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Evaluation of Histopathological Changes in Placenta of Low Birth Weight Babies Delivered at a Tertiary Care Centre

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ABSTRACT

Introduction: Antenatal health-care given to pregnant women has great influence on the rates of perinatal morbidity and mortality. Amongst different causes of perinatal mortality, low birth weight is the single most significant factor. Therefore, routine histopathological examination of the placenta from all the low birth weight babies should be done to find out the likely causes. This study aimed to assess the pathological changes in placenta in association with low birth weight babies.

Methods: A descriptive observational study was conducted from 1 April, 2022 to 31 March, 2023 in the Department of Obstetrics and Gynaecology and the Department of Pathology of Lumbini Medical College-Teaching Hospital after obtaining ethical clearance from the Institutional Review Committee (IRC-LMC-06/P-24) at Lumbini Medical College and Teaching hospital, Palpa, Nepal. A total of 83 placentas of low birth weight babies were included. The weight of the baby and placenta was taken within the first hour of birth. All the collected placentas with a portion of cord attached were sent to Department of Pathology for histopathological study and the reports were collected. All the quantitative data were expressed in frequencies and percentages.

Results: The fetoplacental ratio was 5.99:1. The mean placental diameter was 14.73 centimetres while thickness was 2.95 centimetres. The umbilical cord was inserted centrally in 45, eccentric in 31, marginally in 6 cases and velamentous in 1 case.

Microscopically, syncytial knot formation (75; 90.4%), perivillous fibrin deposition (49; 59%), hyalinisation (45; 54.2%), calcification (59; 71.1%), infarction (49; 59%) and hemorrhage (45; 54.2%) were found in placentas of low birth weight babies.

Conclusions: Histological aberrations like presence of syncytial knots (90.4%), perivillous fibrin deposition (59%), hyalinisation (54.2%), calcification (71.1%), infarction (59%) and hemorrhage (54.2%) are observed in high rates in placentas of women with low birth weight babies.

Keywords: Calcification; Fibrinoid necrosis; Infarction; Low birth weight babies; Syncytial knots.



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INTRODUCTION

Low birth weight (LBW) is the single most significant factor leading to perinatal mortality [1] with a prevalence of 23.6% in Nepal.[2] Uteroplacental vascular insufficiency is a key factor in low birth weight,[3] often resulting in smaller placentas that share the same growthlimiting influences as the fetus. The placenta has considerable reserves and may tolerate the loss of up to 30% of its villi without any obvious effect on fetal growth. [4] In many cases, the placenta is dysfunctional, with abnormalities such as villous infarction, abnormal spiral artery remodelling, chronic villitis, perivillous fibrinoid deposition, hyalinisation, cytotrophoblastic proliferation, calcification and increased syncytial knots. [5,6]

Understanding placental pathology is crucial for identifying the causes of low birth weight, as it directly impacts fetal growth. Despite this, 20–30% of LBW cases remain unexplained. [7] Histological examination of placentas from low birth weight infants have shown significant pathology, highlighting the need for further investigation to clarify these underlying mechanisms.

This study aims to assess the pathological changes in placentas of low birth weight infants in Nepal. Identifying key placental factors can enhance clinical understanding, guiding interventions to reduce low birth weight and improve maternal and neonatal health outcomes.

METHODS

It was a hospital based descriptive observational study conducted in the Department of Obstetrics and Gynaecology and the Department of Pathology of Lumbini Medical College-Teaching Hospital. The approval for the study was taken from the Institutional Review

Committee (IRC-LMC-06/P-24). Written informed consent was taken from all the patients.

Placentas of newborns weighing <2500 grams who delivered at our centre were included in the study. Placentas of women suffering from diabetes mellitus, syphilis, tuberculosis, multiple pregnancy and damaged placenta were excluded from the study. Fetuses with congenital anomalies were also excluded from the study.

The sample size was calculated using the following formula:

 $N \ge Z^2 pq/e2$

Where, n=minimum sample size Z= 1.96 for 95% confidence interval P= prevalence, taken as 30.4% from an article published in 2006[8] where prevalence of infarction in placentas of low birth weight babies was 30.4%

q=1-p

Taking estimated error (e) as 10%, the minimum sample size was calculated to be 81.

