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EXPLORING THE MORPHOMETRIC AND HISTOPATHOLOGICAL CHANGES OF PLACENTAS IN PREGNANCIES COMPLICATED BY MATERNAL ANAEMIA

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ABSTRACT:

Background: Maternal anaemia constitutes a persistent public health challenge in developing nations, carrying substantial risks for both maternal health and fetal development. The placenta, which serves as the crucial feto-maternal organ, often displays pathological changes that reflect systemic maternal conditions like anaemia. Consequently, this study was undertaken to conduct a comparative analysis of the morphometric and histopathological features in placentas from anaemic versus non-anaemic mothers, aiming to elucidate the structural impact of maternal anaemia on this vital organ.

Methods: In this comparative study, we prospectively collected and examined a total of 130 placentas, including 65 from anaemic and 65 from non-anaemic pregnant women. Detailed morphometric parameters such as weight of placenta, diameter, thickness of placenta, circumference, area of chorionic plate, number of cotyledons, cord insertion were recorded. Histopathological examination was performed to assess features such as syncytial knots, villous maturation, fibrinoid necrosis, calcification, intervillous thrombi, intervillous space dilatation, cytotrophoblastic proliferation, and vascular changes. Statistical analysis was carried out using SPSS v21.0, with independent-sample t-tests applied for comparison.

Results: Placentas from anaemic mothers demonstrated significantly reduced weight, diameter, thickness, circumference, and chorionic plate area ($p < 0.01$). Histologically, anaemic group placentas showed a higher incidence of syncytial knots, delayed villous maturation, fibrinoid necrosis, and other degenerative changes ($p < 0.01$), indicating compromised placental function.

Conclusion: Maternal anaemia is associated with distinct alterations in placental morphology and histology, which may adversely affect fetal development. The results of this study underscore the critical importance of timely diagnosis and treatment of anaemia during gestation to mitigate adverse perinatal events.

Keywords: Maternal anaemia, placental morphology, placental histopathology, fetal development, placental insufficiency

INTRODUCTION:

Maternal anaemia presents a major public health challenge, with a high prevalence in developing nations such as India. The World Health Organization (WHO) provides a clinical definition for this condition during pregnancy as any case where haemoglobin levels fall below 11.0 g/dL. Among the various types, iron-deficiency anaemia (IDA) is the most frequently observed. [1] Globally, approximately 37% of pregnant women are affected by anaemia, with higher prevalence observed in South Asian regions. The finding that 57% of Indian women of reproductive age are anaemic, as reported by the National Family Health Survey (NFHS-5), points to a health crisis that is both long-standing and exceptionally widespread. [2,3]

The aetiology of maternal anaemia is multifactorial, encompassing nutritional deficiencies, infectious diseases, and genetic disorders. The primary reason for this is iron deficiency, which often stems from the combined effect of insufficient iron in the diet and the body's heightened demand for it during pregnancy. Beyond iron deficiency, the etiology of anaemia is often multifactorial, with other common causes including insufficient levels of folate and vitamin B12, parasitic infections, and underlying chronic diseases. [4]

The placenta's function as the primary site of feto-maternal nutrient and gas exchange is central to healthy fetal growth. Consequently, the hypoxic stress induced by maternal anaemia often instigates compensatory changes in placental morphology and histology as the organ attempts to maintain adequate fetal oxygenation and nutrition. [5]

Studies have shown that placentas from anaemic mothers undergo structural changes, most notably a decrease in the volume and surface area of the intermediate and terminal villi. These changes may compromise the placenta's diffusing capacity, potentially impacting fetal growth. [6]

Histopathological studies have revealed significant differences in placentas from anaemic mothers compared to non-anaemic counterparts. Notable findings include increased capillary proliferation within chorionic villi, dilated terminal villi capillaries, and widened intervillous spaces. These adaptations are thought to be compensatory mechanisms in response to chronic maternal hypoxia. [7]

Despite these adaptations, the efficiency of placental function may still be compromised in anaemic pregnancies. Reduced oxygen and nutrient transfer can adversely affect fetal growth and development. Furthermore, the degree of placental alteration may correlate with the severity of maternal anaemia, emphasizing the importance of early detection and management. In the Indian context, where anaemia prevalence among pregnant women remains high, understanding the specific morphometric and histopathological changes in the placenta is crucial. Ultimately, this knowledge can be used to develop more effective clinical interventions and public health policies designed to lessen the harmful effects of maternal anaemia on pregnancy.

