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Original Article

Paediatrics Section

Comparison of Placental Histopathological Findings with Good and Adverse Neonatal Outcomes- A Prospective Observational Study

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ABSTRACT

Introduction: The placenta plays a crucial role in the growth and survival of foetus by performing most of the vital functions for the foetus before delivery. Histopathological examination of placenta can help in investigating the mechanism of placental dysfunction, which can further help in devising more precise intervention strategies and can contribute to more effective therapies in the future.

Aim: To compare the placental histopathological findings of patients with adverse neonatal outcomes and good neonatal outcomes.

Materials and Methods: This was a prospective observational study conducted on 200 antenatal cases with gestational age >34 weeks were enrolled in the study from IPD of Department of Obstetrics and Gynaecology, Swaroop Rani Hospital, Prayagraj, Uttar Pradesh, India, over a period of 1 year. They were followed-up till delivery and assessed for neonatal outcomes. On the basis of neonatal outcome, patients were divided into two groups- group A with normal neonatal outcomes and group B with adverse neonatal outcomes. A gross and histopathological examination of placenta was performed for each case. The results were compiled and statistically analysed to compare the findings between the groups. The p-value was calculated using Chi-square score and value of <0.05 was considered significant.

Results: Out of 200 cases, 143 belonged to group A (with normal neonatal outcomes), in which majority 121 (84%) had normal placental histopathology, 8 (5.5%) had villous infarcts, 9 (6.2%) had syncytial knots and 5 (3.4%) had calcifications. Mean placental weight in group A was 425.88 grams while that in group B was 363.70 grams (p-value <0.0001). Group B (with adverse neonatal outcomes) had 57 cases, 8.8% cases were delivered via vaginal delivery, with low Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) score in 53 (26.5%), need for Neonatal Intensive Care Unit (NICU) admission in 57 (28.5%), need for mechanical ventilation in 12 (6%) and death in 6 (3%) cases. Villous infarcts was the placental histopathological feature in all cases with neonatal complications low APGAR score, NICU admission, those requiring mechanical ventilation or neonatal death. Out of these 57 cases, 8 (14%) had normal placental histopathology while 15 (26.3%) had infarcts, 12 (21%) syncytial knots, 9 (15.8%) had calcifications, and 13 (22.8%) had necrosis. Statistically significant difference (p-value <0.05) was found between the two groups in terms of abnormal histopathological findings and mean placental weight.

Conclusion: Neonates with adverse outcomes had abnormal placental histopathological findings like villous infarcts, syncytial knots, calcifications, and necrosis.

Keywords: Calcification, Malformations, Necrosis, Ventilation

INTRODUCTION

Placenta is the main connecting link between a mother and her foetus. It functions as respiratory, excretory and endocrine organ in the growing foetus and also shares the same stress and strain to which a foetus is exposed. The pathological processes interfering with placental functions may result in various abnormalities of foetal growth and development, malformations, still births or Central Nervous System (CNS) abnormalities [1]. The macroscopic and microscopic examination of placenta may point towards the cause of adverse neonatal outcome [2]. The knowledge gained from placental examination can be of help to both the obstetrician in understanding the pathogenesis of maternal and foetal complications as well as the neonatologist in management of neonatal morbidity. Still the placenta is one of the most misunderstood and neglected tissue in the human anatomical and pathological study.

The various placental histopathological findings can be seen depending on the maternal condition like increased syncytial knots can be seen in cases of Pregnancy Induced Hypertension (PIH) and Intrauterine Growth Restriction (IUGR) [3]. Calcifications can also be seen as a common histopathological finding in cases of PIH. Necrosis can be commonly seen in cases with Gestational Diabetes Mellitus (GDM) [4]. Kartheek BVS et al., found that perinatal adverse outcomes were higher in cases with abnormal histology of placenta [5]. Similarly, Kumar S and Sudarshan V, concluded that the placentas in low birth weight babies had higher villitis, syncytial knotting and cytotrophoblast proliferation [6]. Ramachandran A, found that the placental histological features of vessel wall thickening and infarction was associated with abnormal foetal and neonatal outcome [2].

