



PLACENTAL PATHOLOGY IN INTRAUTERINE GROWTH RESTRICTION AND ITS RELATION TO PERINATAL OUTCOME

Gynaecology

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ABSTRACT

AIMS AND OBJECTIVES:

- 1) Histopathological examination of placenta of IUGR babies.
- 2) Determine the frequency and cumulative number of placental abnormalities.
- 3) To correlate the data with perinatal outcome in terms of fetal weight, apgar scores and perinatal mortality.

METHOD OF STUDY: Analytical study for a duration of six months. Analysis of the placentas of IUGR babies both microscopically and macroscopically and the results are correlated with the perinatal outcome.

RESULTS AND ANALYSIS: 100 placentas of mothers who delivered IUGR babies were analysed. Majority of women were primigravida and in the age group of 21-30 years. 45 cases were of unexplained etiology. 66 cases had abnormal Doppler flow and 34 cases had gross macroscopic abnormalities of placenta. Histopathological examination revealed multiple placental abnormalities with >3 lesions in 83 cases. Weight of placenta and weight of baby was significantly reduced with 3 or more lesions. The incidence of neonatal complications were significantly increased with multiple lesions. Apgar score at birth was also significantly reduced with multiple lesions. All cases (19 out of 100 cases) of perinatal mortality were in the group with multiple placental lesions.

CONCLUSION: Increased frequency of placental lesions and increased number of lesions were significantly associated with IUGR. Increased number of placental lesions were commonly observed in cases with abnormal Doppler waveforms. Multiple placental lesions were associated with low birth weight, low placental weight, increased frequency of neonatal complications and increased perinatal mortality.

KEYWORDS

AIM OF STUDY:.

1. Histopathological examination of placenta of term IUGR babies.
2. Determine the frequency and cumulative number of placental abnormalities
3. To correlate the data with the perinatal outcome in terms of fetal weight, apgar scores and perinatal mortality.

MATERIALS AND METHODS :

The study was carried out in the Department of Obstetrics and Gynaecology, GRH, Madurai. 100 placentas of IUGR babies were collected during the study period from September 2017 – December 2018.

Inclusion Criteria : Placentas of pregnant women who delivered term IUGR babies. (Birth weight less than 10th percentile according to standard normal curves).

Exclusion Criteria : 1. Known congenital anomaly in fetus 2. Twin pregnancies 3. Prematurity 4. Unreliable LMP without first trimester scan

Method of study : In this study, mothers who delivered IUGR babies were enrolled as cases. Ultrasound parameters including fetal biometry, estimated fetal weight, amniotic fluid index and Doppler USG of the umbilical artery were noted. Immediately after delivery, the newborn is weighed and the birth weight percentiles were determined by previously published normal curves by Alexander GR in 1996. The placentas were weighed and macroscopic examination done which includes the placental diameter, thickness, colour, calcification and other abnormalities noted. The placentas are sent to Pathology department for histopathological examination by a senior pathologist. Placental histologic data includes decidual vasculopathy, fetal thrombotic arteriopathy, chorangiosis, acute inflammation, chronic villitis and intervillous thrombosis. The frequency and cumulative number of placental abnormalities in IUGR babies were determined and the relationship to perinatal outcome was determined in terms of fetal weight, Apgar scores and perinatal mortality.

RESULTS AND OBSERVATIONS

Total of 100 cases of IUGR were included in the study. The observations and results of the study are presented in the following pages.

80% of patients are in the age group 21-30 years, and only 5% above 31 years. About 51% had oligohydramnios AFI < 5 cm, and 36% had reduced liquor AFI : 6-10 cm. 48% of them were primigravida. 58% of patients belong to class V socioeconomic status. About 87% of patients had weight gain of 6-10 kgs, only 12% had weight gain > 11 kgs.

Table 1: Parity Distribution

Gravida	No. of cases	Percentage
1	48	48
2	31	31
3	17	17
4 and above	4	4
Total	100	100

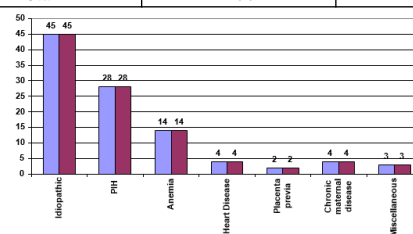


Chart 1: Etiology

Table 2: Distribution of cases based on Umbilical artery Doppler changes

Umbilical artery Doppler changes	Frequency	Percentage
Normal flow	34	34
Reduced flow	34	34
Absent flow	28	28
Reversal of flow	4	4
Total	100	100

Out of 100 cases 34 had normal flow, 34 had reduced flow, 28 had absent diastolic flow. The rest 4 had reversal of flow.

