Original Article

Gynae & Obs

Histomorphological Features of Placentae in Pregnancies Complicated with Intrauterine Growth Restriction

1. Muhammad Zia-ur-Rehman 2. Saima Habib 3. Shafiq Ullah 4. Ehsan Ullah 5. Zaffar Iqbal Malik

1. Asstt. Prof. of Anatomy, SZMC, Rahim Yar Khan 2. PGR; Obs and Gynae, SZMC, Rahim Yar Khan 3. Asstt. Prof. of Anatomy, NMC, Multan 4. Dept. of Pathology, QAMC, Bahawalpur 5. Demonstrator, Anatomy Dept., SZMC, Rahim Yar Khan

ABSTRACT

Background: Fetal growth retardation is most commonly caused by placental letdown to meet the increasing demand for oxygen and nutrients of the developing fetus. Intrauterine growth restriction (IUGR) is common happening in Pakistani setup especially in rural areas. Current literature suggests that placental causes are more common than the maternal causes in intrauterine growth restriction. Macroscopic and microscopic examination of placenta can help us to identify the patho-physiology of placental involvement. This is reasonable especially in those cases of intrauterine growth retardation which are not perplexed by maternal causes.

Objective: To identify macroscopic and microscopic features of placenta in pregnancy complicated with IUGR.

Study design: Descriptive study.

Place and Duration: This study was conducted at Sheikh Zayed Medical College/Hospital, Rahim Yar Khan in collaboration with Department of Pathology Quaid-e-Azam Medical College, Bahawalpur and Anatomy Department, Nishtar Medical College, Multan. Study duration was two years from July, 2010 to June, 2012.

Materials and Methods: One hundred and fifty placentae, 85 from cases of intrauterine growth retardation and 65 from normal (control) were enrolled for the study. Fetal and placental weights and placental diameter and thickness were measured. Tissue for histological examination was obtained from: i) Umbilical cord ii) membranes and iii) three placental zones. The tissues were processed and stained with Haematoxlyin, Eosin and Mallory's Trichrome. The prepared tissues were studied microscopically for villous and intervillous lesions utilizing various criteria.

Results: Macroscopically there was significant decrease in placental weight, fetal weight, and placental diameter and thickness. Microscopic findings were increased fibrinoid necrosis (46.7%), increased perivillous fibrinoid deposition (16.7%), increased syncytial knots (60%) and increased placental infarction (1.8%).

Conclusion: These findings document comparatively higher frequency of fibrinoid necrosis and perivillous fibrinoid deposition. This draws ours attention to the predominant role of placental causes in cases of idiopathic intrauterine growth retardation.

Key Words: IUGR, placenta, perivillous fibrin deposition, synctial knots, fibrinoid necrosis.

INTRODUCTION

Intrauterine growth restriction (IUGR) is a state in which weight of the baby is below the tenth percentile of average for the gestational age. Among the several causes of IUGR, the placental causes are considered as one of the most important. Placenta has risen as an important organ because it provides insight of past events of intrauterine life. Both gross and microscopic examinations of placenta from IUGR fetuses can be of great significance in guiding the clinicians and pathologists to identify the avoidable causes of IUGR and thus help the patients in planning and managing the future pregnancies.

Intrauterine growth restriction (IUGR) can be defined as the disease associated with placenta with which babies are diagnosed when they are smaller in weight as expected. This can be easily diagnosed through ultrasound, which indicates that the weight of a baby in a mother's womb is less than the tenth percentile for their gestational age[1]. Barut et al., and Cox and Marton has specified that the fetal growth depends on the interaction of genetic and epigenetic determinants that functions against an environment of maternal, fetal and placental influences[2,3].

Intrauterine growth restriction is a failure to achieve the growth potential caused by these defined factors. The study of Hendrix and Berghella provides that the causes of IUGR are diverse and include infections, placental disorders, metabolic factors, aneuploidies and non- aneuploidies syndromes[4].

