Journal of Pathology of Nepal (2024) Vol. **14**, 2156 -2160

Journal of
PATHOLOGY
of Nepal
www.acpnepal.com

Original Article

Study of placenta histopathology in low birth weight deliveries: A prospective cross-sectional study at Nobel Medical College Teaching Hospital

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Keywords:

Chorioamnionitis;
Low birth weight;
Placenta;
Pregnancy;

ABSTRACT

Background: Placenta is the most important organ that represents the status of the mother and fetus. Its examination on gross and microscopy can reveal varied pregnancy-relateddiseases, decreasing future adverse pregnancy outcomes. This study aims to examine the placenta histopathologically among low birth weightpregnancies.

Materials and methods: A prospective case-control study was conducted in the Department of Pathology over one year.The placenta of low birth weight (weight < 2.5 kg) term pregnancies were histopathologically examined. The maternal demographics, co-morbidity, gravida, and hemoglobin levels were recorded. Descriptive statistics, and student t-test or Chi-square test were used for two-group analysis.

Results: Thirty-two consecutive patients enrolled in each group. A significant proportion of the patients in the study group were anemic (9.2 vs. 11.5 gm/dl; p=0.03). Pregnancy-induced hypertension rate was significantly higher in the study group (31% vs. 9%; p = 0.042). Gross observations in low birth weight pregnancies were sub-chorionic fibrin deposition (75%), calcification (37%) and infarction (31%). On microscopy, chorionic vessel thrombosis was significantly higher in the study group (56% vs. 6%; p= 0.003). Furthermore, chorioamnionitis (34%) and placental floor infarction (12%) were also observed in a significantly higher number of placentas in the study group.

Conclusions: Anemia and pregnancy-induced hypertension are important associated factors for low birth weight pregnancies. Pathological examinations reveal higher fibrin deposition, infarction, calcification, sub-chronic vessel thrombosis, and chorioamnionitis in low birth weight placenta.

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Received : January 31, 2024; **Accepted :** February 30, 2024

Citation: Choudhary PK, Baral R, Nepal N, Yadav M, Choudhary S, Bhandari R, Shrestha O. Study of placenta histopathology in low birth weight deliveries: A prospective cross-sectional study at Nobel Medical College Teaching Hospital. J Pathol Nep 2024;14(1): 2156-60. DOI: 10.3126/jpn.v14i1.66310

INTRODUCTION

The placenta is the most important vestigial organ (following delivery) which represents the status of the mother and fetus. Routine histopathological examination can depict many important hidden ailments of the fetus and mother.[1,2] On the contrary, it is not routinely examined histopathologicallyafter delivery and is usually discarded after gross inspection. As we know, any tissue from the body following surgery must be subjected to examination by the pathologists, as it gives us the opportunity the study it and treat any silent diseases. Further, during future planning of the pregnancy, preventive measures can be taken by the mother with its

result to decrease any adverse outcome like low birth weight (LBW) babies. Hence, placental pathology is necessary to understand common pregnancy complications and achieve an improved taxonomy of obstetrical disease.[3,4] Moreover, the potential use of placental pathology for phenotypic classification, improved understanding of the biology of adverse pregnancy outcomes, the development of treatment and prevention, and patient counseling has never been studied in our setup in Nepal.[5]

In the present study, we took up this issue to aim at the pathology of the placenta in LBW pregnancies and reveal any high risk features in it.

MATERIALS AND METHODS

This was a prospective case-control study of singleton pregnancies delivered between June 2022 to July 2023 in the Department of Pathology at Nobel Medical College Teaching Hospital, Biratnagar.The institute is a referral center in eastern Nepal with approximately 3,000 deliveries in a year. Pregnancy with LBW babies was included in the study. Those fetus with congenital anomalies were excluded from the study. The study protocol was approved by the Institute's ethical committee (469/2021) and informed written consent was taken from the patients for the histopathological study of the placenta. The informed consent was taken from at-risk mothers with predicted low birth weight (e.g.- low socioeconomic status, short maternal status, anemia, low amniotic fluid volume, pre-term birth, com-morbidity, and less maternal weight gain during the second and third trimester of pregnancy). The final histopathological report was informed to the patient and the treating physician for any further treatment. A low birth weight was defined asa weight less than 2500gm within the first hour of the birth.