This study aims to explore and compare the morphometric and histopathological features of placentas from anaemic and non-anaemic pregnant women. By analyzing placental specimens, we seek to elucidate the structural adaptations associated with maternal anaemia and their potential implications for fetal health. The findings may contribute to a better understanding of placental pathology in anaemic pregnancies and underscore the need for effective interventions to address maternal anaemia.

MATERIALS AND METHODS:

Prior to beginning the research, we secured approval from the Institutional Ethics Committee. The study was then carried out as a prospective comparative analysis over the following year, from January 2024 to December 2024. For this study, we collected placentas from mothers who delivered at full term (37 weeks of gestation or later). We then divided these participants into two groups based on the haemoglobin levels measured in their third trimester: Group A (anaemic mothers) had haemoglobin levels <11 g/dL, and Group NA (non-anaemic mothers) had levels >11 g/dL, in line with WHO guidelines.

Inclusion Criteria:

- Placentas from term deliveries (≥37 weeks gestation).
- Singleton pregnancies.
- Availability of complete maternal clinical data, including haemoglobin levels.

Exclusion Criteria:

- Preterm deliveries (<37 weeks gestation).
- Mothers with comorbid conditions such as gestational hypertension, diabetes mellitus, infections, or other systemic illnesses.
- Placentas with gross abnormalities unrelated to anaemia, such as abruptio placentae or infarcts due to thrombosis.

Sample Size Determination:

We performed a power analysis using G*Power software to determine the necessary sample size. To achieve 80% power for detecting an effect size of 0.5 at a significance level of 0.05, we concluded that 65 participants per group were required, leading to a total study size of 130.

Data Collection Procedures:

Gross Examination:

Immediately after delivery, placentas were collected and rinsed with normal saline to remove blood clots. The following parameters were recorded:

- Weight (measured using a digital weighing scale after trimming membranes and umbilical cord).
- Diameter (measured at the widest point using a measuring tape).

- Thickness (measured at the center using a calibrated ruler).
- Number of cotyledons.
- Type of umbilical cord insertion (central, eccentric, marginal, or velamentous).
- Circumference- The circumference of the placenta was measured in centimeters (to one decimal place) using a thread wrapped fully around its outer edge. The thread was then cut where it overlapped after completing one full circle. This cut piece was straightened and its length measured using a digital caliper.
- The mean chorionic plate area (A) was also calculated by applying the formula for the area of an ellipse: $A=(\pi \times dL \times dS)/4$, where dL and dS represent the largest and smallest diameters of the plate, respectively

Histopathological Examination:

We collected tissue samples for histological analysis from two distinct locations on each placenta: the central region and the periphery. The specimens underwent a 24-hour fixation in 10% neutral buffered formalin, followed by standard processing and paraffin embedding. Sections were then cut to a thickness of 4–5 µm using a microtome and stained with hematoxylin and eosin (H&E). Microscopic evaluation was performed under light microscopy to assess:

- Villous maturation and morphology.
- Syncytial knot formation.
- Cytotrophoblastic proliferation.
- Fibrinoid necrosis.
- Calcifications.
- Intervillous space characteristics.
- Vascular changes within chorionic villi
- Endothelial changes in blood vessels

Each slide was initially examined under low power magnification (×10). The specified histopathological features were assessed in three randomly selected, non-overlapping fields. For each parameter, the observed values across these fields were noted, and both the range and mean per low power field (lpf) were calculated and documented. These parameters were evaluated based on established histopathological criteria and previous studies. [9]