IUGR is known to place the fetus and neonate at risk of disability or death in the perinatal period and predisposes the child to a lifelong increased risk for hypertension and cardiovascular diseases [5, 6, 7]. Redline, Salgado & Pathmeswaran, Mayhew and Charnock-Jones state that the magnitude of the risk differs and it depends on the prior risk of the population studied in previous literature and the definition applied for the diagnosis of IUGR. A common definition of IUGR is

an estimated fetal weight that is less than the tenth percentile for gestational age however, a better predictor of perinatal mortality and morbidity is considered as a fetal weight less than third percentile [7, 8, 9].

The trophectoderm of the blastocyst is the epithelium responsible for the evolution of the human placenta. It is known that the differentiation of trophectoderm establishes the multiple trophoblast cell lineages with different biological activities[10, 11]. The results of Murray, Baergen and Janson & Powell highlight that the sub-optimal growth in abdominal circumference along with the increased fetal head to abdominal circumference ratio reflects the placental dysfunction[6, 11, 12].

According to Beaconsfield & Birdowood (1982), the placenta is one of the organs that readily present in every human being and the abnormalities of the placenta usually have a strong relationship with the outcomes of the abnormalities in fetus[5]. In literature, number of previous studies in the context of placental micro and macro features and its structure in case of IUGR have been conducted that shown the considerable reduction in overall dimension of villi, villous fibrosis and thickness of membrane[6,7].

The infant born with intrauterine growth retardation is recognized as having an increased risk of in-utero mortality, neonatal morbidity and long-term neurological complications[13, 14]. Known causes of IUGR can be traced in up to 40% of cases, including maternal diseases and fetal or placental factors [15,16] and the remainder of IUGR cases are idiopathic in origin. Among the large numbers of maternal factors, maternal hypertension (especially preeclampsia or eclampsia) is one of the most important factors in IUGR. Pregnancy induced hypertension associated with placental pathology include infarct, retroplacental hemorrhage, accelerated maturation, fibromuscular hyperplasia and obliterative endarteritis of the fetal stem artery, villous edema, stromal fibrosis, increased syncytial knots, hyperplasia of cytotrophoblast, trophoblast basement membrane thickening, deficiency of the vasculo-syncytial membrane, excessive fibrinoid necrosis and acute decidual atherosis[13,14].

Maternal factors include heart disease, pulmonary or renal disease, anemia and connective tissue diseases. Fetal factors include chromosomal abnormalities, ventral wall defect and genitourinary defects. The known placental pathology of an IUGR infant includes decrease of placental growth, maternal angiopathy, chronic villitis, increase of perivillous fibrin, fetal thrombotic arteriopathy, avascular villi as its secondary feature, umbilical cord anomaly, infarct, cytotrophoblastic hyperplasia and basement membrane thickening etc[14,15]. Histological examination of the placentae from IUGR fetuses can supplement clinical knowledge of the cause of IUGR.

Thus, by considering these circumstances, the aim and objective of this study is to identify the macroscopic and microscopic features of placenta in idiopathic IUGR along with its impacts on fetal growth, also to compare the placental features in both normal and intrauterine growth retardation pregnancies.