The placental histopathology can play a major role in evidential support for medico-legal cases in event of unexplained neonatal morbidity and mortality. Also, it can help in identifying the causes that can adversely affect the subsequent pregnancies. The primary aim of the study was to compare the placental histopathological findings of patients with adverse neonatal outcomes and good neonatal outcomes.

MATERIALS AND METHODS

This prospective observational study was done at IPD of Department of Obstetrics and Gynaecology, Swaroop Rani Hospital, Prayagraj,

Uttar Pradesh, India) after obtaining clearance from Institutional Ethics Committee (ECR/922/inst/UP/2017). The study analysed placental histology and its association with the neonatal outcome in 200 cases.

Inclusion criteria: All pregnant women from IPD Department of the hospital with >34 weeks of gestation without any high risk and willing to gave consent for participation in the study were included.

Exclusion criteria: Patients with multiple pregnancies, with systemic or obstetrical complication eg. hypertensive disorders, diabetes, severe anaemia, chorioamnionitis etc., or congenital malformations in the foetus were excluded from the study.

Procedure

Patients who met the inclusion criteria were enrolled in the study after taking informed consent. General, systemic and obstetrical examination was done. They were followed-up till delivery for neonatal outcome and placenta was sent for histopathological examination. On the basis of neonatal outcome the patients were divided into two groups:

- Group A (N=143) (with good neonatal outcomes)
- Group B (N=57) (with adverse neonatal outcomes). Neonatal outcome was defined as adverse on the basis of birth weight <2.5 kg, APGAR Score <7/10 at 5 minutes, need for NICU admission and neonatal death.

Method of placental examination: Gross examination of placenta and four samples from it (two from maternal and foetal surfaces, one of membranes and one of umbilical cord) were stored in 10% formalin solution and later examined. Histopathological findings like infarction, intervillous thrombosis, fibrinoid necrosis, syncytial knots, and calcification were compared with the neonatal outcomes.

STATISTICAL ANALYSIS

Data was analysed using Statistical Package for Social Sciences (SPSS) version 26.0. Descriptive analysis for non parametric variables were expressed in proportion and parametric variables in mean and standard deviation. The p-value was calculated using Chi-square test and a p-value of <0.05 was considered significant.

RESULTS

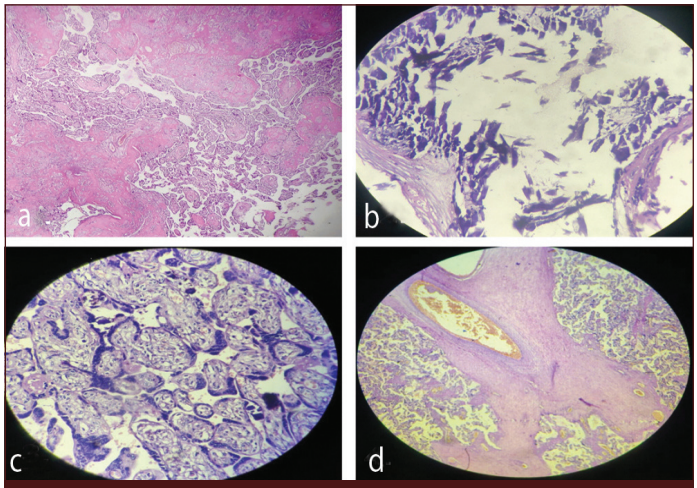
Out of the 200 pregnancies included in the study, 143 belonged to group A (with no neonatal complication) and 57 belonged to group B (pregnancies with any neonatal complication). In group B only 8.8% cases were delivered via vaginal delivery. Amongst preterm neonates (those delivered before 37 weeks) 56.1% cases were found to have adverse neonatal outcomes while those who were delivered beyond 37 weeks of gestational age had adverse neonatal outcome in 43.9% cases (p-value=0.005) [Table/Fig-1].

