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HISTOLOGY OF PLACENTA IN INTRAUTERINE GROWTH RESTRICTED PREGNANCY

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ABSTRACT: INTRODUCTION: Placenta is found in all eutherian mammals. Study of placenta helps to gather information regarding the prenatal life of the fetus. Intrauterine growth restriction (IUGR) of the fetus occurs due to decreased supply of necessary elements to the fetus via the placenta and as a result some typical histological changes occur in placenta. **AIMS AND OBJECTIVE:** We wanted to study the histological features of placenta in IUGR pregnancy and to compare them with uncomplicated pregnancy. **MATERIALS AND METHODS:** In the Group A(study group)we had included 50 placentas from mother of IUGR babies with birth weight less than 10th percentile of normal weight and in Group B(control group)there were 50 placentas from uncomplicated pregnancies. Placentas from mothers with IUGR due to congenital anomaly or infection were excluded. Tissues of placenta were taken and after preparation of slides different histological features like fibrin deposition, cytotrophoblastic hyperplasia, villous pattern, infarction, and calcification were noted. The two groups were compared statistically. **RESULT ANALYSIS:** In our study Risk ratio 1.36 indicates that in Study group A fibrin deposition was 1.36 times (36%) more than that of control group (risk ratio above or below 1 quantifies the relative increase or decrease in risk associated with).Syncytial knot formation were 1.05 times (5%) more in study group. Calcification 1.6 times (60%) and infarction 1.9 times (90%) higher in study group than control group. Significantly in placenta of study group Cytotrophoblastic hyperplasia (2.56 times more than control group), villous obliteration (3.57 times more than control group) and stromal fibrosis (2.33 times more than control group) were more than the control group. **CONCLUSION:** The present study depicted specific histological changes of placentas of IUGR pregnancy, thus explaining the role of examination of placenta to acquire knowledge about the prenatal life.

KEYWORDS: Placenta, Placental histology, IUGR.

INTRODUCTION: Placenta is an organ present in all eutherian mammals. It connects the developing fetus to the uterine wall of mother. The placenta supplies oxygen, nutrients to fetus and allows disposal of fetal wastes via maternal kidney. Human placenta is discoid, choriodecidual organ. Placenta can provide much insight into prenatal life. Study of placenta would help us to evaluate the adverse circumstances faced by the fetus in utero. The results often help us in caring for the neonate.

Intrauterine growth restriction (IUGR) is a term used to describe a condition in which the fetus is smaller than expected for the number of weeks of pregnancy. According to WHO(1995)an infant suffering from IUGR is defined as being below the10% percentile of the recommended gender specific birth weight for gestational age reference curve. A fetus with IUGR also may born at term (after 37wks of pregnancy or prematurely (before 37 wks).Newborn babies with IUGR often described as small for gestational age (SGA).

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Intrauterine growth restriction results when a problem or abnormality prevents cells and tissues from growing or causes cells to decrease in size. This may occur when the fetus does not receive the necessary nutrients and oxygen needed for growth and development of organs and tissues or because of infection.

The findings in IUGR placenta suggest that there is a restriction of maternal utero-placental blood flow in many instances of fetal growth restriction. This is not however the whole story. It has been suggested that cytogenic abnormalities may be associated with utero-placental ischemia.

Impairment of fetal growth in IUGR can have adverse consequences in terms of mortality, morbidity, growth and performance. In our study we intended to detect the typical histological findings of placenta of pregnancies associated with IUGR. The findings provide a record and can be used to plan the future care of mother and child. Tyson R and Barton C (2008)¹ in their study suggested that evaluation of the placenta is extremely important in attempting to understand the pathophysiology of IUGR. Only with careful gross and histological evaluation, along with clinical pathologic correlation, can the underlying causes and recurrence risks be understood.

AIMS & OBJECTIVES: We had done the study to find out characteristic histological features of IUGR placenta. To compare the histological features of IUGR placenta with that of the placenta of uncomplicated pregnancy was another aim of our study so that the changes of the placenta in IUGR could be clearly pointed out.