Table 3: Distribution of cases based on Macroscopic Abnormalities

Macroscopic Abnormalities	Frequency	Percentage
Present	34	34
Absent	66	66
Total	100	100

As shown in the table ,66% had normal macroscopy, the remaining 34% had one or more of the following abnormalities. Calcification, unduly small placenta, necrosis, retroplacental clots.

Table 4:Based on Microscopic abnormalities of placenta

Placental histopathology	Frequency	Percentage
Placental Infarcts	60	60
Decidual vasculopathy	42	42
Syncytial knots	58	58
Chorioamnionitis	33	33
Stromal fibrosis	38	38
Chronic villitis	18	18
Hemorrhagic endovasculitis	15	15
Increased Trophoblastic proliferation	15	15
Increased perivillous fibrin	9	9
Basement membrane thickening	16	16
Calcifications	13	13

As per the table and pie chart, placental infarcts were found in 60%, syncytial knots in 58%, decidual vasculopathy in 42%, the remainder being chorioamnionitis 33%, stromal fibrosis 38%, chronic villitis 18%, hemorrhagic endovasculitis 15%, basement membrane thickening 16%, calcification 12%. Increased trophoblastic proliferation in 15% of cases.

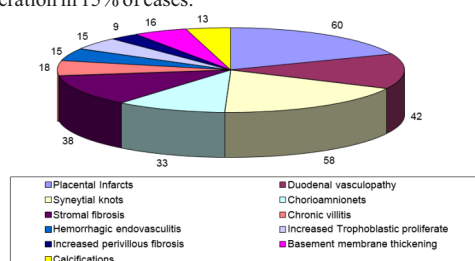


Chart2:Microscopic abnormalities of placenta

Among 100 cases, 44 had more than or equal to 4 placental lesions, 39 had 3 lesions, 11 had 2 lesions and only 6 had single lesion.

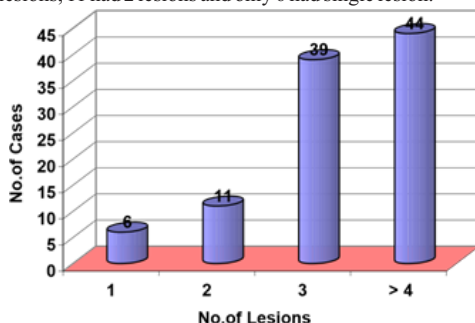


Chart 3: Placental Lesions

Table5:Comparison of umbilical artery Doppler waveforms with placental pathology

Doppler waveforms	No.of placental lesions				Total
	1	2	3	4	
Abnormal flow	1(1%)	2(2%)	27(27%)	36(36%)	66
Normal flow	5(5%)	9(9%)	12(12%)	8(8%)	34
Total	6	11	39	44	100

Increased number and frequency of placental pathologies were more commonly observed in cases with abnormal Doppler waveforms when compared with normal Doppler waveforms with difference being statistically significant with $p < 0.001$.

Table-6 :Abnormal Doppler waveforms in relation to the number of Placental lesions

No of placental lesions	Reduced diastolic flow	Absent flow	Reversal of flow	Total
1	1(1.5%)	-	-	1
2	1(1.5%)	-	1(1.5%)	2
3	13(19.6%)	13(19.6%)	1(1.5%)	27
≥ 4	19(28.7%)	15(22.7%)	2(3%)	36
Total	34	28	4	66

Out of the 66 cases with Doppler abnormalities, 27 cases had 3 lesions and 36 of them had four or more lesions. ($p < 0.001$) significant.

Table7:Distribution of cases based on type of Delivery

Mode of Delivery	Frequency	Percentage
Vaginal	46	46
Instrumental	4	4
LSCS	50	50
Total	100	100

As mentioned above, 46% had vaginal delivery, 4% had instrumental delivery, 50% were delivered by LSCS.