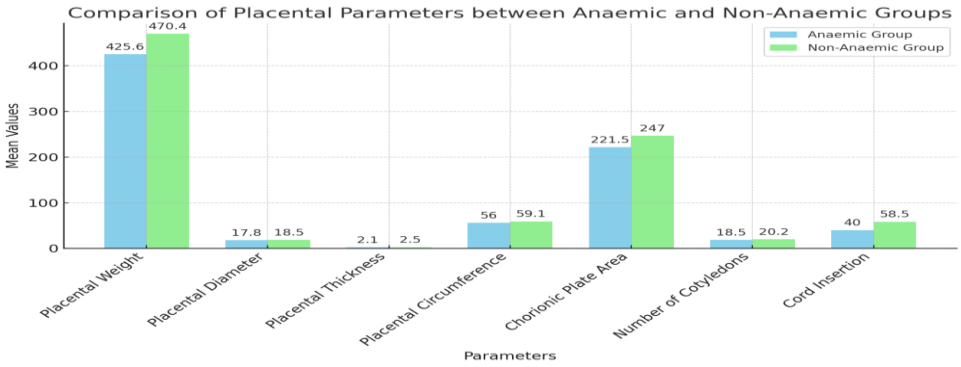
All data were compiled in Microsoft Excel and subsequently analyzed using SPSS version 21.0. Continuous data were expressed as mean with standard deviation, and categorical data were summarized using percentages and frequencies. To compare the two groups, independent-sample t-tests were used for continuous data and chi-square tests for categorical data. A p-value of less than 0.05 was considered the threshold for statistical significance.

RESULTS:

The comparison of placental morphometric parameters between the anaemic and non-anaemic groups revealed significant differences in several key measurements as shown in Table 1. The average placental weight in the anaemic group was 425.6 ± 60.3 g, which was notably lower than the 470.4 ± 55.8 g observed in the non-anaemic group ($p = 0.002$). Similarly, the placental diameter was significantly smaller in the anaemic group (17.8 ± 1.2 cm) compared to the non-anaemic group (18.5 ± 1.1 cm), with a p-value of 0.004.

In terms of placental thickness, the anaemic group showed a thinner placenta (2.1 ± 0.4 cm) in comparison to the non-anaemic group (2.5cm ± 0.3 cm), with this difference reaching a high level of significance ($p < 0.001$). The placental circumference was also significantly smaller in the anaemic group (56.0 ± 3.5 cm) compared to the non-anaemic group (59.1 ± 3.2 cm), with a p-value of 0.005 (Figure 1).

Figure 1: Comparison of macroscopic placental parameters between anaemic and non-anaemic mothers



The analysis of the chorionic plate area demonstrated that the anaemic group had a smaller area (221.5 ± 18.4 cm²) than the non-anaemic group (247.0 ± 16.7 cm²), with a significant difference. The anaemic group exhibited a significantly lower number of cotyledons compared to the non-anaemic group (18.5 ± 2.1 vs. 20.2 ± 2.0, respectively; p=0.001). Similarly, central cord insertion was less frequent in the anaemic group (40.0%) than in the non-anaemic group (58.5%; p=0.038).

