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Comparison of Placental Histopathology in IUG Rand Normal Term Infants: A Cross-Sectional Study

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Abstract:
Introduction: *Healthy development of fetus is dependent on normal placental development. Alteration in the placental development is the main etiopathological factor for IUGR. The present study aims to compare the histopathological findings of placenta in IUGR and normal term delivery.*
Materials and Methods: *This cross sectional study was done at an Army zonal Hospital from Jan 2016 to Jan 2017. Sixty placenta were studied of which 30 belonged to the IUGR group and other 30 were from normal term fetus(Control group). Inclusion criteria was maternal age between 20 to 35 yrs, Gestational age between 32 to 40.5 wks with IUGR(USG confirmed) or normal healthy fetus. Exclusion criteria were twin pregnancy, gestational age <32wks, and diabetes. Data of mother, newborn and placenta were recorded after delivery. The subjects were matched for age, height, weight, social status. Data were analyzed using SPSS software version 16.*
Results: *Infarction rate, thrombosis, tissue ischemia, intervillous haemorrhage and intervillous fibrin deposition were significantly higher in IUGR group. Mean placenta weight was lower in IUGR group (380 gms vs. 510 gms).*
Conclusion:*Placenta of IUGR newbornswere smaller with more microscopic infarction. The findings suggest that chronic ischemia and associated secondary changes probably lead to improper perfusion and IUGR. The gross and microscopic measurements of a placenta are more objective and seem to offer a good way to get proper information about IUGR. Therefore a detailed history of placental study should be taken during ANC visit of a lady with previous history of IUGR and manage the case accordingly.All IUGR fetuses must be considered at risk for poor placental circulation and hypoxia along with compromised nutrition. This study therefore indicates that study of fetal blood supply must be done as a part of surveillance of IUGR cases by Doppler study and other tests of fetal well-being must be carried out during antenatal period frequently and they must be delivered as soon as the fetal maturity is reasonably assured or there are any signs of fetal compromise.*
Keywords:*IUGR, Placenta, Calcification, Thrombosis, infarction, intervillous fibrin*

I. Introduction

Intra uterine growth restriction (IUGR) is most commonly defined as weight of fetus less than tenth centile for that gestational age[1]. Intra uterine growth restriction is a common clinical sign for chronic fetal hypoxemia. FGR is one of the leading causes of perinatal morbidity and mortality[2,3]. Placenta is a vital organ for normal development of a healthy fetus as it is the media of transfer of essential nutrients and oxygen from mother to fetus and the waste products of metabolism from fetus to the mother. Any aberration in its development may have catastrophic effect on both the fetus and mother in the form of IUGR, IUFD and preeclampsia, Abruptio placenta respectively.A placenta is like a diary of gestational life[4] . It should be studied carefully. The etiology of IUGR can be divided into maternal, fetal, placental and unknown causes but placenta holds the main role in the basic pathophysiology of IUGR[5].Impaired placentation is thought to underlie most cases of IUGR especially early IUGR and early onset pre-eclampsia which is characterised by placental pathology associated with hypoxia and reperfusion damage caused by impaired remodelling of spiral arteries[3,6].

In a histopathological evaluation of placenta in IUGR pregnancies, the weight of IUGR placenta was less than normal placenta. Infarction and intervillousfibrinoid deposition were higher in IUGR placenta. In addition thickening of basal membrane and cytotrophoblast hyperplasia were more common among IUGR placenta. All the main histopathological findings pointed to placental blood flow reduction and fetal blood flow restriction[7] .

The present study was conducted to compare the pathological changes in IUGR with placental histology in term normal infants so as to establish a relationship between placental pathology and IUGR. This study may be useful in deciding and managing future pregnancies. Prevention of the perinatal complications in fetuses with growth restriction is possible by effective antenatal identification and management.

II. Materials & Methods

This cross sectional study was done at an Army zonal Hospital from Jan 2016 to Jan 2017. Sixty placenta were studied of which 30 belonged to the IUGR group and other 30 were from normal term fetus (Control group). The day a sample of placenta of IUGR case was sent, a placenta from normal full term delivery without any associated comorbidity was sent for gross and HPE .