Table 8:Based on weight of the placenta

Weight of placenta	Frequency	Percentage
≤ 350	51	51
350 – 400	39	39
≥ 400	10	10
Total	100	100

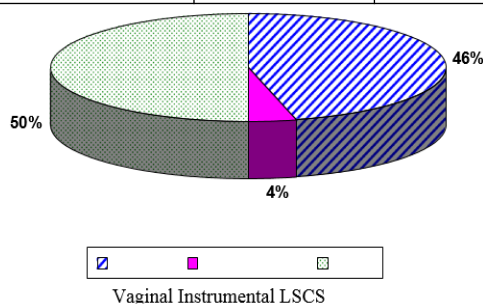


Chart 4:Mode Of Delivery

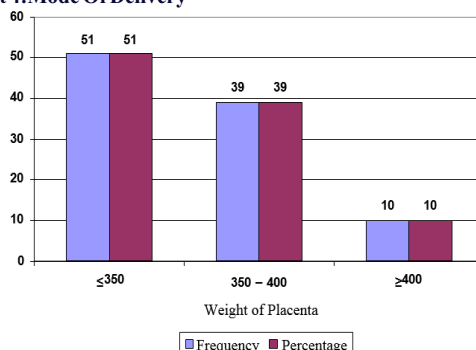


Chart 5:Based on weight of the placenta

Table 9:Distribution based on weight of the baby

Weight of baby	Frequency	Percentage
<1.5 kg	6	6
1.5-2kg	51	51
2.1-2.5kg	43	43
>2.5kg	-	-
Total	100	100

43 babies had birth weight between 2.1-2.5 kg (<10th percentile), 51 babies had birth weight between 1.5-2 kg (<5th percentile), the remaining 6 babies had birth weight less than 1.5 kg.

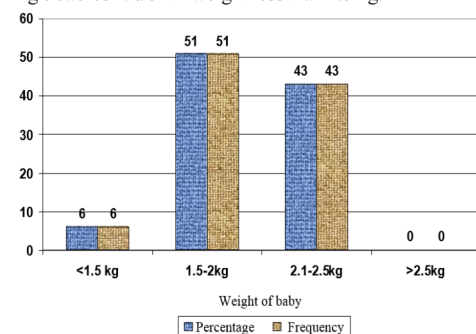


Chart 6:Distribution based on weight of the baby

Table 10:Based on number of placental lesions

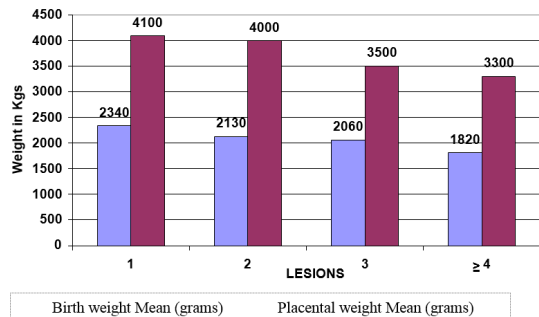
No.of Lesions	Frequency	Percentage
1	6	6
2	11	11
3	39	39
≥4	44	44
Total	100	100

The total cumulative number of placental lesions had a significant correlation with placental birth weight and fetal weight. As the number of lesions increases the birth weight and the placental weight decreases, the relation being statistically significant with p value <0.001.

Table 11:Comparison of Birth weight and placental weight in relation to number.of placental lesions.

No.of lesions	Birth weight Mean(grams)	Placental weight Mean(grams)
1	2340	410
2	2130	400
3	2060	350
≥ 4	1820	330

The total cumulative number of placental lesions had a significant correlation with placental birth weight and fetal weight. As the number of lesions increases the birth weight and the placental weight decreases, the relation being statistically significant with p value <0.001.

**Chart 7:Comparison of Birth weight and placental weight in relation to No. of placental lesions.****Table – 12 Fetal outcome in relation to number of placenta lesions**

No.of lesions	Apgar (Median)		Neonatal complications			
	1	5	HIE	RDS	MAS	Sepsis
1	7	8	0	0	0	1(1.2%)
2	6	8	0	3(3.8%)	2(2.5%)	1(1.2%)
3	5	7	4(5.1%)	12(15.3%)	10(12.8%)	1(1.2%)
>4	2	4	4(5.1%)	18(23%)	18(23%)	4(5.1%)
Total			8	33	30	7

