# Histopathological Study of Villous Hypervascularity and Chorangiosis at Different Maternal Hemoglobin Levels

Nazma Kiran<sup>1</sup>, Sahar Mudassar<sup>2</sup>, Bushra Adeel<sup>3</sup>

#### ABSTRACT

**Introduction:** Placenta has a remarkable reserve capacity to survive in the harmful environment, but some of the damaging factors, especially maternal anemia may have negating effects on placenta which might compromise the fetal well-being. Decreased hemoglobin level in pregnancy is associated with villous hypervascularity and chorangiosis, which can be assessed for diagnostic purposes because it has been considered as a result of placental hypoxia caused by maternal anemia. The objective of this study is to assess the morphological pattern of villous hypervascularity and chorangiosis at different maternal hemoglobin levels.

**Material and methods:** This descriptive study was carried out over a period of 2 years in a tertiary care hospital. Nonprobability convenience sampling was done. Placentas were obtained from 100 full-term pregnant women having different hemoglobin levels. After processing and staining, the slides were examined under light microscope and number of blood vessels were calculated in 10 villi in 10 non-infarcted areas in 3 random fields per each slide under 10X objective.

**Results:** At normal hemoglobin level, all the chorionic villi showed normal number of blood vessels, while at 10.0-10.9 gm/dl, 50% (12 out of 24 cases), at 7-9.9 gm/dl, 36.4% (12 out of 33 cases) and at < 7 gm/dl, 72.2% (13 out of 18 cases) placental specimens showed hypervascularity. Chorangiosis was not seen at hemoglobin level  $\geq$  10.0 gm/dl while 18.1% (6 out of 33 cases) having hemoglobin level  $\leq$  7.0 gm/dl (5 out of 18 cases) showed chorangiosis

**Conclusion:** In current study number of capillaries per chorionic villi were found to be significantly more at decreasing concentration of hemoglobin, displaying adaptive alterations

**Key words:** Low Hemoglobin Concentration, Villous Hypervascularity, Placental Morphology, Chorangiosis, Placental Hypoxia

#### **INTRODUCTION**

Placenta maintains a fundamental connection among the mother and the fetus. Placenta has a remarkable reserve capacity to survive in the harmful environment, but some of the detrimental factors, especially maternal anemia may have adversative effects on placenta which might compromise the fetal well-being. The studies of different authors and researchers revealed that careful examination of the placenta may explain the etiology and pathogenesis of a number of maternal and fetal diseases.<sup>1</sup>

Decreased hemoglobin level in pregnancy is associated with variable histomorphological changes in placenta, which show a strong connection with poor fetal outcome.<sup>2</sup> One of

the morphologic features of placental chorionic villi is their vascularity, which can be assessed for diagnostic purposes. The normal values of vascular profiles are ranging from 2 to 6 per terminal villus and larger numbers of vessels are defined as hypervascularity. Extreme hypervascularity of the chorionic villi is known as chorangiosis, the term introduced by Altshuler 30 years ago and defined as at least 10 vessels per terminal villus in 10 chorionic villi per 10x objective microscopic field in at least 10 random areas of cotyledons.<sup>3,4</sup> Chorangiosis has been considered as a result of placental hypoxia linked with abnormal outcomes. It is unknown whether these abnormal outcomes are a consequence of chorangiosis itself or of related other placental pathology. Presence of diffuse patterns of hypoxic placental injury imparts prognostically undesirable significance to increased vascularity of the chorionic villi.5

Chorangiosis is linked with adverse perinatal outcomes, however the definitive mechanism is still unknown but the interaction of fetal, placental and maternal factors may well combine to produce such pathologic change. Whatever the cause, chorangiosis can be considered as a sign of possible clinical significance.<sup>6</sup>

Fetal blood vessels of the placenta adapt in different forms of hypoxic stress i.e. maternal anemia. Increased capillarization of terminal villi is seen in maternal iron deficiency anaemia.<sup>7</sup> Charnock-Jones et al in 2004 stated that fetoplacental angiogenesis differ in certain pregnancy pathologies. In hypoxia, morphological changes are seen in capillary growth, vascular endothelium, capillary shape and size and villous capillarization.<sup>8</sup>