Inclusion criteria was maternal age between 20 to 35 yrs, Gestational age between 32 to 40.5 wks with IUGR(USG confirmed) or normal healthy fetus.

IUGR was clinically suspected and then confirmed by USG showing growth lag of more than 3 Wks .These cases were further followed by regular close fetal surveillance in the form of Daily fetal movement count, Non stress test and umbilical flow velocimetry studies and USG for interval growth. Surfactant induction (Inj Betamethasone 12 mg IM 24 hrly 2 doses) was given once IUGR was confirmed.IUGR cases weredelivered as soon as the fetal maturity was reasonably assured or there are any signs of fetal compromise.

Exclusion criteria were Twin pregnancy, GA < 32 wks, GDM.

A thorough history, general and systemic examination of patient was done.

Placenta obtained after delivery was sent immediately in 10 % formalin to the lab for gross and histopathological examination by pathologist. Gross examination was carried out on the same day on intact specimen and after bread- loafing. The following parameters were noted:

- Cord insertion –central or eccentric
- Number of vessels in the cord
- Membrane insertion – marginal or circumvallate
- Membrane discolouration – meconium stained or yellow
- Areas of infarction, calcification, fibrin deposition.

Sections are taken from cord, membranes and parenchyma. Sections from membranes include the rupture site. These are rolled and processed further. The sections from parenchyma include all relevant pathological areas and atleast one "normal" area. These are full thickness sections including the chorionic plate. The sections are further fixed overnight in 10% formalin and processed. Routine Hematoxylin and Eosin stains are employed for all sections.

The results obtained were analysed to study the correlation between placental findings and the delivery outcomes. Statistical correlation was done using SPSS software version 16.

$P < 0.05$ was taken as critical level of significance.

III. Results

Maternal characteristics of the study group and the control group is shown in Table 1.

Table 1

	Study Group (30)	Control Group (30)
Mean Age	26.6 Yrs	26.4 Yrs
Mean Wt	64.3 kg	66.9 kg
Mean Gestational Age	36.95 Wks	38.7 Wks
Significant Contributory Finding	3 PIH, 2 APLA positive, 1 Thrombophilia	-
Average Birth Weight	2.24 kg	3.01 kg

The gross findings of placenta of the study group and the control group is shown in Table 2:

Table 2

	Study Group (30)	Control Group (30)
Average Placental weight	380 gms	510 gms
Cord insertion	Central - 11 Eccenteric - 19	Central - 19 Eccenteric - 11
Membrane discolouration	Green - 5 Yellow - 1	Green - 1 Yellow - 0
Membrane insertion	Marginal - 29 Circumarginate- 2	Marginal - 30 Circumarginate- 0
Gross infarction	6	2
Calcification	1	0

The microscopic findings of placenta of the study group and the control group is shown in Table 3:

Table 3

	Study Group (30)	Control Group (30)	P value
Placental infarction	19	02	<0.001
Ischemic changes	26	04	<0.001
Thrombosis	15	02	<0.01
Calcification	14	04	<0.001
Chorangiosis	03	0	Not significant
Intervillousfibrinoid deposition	26	05	<0.001
Cord vasculitis	0	0	Not significant
Choroioamnionitis	3	0	Not significant
Intervillous hemorrhage	25	0	<0.001

Grading of intervillousfibrinoid deposition seen in the study group is shown in Table 4:

Table 4

Intervillousfibrinoid deposition	Study Group (30)	Control Group (30)
<5%	8	3
5%- 10%	8	2
>10%	10	0

