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RESEARCH ARTICLE

A comparative study of placental histomorphological changes in a normal pregnancy and an intrauterine growth restriction pregnancy

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ABSTRACT

Objectives: The wellbeing of a fetus depends a lot on the proper functioning of the placenta. The placental pathology can be seen at a gross and microscopic level. Intrauterine growth restriction and other pathological conditions can be the result of these changes in the placenta. The aim is to study and compare the gross and histopathological changes in the placenta of normal and intrauterine growth restriction pregnancies. **Methods:** It is a prospective observational study conducted in a tertiary hospital. The study was conducted on 71 pregnant women with IUGR fetus and 129 normal fetuses attending a tertiary hospital OPD and labour room between 2016 and 2018. Mother, placenta, fetus and newborn data were recorded before and after delivery. After checking the inclusion and exclusion criteria, pregnancies with IUGR were taken as cases and normal pregnancies as controls. All the data were collected and tabulated and then analyzed with appropriate statistical tools "MedCalc". **Results:** There are statistically significant differences found in gross and histological changes in the placenta of IUGR and the control group. Among gross features, in FGR group, mean weight of the placenta was 363.52 grams, calcification was found in 33.80% cases and infarction in 26.76% of cases and in control group, mean weight of the placenta was 547.16 grams (P value < 0.0001), calcification was found in 15.50% cases (P value-0.0049) and infarction 8.53% cases (P value - 0.0012). Among histopathological features, in FGR group, perivillus fibrin deposit (PFVD) was found in 38.03% of cases, syncytial knot found in 30.99% of cases and fibrinoid necrosis found in 29.58% cases. In control group, PFVD was found in 20.16% of cases (P value - 0.0101), syncytial knot was found in 14.73% of cases (P value - 0.0110) and fibrinoid necrosis found in 9.30% cases (P value - 0.0005). **Conclusions:** The abnormal gross pathological and histopathological changes like calcifications, infarction, perivillus fibrin deposit, fibrinoid necrosis and syncytial knot are seen in a statistically significant higher percentage in pregnancies with intrauterine growth restriction.

Keywords: Intrauterine growth restriction, fibrinoid necrosis, placenta, placental infarction, fetal growth restriction.

Human fetal growth, differentiation and maturation occur in a sequential pattern. Fetal growth has been divided into 3 phases. The initial phase of hyperplasia occurs in the 1st 16 weeks and is characterized by a rapid increase in cell number. From the 17th to the 32nd week in the second phase, there occurs both cellular hyperplasia and hypertrophy. After 32 weeks, fetal growth is by cellular hypertrophy and during this phase, most of the fetal fat and glycogen is accumulated[1]. Intrauterine growth restriction (IUGR) is most commonly defined as the weight of a fetus less than a tenth centile for that gestation [2]. It is a pathological condition in which the fetus has not achieved its genetic growth potential, regardless of fetal size [3]. IUGR and SGA are not synonymous. It is estimated that the majority of IUGR fetuses are SGA, while 50-70% of SGA fetuses have growth appropriately but are constitutionally small [4]. IUGR is

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sometimes defined as SGA with abnormal doppler indices such as umbilical artery (UA), and pulsatility index (PI) above the 95th centile [5]. Intrauterine growth restriction is a common clinical sign of chronic fetal hypoxemia [6]. IUGR is the second leading cause of perinatal morbidity and mortality, followed only by prematurity [1].

The placenta plays a prominent role in the optimum development of a healthy fetus as it is the organ for the transfer of essential nutrients and oxygen from mother to fetus and the waste products of metabolism from the fetus to the mother. A placenta is like a diary of gestational life [7].

Any aberration in its development may have a catastrophic effect on both the fetus and mother in the form of IUGR, IUFD, miscarriage, unsuccessful pregnancy and preeclampsia and abruptio placenta respectively [7]. Furthermore, it seems that the incidence of central nervous system damage and neural development complication increase in these infants [8] and increase the risk of adult diseases like cardiovascular disease and diabetes [9].

The fetus and the placenta are genetically similar, so their growth potential will be corresponding. Not surprisingly, 'placental insufficiency' is invoked commonly in cases of impaired foetal growth [10].

