mothers among 284 pregnancies.[32] Langenveld et al further emphasized that infants of preeclamptic mothers frequently experience severe respiratory complications such as RDS, transient tachypnea of the newborn (TTN), and increased requirements for CPAP or mechanical ventilation.[33] In our cohort, TTN occurred in 37.5% of infants born to preeclamptic mothers, although this did not reach statistical significance (p>0.05). Preeclampsia contributes to neonatal morbidities including small for gestational age (SGA), RDS, TTN, and feeding difficulties in late preterm infants, likely through mechanisms involving uteroplacental insufficiency, vascular dysfunction, and pathological inflammation.[33] These findings align with recent prospective analyses highlighting preeclampsia as a major determinant of placental malperfusion lesions and neonatal complications.[18]

Oligohydramnios, another maternal risk factor, has been previously associated with TTN, as reported by Brzezinski-Sinai et al in a study of 144 pregnant women. In contrast, our study found oligohydramnios in 17.7% of cases but did not identify a significant association with respiratory morbidities (p>0.05).[34] Karahanoglu et al analyzed 1,213 cases of oligohydramnios and reported frequent hyperbilirubinemia among affected infants, which was attributed to feeding intolerance.[35] Consistent with this, our study found significant associations between oligohydramnios and hyperbilirubinemia (p=0.020) as well as feeding intolerance (p=0.005). Oligohydramnios, potentially resulting from placental insufficiency, fetal hypovolemia, or intrauterine growth restriction, may adversely affect fetal lung development.[34] Recent work also suggests that oligohydramnios in late preterm pregnancies may interact with placental villous immaturity to amplify neonatal morbidity risks.[19]

We observed significant associations between placental histopathological findings and neonatal morbidities. Chronic inflammation, one of the placental pathologies, has been linked to neonatal sepsis and cerebral morbidities in previous studies. Yamada et al in a cohort of 272 infants, demonstrated that chronic inflammation is associated with neonatal sepsis, intracranial hemorrhage, chronic lung disease, and necrotizing enterocolitis.[36] Similarly, Chisholm et al reported chronic inflammation in 34 of 102 infants, associating it with post-hemorrhagic hydrocephalus and neonatal sepsis.[25] In our study, chronic inflammation was significantly associated with polycythemia (p=0.046), feeding intolerance (p=0.015), and recurrent hospitalizations (p=0.035). It has been suggested that placental chronic inflammation may induce hypoxia and placental insufficiency, contributing to neonatal morbidity.[36] These results are reinforced by new histopathological evaluations linking maternal infection-driven inflammation to neonatal systemic morbidity.[11]

Maternal uterine malperfusion, another significant placental pathology, has been correlated with adverse neonatal outcomes. Studies by Wright et al, Weiner et al, and Scifres et al have demonstrated associations between maternal uterine malperfusion, preeclampsia, and SGA infants.[37-39] In our cohort, maternal uterine malperfusion was significantly associated with hyperbilirubinemia (p=0.043) and intracranial hemorrhage (p=0.035). It was also more prevalent among mothers with preeclampsia (p=0.001) and gestational diabetes mellitus (p=0.017). Maternal uterine malperfusion is known to cause uteroplacental perfusion disorders and neonatal morbidities.[38] While the relationship between maternal uterine malperfusion and hyperbilirubinemia aligns with existing literature, its association with intracranial hemorrhage has not been previously documented. Notably, the two infants with intracranial hemorrhage in our study were born at 34 weeks of gestation and exhibited maternal uterine malperfusion on placental pathology, with one case involving a mother with placenta previa. This finding warrants further investigation to elucidate the implications of maternal uterine malperfusion on neonatal outcomes. Recent reviews confirm that maternal vascular malperfusion lesions are highly predictive of neonatal complications in late preterm infants and should be systematically incorporated into perinatal risk assessments.[18]