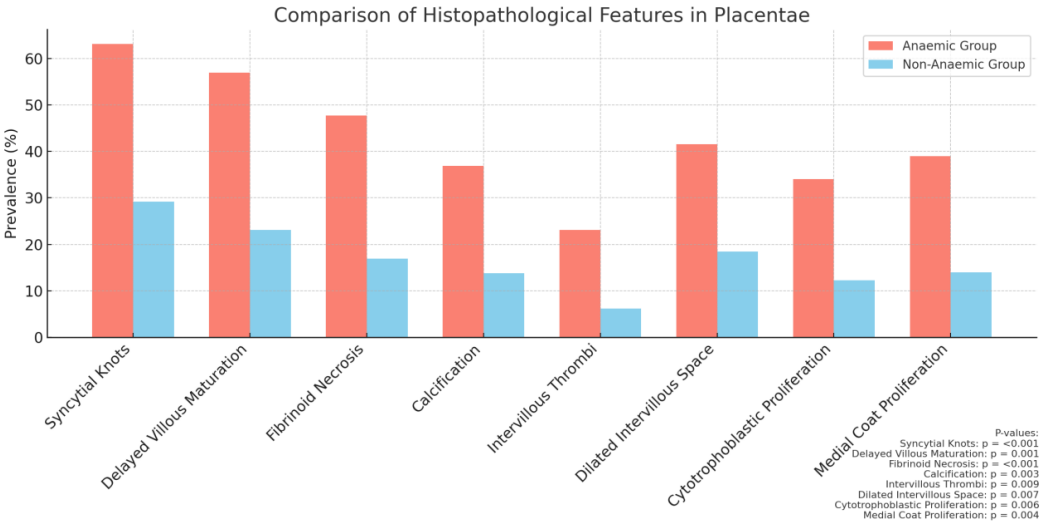
Table 1: Gross Morphometric Analysis

Parameter	Anaemic Group	Non-Anaemic Group	p-value
Placental Weight (g)	425.6 ± 60.3	470.4 ± 55.8	0.002 **
Placental Diameter (cm)	17.8 ± 1.2	18.5 ± 1.1	0.004 **
Placental Thickness (cm)	2.1 ± 0.4	2.5 ± 0.3	<0.001 **
Placental Circumference (cm)	56.0 ± 3.5	59.1 ± 3.2	0.005 **
Chorionic Plate Area (cm²)	221.5 ± 18.4	247.0 ± 16.7	<0.001 **
Number of Cotyledons	18.5 ± 2.1	20.2 ± 2.0	0.001 **
Cord Insertion (Central %)	40.0%	58.5%	0.038 *

The histopathological comparison between the two groups, detailed in Table 2, revealed several significant differences. In the anaemic group, placental samples more frequently displayed features such as increased syncytial knot formation (63.1%) and evidence of delayed villous maturation (56.9%), in contrast to lower rates observed in the non-anaemic group (29.2% and 23.1%, respectively). These differences were statistically significant ($p < 0.001$ and $p = 0.001$).

The placentas from the anaemic group also exhibited a range of other significant pathological changes when compared to the non-anaemic group (Figure 2). These included a higher incidence of fibrinoid necrosis (47.7% vs. 16.9%; p<0.001), calcification (36.9% vs. 13.8%; p=0.003), intervillous thrombi (23.1% vs. 6.2%; p=0.009), and dilated intervillous spaces (41.5% vs. 18.5%; p=0.007).

Figure 2: Clustered bar chart comparing the prevalence of histopathological features between anaemic and non-anaemic groups



The anaemic group also demonstrated significant proliferative changes. Both cytotrophoblastic proliferation (34.0% vs. 12.3%; p=0.006) and medial coat proliferation in vessels (39.0% vs. 14.0%; p=0.004) were observed at a significantly higher rate compared to the non-anaemic group. These results

highlight several key differences in both gross morphometric and histopathological features of placental development between the anaemic and non-anaemic groups, suggesting a significant impact of anaemia on placental structure and function.

Table 2: Histopathological Findings

Histological Feature	Anaemic Group	Non-Anaemic Group	p-value
Increased Syncytial Knots (%)	63.1%	29.2%	<0.001 **
Delayed Villous Maturation (%)	56.9%	23.1%	0.001 **
Fibrinoid Necrosis (%)	47.7%	16.9%	<0.001 **
Calcification (%)	36.9%	13.8%	0.003 **
Intervillous Thrombi (%)	23.1%	6.2%	0.009 **
Dilated Intervillous Space (%)	41.5%	18.5%	0.007 **
Cytotrophoblastic Proliferation (%)	34.0%	12.3%	0.006 **
Medial Coat Proliferation of Vessels (%)	39.0%	14.0%	0.004 **
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Dilated Intervillous Space (%)	41.5%	18.5%	0.007 **
Cytotrophoblastic Proliferation (%)	34.0%	12.3%	0.006 **
Medial Coat Proliferation of Vessels (%)	39.0%	14.0%	0.004 **

DISCUSSION:

This study underscores the profound impact of maternal anaemia on both the gross morphometry and microscopic architecture of the placenta. Anaemia in pregnancy, driven primarily by iron deficiency, remains a major nutritional disorder for women in developing nations. According to global figures, more than four in ten pregnant women are affected, and this problem is most heavily concentrated in South Asia and Sub-Saharan Africa. [10]