All newborns delivered in Department of Obstetrics and Gynaecology were weighed in grams using Ebsa-20 Kinlee Digital Electronic Household Baby Infant Weighing Balance Scale within the first hour of birth. Placentas of 83 new-borns weighing <2500 grams were weighed using the same machine and fetoplacental ratio was calculated. The mode of delivery was noted. The general shapes of placentas were assessed. The position and insertion of umbilical cord on the fetal surface of placenta were observed. The length of umbilical cord was measured in centimetres using a standard measuring tape. The diameter and thickness of placentas were also noted. All the placentas were immersed in 10% formalin and microscopic and gross examination of placenta was carried out in the Department of Pathology. Microscopic parameters assessed in placenta were presence of syncytial knots,

cytotrophoblastic proliferation, perivillous fibrin deposition, hyalinised chorionic villi, placental infarction, calcification, haemorrhage, oedema and congestion of chorionic villi. Also, history regarding the pregnant woman's age, parity, obstetric history, gestational age, past and present medical history like diabetes, syphilis, tuberculosis and personal history were taken through a structured questionnaire and antenatal records. Routine haematological and biochemical investigations were also noted.

Lastly, these data were collected in structured proforma and entered to and analysed with Statistical Package for the Social Sciences (SPSS) software version 22. All the quantitative data were expressed in frequencies and percentages.

Results

A total of 83 placentas from low birth weight babies were studied for both gross and histological features during the study period.

The prevalence of low birth weight babies was 7.19% (with 95% CI 1.65 to 12.73%). Table 1 presents the demographic characteristics of the pregnant women.

Table 1. Demographic characteristics of pregnant women who delivered low birth weight babies (n=83)

Variables	Overall values (Mean ± SD)
Mean maternal age (years)	25.70 ± 6.03
Mean maternal height (centimeters)	150.93 ± 7.34
Mean maternal weight (kilograms)	59.47 ± 11.13
Mean maternal BMI (kilogram/ meter²)	25.92 ± 4.55
Mean gestational age at delivery ± SD (weeks)	37.76 ± 2.61
Mean birth weight \pm SD (grams)	2108.61 ± 370.38

Majority (84.4%) of the pregnant women belonged to the age group of 18 to 35 years with a mean age of 25.70 ± 6.03 years while seven (8.4%) pregnant women were less than 18 years and six (7.2%) patients were more than 35 years.

Forty-two (50.6%) and 41 (49.4%) pregnant women were primigravida and multigravida respectively.

Thirty-three (39.8%) were delivered before 37 completed weeks and 50 (60.2%) delivered after 37 weeks.

Out of total 83 low birth weight babies, most of them were delivered via Lower Segment Caesarean Section (49; 59%) while 34 (41%) were delivered vaginally. However, there were no instrumental deliveries.

The mean birth weight was 2108.61 ± 370.38 grams (range: 940-2495 gm). Fig. 1 describes the distribution of low birth weight babies according to their birth weight (categorising into LBW, VLBW, ELBW).

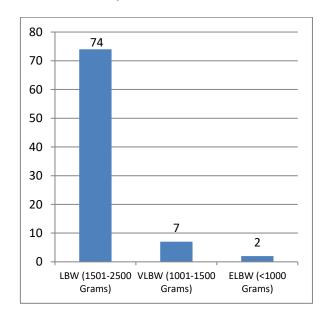


Fig.1. Distribution of low birth weight babies

VLBW: Very Low Birth Weight

ELBW: Extremely Low Birth Weight

Macroscopic and microscopic features of placenta

In Table 2 we present the morphological features of placenta.

Table 2. Morphological features of placenta (n=83)

Variables	Overall values (Mean ± SD)
Mean placental weight	$378.84 \pm$
(grams)	108.26
Mean fetoplacental ratio	5.99: 1
Mean length of placenta (centimeters)	14.73 ± 2.07
Mean thickness of placenta (centimeters)	2.95 ± 1.31
Mean length of umbilical cord (centimeters)	54.71 ± 8.86

The placental weights of low birth weight babies ranged 116-650 grams. The umbilical cord was inserted centrally, eccentric, marginally and velamentous in 45 (54.2%), 31 (37.3%), 6 (7.3%) and 1 (1.2%) cases respectively. However, there were no abnormality in number of blood vessels as all the umbilical cord contained two umbilical arteries, one umbilical vein and wharton's jelly. All umbilical cord and membranes were grossly normal.

In Figure 2 we present data of microscopic features of placenta found in Low Birth Weight Babies. Presence of syncytial knots, perivillous fibrin deposition, hyalinisation, calcification, infarction and haemorrhage were found in majority of placentas of low birth weight babies.

