



## Research Article

# Histological Study of Human Placenta in Normal and Anemic Cases

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### Abstract

**Background:** Placenta forms a functional unit between the mother and the fetus and any pathological event that concerns the mother or the fetus will influence the normal function of the placenta. Anemia is commonest hematological disorder that occurs in pregnancy and the commonest cause of anemia during pregnancy is iron deficiency which may be due to nutritional deficiency or increased demand of oxygen in pregnancy. Anemia leading to hypoxia cause changes in structure of placenta. It also exerts profound changes on the maternal circulatory system and has serious effects both on mother and fetus<sup>7</sup> and it is responsible for 20-40% of maternal deaths directly or indirectly.

**Objective:** To analyze the spectrum of histopathological changes in placenta in normal and anemic cases.

**Material and Methods:** A total of 90 placentae were collected soon after deliveries from normal and caesarean sections of which, 45 placentae were from mothers with anemia and 45 placentae were from normal term mothers who formed the control group. Placental tissue was taken for histopathological processing viz: Fixation, Dehydration, Clearing, Embedding and Sectioning and staining was done after that Immunostaining for paraffin sections was done.

**Results:** The area of syncytial knot formation, cytotrophoblastic cellular proliferation, fibrinoid necrosis was found higher among the cases as compared to controls which is statistically significant. Hyalinised area was the most common finding among cases while Stromal fibrosis was least finding.

**Conclusion:** Anaemia in pregnancy alters the placental morphology and adequate treatment of anaemia may therefore be critical to normal placental function.

**Keywords:** Anemia, Fibrinoid necrosis, Placenta, Syncytial knot formation.

### Introduction

The placenta forms a functional unit between the mother and the fetus and any pathological event that concerns the mother or the fetus will influence the normal function of the placenta<sup>1,2</sup>, resulting in morphological and histopathological changes.

It acts like a sieve, moving oxygen and nutrients from the mother's body to baby and taking carbon

dioxide and waste materials from the baby into mother's body for elimination. The blood vessels of the mother and baby are incredibly close together at the site where the placenta is attached to uterus. However, remarkably the blood flows always completely separate whilst facilitating vital exchange. The placenta can help to protect the fetus against certain xenobiotic molecule, infections and maternal diseases. Early placental

development is characterized by the rapid proliferation of the trophoblast and development of chorionic sac and villi<sup>3</sup>. Placenta is classified into 2 types one is disperse and other is magistral<sup>4</sup>. Placental weight is around 500–600 g usually one-sixth of the fetal weight and thickness is 2.5 cm<sup>5</sup>. Anemia is commonest hematological disorder that occurs in pregnancy. The World Health Organization (WHO)<sup>6</sup> recommends that hemoglobin ideally should be maintained at or above 11.0 g/dl, and should not be allowed to fall below 10.5 g/dl in the second trimester

The commonest cause of anemia during pregnancy is iron deficiency which may be due to nutritional deficiency or increased demand of oxygen in pregnancy. Anemia leading to hypoxia cause changes in structure of Placenta. It also exerts profound changes on the maternal circulatory system and has serious effects both on mother and fetus<sup>7</sup> and it is responsible for 20-40% of maternal deaths directly or indirectly through cardiac failure, preeclampsia, antepartum hemorrhage, postpartum hemorrhage and puerperal sepsis<sup>8</sup>.

Anemia during pregnancy increases the risk of fetal growth retardation and low birth weight, premature delivery, increased perinatal mortality, and reduced resistance to infection of both mother and baby. Hence, the present study was taken to analyze the spectrum of histopathological changes in placenta in normal and anemic cases.

## Material and Methods

**Study Population:** This was laboratory based Cross sectional descriptive type of observational study carried out in Department of Anatomy, Zydus Medical College and Hospital, Dahod over a period of one year. A total of 90 placentae were studied, of which, 45 placentae were from mothers with anemia (Hb < 11g/dl) who formed the anemia group and 45 placentae were from normal term mothers (Hb ≥11g/dl) who formed the control group.

## Methodology

The placenta was collected soon after deliveries from normal and caesarean sections. The collected placenta was washed under the running tap water and examined thoroughly. The specimen was transported to the Department of Anatomy in formalin (10%) filled plastic container. Placental tissue was taken for histopathological processing viz: Fixation, Dehydration, Clearing, Embedding and Sectioning and staining was done after that Immunostaining for paraffin sections was done.

## Statistical Analysis

The results are presented in Mean±SD. The Chi-square test was used to compare the categorical variables between cases and controls. The Unpaired t-test was used to compare the continuous variables between cases and controls. The Pearson correlation coefficient was calculated. The p-value<0.05 was considered significant. All the analysis was carried out by using SPSS 16.0 version (Chicago, Inc., USA)

## Results

A total of 90 samples were included in the study. The area of syncytial knot formation was observed higher among the cases (64.56±2.37) compared to controls (25.02±1.40) which is statistically significant (p=0.0001) (Table 1)

The area of cytotrophoblastic cellular proliferation was found higher among the cases (3.00±1.43) compared to controls (2.49±1.03) which is statistically significant (p=0.04) (Table 2)

The area of fibrinoid necrosis was higher among the cases (5.96±1.39) compared to controls (3.07±1.45) which is statistically significant (p=0.0001) (Table 3)

Hyalinised area was the most common finding among cases (71.1%) followed by Intervillous haemorrhage (64.4%), Area of calcification (60%) and Stromal fibrosis (51.1%). There was significant (p=0.0001) difference in the histological findings between cases and controls. (Table 4).