MATERIALS AND METHODS

A total of 150 placentae were studied. The placentae were collected from Obstetrics and Gynecology department of Sheikh Zayed Medical College/ Hospital Rahim Yar Khan and study was conducted at anatomy department Sheikh Zayed Medical College/ Hospital Rahim Yar Khan in collaboration with department of Pathology, Quaid-e-Azam Medical College, Bahawalpur and Anatomy Department, Nishtar Medical College, Multan. Study duration was two years from July, 2010 to June, 2012. The samples were divided into two groups, that is, control group (normal placentae) and study group (IUGR placentae). Out of one hundred and fifty samples, eighty five (85) placentae were collected from the documented cases of intrauterine growth restriction i.e. study group (birth weight less than 2500 grams). Remaining sixty five (65) placentae were obtained from the normal pregnancies i.e. control group. The birth weights of new born babies were taken and foeto-placental ratio was calculated in each case. Macroscopically the general shape of the placenta was observed and the weight was noted after trimming the membrane and umbilical cord. The diameter and thickness of the placentae were noted and the insertion of umbilical cord on the surface of the placenta was observed. Transverse cuts were made through the maternal surface at the distance of 1-2 cm in bread loaf manner and examined for pale areas. All placentae were immersed in 10% formalin overnight and examined on the next day. In each case, blocks containing cord, membrane and full thickness of villous tissue were prepared. Whole thickness villous tissue blocks were obtained from three zones viz, central zone, peripheral zone and intermediate zone between the first two zones, to include all areas of placentae.

Then all the tissues were processed and stained with Haematoxlyin and Eosin. A special stain, Mallory's Trichrome was also used. Microscopic study of placenta was carried out utilizing a set of standard criteria for villous and intervillous lesions [21]. For studying these criteria, eight random microscopic fields were chosen and 100 villi were counted in each field with the help of optical grid scale and studied for the presence of following criteria:

Villous lesions

a) Syncytial knots > 30% in one field
b) Fibrinoid necrosis > 5% in one field
c) Placental infarction > 5% in one field

Intervillous space

a) Perivillous fibrinoid deposition > 5% in one field

b) Presence of calcification.

Statistical analysis was carried out by using the SPSS 16.0 version. Descriptive statistics were applied to calculate mean and standard deviation of quantitative variables.

RESULTS

All the data were computed and analyzed; the results are following:

The mean placental and fetal weights in IUGR cases were 375 ± 77.86 grams and 1912 ± 392.19 grams which were significantly decreased ($p<0.001$) as compared to the control group (561 ±50.25 grams and 2921 ±318.45grams) respectively. Macroscopically feto-placental ratio in study group was 5:2 which was slightly more than the control group (5:1). The mean diameter and thickness were 16.8 cm and 1.86 cm which were decreased as compared to the control group (22 and 2.19 cm) respectively. The insertion of umbilical cord was eccentric in 18 cases in comparison to the control group which were 14 (Table 1).

Table No.1: Distribution of various parameters in both groups

Parameters	Placental Condition	n	Mean	Std. Deviation	Std. Error Mean
Fetal Weight	IGUR	85	1912.9529	392.19043	42.53902
	Normal	65	2921.0000	318.45231	39.49915
Placental Diameter	IGUR	85	16.8941	3.00406	.32584
	Normal	65	22.0000	.00000	.00000
Placental Ratio	IGUR	85	5.1436	1.23025	.13344
	Normal	65	5.2398	.75570	.09373
Placental Thickness	IGUR	85	1.8600	.98503	.10684
	Normal	65	2.1985	.18157	.02252
Placental Weight	IGUR	85	375.9412	77.86395	8.44553
	Normal	65	560.4615	50.25500	6.23337

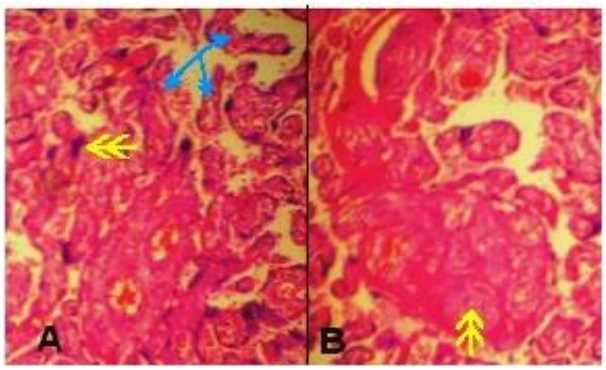

Figure No.1: Showing from control group A- Tertiary chorionic villi (blue arrows). Syncytial knots are seen in moderate numbers i.e. <30% in one field (yellow arrowhead). B- Perivillous fibrinoid deposition seen in moderate quantity i.e. < 5% in one field (yellow arrow head)