The aetiology of IUGR can be divided into maternal, fetal, placental and unknown causes but the placenta holds the main role in the basic pathophysiology of IUGR [11]. Impaired placentation is thought to underlie most cases of IUGR, especially early IUGR and early onset pre-eclampsia which is characterized by placental pathology associated with hypoxia and reperfusion damage caused by impaired remodelling of spiral arteries [7, 12].

In the gross evaluation of the placenta in IUGR pregnancies, the weight of the IUGR placenta was less than the normal placenta. Infarction and intervillous fibrinoid deposition were higher in the IUGR placenta. All the main histopathological findings pointed to placental blood flow reduction and fetal blood flow restriction [13].

The present study was conducted to compare the placental histopathological changes in IUGR and normal pregnancy to establish a relationship between placental pathology and IUGR. This study may help detect, evaluate and manage future pregnancies.

Materials and methods

This research is a prospective observational study that was conducted on pregnant women with IUGR fetuses and non-IUGR foetuses after approval of the ethical committee of JLN Hospital and Research Centre, Bhilai, Chhattisgarh. The study was carried out in the department of obstetrics and gynecology of JLN Hospital and Research Centre, Bhilai, between 2016 and 2018. During this period pregnant women with normal singleton fetus were recruited into a control group. All patients attending our obstetrics and gynaecology OPD were examined routinely.

Pregnant women on their antenatal visit to a hospital in OPD/IPD were selected as a case based on inclusion and exclusion criteria.

In our study inclusion criteria were -

1. Maternal age between 18 -35 years,
2. Gestational age between 32 to 41 weeks with pregnancy diagnosed with IUGR (USG -confirmed) and non IUGR pregnancies,
3. Singleton pregnancy.

The exclusion criteria were -

1. Multifetal pregnancy,
2. Pregnancy with hypertension or diabetes mellitus, gestational age <32wks,
3. History of irregular cycles, mistaken dates, congenital malformation,
4. Female not giving consent for the study.

By fulfilling inclusion and exclusion criteria, patients were counselled for the study and informed consent was taken from the patient.

Antenatal detailed history and general and systemic examination were done. IUGR was clinically suspected and then confirmed by USG showing weight less than the 10th percentile for their gestational age. These cases were further followed by regular close fetal surveillance in the form of daily fetal movement count, nonstress test, uterine, middle cerebral & umbilical artery doppler studies and USG for interval growth. IUGR cases were delivered as soon as the fetal maturity was reasonably assured or there are any signs of fetal compromise. After delivery, all information related to pregnancy, newborn, and morphological assessment of placentae like placental weight, cord insertion, true knot, false knot, and calcification were collected and recorded.

After gross examination of the placenta; the placenta in formaldehyde solution was transferred to a pathological laboratory. There it was examined by a pathologist. The pathologist was kept blind for all the samples. After macroscopic evaluation, multiple sections of each placenta, umbilical cord and placental membrane were taken for tissue processing. Samples were processed for 18 hours in a tissue processor and various solutions (Alcohol, Xylol). The tissue is infiltrated with histological wax and sections of 3-4 microns thickness were prepared and stained with hematoxylin-eosin stain.

After studying these samples, the pathologist comments on the microscopic section with information such as haemorrhage & necrosis of parenchyma, signs of ischemia & chorioamnionitis, thrombosis, infarction, intervillous fibrin & calcification.

The neonatal parameters including birth weight, body length, head circumference and abdomen circumference were measured for all the babies**.** The gross and histopathology reports obtained were correlated with the antenatal history and postnatal outcomes.

Statistical analysis - All the data were selected and tabulated and then analyzed with appropriate statistical tools "MedCalc". The result was presented as proportions or mean with standard deviation depending on the type of data. Mean, median, standard deviation and variance were calculated and the following statistical significance tests were applied.

1. To test for the significance of observed mean differences student's unpaired T-test was used.
2. "Chi-square test" and "Fisher's exact test" was also used for the statistical significance test.
3. Test of significance for difference of proportions.

Finally, the calculated value was compared with the tabulated value at a particular degree of freedom and finds the level of significance. A "p-value" considered to be non-significant if > 0.05 and significant if <0.05.