The observed reduction in weight of placenta, diameter, thickness of placenta, and area of chorionic plate in anaemic mothers compared to their non-anaemic counterparts is consistent with several previous studies that associate maternal anaemia with placental hypotrophy [11,12]. It is probable that these structural alterations are a direct consequence of chronic hypoxia and uteroplacental insufficiency. This state, triggered by maternal anaemia, compromises the placenta's ability to effectively transfer vital oxygen and nutrients to the fetus[13]. The reduction in cotyledon count observed in our study further supports the hypothesis that placental maturation is compromised in anaemic pregnancies. A study by Bhanarkar U et al. demonstrated that anaemic placentas had significantly fewer and irregular cotyledons, affecting the surface area available for exchange [14]. Cord insertion patterns also differed significantly, with central insertion being less frequent in the anaemic group. Abnormal cord insertions, such as marginal or velamentous insertions, have been linked to placental insufficiency and are more common in compromised pregnancies, including those affected by anaemia [15].

Histologically, the placenta from anaemic mothers exhibited a marked increase in syncytial knots and delayed villous maturation. These features are well-established indicators of placental stress and chronic hypoxia. Syncytial knots represent terminal differentiation of the syncytiotrophoblast and have been shown to increase in conditions of utero-placental underperfusion [16]. Delayed villous maturation, meanwhile, reflects disrupted differentiation and branching morphogenesis, a phenomenon previously described in anaemia and preeclampsia [17].

The presence of fibrinoid necrosis and calcification was also significantly higher among anaemic placentas. Fibrinoid necrosis indicates tissue injury and degeneration, while calcification is often regarded as a sign of accelerated ageing or terminal placental maturation. These features suggest that the placentas in anaemic pregnancies experience premature senescence, likely due to oxidative stress and chronic inflammation. This observation is consistent with the work of Soni RB et al., who also noted extensive fibrinoid necrosis and the deposition of perivillous fibrin in placentas from anaemic mothers. [18] Furthermore, the higher prevalence of intervillous thrombi and the presence of dilated intervillous spaces in the anaemic group are indicative of impaired maternal blood flow and circulatory stasis within these placental areas. These vascular lesions may reflect sluggish perfusion and increased blood viscosity secondary to iron-deficient states. Cytotrophoblastic proliferation observed in anaemic placentas is a

compensatory mechanism aimed at improving oxygen and nutrient transfer but also reflects immature villous development [19]. Notably, medial coat proliferation of fetal blood vessels—a feature seen more frequently in the anaemic group—has been linked to chronic fetal hypoxia and increased resistance in fetoplacental circulation. This vascular adaptation is thought to increase perfusion pressure and mitigate the effects of placental insufficiency [20].

The clinical implications of these findings are far-reaching. The structural alterations found in the placentas of anaemic mothers are strongly linked to a range of poor perinatal outcomes. These include intrauterine growth restriction (IUGR), low birth weight, preterm labor, and in the most severe cases, intrauterine fetal demise [21]. These placental alterations reflect a state of suboptimal intrauterine environment, corroborating the hypothesis that the placenta serves as a mirror of maternal health. Routine antenatal surveillance for anaemia, coupled with early nutritional interventions, is therefore crucial in minimizing these risks [22]. One of the primary limitations of this study is that the severity of anaemia was not stratified, which could have provided deeper insights into dose-response relationships between haemoglobin levels and placental changes. Other potential confounders such as maternal nutritional status, comorbidities and socioeconomic factors were not accounted for, which may influence placental morphology.

CONCLUSION:

The findings of this study reinforce the fundamental importance of maternal haemoglobin status for maintaining a healthy placenta throughout pregnancy. Significant gross and microscopic changes were noted in placentas from anaemic mothers, reflecting compromised vascular development and altered villous architecture - hallmarks of a stressed intrauterine environment. These alterations may have downstream effects on fetal growth and pregnancy outcomes. Early diagnosis and management of anaemia during pregnancy are essential not just for maternal well-being, but also for safeguarding optimal placental development and fetal health. The findings also highlight the importance of routine placental examination in anaemic pregnancies, which may offer valuable postnatal insights into antenatal complications and guide future care strategies.

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