MATERIALS & METHODS: We had collected 50 placentas from mother of IUGR babies, denoted as Group A (study group) with birth weight less than 10th percentile of normal weight and 50 placenta of uncomplicated pregnancy denoted as Group B (Control group), from the labor room after vaginal delivery or from the OT after caesarian section. The study was conducted in Medical College, Kolkata. The selected mothers in both the groups were between 20-35yrs of age and were primi, second or third gravida. IUGR was confirmed in each case clinically as well as ultrasonographically. In our study group (Group A) we included IUGR due to utero-placental insufficiency such as pre-eclampsia, essential hypertension, gestational Diabetes and exclude IUGR due to congenital anomaly, intrauterine infection. In group B, the selected cases had no foeto-maternal complications after routine procedures.

After delivery placentae were collected in both groups immediately for histological examination. Tissues were collected from the following sites for the histological examination 1) near the insertion of umbilical cord 2) Margins-12, 3, 6, 9'O' clock position 3) centre of placenta 4) infarcted and calcified area. After proper tissue preparation sections were stained by Haematoxylin & Eosin (H & E) stain. All the important histological features such as fibrin deposition, villous pattern, syncytial knots, infarction, calcification, stromal fibrosis were noted in placentae. Statistical analysis was done and the results were noted.

RESULT ANALYSIS: We had included 50 consecutive cases of pregnancy with IUGR which had fulfilled the inclusion criteria in Group A (Study group) and 50 consecutive cases of uncomplicated pregnancy in Group B (Control group). The mean age of mother in Group A was 23.2 years and Group B was 22.8 years. All the cases and control were from comparable economic status. Regarding the associated obstetric complications, in Group A, 11 mothers had Pregnancy induced hypertension (PIH) and three mothers had Gestational Diabetes mellitus (GDM).

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In our study we found some characteristic histological features in IUGR placenta such as villous obliteration, cytotrophoblastic hyperplasia and stromal fibrosis. other histological features such as infarction, calcification, fibrin deposition, syncytial clot formation present both in IUGR placenta and control group, but in IUGR group they are present in more number of placenta than control group. Histological features were compared in both study and control group.

	Study group (IUGR) A	Control group B	
Fibrin deposition +	19 A ₁	12 B ₁	N ₁ =31
Fibrin deposition -	31 A ₀	38 B ₀	N ₀ =69
Table 1: Risk estimator of study group $P_1=A_1/N_1=0.613$. Risk estimator of control group $P_0=A_0/N_0=0.449$			

Risk difference= $P_1 - P_0=0.164$. Risk ratio= $P_1/P_0=1.36$.

Risk ratio 1.36 indicates that in study group (IUGR) fibrin deposition was 1.36 times more than that of control group. The segment of risk ratio above (or below) 1 quantifies the relative increase or decrease of risk associated with. So in IUGR risk of fibrin deposition in placenta is $(1.36-1) = 0.36 \times 100 = 36\%$ more than control group.

	Study group	Control group	
Syncytial knot formation +	17	5	N ₁ =22
Syncytial knot formation -	33	45	N ₀ =78
Table 2: Indicates that risk ratio=1.05, so that in study group Syncytial knot formation was 1.05 times or $(1.05-1) \times 100 = 5\%$ more than control group			

Calcification +	Study group 6	Control group 2	N ₁ =8
Calcification -	44	48	N ₀ =92
Table 3: Risk ratio=1.6			

	Study group	Control group	
Infarction+	14	3	N ₁ =17
Infarction-	36	47	N ₀ =83
Table 4: Risk ratio=1.9			

Table 3 and 4 indicates that in IUGR calcification in placenta is 1.6 times (60%) and infarction is 1.9 times (90%) higher than control group.

	Study group	Control group	
Cytotrophoblastic hyperplasia+	18	0	N ₁ =18
Cytotrophoblastic hyperplasia-	32	50	N ₀ =82
Table 5: Risk ratio= 2.56			

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Table: 5 indicate that in IUGR Cytotrophoblastic hyperplasia was 2.56 times higher than co Cytotrophoblastic hyperplasia control group.

	Study group	Control group	
Stromal fibrosis+	12	0	N ₁ =12
Stromal fibrosis-	38	50	N ₀ =88
Table 6: Risk ratio =3.57			

	Study group	Control group	
Villous obliteration+	31	0	N ₁ =31
Villous obliteration-	19	50	N ₀ =69
Table 7: Risk ratio = 2.33			

Table 6 and Table 7 indicate that in IUGR placenta (Group A) villous obliteration was 3.57 times and stromal fibrosis is was 2.33 times higher than that of control group (Group B).