The microscopic features studied in the placentae of control and study groups indicate that the normal cases had shown moderate quantity of syncytial knots and perivillous fibrinoid as given in the figure 1, also the least amount of fibrinoid necrosis was found in the control group. The higher number of syncytial knots were identified in the cases with IUGR while the low number of syncytial knots were identified in the control group which are 60% and 44% respectively, shown in figure 2 and 3. Moreover, the result exhibits fibrinoid necrosis in a number of cases with IUGR, which is significantly higher than the control group, since it is found 46.7% of cases in the study group and 8% of cases in a control group (figure 4).

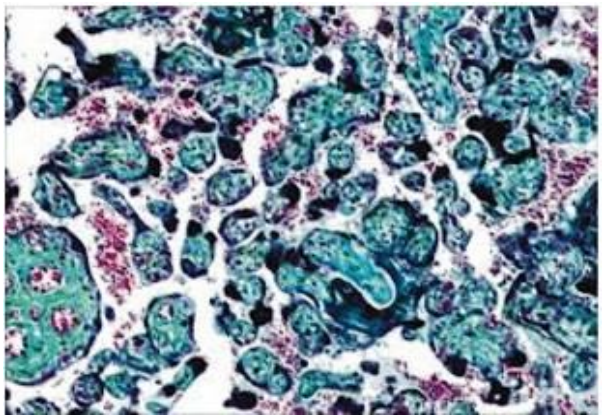

Figure No.2: Increased synctial knots in study group.

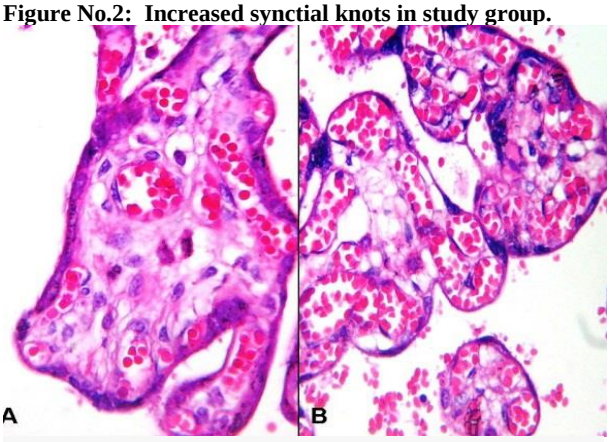

Figure No.3: A; Normal placental tissue B; Increased syncytial knots and villous vascular structures in IUGR placental tissue (H&E A; B; ×200)