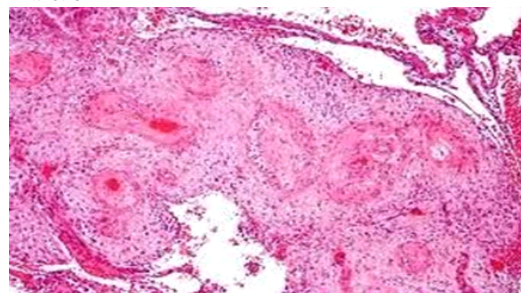
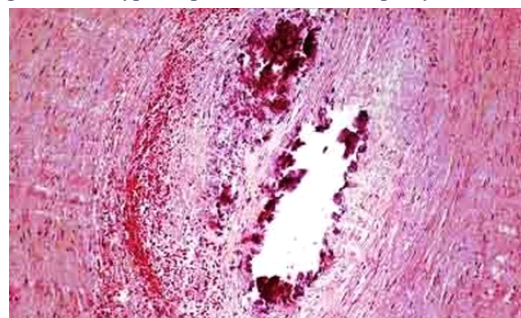
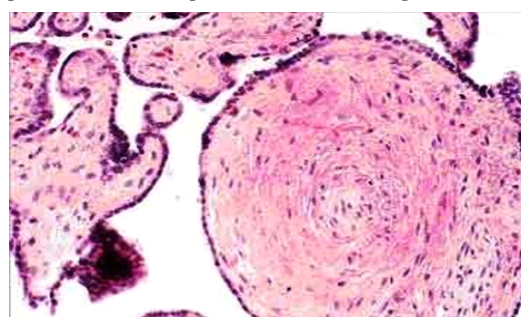
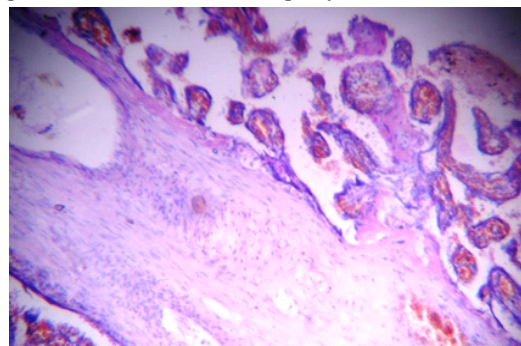
Increased number of placental lesions was associated with a decreased fetal apgar score and increased frequency of neonatal complications. Babies with single placental lesion had a 1 min apgar score of 7 compared to 2 for babies having 4 or more lesions. Similarly the rate of neonatal complications increased significantly when number of lesions were more than 4(p<0.001)

Table 13:Number of placental lesions in relation to perinatal mortality

No of placental lesions& frequency	Doppler abnormalities	Still birth	Admission in NICU	Neonatal death
1 6%	1	0	6 (min-2days Max-3 days)	0
2 11%	2	0	11 (min-2 days Max-5 days)	0
3 39%	27	0	39 (min-4 days Max-21days)	5
≥4 44%	36	3	41 (min 5 days Max-28 days)	11
Total 100	66	3	97	16

Out of 100 cases, 83 cases had 3 or more placental abnormalities.Out of 66 cases with Doppler abnormalities,63 cases had 3 or more

placental lesions.3 babies were still born who had >4 placental lesions, 16 cases of neonatal death of which 5 babies had 3 lesions and 11 babies had >4 placental lesions.

**Figure – 1: Gross examination of the placenta showing yellow areas of infarction****Figure No. 2: Hypertrophic decidual vasculopathy****Figure No. 3: Microscopic examination showing calcification****Figure No. 4: Thrombotic vasculopathy****Figure No. 5: Stromal fibrosis**

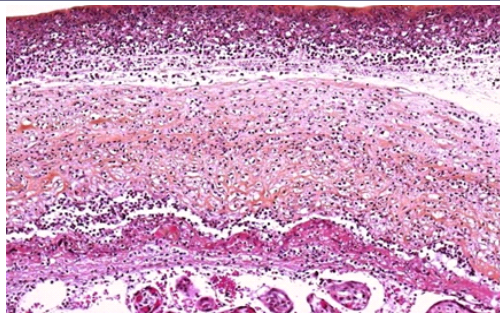


Figure No. 6: Chorioamnionitis

DISCUSSION

IUGR is related to a variety of clinicopathologic factors including maternal, uterine and fetal factors. Recent studies of placental examination of IUGR pregnancies provide good evidence for the occurrence of distinctive structural and histological abnormalities.

In this study, majority of cases were primiparous women (48%) in the age group of 21-30 years (80%). A study by Robert M. Kliegman et al showed that low socioeconomic status have been associated with poor fetal nutrition. About 58% of patients belong to class V socioeconomic status and 30% belong to class IV socioeconomic status.

In this study, 45% cases of IUGR are of unexplained etiology and PIH contributed to 28%. Park et al, Kim et al, Chun et al 2002 showed that IUGR groups had higher incidence of oligohydramnios than controls. Our study proved similar results.

In this study, 34% of cases had macroscopic abnormalities of placenta. The placentas from pregnancies complicated by IUGR tend to be smaller than those from normal uncomplicated pregnancies. (Thame et al 2001, 2004, Khadija qamar et al). In the present study, the placental weights were significantly lower especially in those with 3 or more number of placental lesions.