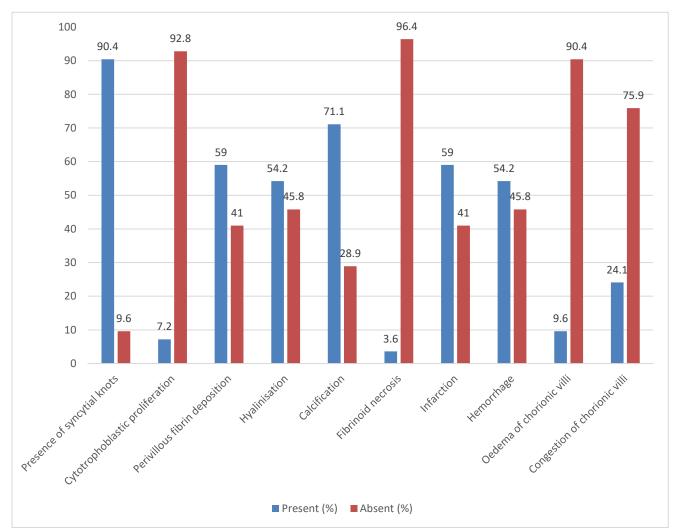


Fig. 2. Histological changes in placenta (n=83)

DISCUSSION

The prevalence of low birth weight babies was found to be very low (7.19%) in the present study. However, the prevalence of low birth weight was found to be significantly high among other institutional deliveries of the country. The prevalence of low birth weight was found to be high (23.6%) in a previous study conducted in 2019. [2] Likewise, two studies conducted in the past also reported higher prevalence of 9.8% [9] and 15.3% [10] as compared to this study. These variations might be probably due to geographical differences and differences in community. This lower prevalence may also be because most of the newborn might have missed the diagnosis as most women in western part of Nepal are still unaware regarding regular antenatal check-ups and prefer home delivery and some deliver in nearby health post and are discharged from there itself.

The mean placental weight was 378.84 ± 108.26 grams. The minimum and maximum placental weight was 116 grams and 650 grams respectively. The mean placental weight of IUGR (Intrauterine Growth Restriction) group was 383 grams in one study. [11] In another study, the placental weights in the IUGR group ranged from 180 to 458 grams, with a mean of 333.32 grams (S.D. \pm 75.59). [12] These findings were comparable to those of the current study.

In the current study, fetoplacental ratio is increased (Mean=5.99), unlike in other studies where placental weight and the fetal-placental weight ratio in IUGR cases were significantly lower. [13] This difference could be attributed to the inclusion of low birth weight babies in our study, while the other studies focussed on IUGR babies.

It was observed that the placentas associated with low birth weight babies were smaller in diameter. These findings were consistent with those of another study, which reported that mean diameters of normal placentas of low birth weight babies were 17 cm by 16 cm. [14]

In terms of mean umbilical length, the findings of the current study were 57.2 ± 9.7 cm which is consistent with those of a previous study. [15]

On gross examination of the placentas, it was found that in the majority of low birth weight babies cases positions of insertion of umbilical cord were central (54.2%) followed by eccentric (37.3%) as shown in figure 3. Additionally, six placentas (7.3%) had marginal insertion and one placenta (1.2%) had velamentous insertion out of 83 cases. This differed from a previous study where the majority of IUGR cases had eccentric cord insertions, with two placentas showing marginal insertion and one showing velamentous insertion out of 28 cases.[14] Another study also reported that 66.67% of umbilical cords in low birth weight babies had eccentric attachment.^[16] Other research observed velamentous insertion in the majority of cases, [17] while yet another study found marginal insertion to be a significant finding in the placentas of IUGR fetuses.[18] These discrepancies may arise due to the fact that our study focused on placentas of low birth weight babies, while the other studies were conducted on placentas of IUGR babies.

Syncytial knots (Figure 4) are indicative of compromised fetal circulation. ^[19] In our study, a higher incidence of syncytial knots was observed in low birth weight babies cases (90.4%). Similar findings have been reported in other studies, where the presence of syncytial knots was also noted to be more common in low birth weight babies cases. ^[20, 21] Additionally, the occurrence of syncytial knots was observed in more than 30% of cases in a significant proportion of low birth weight babies cases, which was higher compared to normal birth weight babies. ^[22]

Cytotrophoblastic proliferation was absent in 92.8% of our cases. An increase in cytotrophoblastic cell proliferation has been observed in the placenta of low birth weight cases in studies done in 2003 and 2014. [23,24] It is suggested that cytotrophoblastic cell proliferation and excessive syncytial knot formation occur as a response to reduced perfusion of the placenta, which ultimately leads to the birth of low birth weight babies. [25]