In group A, majority (84.6%) cases had normal placental histopathology. Amongst group B, majority (26.3%) had villous infarcts followed by necrosis in 22.8% cases and syncytial knots in 21% cases. Mean placental weight in group A was 425.88 grams while that in group B was 363.70 grams with significant p-value of 0.0001 [Table/Fig-2,3].

Villous infarcts were the single most ominous placental histopathological feature in all cases with low APGAR score, NICU admission, those requiring mechanical ventilation or neonatal death. The neonatal complications observed in the present study was from the subjects of Group B. It was associated with 50% cases of neonatal mortality [Table/Fig-4].

Obstetric findings of pregnant females	Group A (Good neonatal outcome) (N=143)	Group B (Adverse neonatal outcome) (N=57)
Gravida		
Primigravida	42 (29.4%)	13 (22.8%)
Multigravida	101 (70.6%)	44 (77.2%)
p-value	0.348	
Mode of delivery		
Normal vaginal delivery	120 (84%)	05 (8.8%)
Lower segment caesarean section	23 (16%)	52 (91.2%)
p-value	**0.00001**	
Gestational age at time of delivery		
Gestational age at the time of delivery <37 week	50 (35%)	32 (56.1%)
Gestational age at the time of delivery >37 week	93 (65%)	25 (43.9%)
p-value	**0.005**	

[Table/Fig-1]: Comparison of maternal characteristics.
p-value <0.05 considered significant



[Table/Fig-2]: Histopathology pictures of placenta showing: a) normal placental with chorionic villi (4x); b) calcifications (40x); c) Syncytial trophoblastic knots (10x); d) fibrin deposition (10x).

Histopathological finding	Group A (N=143)	Group B (N=57)	p-value
Normal	121 (84.6%)	08 (14%)	**0.00001**
Villous infarcts	08 (5.6%)	15 (26.3%)	**0.0003**
Syncytial trophoblastic knots	09 (6.3%)	12 (21%)	**0.0021**
Calcifications	05 (3.5%)	09 (15.8%)	**0.0020**
Necrosis	00	13 (22.8%)	**0.0001**
Mean placental weight (gram)±SD	425.88±32.44	363.70±50.27	**0.0001**

[Table/Fig-3]: Comparison of placental histopathological findings.
p-value <0.05 considered significant

Placental histopathology	APGAR score <7/10 (N=53)	NICU admission (N=57)	Mechanical ventilation (N=12)	Death (N=06)
Normal	07 (13.2%)	08 (14%)	00	00
Villous infarcts	15 (28.3%)	15 (26.3%)	04 (33.3%)	03 (50%)
Syncytial trophoblastic knots	10 (18.8%)	12 (21%)	02 (16.7%)	00
Calcification	08 (15%)	09 (15.7%)	04 (33.3%)	02 (33.3%)
Necrosis	13 (24.5%)	13 (22.8%)	02 (16.7%)	01 (16.7%)

[Table/Fig-4]: Placental histopathology findings and neonatal complications.
APGAR: Appearance, pulse, grimace, activity, and respiration; NICU: Neonatal intensive care unit

DISCUSSION

The mother, placenta and foetus form a composite triad of dynamic equilibrium and dysfunction of any one of them can affect the others [7]. The histopathological examination of placenta can be implemented in drawing conclusions in unexplained cases of adverse neonatal outcomes. Also, placental tissue can be easily collected in such cases where foetal or neonatal autopsy is much more complex and cumbersome procedure and has religious issues. Fox H stressed the importance of analysing the placental pathology quantitatively and has stated that the importance of the lesions could be realised only when assessed in relation to foetal growth and maturation [8]. The American College of Pathologists and American College of Obstetricians and Gynaecologists (ACOG) has provided guidelines for the examination of placenta [9].

