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Histopathology

MORPHOLOGICAL STUDY & HISTOLOGICAL CHANGES THAT TAKES PLACE IN HUMAN PLACENTA DUE TO NUTRITIONAL ANAEMIA

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ABSTRACT Anaemia is most common nutritional disorder in world. Nutritional Anaemia in pregnancy is a well recognized obstetric hazard, observed more frequently in developing countries. Severity of anaemia among pregnant women was judged by the criteria suggested by World Health Organization. The present study was undertaken to analyze the morphological and histological changes in the placentae of anaemic mother compared with normal mothers. On Gross examination of placenta showed increased areas of infarction & calcification with increasing the severity of anaemia. In the present study number of cotyledons decreases with severity of anaemia. The histomorphological observations showed increased stromal fibrosis, syncitial knots, fibrinoid necrosis, medial coat proliferation of blood vessels, intervillous hemorrhage, calcification, hyalinization of villi & cytotrophoblastic cell proliferation in study group than the control group. This is might be due to an adaptation to maternal hypoxia. It was found that period of gestation decreased with severity of anemia. Various workers have attributed this to either degenerative changes or increased intervillous fibrinoid deposition causing premature delivery where placenta could not further compensate caused by hypoxia. Placentas from anemic mother have comparatively low weight. This is attributed to retarded growth of placenta due to decrease in total placental DNA.

KEYWORDS : Anaemia, Placentae, infarction, calcification, fibrinoid necrosis

INTRODUCTION

Anaemia is most common nutritional disorder in world. Nutritional Anaemia in female during pregnancy is very common. It is a pathological condition, which affects maternal blood, leading to hypoxia (oxygen carrying capacity of red blood cells is insufficient), which cause changes in structure of Placenta. Anaemia also exerts profound changes on the maternal circulatory system and has serious effects both on mother and fetus.

Placenta is a developing organ during pregnancy for providing nutrition, oxygen supply for the fetus and to eliminate excretory wastes, acts as protective barrier. So it is a vital organ which is absolutely essential for survival, growth and development of fetus. If the placenta has got affected due to anaemia it adversely affects for the growth of the fetus. Neonates may get pathological conditions like, birth asphyxia, prematurity, IUGR, low birth weight and also the placenta varies in its measures that includes its weight, morphometry, number of cotyledons and its thickness. Hence a good fetal outcome depends on mother's health and her diet during antenatal period [16].

Severity of anaemia during pregnancy is a potentially hazardous haematological disorder. It is associated with late abortions, prematurity, low birth weight and stillbirths [20], [15]. The commonest cause of anaemia during pregnancy is iron deficiency which may be due to nutritional deficiency or increased demand of oxygen in pregnancy. Any diseases associated with pregnancy like hematological disorder, diabetes and hypertension affects placenta, which also affected morbidity and mortality statistics of pregnancy and fetal outcome. The sum of which is increased perinatal loss. The world health organization reports (WHO) estimated that anaemia is responsible for 12-28% of fetal loss, 30% perinatal death, and 7-10% of neonatal death [26].

The global prevalence of anaemia in pregnancy is 55.9% [3]. Anaemia in pregnancy is a well recognized, observed more frequently in developing countries. In India incidence of anaemia in pregnancy has been noted as high as 40-80%. About 4-16% of maternal deaths are due to anaemia. It also increases the maternal, foetal and neonatal mortality & morbidity significantly [28]. According to WHO [31], the severity of anaemia is classified as mild degree (9-11 gms%), moderate (7-9 gms%), severe (4-7gms%) and very severe (< 4 gms%).

Placenta is a focus of increasing interest in modern obstetrics because significant pathology afflicts the placenta, often before affecting the fetus. Placental abnormalities therefore can be an 'early warning system' for fetal problems. The evaluation of placenta thus becomes essential in high risk pregnancy. With nations commitment for 'Health for all' the successful outcome of all the pregnancy depended much to the horticulture of placental tree.

The present study is to analyze placental changes in anemia by histomorphological methods because these changes serve as a guide to the duration and severity of disease.

AIMS & OBJECTIVES

1. To study the morphology of placenta in anemic subjects and to compare it with the placenta of subjects with normal hemoglobin.
2. To analyze the histological changes in placenta due to anemia.

MATERIALS & METHODS

Type of study: Observational study

Place of study: Study will be conducted in Shri Sathya Sai Medical College, Hospital & Research Institute (SSSMCRI), Department of Anatomy.

Sample size: In the present study 40 placenta were utilized.

Sample collection: The placentas were collected from labor room from period of January 2017 to September 2017, along with detailed case history immediately, from mothers who delivered either normally or by Caesarean section, from the Department of Obstetrics and Gynaecology, Shri Sathya Sai Medical College, Hospital & Research Institute.