Results

Of 200 placentas, 71 were from the IUGR pregnancies (case group) and 129 were from normal pregnancies (control group). In our study population in case 48 out of 71 (67.61%) and in control 98 out of 129 (75.97%) were between 20-30 years of age. However, this difference was not statistically significant. The mean gestational age at delivery was in IUGR (case) group 37.03 years and in the control group 38.97 years. This difference was statistically significant (p<0.0001) (table 1).

In the case group vaginal delivery rate was 36.62% and LSCS was 63.38%, and in the control group vaginal delivery rate was 55.04% and LSCS was 44.96%. This difference was statistically significant (p <0.0001) (table 2).

The mean birth weight of babies in the IUGR group was 2126±169.41 gm and in the control group 3014.63±222.62 gm. This difference was statistically significant (p <0.0001) (table 1). In our study, as compared to the control group, the mean weight of the placenta in the IUGR group was less and this difference was statistically significant (p<0.0001) (table 1). The mean head circumference is 32.54± 1.08 cm in the IUGR group and 33.54±1.24 cm in the control group. This difference was statistically significant (p <0.0001) (table 1). In the IUGR group, the mean of HC/AC was 1.059±0.035 cm and in the control group it was 0.948±0.026 and this difference was statistically significant (table 1).

Table 1: Fetomaternal variables

Variables	Number	Mean±SD	P - value
Age (years)	Case (71)	27.73±3.12	0.2131
	Control (129)	27.13±3.22	
SFH (centimetres)	Case (71)	33.12±1.43	<0.0001
	Control (129)	35.57±0.83	
Gestational age (weeks)	Case (71)	37.03±0.51	<0.0001
	Control (129)	38.97±0.76	
Birth weight (gms)	Case (71)	2126.90±169.41	<0.0001
	Control (129)	3014.63±222.62	
Placental weight (gms)	Case (71)	363.52±38.29	<0.0001
	Control (129)	547.16±94.48	
Head circumference (cms)	Case (71)	32.54±1.08	<0.0001
	Control (129)	33.54±1.24	
Abdominal circumference (cms)	Case (71)	30.76±1.62	<0.0001
	Control (129)	35.40±1.45	
HC/AC	Case (71)	1.059±0.035	<0.0001
	Control (129)	0.948±0.026	

Table 2: Comparison of mode of delivery between two groups

Mode of delivery	Case (n=71)		Control (n=129)	
	No.	Percentage	No.	Percentage
CS	45	63.38%	49	37.98%
VD	21	29.58%	77	59.69%
Instrumental	5	7.04%	3	2.33%

Table 3: Evaluation of variables of the placenta in IUGR and normal pregnancies

Variables	Case (71)		Control (129)		P value
	No	%	No	%	
Calcification	24	33.80	20	15.50%	0.0049
Infarction	19	26.76	11	8.53	0.0012
Perivillous fibrin deposition	27	38.03	26	20.16	0.0110
Fibrinoid necrosis	21	29.58	12	9.30	0.0005
Syncytial knot	22	30.99	19	14.73	0.011
Intervillus haemorrhage	10	14.08	18	13.95	0.85
True knot	2	2.82	0	0	0.15
False knot	2	2.82	0	0	0.15

In this study, the gross morphology of the placenta like calcification was found more often in the IUGR group in comparison to in the control group. In our study, perivillous fibrin deposition, infarction, syncytial knot, calcification, and fibrinoid necrosis were higher in the IUGR placenta as compared to the normal placenta. This was a statistically significant difference (table 3).

Discussion

In IUGR, the weight of the infant is at or below the 10^{th} percentile for the expected birth weight at a given gestational age. IUGR is associated with interference with circulation and the development or growth of the fetus or with nutrition and general health of the mother. IUGR may be a normal fetal response to oxygen or nutritional deprivation.

Therefore, the issue is not IUGR, but rather the ongoing risk of malnutrition or hypoxia. IUGR infants more frequently show multiple types of lesions in their placenta. The placenta is a dynamic organ which is unique in its development and function. The placenta mediates the intrauterine interaction between a mother and her baby, it is directly responsible for mediating and/or modulating the maternal environment necessary for normal fetal development.