During delivery of the fetus (vaginal vs. caesarian), baseline data including, maternal age, parity, gestational age, comorbidity (gestational diabetes mellitus, pregnancy-induced hypertension (PIH), and treated chorioamnionitis), hemoglobin level, serology for Hepatitis B, C and Human Immunodeficiency Virus (HIV) and previous LBW were recorded.

The placental histological examinations were performed and confirmed by the two senior pathologists of the department (PC and NS). After delivery, placentas wereweighed, placed in 4% buffered formalin, and allowed to fix for at least 48 hrs. Any gross lesions and umbilical cord descriptionswere documented and sampled, along with the standard samples. The standard sample included two cross-sections of normal-appearing placenta parenchyma within the central two-thirds of the placental disc. The samples were embedded in paraffin and cut into 5µm thick slides. The slides were stained with Hematoxylin and Eosin and assessed by the pathologists. Findings were documented in the pathology report.

An equal number of the control group with normal weight of the fetus (2.5-3.5 kg) were consecutively enrolled in the study for the histopathological examination of the placenta. Similar to the cases, their clinical parameters were also studied.

Statistical analysis: The data were entered in a Microsoft excel sheet and processed using SPSS vol.17. Results were presented as mean, mode, percentage, and standard deviation where appropriate. Descriptive statistics were used, and student t-test or Chi-square test were used for two group analyses where appropriate. P values less than 0.05 were considered significant.

RESULTS

There were 32 consecutive patients enrolled in the study in each group. The mean ages of the patients in the study group (LBW) and the control group were 22 years and 24 years, and both groups were comparable. Sixty-two percent of the patients in the study group were primipara and the mean gestational age for delivery was 37 weeks. A significant proportion of the patients in the study group were anemic with a mean hemoglobin level of 9.2 gm/dl (vs. 11.5 gm/dl; p=0.03). Looking at the co-morbidity, the pregnancy-induced hypertension rate was significantly higher in the study group (31% vs. 9%; p = 0.042). (Table 1) None of the patients in either group were positive for hepatitis B and C and HIV infections, however, one of the patients in the study group was infected with COVID-19 infection during the 16 weeks of pregnancy.

Table 1: Patients characteristics among study population (n=32)

Parameters	Low Birth weight (n=32)	Control (n=32)	P-value
Maternal age (yr), mean±SD	22±3.7	24±5.1	0.44
Primipara, n (%)	20 (62.5%)	15 (46.8%)	0.56
Gestational age, weeks	37±2.6	38±1.5	0.21
Hemoglobin, g/dl (mean)±SD	9.2±3.1	11.5±2.8	0.03
Gestational Diabetes mellitus, n (%)	6 (18.7%)	4 (12.5%)	0.84
Pregnancy Induced Hypertension,n (%)	10 (31%)	3 (9%)	0.042
Birthweight (kg), mean (SD)	2.3±1.4	3.0±0.4	0.02

DOI : 10.3126/jpn.v14i1.66310

The mean weight of the placenta in the study and the control groups was 252 vs. 335 gm and was significantly lower in the study group (p=0.004). There were two umbilical cord artery anomalies in the study group, with a single artery and vein. Grossly, a significant proportion of the placenta in the LBW pregnancies had subchorionic fibrin deposition (75%), calcification (37%), and infarction (31%), which were the major findings compared to the controls.