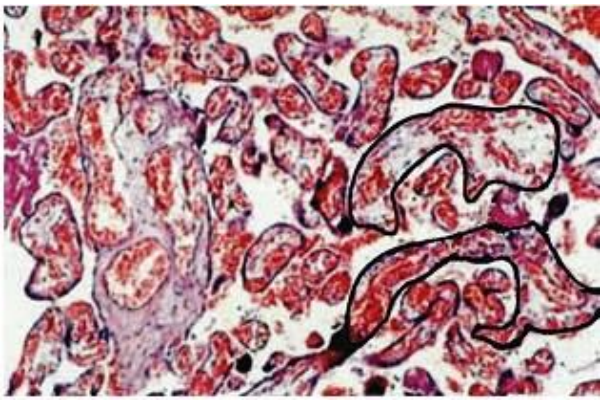

Figure No.4: Fibrinoid necrosis

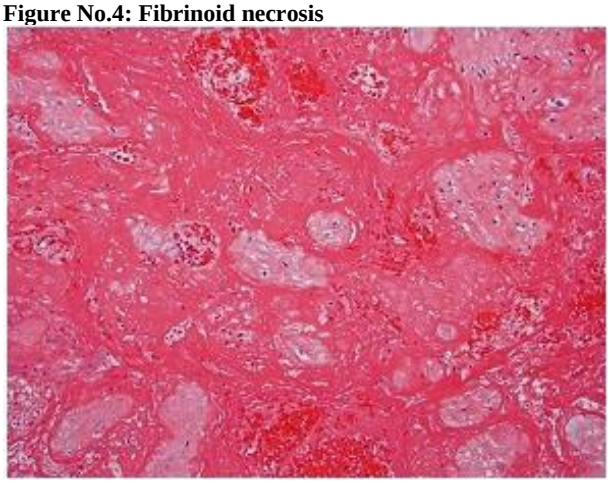

Figure No.5: Perivillous fibrin deposition with expansion of intervillous space

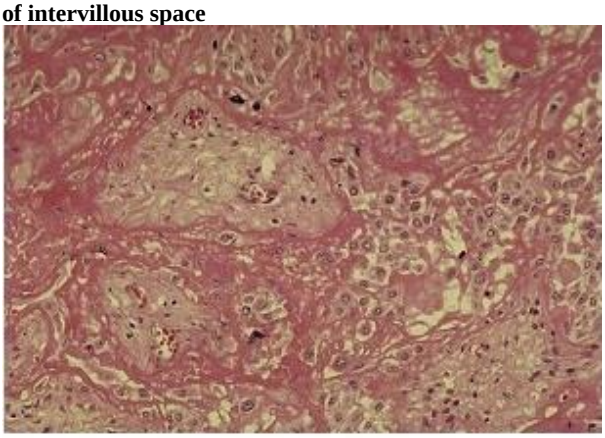

Figure No.6: Perivillous fibrin deposition with cytotroblast proliferation

The placental infarction was found in 1.8% cases of the study group; on the other hand in the control group no single case was identified. Likewise, in the study group 16.7% cases were identified with the perivillous fibrinoid infarction (figure 5 & 6), while in the control group, the percentage of perivillous fibrinoid infarction is comparatively low since it was only 1.8%. In IUGR cases presence of calcification was observed in 60% while in control group it was identified in 56% of cases only.

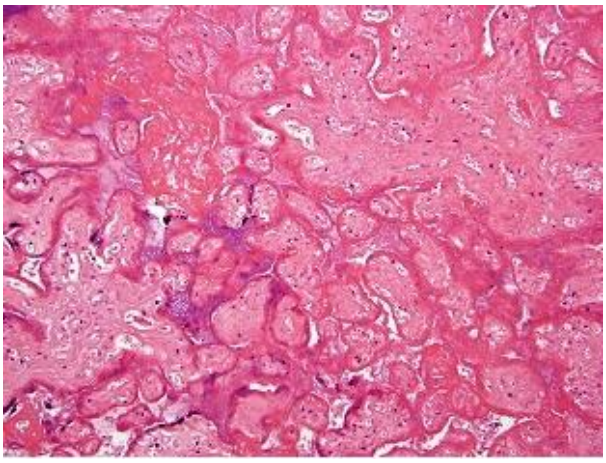

Figure No.7:-Ghost villi with thick trophoblast membranes

DISCUSSION

IUGR is an important cause of perinatal morbidity and mortality. The incidence of IUGR in developed countries is 3%, while in developing countries it reaches 15-20%. It is one of the most commonly recognized abnormalities of the fetal condition and is a compounding factor in 26% or more of stillbirths[29, 30, 31].

In order to understand the patho-physiology of IUGR, evaluation of placenta is particularly important because only gross and microscopic examination of placenta can determine the primary cause, recurrence associated with IUGR and its impact on the fetal growth and weight [17,18]. There is a debate going on in cases of IUGR[19, 20] whether placental inefficiency is a primary cause, contributory factor or a result of extraneous factors (infection, genetic, nutritional etc). Placental insufficiency in some form is associated with the majority of IUGR cases [4]. In the present study the placental variables were considerably reduced as compared to the control group. Malik et al. (1968) has reported the similar findings. Placental and newborn weights were considerably reduced and were similar to findings reported in previous studies [21,7,22,23].