Placental infarction, indicative of maternal uterine malperfusion, is a critical factor contributing to neonatal complications, including intrauterine growth restriction, fetal hypoxia, and intrauterine fetal death.[14,15] Even small infarcts involving 5-10% of the placental volume have

been associated with perinatal complications, underscoring their clinical significance. Additionally, placental hematomas, another manifestation of maternal uterine malperfusion, have been linked to perinatal morbidity and mortality.[14,15] In our study, placental hematoma was observed in 11.2% of infants, with RDS and transient tachypnea of the newborn each present in 14.3% of cases (p>0.05). Interestingly, we found a significant association between placental hematoma and a single case of pneumothorax (p = 0.005). Recent literature supports the clinical relevance of placental hematomas, highlighting their association with neonatal hypoxia and increased NICU admission.[19]

Fetal obliterative vasculopathy, a rare pathology observed in 3.2% of our cases, has been associated with neonatal complications. Chisholm et al identified fetal obliterative vasculopathy in 26 of 102 infants and linked it to necrotizing enterocolitis, retinopathy of prematurity, thrombotic events, and bronchopulmonary dysplasia.[25] They emphasized that thrombi within large placental vessels may cause systemic vasculopathy, disrupting oxygen distribution and leading to hypoxia. Given that polycythemia can cause significant morbidity in newborns including microthrombi and hypoxia in target organs our findings are consistent with existing literatüre.[25] Newer reports also indicate that fetal vascular malperfusion lesions play a role in the pathogenesis of neurodevelopmental impairments in survivors.[12]

Birth weight closely correlates with placental weight and villous surface area.[13] In our study, placentomegaly was observed in 16.1% of cases and was significantly associated with feeding intolerance (p=0.011) and early neonatal sepsis (p=0.022). Chisholm et al reported placentomegaly in 37.3% of infants, associating it with RDS.[25] Placentomegaly may increase the risk of adverse perinatal outcomes by decreasing uteroplacental blood flow. Berceanu et al found a significantly high prevalence of placentomegaly (58.4%) in a cohort including 53 diabetic and 16 gestational diabetic pregnancies.[40] In our cohort, 40% of placentomegaly cases occurred in mothers with gestational diabetes, and 75% of their infants developed hypoglycemia, although these findings were not statistically significant (p>0.05). More recent studies confirm that placentomegaly is an independent risk factor for neonatal metabolic disturbances and sepsis.[11]

Perivillous fibrin accumulation within the intervillous space is observed in approximately 20% of term placentas and is generally not considered pathologic unless it exceeds 40% of placental volume. Villous edema, however, is associated with fetal hypoxia and growth restriction.[15] Full-thickness perivillous fibrin deposition, a rare pathology, was not associated with neonatal morbidities in either our study or the literatüre.[25] Nonetheless, updated pathological reviews indicate that extensive fibrin deposition should not be underestimated, as it can signify severe maternal vascular pathology.[18]

Maternal risk factors were also examined in relation to placental pathology. Maternal uterine malperfusion, closely linked to neonatal morbidities, was more common in mothers with preeclampsia (p=0.001) and gestational diabetes (p=0.017). Maternal infection was significantly associated with chronic placental inflammation (p=0.038). Careful placental examination in mothers with infections is therefore crucial to identify chronic inflammation, which may contribute to neonatal morbidity. Integrating the assessment of maternal risk factors and placental histopathology is essential for the prevention of neonatal morbidities. Recent clinical guidelines stress the integration of histopathological findings with maternal risk profiling to enhance neonatal outcome prediction.[17,18]

CONCLUSION

Detailed placental assessment offers critical insight into the intrauterine environment, enabling early identification of neonates at risk. The high prevalence of placental abnormalities in late preterm infants highlights the necessity of systematic evaluation. Our findings underscore the interplay between maternal conditions and placental pathology in shaping neonatal morbidity and mortality. Integrating these assessments into perinatal care can guide targeted interventions, improve neonatal outcomes, and inform evidence-based clinical strategies, emphasizing the pivotal role of the placenta in neonatal risk stratification.

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