Macara et al worked on the structural analysis of placental villi from growth restricted pregnancies with abnormal umbilical artery Doppler waveforms. They found that the terminal villi from the IUGR cases were smaller in diameter than those of controls and had increased syncytial nuclei, thickened basal lamina and increased stromal deposition of collagen and fibrin. In our study, the 5 main histopathological lesions documented are placental infarcts (60%) which are mainly due to ischaemia followed by syncytial knots in 58% of patients, decidual vasculopathy in 42% of patients, stromal fibrosis in 38% and chorioamnionitis (33%).

The overall incidence of infarction is increased in placenta growth restricted infants. (Bjoro et al, Suska et al, Salafia et al) and Laurini et al have claimed that infarction is the only placental lesion that correlates with growth restriction. In our study, 60% of babies had placental infarct.

The finding of ischemic type changes in many placentas from pregnancies with Idiopathic intrauterine growth restriction suggests that there is diminished maternal blood flow in such cases and this has been confirmed by Doppler studies of uteroplacental circulation. (Trudinger et al, Mc Cowarr et al, Jacobson et al, Beroley et al, Schulmann et al, Iwata et al, Nicolaides et al). There is a clear correlation with abnormal Doppler wave form and the presence of ischemic type of changes in the placenta. In our study, increasing number of placental lesions had significant correlation with abnormal Doppler wave forms.

Placental pathology and its relation to perinatal outcome

Liaquat All minnas et al, Muhammad yunas khan et al: 2009 showed that mean birth weight was lower in fetus with multiple placental abnormalities. Majority of babies (57%) had low birth weight with mean birth weight of 2.06 kg when there are 3 lesions and a mean of 1.82 kg when there are 4 or more lesions.

A study by Rose M. Viscardi et al and Chen Cin J. Sun et al has proved that severity of placental abnormalities expressed as the cumulative number of lesions is a significant risk factor for IUGR and increased perinatal mortality. Our study proved the similar results. Increased

number of placental lesions were associated with a decreased fetal apgar score and increased frequency of neonatal complications. Babies with single placental lesion had a 1 min apgar score of 7 compared to 2 for babies having 4 or more lesions. Similarly the rate of neonatal complications increased significantly when number of lesions were more than 4 ($p < 0.001$)

The perinatal mortality increased with number of placental lesions. All the 3 cases of stillbirth were with multiple lesions. There were 16 cases of neonatal death with 3 or more lesions.

Assessment of placental pathology is an invaluable tool in determining the pathophysiology behind the growth restriction. It is also useful in determining the underlying mechanisms leading to pregnancy complications and for guiding future investigations. The consequences of aberrant fetal growth secondary to placental dysfunction extend beyond the intrauterine phase of existence. A variety of adult chronic illness including cardiovascular disease, dyslipidemia, type II diabetes, obesity are now felt to be manifestations of fetal malnutrition usually resulting from placental changes precluding optimum function. Therefore placental examination may represent a means of investigating the intrauterine past to explain the present condition of the neonate. The results of this study provide new evidence for the relationship between intrauterine events, reduced growth velocity and postnatal consequences. Specific patterns of placental pathological findings may be predictive of specific adverse neonatal outcomes.

Over the past 10-15 years medicolegal implications of placental pathologic examination have been emphasized. In obstetric malpractice litigations involving perinatal death, neurologic damage or mental impairment, the presence of chronic placental abnormalities (such as infarcts, small placental size, membranous cord insertion, maternal decidual vasculopathy, chorangiosis, nucleated fetal RBCS etc) may suggest that fetal damage occurred antenatally rather than perinatally. A recent analysis of obstetric malpractice claims concluded that many more neurologically impaired infant claims could be successfully defended if placenta specimens were available for examination at the time a claim is made'.

CONCLUSION

1. Histopathological examination of placenta in cases with IUGR revealed pathological changes like infarction, inflammation and fetal thrombotic vasculopathies.
2. Increased frequency of placental lesions and increased number of lesions were significantly associated with IUGR.
3. Increased number of placental lesions was commonly observed in cases with abnormal Doppler waveforms compared with normal Doppler waveforms with difference being statistically significant with p value < 0.001 .
4. Multiple placental lesions were associated with low birth weight, low placental weight and increased frequency of neonatal complications and increased perinatal mortality. ($p < 0.001$)
5. It is well recognized that all institutions do not have pathologist with experience in doing placental pathology. If protocols are instituted such that placentas from all cases of IUGR are subjected to histopathological examination, it will allow a more complete understanding of the pathophysiology of fetal growth restriction, knowledge of risk of additional complications to the mother and the neonate and the risk of recurrence in subsequent pregnancies.

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