This study was conducted to compare the placental histopathological findings with good and adverse neonatal outcomes. In group B with adverse neonatal outcomes villous infarcts (26.3%) were the most common finding followed by necrosis in 22.8% cases. Also, the mean placental weight in group B i.e., with adverse neonatal outcome was significantly lower than group A i.e., with good neonatal outcomes (p-value <0.05). Sato Y et al., studied the placental findings, maternal and foetal factors in the cases of IUGR. It was found that the prevalence of infarction (33%) and foetal vessel thrombosis (22%) were higher in IUGR cases than those in normal growth pregnancies [10]. Similarly, Cibils LA had reported that the placenta from hypertensive patients were smaller than the normal [11]. This suggests that the pathologic process interferes with the normal placental growth and function.

Amongst neonates with adverse outcomes, it was found that villous infarcts were the most common finding in each category. Syncytial knots and necrosis were indicative of adverse neonatal outcome. A 50% of cases of neonatal mortality showed villous infarcts in placental histopathology. Calcifications and necrosis had grave prognosis and associated with greater need for mechanical ventilation and risk of neonatal mortality. In the study conducted by Madazli R et al., placenta from IUGR cases had a significantly increased number of villous infarcts, cytotrophoblastic proliferation and thickening of villous trophoblastic basement membrane [12]. Also, in a study by Kartheek BVS et al., perinatal mortality (2.22%), low APGAR score (90.9%), IUGR (4.44%) were higher in cases with abnormal histology of placenta compared to normal cases [5]. The adverse neonatal outcome was probably due to ischaemia resulting from decreased uteroplacental blood flow [13].

Human placenta is described as haemochorioendothelial [14]. Maternal blood bathes the syncytiotrophoblast and villi and is separated from the foetal blood by endothelium lining of foetal blood vessels. Deviation from normal physiology is reflected in placental morphology and functions. The pathophysiology behind various placental histopathological findings also explains the neonatal outcomes. Syncytial knots are aggregates of small, closely packed densely staining nuclei protruding from the villous surface into the intervillous space. High villous syncytial count i.e., more than 30% of villi showing syncytial knots are considered excessive [15]. These are formed as a result of villous hypovascularity which result in accelerated or augmented sequestration of aged nuclei for the optimal use of the trophoblasts available for transfer purpose [16]. An increased syncytial knot in placentae suggests that an attempt was being made to form new villi so as to increase an effective surface area for exchange [17].

Calcification is common in human placentae and is a normal physiological process of maturation and aging. However, premature and excessive calcification of placenta is pathological which causes uteroplacental insufficiency and compromises foetal blood supply and growth. The maturation of placenta, because of excess calcification is associated with a higher incidence of poor foetal outcomes [18,19]. Villous infarction is death of placental tissue which occurs due to compromised blood flow. It presents as yellowish white or blood-stained deposits of fibrin (a fibrous protein) on the surface or in the substance of the placenta [20]. Small infarcts and those at the margin are usually clinically insignificant because of presence of extensive placental reserve. Necrosis is cell death due to impaired blood and oxygen supply due to insults like ischaemia, infections, toxins, immunological reactions and trauma. Fibrinoid necrosis involving upto three percent of placental villi is considered abnormal. Necrosis can be a degenerative change in villous trophoblast [21]. It is seen as a nodular mass of homogeneous acidophilic material in the villi. Blood supply of the foetus is reduced due to decrease in the amount of functional placental tissue.

Limitation(s)

All pathological examinations were not done by a single pathologist, thus there may be a variation in specimen collection and interpretation of pathological slides. Also, proteomic or genomic study on the placental tissue would have provided more information.

CONCLUSION(S)

In the present study, adverse neonatal outcomes were associated with abnormal placental histopathology in 85.9% cases. Villous infarcts were found in majority (26.3%) of cases with adverse neonatal outcomes and in 50% cases with neonatal mortality. Only 15.3% cases with good neonatal outcomes had abnormal placental histopathological findings. Among which syncytial trophoblastic knots were the most common finding. The mean placental weight was lower in group with adverse neonatal outcomes. Placental histopathological examination can help in identifying the cause of neonatal morbidity and mortality. Also, the association between clinical and placental histopathology helps in diagnosis of causes that effect subsequent pregnancies and findings relevant to care of newborn.

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