**Table 1** Comparison of area of syncytial knot formation between cases and controls

Groups	Area of syncytial knot formation (Mean±SD)
Cases	64.56±2.37
Controls	25.02±1.40
p-value <sup>1</sup>	0.0001*

<sup>1</sup>Unpaired t-test, \*Significant**Table 2** Comparison of area of cytotrophoblastic cellular proliferation /LPD between cases and controls

Groups	Area of cytotrophoblastic cellular proliferation (Mean±SD)
Cases	3.00±1.43
Controls	2.49±1.03
p-value <sup>1</sup>	0.04*

<sup>1</sup>Unpaired t-test, \*Significant**Table 3** Comparison of area of fibrinoid necrosis /LPD between cases and controls

Groups	Area of fibrinoid necrosis (Mean±SD)
Cases	5.96±1.39
Controls	3.07±1.45
p-value <sup>1</sup>	0.0001*

<sup>1</sup>Unpaired t-test, \*Significant**Table 4** Distribution of histopathological findings among the cases

Histological findings@	Cases (n=45)		Controls (n=45)		p-value <sup>1</sup>
	No.	%	No.	%	
Area of calcification	12	26.7	27	60.0	0.0001*
Stromal fibrosis	11	24.4	23	51.1	0.0001*
Intervillous hemorrhage	0	0.0	29	64.4	0.0001*
Hyalinised area	6	13.3	32	71.1	0.0001*

<sup>1</sup>Chi-square test, @Multiple response, \*Significant

## Discussion

Histopathological examinations of the placenta can reveal changes which may be associated with maternal disorders and also result in fetomaternal complications. Placental studies are quantitative rather than qualitative as some changes take place in placenta before it separates from the uterus. The changes are considered pathological when the extent of involvement is greater than normal<sup>9</sup>.

Lao and Tam<sup>10</sup> concluded that placental size increased relative to infant size in pregnancies complicated by anemia, but whether this phenomenon reflected actual placental hypertrophy or failure of fetal growth to keep up with placental growth remains to be determined. Dhall<sup>11</sup> also found significant increase in the number of syncytial knots in these placentas. Villous hypovascularity, increased syncytial knots

and fibrinoid necrosis were also noted by Joshi et al<sup>12</sup>.

Syncytial knots are composed of aggregates of small, closely packed densely staining nuclei protruding from the villous surface into the intervillous space. In the literature, it is hypothesized that villous hypovascularity leads to formation of syncytial knots, indicating sequestration of aged nuclei is being accelerated or augmented so as to use optimally the amount of trophoblast available for transfer purpose<sup>9</sup>. Increased syncytial knots in placentae in anemia suggested that an attempt was being made to form new villi so as to increase an effective surface area for exchange<sup>11</sup>.

In this study, the area of syncytial knot formation was observed to be significantly ( $p=0.0001$ ) higher among the cases (64.56±2.37) compared to

controls (25.02±1.40). Our results are in accordance with study conducted by Sabharwal et al<sup>13</sup> and Gyatri et al<sup>14</sup> who also reported high villous syncytial counts among the cases as compared to controls. However Rangnekar and Darbari et al<sup>15</sup>, Adil and Nausheen et al<sup>16</sup> and Rohini et al<sup>17</sup> reported low incidence of excessive syncytial knots in anemia groups. There are studies<sup>18,19</sup> who did not find any difference in the incidence of syncytial knots in anemia and control group.

Fibrinoid necrosis is seen as a nodular mass of homogenous acidophilic material in the villi. Fibrinoid necrosis has been considered as a hallmark of immunological reactions within the trophoblastic tissue<sup>20</sup>.

In this study, the area of fibrinoid necrosis was significantly ( $p=0.0001$ ) higher among the cases (5.96±1.39) compared to controls (3.07±1.45). Our results are in concordant with earlier studies<sup>13,14,16</sup>. However Rangnekar and Darbari<sup>15</sup> has reported decreased incidence of villi with fibrinoid necrosis, in severe anemia subgroup.

In the present study, hyalinised area was the most common finding among cases (71.1%) than intervillous hemorrhage (64.4%) followed by area of calcification (60%) and stromal fibrosis (51.1%). There was significant ( $p=0.0001$ ) difference in the histological findings between cases and controls. Our findings are concordant with various studies<sup>13-17</sup> who all reported increase in villous stromal fibrosis in the anemia cases.

In contrary to earlier reports in the present study, the gross examination of the placentae from anemic mothers showed lower incidence of calcification and infraction<sup>21</sup>. This might be probably due to the decreased size of placentae.

Anemia especially, severe anemia in pregnancy alters the placental histomorphology. To avoid the placental malformation, prompt treatment of anemia is required. Cytotrophoblastic cellular proliferation was significantly higher in anemic group which might be also an adaptive response to decreased oxygen supply<sup>22</sup>. All these changes in placentae of anemic mothers may be the cause of

worse fetal outcome and maternal hazards. This signifies there is a need of assessment of placenta at the time of delivery.

### Conclusion

Histopathological changes showed significant microscopic changes in placentae of anemia group as compared to controls. Placenta in severe anemia showed excessive syncytial knots, increased fibrinoid necrosis of the villi, increased villous stromal fibrosis. Quantitative determination of placental changes is essential in study of placenta as normal pregnancies can also show significant placental changes. Severe anemia in pregnancy alters the placental morphology and adequate treatment of anemia may therefore be critical to normal placental function.

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