Fig 1 A- F are showing the pathological findings in IUGR placenta

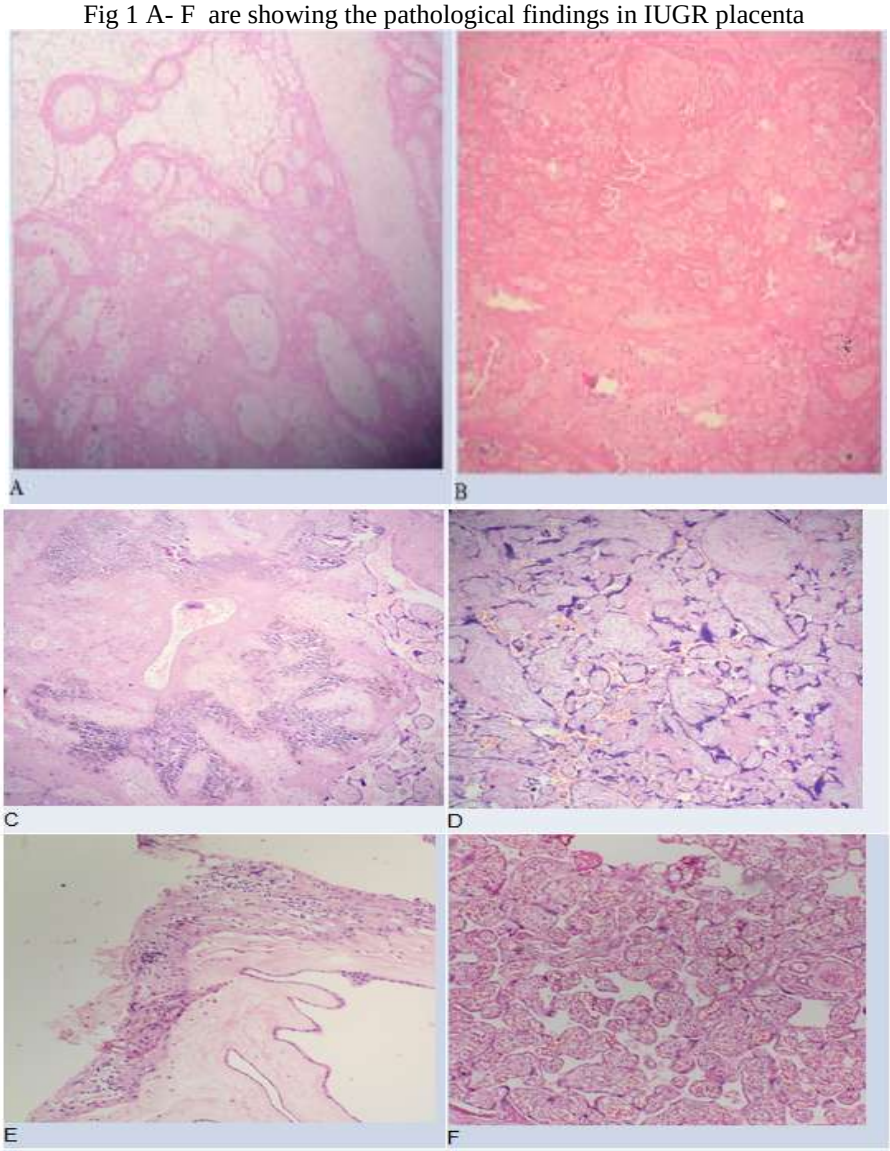

Fig 1A,B- Placental infarct . **Fig 1C** - Calcification with intervillousfibrinoid deposition.
Fig 1D - Increased syncytial knots and intervillousfibrinoid deposition.
Fig 1E -Chorioamnionitis.**Fig 1F** - Chorangiosis

Fig 2 A,B are showing the microscopic appearance of normal placenta from a normal term delivery