Marked villous hypervascularity is seen in longstanding hypoxic placental injury. The is related to low oxygenation of blood reaching the uterus and placenta which characteristically shows diffuse hypervascularity of villi.<sup>9</sup>The incidence of chorangiosis is decreased in the second trimester and rises in the third trimester, in which it is lower in preterm than full term pregnancies.<sup>10,11</sup>

The effect of anemia in pregnancy can be varied and

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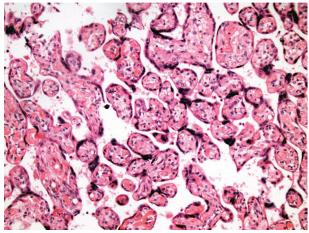
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Hemoglobin levels g/dl	Number of cases (n)	Hemoglobin level (g/dl) Mean±SD
Normal >11g/dl	25	11.8±0.64
n:25		
Mild anemia 10.0-10.9 gm/dl	24	10.3±0.30
n:24		
Moderate anemia 7-9.9 gm/dl	33	8.6±0.55
n:33		
Severe anemia <7g/dl	18	6.4±0.25
n:18		
· · · ·	Table-1: Hemoglobin levels.	

Hemoglobin levels g/dl	Blood vessels		
	Normal n	Hypervascularity n	Chorangiosis n
	(%age within group)	(%age within group)	(%age within group)
Normal >11g/dl	25	0	0
n:25	(100%)	(0%)	(0%)
Mild anemia 10.0-10.9 gm/dl	12	12	0
n:24	(50%)	(50%)	(0%)
Moderate anemia 7-9.9 gm/dl	15	12	6
n:33	(45.5%)	(36.4%)	(18.1%)
Severe anemia <7g/dl	0	13	5
n:18	(0%)	(72.2%)	(27.8%)
Table-2: Number of blood vessels at different hemoglobin levels.			



**Figure-1:** Photomicrograph of placental tissue at hemoglobin level of 6.8gm/dl revealing chorangiosis (H&E stain x 100)

damaging to both mother and the fetus; this encouraged us to carry on the present study. That's why an attempt has been made to confirm, agree or disagree the findings of the former workers in this field.<sup>1</sup> The objective of this study was to assess the morphological pattern of villous hypervascularity and chorangiosis at different maternal hemoglobin levels.

# MATERIAL AND METHODS

This descriptive study was carried out at Alfalah Hospital, Islamabad, Pakistan from December 2016 to November 2017. Non-probability convenience sampling was done. Placentas were obtained from 100 full-term pregnant women having different hemoglobin levels. The placentas of the mothers having systemic disorders i.e. hypertension, asthma, diabetes mellitus, and antepartum hemorrhage were not included in the study. Placentas were collected immediately after removal, washed in tap water and were preserved in 10% formal saline. The placenta was cut into 1 cm thick sections and three sections were taken, one close to umbilical cord, one from periphery and one from the mid of these two points. The tissues were processed and stained by H & E stain.<sup>12</sup> The slides were examined under light microscope and number of blood vessels were calculated in 10 villi in 10 non-infarcted areas in 3 random fields per each slide under 10X objective.<sup>5</sup>

# STATISTICAL ANALYSIS

Data was analyzed using SPSS-30. Percentages and mean values were calculated for different variables.

# RESULTS

Among the 100 placentas, 25 cases exhibited normal hemoglobin level (>11g/dl). Hemoglobin level 10.0-10.9 gm/dl (mild anemia) was found in 24 cases with mean hemoglobin level of 10.3g/dl. Maximum number of cases (n 33) revealed hemoglobin level of 7-9.9 gm/dl (moderate anemia). Hemoglobin level < 7gm/dl (severe anemia) was found in 18 cases (Table-1).