Discussion: Regarding histological features of placenta we found various differences between placenta of uncomplicated pregnancy and placenta of IUGR pregnancy. Mardi K, Sharma J(2003)² suggested that there is highly significant increase in the incidence of infarction, intervillous fibrin deposition, stromal fibrosis and syncytial knotting were found in IUGR placentas compared to full term normal placentas on microscopic examination. Regarding fibrin deposition, in IUGR group fibrin deposition was found in 19 placentas and in control group fibrin deposition was found in 12 placenta out of total 50 placentas. Katzman PJ, Genest DR (2002)³ observed in their study that massive perivillous fibrin deposition may be more common and more strongly associated with IUGR than normal placenta.

Cytotrophoblastic hyperplasia was found in 18 placentas in study group (Picture: 4). This was not present in control group. Vander Veen F, Fox H.(1983)⁴ observed that in IUGR placenta at the light microscopic level the only significant finding was an excess of villous cytototrophoblastic cells whilst electron microscopy showed these placenta to be characterized by villous cytotrophoblastic hyperplasia, focal syncytial necrosis. It was thought that most of the observed abnormalities are due to uteroplacental ischemia and it is possible that the fetal vascular abnormalities are a reflection of the fetal growth retardation.

In our study group villous obliteration was found in 31 IUGR placentas (Picture: 1) out of 50 placentas. This feature was absent in control group. Egbor M, Ansari T, Morris N, Green C, Sibbons P. (2006)⁵ reported that the mean total volumes of villi (terminal and intermediate) of IUGR placentas were found to be significantly lower than that of control placentas. Biswas et al (2008)⁶ had similar observations and commented that since the surface area of the villi presents the interface between maternal and fetal circulation, its reduction might be the cause of idiopathic intrauterine growth restriction of the fetus.

Regarding syncytial knot formation it was found in more number of placenta in IUGR (17 placenta) than in control group (5 placenta). According to Burton et al (2009)⁷ generation of reactive oxygen species under oxidative stress could be the major reason of abnormal vascular remodeling and production of increased syncytial knots. Sankar KD, Bhanu PS, Kiran S et al. (2012)⁸ in their study

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reported similar findings with the oxidative stress injury disrupting syncytiotrophoblast arrangement and resulting in increased vasculosyncytial membrane thickness and syncytial knot density.

Regarding infarction of placenta it was present in 14 IUGR placentas (Picture: 3) out of 50 placentas and in control group infarction was present in 3 placentas out of 50 placentas. Heazell AE, Martindale EA. (2009)⁹ suggested that some placental abnormalities found were associated with clinical causes of still birth, such as placental infarction and IUGR. Burke C, Globe G (2005)¹⁰ suggested that apoptosis was strongly associated with IUGR and placental infarction. Regarding calcification in IUGR group it was found in 6 placenta and in control group in 2 placenta. Rathod KB, Jaiswal KN et al (2007)¹¹ showed pathological changes of placenta in the form of infarction, calcification, increased syncytial knots.

Regarding stromal fibrosis in IUGR group stromal fibrosis was found in 12 placentas (Picture: 2). This feature was absent in placenta of control group. Wang ZJ, Yu YH et al. (2002)¹² showed that pathological changes exemplified by stromal fibrosis, fibrinoid necrosis and leukocyte infiltration of villi, increase in villous syncytial nodules, hyperplasia of cytotrophoblasts were more prevalent in the placentas of PIH complicated by IUGR than in normal woman.

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Ethical clearance: The study was approved by the Institutional ethics committee of Medical College, Kolkata.

PICTURE : 1

IUGR placenta showing villous obliteration

H & E stain, 10 X magnification

PICTURE : 2

Area of stromal fibrosis in higher (40 X)

magnification, H & E stain

PICTURE : 3

Placenta with areas of infarction, 40 X

magnification, H & E stain

PICTURE : 4

Placenta with area of cytotrophoblastic hyperplasia,

10 X magnification H & E stain

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