Perivillous fibrin deposition (Figure 5) in intervillous space is a consequence of thrombosis of maternal blood. The villi embedded in this fibrin are not infarcted but are unable to participate in any transfer activity. Interestingly, such deposition of fibrin tends to develop in placentas with good maternal blood supply. The greater the blood flow, greater the turbulence and stasis and greater is the perivillous fibrin deposition. [26] Our study reported incidence of perivillous fibrin deposition in 59% cases. Other studies have reported varying incidences, with one study showing a significantly higher presence of perivillous fibrin deposition, [27] while another observed an incidence of 16.7%.[22] Additionally, perivillous deposition was more frequently found in placentas of low birth weight babies in another study. The variable findings and uncertainty surrounding the pathophysiology of fibrin deposition highlight the need for further research.

Hyalinization was present in 45 (54.2%) cases of placentas from low birth weight babies. Additionally, the number of hyalinized areas (greater than 5) was significantly higher in cases of intrauterine growth restriction (IUGR) (101) compared to the control group (birth weight greater than 2500 grams) (68), as observed in a study. [6]

In our study, calcification was observed in 71.1% of cases. Other studies have reported varying

prevalence rates of calcification, ranging from 8% to 100%. [20,21,28] One study found calcification in 33.33% of placentas from low birth weight babies. The differences in prevalence across studies may be due to subjective reporting and variations in sample size.

Fibrinoid necrosis is well recognized as one of the hallmarks of immune attack on trophoblastic cells. The fibrinoid material in the affected villi contains a considerable quantity of immunoglobulins. [20] Fibrinoid necrosis was observed in only 3.6% cases in our study as compared to 32-38% cases as reported by the other authors. [20, 21, 28] One study remarked presence of fibrinoid necrosis of villi in 66.67% (40/60) cases. [16] This difference may be attributed due to selection of low birth weight babies in our study, as opposed to intrauterine growth restriction cases in other studies.

In a study, the prevalence of placental infarction in low birth weight infants was reported to be 30.4%, [8] while another study observed a rate of 1.8%. [22] In contrast, our study found placental infarction in 49 (59%) cases. This pathology leads to a reduction in the exchange surface, which in turn decreases the transfer of nutrients and oxygen to the fetus, contributing to low birth weight.

In this study we found haemorrhage in 54.2% cases while a study conducted in 2023 reported haemorrhages (Figure 6) in only 18% cases. [29] Also, eight (9.6%) placentas of low birth weight babies were observed to have oedema in our study, which is similar to the findings of a 2014 study that reported villous oedema in seven (11.6%) cases. [16] Congestion of chorionic villi was observed in 20 (24.1%) cases in present study.

This study is limited by its single-institution design. Additionally, grading the histo-

pathological changes and evaluating the extent of these changes across the entire placenta could offer further insight into the relationship between histopathological features and low birth weight babies.

Besides, this study included both term and preterm low birth weight babies without separate analysis. As prematurity itself can influence placental changes, this may have confounded the histopathological findings.



Figure 3: Fetal surface with eccentric attachment of the cord

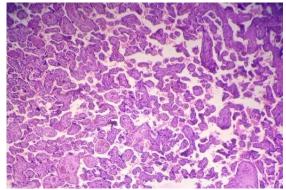


Figure 4: Villi with close aggregations of nuclei (syncytial knots)

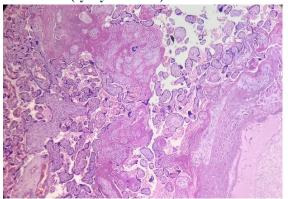


Figure 5: Perivillous and intervillous fibrin deposition

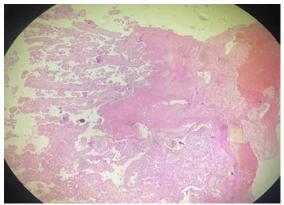


Figure 6: Villi showing sclerosis and area of hemorrhage

CONCLUSIONS

The prevalence of low birth weight babies in this study was found to be lower than most other studies.

Common placental lesions observed among low birth weight were presence of syncytial knots, perivillous fibrin deposition, hyalinisation, calcification and haemorrhage. All placentas in low birth weight cases should be meticulously examined as it can enlarge our understanding of the aetiology of low birth weight and will improve the management of the subsequent pregnancies.

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