At normal hemoglobin level, all the chorionic villi showed normal number of blood vessels, while at 10.0-10.9 gm/dl, 50% (12 out of 24 cases), at 7-9.9 gm/dl, 36.4% (12 out of 33 cases) and at < 7 gm/dl, 72.2% (13 out of 18 cases) placental specimens showed hypervascularity. Chorangiosis was not seen at hemoglobin level  $\geq$  10.0 gm/dl while 18.1% (6 out of 33 cases) having hemoglobin level 7-9.9 gm/dl and 27.8% specimens having hemoglobin level  $\leq$  7.0 gm/dl (5 out of 18 cases) showed chorangiosis (Table-2) (Fig-1).

# DISCUSSION

The placenta is a functional constituent between fetus and mother. Hence, any pathological condition related to mother

or fetus, will disturb the structure and function of placenta. Anemia during pregnancy is considered as a cause of placental hypoxia which in turn give rise to fetal hypoxia and its complications. The number of blood vessels in chorionic villi is of substantial importance and considerable information can be gathered by its careful examination. With this background, the current study was undertaken to evaluate the spectrum of histopathological vascular changes in placenta at different hemoglobin levels.<sup>12</sup>

In current study number of capillaries per chorionic villi were found to be significantly more at decreasing concentration of hemoglobin. The effects of hypoxia on vascularity of villi have been evaluated in Ohio and it was observed that presence of diffuse patterns of hypoxic placental injury adds negative significance to increased vascularity of the chorionic villi.<sup>5</sup> Increased capillaries per chorionic villous in maternal anemia is also confirmed by Soni RB in 2013.<sup>13</sup> Placental chorangiosis was studied by De La Ossa et al and it was found that hypoxic stimulus may lead to an extreme villous capillary proliferative activity, maybe via growth factors such as vascular endothelial growth factor.<sup>6</sup>

Petersen SS et al in 2017 suggested that chorangiosis, an indicator of chronic hypoxia, is related to increased rates of cesarean sections for non-reassuring fetal conditions because of chronic hypoxia coupled with the stress of delivery.<sup>14</sup> Suzuki et al in 2009 studied a possible association of placental oxygenation with the development of chorangiosis. Suzuki et al measured placental tissue oxygen index values via near-infrared spectroscopy before childbirth and compared them to the detection of placental chorangiosis. They found that decreased efficiency of oxygen transfer to the fetal blood circulation in the villi causes low oxygen level in the capillaries of the villi and result in chorangiosis and proved that chorangiosis is a vascular hyperplastic phenomenon of the terminal villi, resulting from chronic low-level hypoxia in the placental tissue.<sup>15</sup>

Some authors confirmed that capillary dilatation rather than proliferation is a morphological change to longstanding hypoxia. The authors regard this opinion as a arguable point because in villous hypervascularity even if villous blood vessels are frequently congested, their numbers of lumens are increased due to branching angiogenesis.<sup>16</sup> It takes several weeks for chorangiosis to develop, but chorangiosis seems to enhance placental resistance to more hypoxic events. In high-risk pregnancies chorangiosis is more predominant in late preterm and near term or term pregnancies.<sup>17,11</sup> Barut et al in 2012 studied placental chorangiosis and found that capillary hyperplasia is due to chronic placental low-grade hypoxemia or hypoperfusion.<sup>18</sup>

#### CONCLUSION

The present study showed marked increase in number of blood vessels per chorionic villi at decreasing levels of maternal hemoglobin. Thus, our study specified a few adaptive modifications which placenta has to adapt to overcome the effects of low maternal hemoglobin values. The more vascularity of the placental chorionic villi, the better off the pregnancy. Pure chorangiosis is connected with significantly fewer pregnancy risk factors, abnormal consequences, and other placental abnormalities. That is why, it can be regarded as an adaptive response to hypoxic placental injury. Maternal ailments have a major role in disrupting the placental angiogenesis and vasculogenesis by creating a hypoxic condition that may affect the fetus badly. Therefore, such conditions need to be recognized early in pregnancy and treated properly as it is possible to maintain a normal circulation and prevent fetal abnormalities if quick intervention is done.<sup>19</sup>

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