Microscopically, the chorionic vessel thrombosis/ obliterative vasculopathy was observed in 56% of the LBW patients compared to only 6% in the control group, which was significant (p= 0.003), and the important findings as PIH was seen in 31% of the study group. Furthermore, chorioamnionitis was seen in 11(34%) of the study group, compared to 3 (9%) in the control group, and was statistically significant (p=0.04). Similarly, the placental floor infarction was also observed in a significantly higher number of placentas in the study group compared to the control (12 vs. 2; p=0.042). (Table 2; fig. 1, 2)

Table 2: Description of Placentae in LBW pregnancies (n=32) and the control group

Parameters		LBW (n=32)	Control (n=32)	P value
Weight of placenta, mean (gm)		252.5±54.2	335.8±35.6	0.004
Umbilical cord length, mean (cm)		46±4.8	49±5.2	0.96
Umbilical cord insertion	Central	15 (46.8%)	28 (87.5%)	0.3
	Ecentric	17 (53.3%)	4 (12.5%)	
Any cord artery anomalies		2 (6%)	0	0.07
Gross features	Meconium staining of fetal surface	8 (25%)	4 (12.5%)	0.089
	Subchorionic fibrin deposition	24 (75%)	5 (15.6%)	0.037
	Calcification	12 (37.5%)	3 (9.3%)	0.002
	Infarction	10 (31.2%)	0	0.001
Microscopic features	Placental dysmaturity	10 (31.2%)	5 (15.6%)	0.052
	Villitis of unknown origin	5 (15.6%)	3 (9.3%)	0.75
	Placental floor infarction	12 (37.5%)	2 (6.2%)	0.042
	Chorionic vessel thrombosis/ Obliterative Vasculopathy	18 (56%)	2 (6.2%)	0.003
	Chorioamnionitis	11 (34%)	3 (9.3%)	0.04
	Retroplacental hematoma	2 (6.2%)	0	0.08

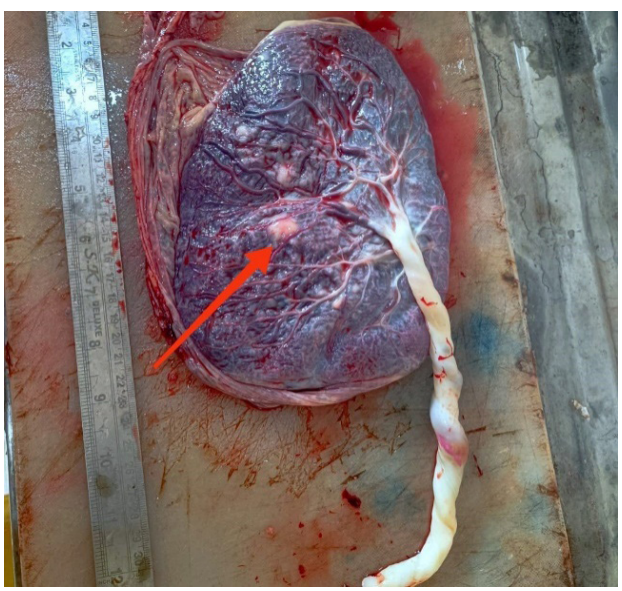

Figure 1: *Grpss image of subchorionic fibrin*

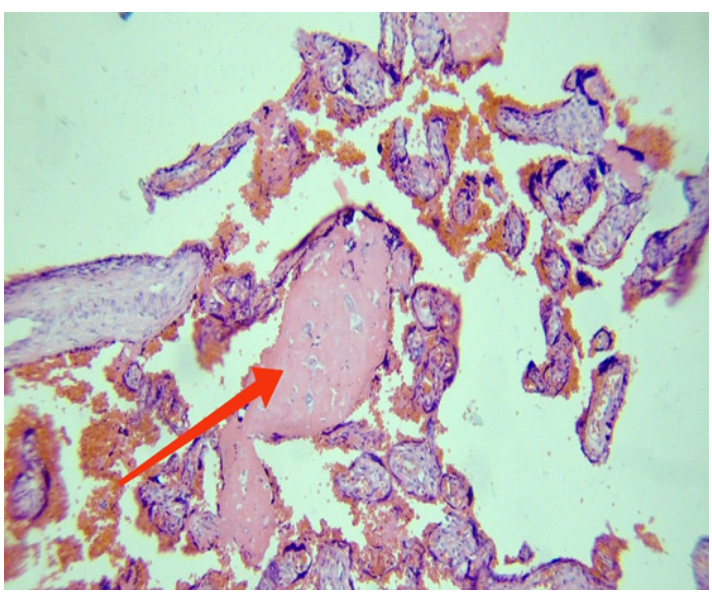

Figure 2: *Photomicrograph showing chorionic villi thrombosis (arrow). (HE stain, X40)*