The hallmark of immune attack on trophoblastic cells is represented as fibrinoid necrosis[24, 5, 2]. A considerable quantity of immunoglobulins is present in the fibrinoid material of the affected villi [13]. In our study fibrinoid necrosis was observed in 46.7 % cases as compared to 32% - 38% cases as reported by the other workers [2, 21, 25]. This difference may be attributed to collection of IUGR cases. In our study we considered only idiopathic IUGR. The high percentage of fibrinoid necrosis as found in the study indicates primary placental involvement in cases of idiopathic IUGR.

Perivillous fibrin deposition in intervillous space is a result of thrombosis of maternal blood. The villi embedded in this fibrin are not infarcted but are incompetent of participating in any transfer activity.

Ironically, such deposition of fibrin tends to develop in placentae with good maternal blood supply. The greater the blood flow, greater the turbulence & stasis and greater is the perivillous fibrin deposition [13]. Perivillous fibrin deposition is derivative of maternal blood in the intervillous space. Platelets adhere to the villous syncytiotrophoblast with subsequent thrombus formation due to turbulence of blood within the intervillous space. The resultant fibrins that engulf areas of syncytiotrophoblast are cut-off from the maternal oxygen and go through ischemic necrosis. Normally perivillous fibrin deposition is present in about 20% of term placentae [26]. Reported incidence of perivillous fibrin deposition by earlier workers was about 36% by Mallik et al and about 21 % by Mirchandani et al [21,26,27,28,29]. The incidence of perivillous fibrin deposition is 16.7 % in the present study. These findings are similar to the studies done by Katzman and Genest and Fuke et, al [30,31] and also by earlier workers. Syncytial knots are indicators of compromise in fetal circulation [13]. Syncytial knots are seen due to aggregation of syncytial nuclei at the surface of terminal villi. In full term placentae, most syncytial knots are thought to be artifacts from tangential sectioning. Syncytial knots are always present increasing in numbers with gestational age and can be used to assess villous maturation. Syncytial knots in higher number are associated with conditions of utero-placental mal-perfusion and are important in placental examination[34]. Frequency of syncytial knots was higher in IUGR cases as compared to the control group. Similar findings have been reported by other workers [26,22,23,32]. The trophoblast nuclei show signs of degeneration such as nuclear pyknosis and karyorrhexis. With time, the villous stroma and syncytiotrophoblast degenerate and eventually only "ghosts" of villi remain (figure 7).

Our study documents a very low frequency of placental infarction (7%) similar to other workers [13, 33.34.35]. Placental calcification is often present in pregnancy at term and regarded as a physiological aging process. However, its earlier onset before 36 weeks gestation (preterm placental calcification) may have an unusual pathological implication [36,37]. We did not find appreciable difference in prevalence of calcification in IUGR and control group. This difference may be ascribed to subjective reporting and variable sample size.

CONCLUSION

Our study highlights some important facts:

1. Baby-placental weights and placental macroscopic variables were significantly reduced.
2. Syncytial knots were seen in 60% cases.
3. Placental involvement was strongly implicated in more than two third cases (47% fibrinoid necrosis and 16.7% perivillous fibrinoid deposition). These findings differ from earlier studies in comparatively higher incidence of placental involvement.
4. These findings represent the predominant role of placenta in idiopathic cases of intra-uterine growth retardation.

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Address for Corresponding Author:
Dr. Muhammad Zia Ur Rehman
Assistant Professor of Anatomy
Sheikh Zayed Medical College, Rahim Yar Khan.
Email; ziaafraisam2000@yahoo.com;
Ph: 0092-3009689829