Study population: - Placentas from SSSMCRI

Selection Criteria For Samples

Inclusion criteria: Subjects having hemoglobin less than 10.9g/dl during pregnancy

Exclusion criteria: Subjects with Anemia complicated with other conditions such as diabetes, hypertension & malignancy.

Control group: In control group subjects with Hb more than 10.9 g/dl.

Ethical clearance and consent: Ethical approval and clearance was taken from institutional review committee of Shri Sathya Sai Medical College & Research Institute before data collection. Informed consent was obtained from each pregnant woman prior to enrollment in the study.

Study Design: Divided into 2 groups

Group - 1 (control group) - Comprised of 20 placentas from mothers having no sign and symptoms of anaemia and their hemoglobin level were recorded to be more than 10.9g/dl.

Group - 2 (Study group) - Comprised of 20 placentas from mothers having anaemia (hemoglobin level< 10.9 gm %). According to WHO [32] report study group redivided into 3 groups depending on the severity of anaemia.

- Group 2a – Mild Anemia (Haemoglobin level 10 -10.9 gm/ dl)
- Group 2b – Moderate Anemia (Haemoglobin level 7-9.9gm/ dl)
- Group 2c – Severe Anemia (Haemoglobin level < 7 gm/ dl)

METHODOLOGY:

1st Step - Placentas were collected along with detailed case history and relevant investigations Soon after the delivery and washed with normal saline. Weight of the placenta was measured by an Electronic Weighing Scale.

2nd Step - After that gross examination of the placenta also observed for the presence of any calcification & Infarction and also the following parameters like shape, number of cotyledons were also noted.

3rd Step - The placentas were then transfer in formalin (10%) filled plastic containers. All the specimens were tagged with number discs before the commencement of the study, for the purpose of identity.

4th Step - Tissues each of 2x2 cm were taken from both group of placentas included both fetal and maternal surfaces, and fixed in 10 % formalin for 24 hours then 5mm section were taken, and further used for Processing & staining with Haematoxylin and Eosin (H & E) to study the histological observations of placenta.

OBSERVATIONS & RESULTS

Among 40 Placentas, 20 cases are normal haemoglobin level (>11g/dl) belongs to control group. According to WHO, Anaemic group divided into 3 groups - Haemoglobin level 10.0-10.9 g/dl (Mild anaemia) was found in 6 cases (30%), Hb level 7 - 9.9g/dl (Moderate anaemia) in 12 cases (60%) & Hb level < 7g/dl (Severe anaemia) was found in 2 cases (10%) only.

In the present study, the mean weight of placenta was significantly lower in anaemic group (377.6 gms) than in the control group (427.28 gms). The mean value of Placental weight at different hemoglobin levels presented in Table – I

Table - I: Weight of Placenta in Anemic & control Group

Group	Placental Weight (in gms) Range	Mean / Average
Control Group (n=20)	260 - 570 g	427.28 g
Study (Anemic) Group (n=20)	230 - 520 g	377.60 g

On Gross examination:

Shape of Placenta: Majority of Placenta showed oval followed by Round shape in mild & Moderate anaemic Group & in control group almost the shape of placentae is oval (65%) & round (20%) shown in Table - II.

Table - II: Shape of Placenta in Anemic & control group

Shape of Placenta	Study Group			Control Group
	Mild (n=6)	Moderate (n=12)	Severe (n=2)	(n=20)
Oval	4 (66.6%)	10 (83.3%)	1 (50%)	13 (65%)
Round	1 (16.66%)	2 (16.66%)	-	4 (20%)
Irregular	1 (16.66%)	-	1 (50%)	2 (10%)
Triangular	-	-	-	1 (5%)

Number of Cotyledons: The number of cotyledons observed in the present study was found to vary between 14 & 33 in anemic group and 16 & 28 in Control group. The mean of cotyledons are same in two groups.

Calcification: observed more common in placenta of anemic cases (65%) than that of Control group (20%).

Areas of Infarction: Anemic group (55%) shows areas of infarction than Control group (5%). (Table - III)

Table - III: Comparison of Histomorphology of Placenta from Control & Anemic group

S. No	Parameters	Control Group (n=20)	Anemic Group (n=20)
1.	Mean Placental weight (Grams)	427.28	377.60
2.	Areas of Calcification	04 (20%)	13 (65%)
3.	Areas of infarction	01 (5%)	11 (55%)
4.	Stromal fibrosis	04 (20%)	15 (75%)
5.	Medial coat proliferation of Blood vessels	01 (5%)	07 (35%)
6.	Intervillous Hemorrhage	00	14 (70%)
7.	Hyalinized areas	02 (10%)	12 (60%)
8.	Calcification	05 (25%)	12 (60%)

Histological Observations:

The placental villi shows significant changes in the study (Anemic) group (Table - III).