The difference of mean age of cases and controls were not statistically significant in our study. The similar result was seen in other studies. N Thilagavathy Sharmila et al study reported that 80% of cases were between 21-30 years of age [13]. Suneeta Singh et al study reported that the mean age of patients in the case group was 26.6 yrs and in the control group 26.4 yrs [14]. Nayereh Ghomian et al study reported that the mean age of patients was in the case group 27.6 yrs and in the control group 27.5 yrs [15].

The mean gestational age at delivery in IUGR cases were lower in comparison to controls and it is statistically significant. The similar results were seen by Suneeta Singh et al were the mean gestational age at delivery in the IUGR group was 36.95 and in the control group 38.7 yrs [14]. Nayareh Ghomian et al study reported that the mean gestational age at delivery in the IUGR group was 37.7±1.9 yrs and in control group 39.1±1 yrs [15].

In our study the vaginal delivery rate was higher in control group and LSCS was higher in cases group. Gurdip Kaur et al study reported in the case group LSCS rate was 37% and in the control group 16% [16]. Rajarajeswari R et al study reported in the case group LSCS rate was 40% and the vaginal delivery rate was 60% [17]. Neha Muniyar et al study reported in the case group LSCS rate was 80% and the vaginal delivery rate was 20% [18].

In our study mean birth weight of babies in IUGR group was statistically significantly lower than the babies of the control group. The similar result were found by Nayereh Ghomian et al [15] and Maria Grazia Clemente et al [19].

In our study, the mean weight of the placenta in the IUGR group was less as compared to the control group and this difference was statistically significant ($p < 0.0001$). Nayereh Ghomian et al in their study found that the mean placental weight was in the case group 440±64.5 gm and in the control group 585.7± 149.4 gm [15]. In a study by Suneeta Singh et al the mean placental weight in IUGR cases was less as compared to the control group [14]. As per the study by Mauliket al the mean placental weight in the IUGR group was less as compared to the control group [20].

In our study the head circumference in IUGR group was significantly less in comparison to control group. In the study by Maria Grazia Clemente et al the mean head circumference in the IUGR group was less as compared to the control group [19].

In our study in IUGR group the HC/AC is significantly higher than the control group. This shows differential slowing of abdominal growth in comparison to head growth. Ann Quinton et al study reported that HC/AC ratio was the best predictor of IUGR and the HC/AC ratio was significantly higher for IUGR babies than for the appropriate for gestational age babies [21].

The present study shows increased placental calcification in IUGR group. In the study of Suneeta Singh et al calcification was found only in the IUGR group [14]. In the study of Hemlatha M et al calcification was found more in the IUGR group than in the control group [22].

So, the morphology and histopathology of the placenta may play an important role in assessing fetal wellbeing. A single uteroplacental or villous lesion does not result in IUGR rather it is more likely due to an accumulation of placental injury for a long period. The severity of placental abnormalities expressed as a cumulative number of placental lesions is a significant risk factor for IUGR.

The size of the placenta in the IUGR group was smaller than the control group. In the IUGR group, the placental weight and fetoplacental weight ratio were lower than in the control group. The neonatal HC/AC ratio was more in the IUGR group than in the controls. The intervillous fibrin deposition, infarction, thrombosis, perivillous fibrin deposition, and the syncytial knot were more in the IUGR group than controls.

Suneeta Singh et al reported higher placental infarction in the IUGR group as compared to normal pregnancy. Hemlatha M et al reported higher placental infarction and fibrinoid necrosis in IUGR pregnancy as compared to the control group [22]. Similarly, Nayereh Ghomian et al found calcification, and infarction more in the IUGR placenta as compared to normal [15]. In the study of N Thilagavathy et al infarction and syncytial knot were more in the IUGR placenta. In the study of S Kotgirwar et al perivillous fibrin deposition, placental calcification, syncytial knot and fibrinoid necrosis were higher in IUGR placenta as compared to normal pregnancy [23].

Conclusions

The abnormal gross pathological and histopathological changes like calcifications, infarction, perivillus fibrin deposit, fibrinoid necrosis and syncytial knot are seen in a statistically significant higher percentage in pregnancies with intrauterine growth restriction in comparison to normal pregnancies. So, the present study is to analyse the histomorphological changes in IUGR and normal placenta gives us insight into the pathophysiology of IUGR and that will guide us for further research to prevent or treat IUGR pregnancies.

Conflict of interest: None. **Disclaimer:** Nil.

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