DOI : 10.3126/jpn.v14i1.66310

DISCUSSION

Low birth weight babies are very common in Nepal in vulnerable populations. The prevalence rate in our part is 12%.[6,7] It is directly related to the mother's health, gravida, malnutrition, hypertensive diseases, infection, inadequate iron intake, and unplanned pregnancy.[8,9] Further the weight of the baby and its well-being is correlated with number of antenatal care visits and check-up by physicians in the hospital.[10] These ailments can be indirectly depicted on the histopathological examination of the placenta following delivery.[11,12] In the present study, the placental abnormalities among LBW babies were observed in 56% of patients.

The major placental microscopic findings were infarction and vascular pathology. It was observed in 40-50% of the patients. It was followed by chorioamnionitis (34%) and hypertensive disease of pregnancy (50%). Pre-eclampsia or eclampsia is known to induce maternal vascular changes which reduce the utero-placental blood flow and can lead to placental infarction.[13] This explains the reasons for LBW babies with placental ischemia and infarct. Moreover, the low placental weight associated with LBW might result from poor placental development due to the maternal vascular changes along with small placentas with decidual arteriopathy, infarcts in central portions, retroplacental hematoma, and intervillous thrombosis.[13, 14]

Similarly, a significant proportion of mother with LBW were having anemia (50%) with mean hemoglobin level of only 9 gm/dl. This often leads to gross and microscopic placental changes like decreased number of cotyledons, insertion of cord towards margin, increased calcification and areas of infarction.[15,16] The calcification and infarction were observed in 37% and 31% of patients which was significantly higher compared to the control group.

Intra-amniotic inflammation is associated with adverse perinatal outcomes whether or not microbes are detected. The acute chorioamnionitis (may be silent or following vaginal infections) incidence as confirmed histologically in various studies is observed in only 5.1% among normal weight births, but as high as 30.0% among LBW.[10, 17, 18] In the present study, it was observed in 28% of our patients.

Around 20% of our mother with LBW babies were adolescents (<20 years old) and of low socioeconomic status. This age group (18-20 yrs.) is a proven risk factor for LBW.[2,7,19] Further, they are still in the growing stage and nutrients they consumed need to be shared by both the mother and the fetus. Hence, this inadequate nutrition and inadequate antenatal care and visits, due to the financial issues leads to ischemia and vascular changes in the placenta with its low weight.[20]

COVID-19 infection, a new disease has also been advocated as a cause for LBW and placental changes.[21] In the present study, one of our mothers was infected with COVID-19 infection during her first trimester. The pathological examination of the placenta however was normal. In a study by Corbetta et al, only 1 of 19 placentas from patients with COVID-19 at <20 weeks of gestation (5%) and 31 of 118 placentas with SARS-CoV-2 infection at >20 weeks of gestation (26%) had no placental lesion. They noted one placenta that met the criteria for SARS-CoV-2 placentitis based on the triad of histiocytic intervillositis, perivillous fibrin deposition, and trophoblast necrosis.[22]

The study is limited by the low sample size, lack of availability of treatment of anemia and PIH of patients with study group, and single-institution study.

CONCLUSIONS

The most common predisposing factors for low birth weight pregnancies observed were anemia and pregnancy-induced hypertension, which was significantly observed compared to the control group. The placenta had a grossly significantly higher number of fibrin deposition, infarction, and calcification. Microscopically, sub-chronic vessel thrombosis, chorioamnionitis, and placental floor infarction were the major findings. Observation of the findings in the study group may help the clinicians treat it in the next pregnancy to avoid LBW pregnancies.

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