1. Stromal Fibrosis: In control group scattered fibrosis were seen whereas in Study group stromal fibrosis tend to increase in villi & intervillous spaces with increase in severity of Anemia (Fig:1)

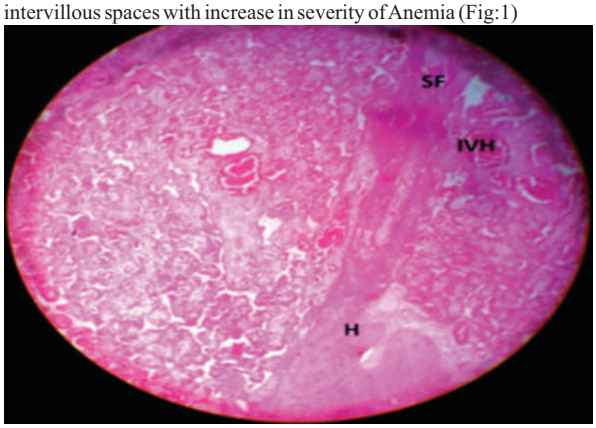

Fig: 1 Showing Stromal Fibrosis, IVH & Hyalinized villi

SF - Stromal fibrosis; IVH - Intervillous hemorrhage; H - Hyalinization of Villi

2. Areas of Fibrinoid necrosis: In anemic group was found to be increased than in Control group. (Fig:2)

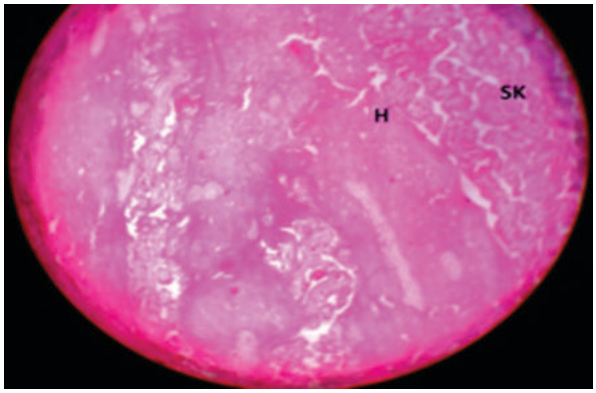

Fig:2 Showing Hyalinization & Increased Syncitia knots

SK - Syncitial Knots

3. Medial coat Proliferation of Blood vessels were also increased in anemic group than in control group

4. Intervillous hemorrhage was completely absent in the control group but observed in Study group (70%). (Fig: 1) & (Fig:3)

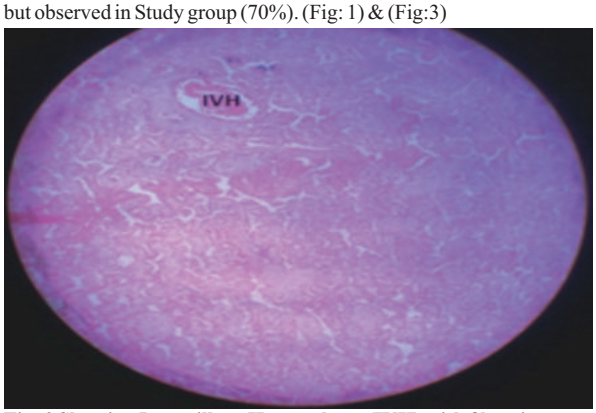

Fig: 3 Showing Intervillous Hemorrhage (IVH) with fibrosis

5. Hyalinized villi & Calcification was commonly found in anemic group (60% & 60%) than in Control group (10% & 25%) respectively. (Fig: 1)
6. Cytotrophoblastic Proliferation &
7. Syncitial Knots also increases with increase in severity of Anemia (Fig: 2)

DISCUSSION

The chorionic villi are the functional unit of placenta. It provides oxygen and nourishment to foetus and also serves as excretory unit [11]. The histological appearance of chorionic villi varies with the gestational age and with the stage of development and maturations of villous tree. Oxygen plays a vital role in the development of placenta, as it is known key factor in the regulation of cytotrophoblastic differentiation, proliferation and invasion in early pregnancy [21]. Anemia in pregnancy is associated with increased incidence of both maternal and fetal morbidity and mortality [7]. Therefore histopathological examination of placental tissue is a valuable tool in predicting the outcome of future pregnancies and their management.

The weight of the placenta is of significant importance and much information can be gathered by proper weight recording. It is functionally substantial as it is related to villous area [1]. Changes in placental weight are debatable. Few studies exhibit increased placental weight while some of the previous data revealed decrease in placental weight.