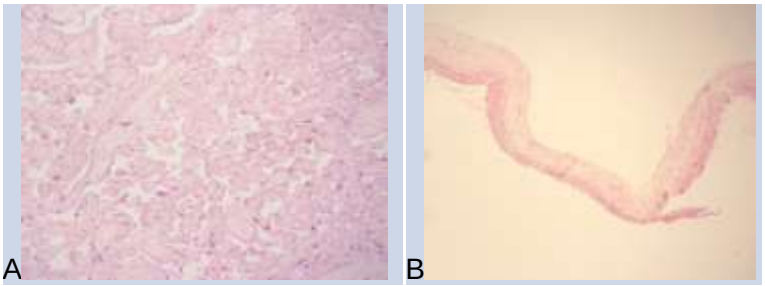

Fig 2A - Normal Mature Placenta .**Fig 2 B** -Section from membranes of mature Placenta

IV. Discussion

Chronic placental insufficiency accounts for majority of IUGR foetuses. In this study we have tried to study the significant placental pathology in IUGR cases.Mean Placental weight of IUGR cases was 380 gm (less than 25th percentile) as compared to the 510 gm (>50th percentile) in control group. Similar finding was seen in other studies[8,9].Few studies suggested circumvallate placenta, circummarginate, velamentous insertion of the cord and placenta previa as possible causes of IUGR[1,10,11]. In this study almost all the placenta had marginal insertion of membranes. No significance can hence be attached to this finding in our study.

IUGR placenta generally shows pathological lesions of two major categories[12] :

i. Due to reduced vascular supply of nutrients and oxygen (eg: infarction, villous hypoplasia, increased syncytial knotting

ii. Due to altered inflammatory response (eg: chorioamnionitis, villitis)

In our study we found signs of chronic placental insufficiency in the form of ischemia, intervilloushaemorrhages, calcification, fibrinoid necrosis, intravillous fibrin deposition in IUGR group placenta in significant number of cases. The p value was < 0.01 for all the above mentioned features as compared to the control group. The same has been quoted in previous studies[9,13-17]. In this study the inflammatory response was seen in only 2 of the 30 cases of IUGR. Redline and Pappin have suggested the association between chronic villitis and growth restriction[19]. Veerbbeketaland Green LG etalalso observed higher level of chronic chorioamnionitisfrom pregnancies with early IUGR and maternal hypertensive disease as compared to normotensive IUGR pregnancies and suggested that pronounce allograft rejection and graft versus host disease in membranes in women with concomitant hypertensive disease[14,20]. This could be due to the small sample size combined with only three cases of PIH in our study. Therefore, it is recommended such pathological findings be examined in a larger sample size in future studiesIntervillousfibrinoid deposition of more than 10% was more common in the study group as was seen in previous studies[9,13,15,16]. Maternal thrombophilias, both inherited and acquired have been seen to be associated with increased fibrinoid deposition in intervillous space. This results in trapping of villi by the fibrinoid material and ultimately necrosis. Therefore, high amount of intervillousfibrinoid deposition is a pathological finding in IUGR-related placenta[22].

Chen etal studied the relationship between preterm placental calcification and adverse pregnancy outcome by ultrasonography and they concluded that early preterm placental calcification is associated with a higher incidence of adverse pregnancy outcome and may serve as an indicator of adverse maternal and fetal outcomes when noted on ultrasonography[21]. Conversely, women with late preterm placental calcification are not at greater risk for adverse pregnancy outcome. In the present study we observed calcification in 46.6 % cases (14/30) of IUGR placentae as compared with 13.33% (4/30).

V. Conclusion

Placenta of IUGR newborns was smaller with more gross finding of calcification and more microscopic infarction. Significant pathologic findings were infarction, thrombosis, ischemia, intervillushaemorrhage and intervillus fibrosis. These findings suggest that chronic ischemia and associated secondary changes probably lead to improper perfusion and IUGR. Therefore all pregnancies diagnosed to have IUGR antenatally must be suspected to have etiology of placental origin unless proved otherwise. The corollary to this is that such IUGR fetuses must be considered at risk for poor placental circulation and hypoxia along with compromised nutrition. This study therefore indicates that study of fetal blood supply must be done as a part of surveillance of IUGR cases by Doppler study and other tests of fetal well-being must be carried out during antenatal period frequently and they must be delivered as soon as the fetal maturity is reasonably assured or there are any signs of fetal compromise.

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