Benirschke [6] and Agbola [2] studied 199 and 25 placenta from anemic mothers respectively and observed that maternal anemic was associated with placental hypertrophy. Agbola [2] also observed that mean placental weight in control group was lower than study group. To the contrary they observed that placental weight of anemic mothers was lower than control group. Hosemann [13] reported that placental weight increases in anemia. Sinclair [28], Dhall [9] concluded that placental weight was lower in anemic mothers compared to healthy mothers though the difference was not significant statistically. In our study, we found that the mean placental weight was lower in anemic mothers (377.6g) compared to Normal mothers (427.28g). When anemic group was studied according to the severity of anemia, it was found that placental weight decreases as the severity of anemic increases, without being statistically significant. So our study correlates with the findings of previously mentioned study. Hypoxia is responsible for the placental changes in women with anemia [5]. Lao TT et al noted increase in the placental weight of anemic patients contrary to the present study [20]. But in present study, severe anemia produced small placentae.

Regarding the gross morphology of placenta, present study showed the placental weight and the number of placental cotyledons were significantly reduced in the severely anemic mothers and had direct relationship with the maternal haemoglobin level. The reduced number of cotyledons in the placenta of mothers with severe anemia indicated a lesser degree of septation and probably a greater proportion of functioning parenchyma, which could be an adaption to a physiological stress, resulting in an improvement of placental function and fetal well being. This fact was also stated by Anpej Huang et al [14] also.

In earlier reports as well as in the present study, the gross examination of the placentae from anemic mothers showed higher incidence of calcification and infarction [22], [23], [24]. This might be probably due to the decreased size of placentae. Calcification is a sign of physiological maturity of placenta [30] so should not be taken as guideline for impending delivery because it is not a pathological process. Although there had been a tendency to increase placental calcification with advancing maturity, there was no initial difference in calcification between mature and post mature placenta and the weight of placenta was found to be directly related to calcification [10]. Incidence of calcification in the present study showed a significant increase in anemia (65%) in comparison to the control (20%). Our findings also correlated with most of the previous studies.

Some Authors in 2003 had confirmed that the most frequent microscopic lesions observed in iron- deficiency anemia were intervillous thrombosis, infarction and fibrosis of placenta [19]. Thus, in anemic mothers, our findings about the necrosis, hyalinization and fibrosis in the placenta are correlated with that of the previous studies.

Placental parenchyma responds to infarction by accumulation of fibrin in the intervillous spaces. As a result the villous vessels are dilated and congested and trophoblastic nuclei cluster together forming trophoblastic or syncytial knots. In present study formation of syncytial knot has been increased in the anemic group. Probably due to the regional functional differentiation of syncytium which leads to the development of vasculosyncytial membrane – a principal site for feto-maternal oxygen transfer [3]. Earlier study showed 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 [4], [8]. The reason behind the increased syncytial knots formation in the anemic group may be explained by findings of Kristina et al (2009) [17] who mentioned that increased syncytial knots are associated with conditions of uteroplacental malperfusion. Hence, previous findings of increased incidence of syncytial knots and cytotrophoblastic proliferation are comparable to that of the present study.

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 [11]. In the present study, significantly increased fibrinoid necrosis in placentae of anemic mothers might be evolved due to degenerative changes in villous cytotrophoblasts [29].

In the present study, stromal fibrosis and medial coat proliferation of fetal blood vessels were also increased in anemic group. This increase incidence of stromal fibrosis may be related to obliterative endarteritis which was found in placentae of anemic group. This fibrosis and obliterative endarteritis may be a result of relative hypoxia [12]. It was also stated by Usha Russia [23] that villous fibrosis increases in amount with increasing grade or severity of anemia.

Cytotrophoblastic cellular proliferation was significantly lower in anemic group which might be also an adaptive response to decreased oxygen supply [26]. All these changes in placentae of anemic mothers may be the cause of worse fetal outcome and maternal hazards. This signifies need of assessment of placenta at the time of delivery.

CONCLUSION

Anemia is not a major problem if treated in time among pregnant women during antenatal visit; otherwise it adversely affects the placental and fetal outcome. The investigation realizes that more often anemic mothers will have poor perinatal outcome and low placental weight compared to normal mothers. In pregnancy anemia has tremendous effect on placental growth that leads to reduction in functions. In present study showed increased areas of infarction & calcification, stromal fibrosis, syncitial knots, fibrinoid necrosis & intervillous hemorrhage with the severity of anemia. This is might be due to an adaptation to maternal hypoxia.

Severe anemia in pregnancy alters the placental histomorphology. To avoid the placental malformation, prompt treatment of anemia is required.

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