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Original Article

Histopathological Changes in Placenta Associated with Intrauterine Growth Retardation (IUGR)

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Abstract:
Background: Intrauterine growth retardation (IUGR) is a term applied to a condition of poor growth of the fetus in utero. It is considered the most common cause of low birth weight and perinatal morbidity and mortality. The placenta shows functional and structural changes in IUGR. Histologic examination of the placentas from IUGR fetuses can supplement clinical knowledge of the causes of IUGR. The aim of this study was to identify the histopathological changes in placenta in IUGR. **Methods:** This is a descriptive cross sectional study which was carried out at the Department of Pathology, Dhaka Medical College, during the period of March, 2017 to February, 2019. Total 57 patients clinically diagnosed as term pregnancy with intrauterine growth retardation and delivered by Caesarean section were selected. **Results:** In this study 79% mothers had known co-morbidities. Significant histopathological changes were found (94.7%, $p<0.05$) in this study and the changes were perivillous fibrin (63.2%), syncitial knot (70.1%), fibrinoid necrosis (33.3%), infarct (33.3%), calcification (31.6%), chronic inflammation (19.3%), stromal fibrosis (17.5%), intervillous haemorrhage (10.5%), avascular villi (10.5%), acute inflammation (7%). The mean baby weight in hypertensive mothers were significantly lower than non-hypertensive mother ($p<0.05$). **Conclusion:** This study showed the histopathological changes in the placenta of IUGR newborn were syncitial knot, perivillous fibrin, fibrinoid necrosis, infarct, calcification, acute inflammation andchronic inflammation, stromal fibrosis, intervillous haemorrhage and avascular villi. These findings suggest that chronic ischemia and associated secondary changes probably lead to improper perfusion and IUGR.

Key words: Intrauterine growth retardation (IUGR), Placental changes

Introduction:
Intrauterine growth retardation (IUGR) is defined as having a weight at or below the 10th percentile for the expected birth weight at a given gestational age[1]. The prevalence of IUGR is reported to be 3-10% of live newborns in developed countries and 15-20% of newborns in developing countries[2].

Known causes of IUGR can be traced in up to 40% of cases, these are maternal diseases, fetal or placental factors and the remainder of IUGR cases is idiopathic in origin. The maternal diseases are hypertension, cardiac disease, pulmonary or renal disease, anemia and connective tissue disease. Among these maternal hypertension related diseases like preeclampsia, eclampsia and pregnancy induced hypertension are the most important factors of IUGR. Fetal factors include chromosomal abnormalities, ventral wall defect, genitourinary defects and intrauterine infection. Histologic examination of the placentas from IUGR fetuses can supplement clinical knowledge of the cause of IUGR[3,4].

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The placenta is the mirror of maternal and fetal status; it reflects the changes occur in IUGR due to maternal hypertension, anemia, diabetes etc. and it also reflects fetal causes like intrauterine infection. As placentas are rarely examined, there is a little knowledge regarding the benefits of routine placental examination based on pregnancy outcome and risk assessment for long term neurodevelopmental sequelae. The working group of College of American pathologist had laid some indications for the examination of placenta based on the patient care and risk management[5,6].

An impairment in the invasion of fetal trophoblastic cells into the maternal decidua has been hypothesized as a cause of placental insufficiency and this leads to IUGR[7,8].

The parameters we see by histological examination of placenta of pregnancies with IUGR include infarction, chronic villitis, chronic chorio-amnionitis, increase perivillous fibrin,increased syncytial knotting, avascular villi, excessive fibrinoid necrosis, acute atherosis in decidual vessels, stromal fibrosis, calcification and intervillous hemorrhage[9].

Though IUGR fetuses are more frequently associated with morphologically and histologically abnormal placentas, it could not be conclusively decided whether these abnormalities are responsible for the intrauterine growth restriction or not. The study of placental pathology can greatly contribute to a better understanding of a complex subject such as IUGR[10].

Methods:

This descriptive cross sectional study was carried out at the Department of Pathology, Dhaka Medical College, during the period of March, 2017 to February, 2019. Ethical issues were addressed accordingly. A total fifty seven cases who were clinically diagnosed as term pregnancy with intrauterine growth retardation and delivered by Caesarean section without induction of labor with the aim to minimize the potential effects of labor itself on placental histology[9]. Placentas were collected and fixed in formalin. After fixation and grossing, light microscopic examination was done with Haematoxylin and Eosin stain. Statistical analysis was done using SPSS-19.

Results:

A total of 57 placentas were collected from the patients clinically diagnosed as term pregnancy with intrauterine growth retardation and delivered by Caesarean section.

Regarding the co-morbidities, 79% mothers had co-morbidities (Figure 1).

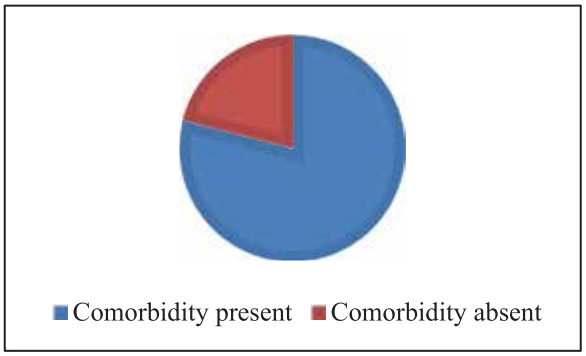


Figure 1: Distribution of the mother according to presence of co-morbidities (n=57).

The co-morbidities were eclampsia, preeclampsia, bronchial asthma, pregnancy induced hypertension, hypothyroidism, rheumatoid arthritis, Hb E disease, anemia and 21.1% cases were idiopathic. The common co-morbidities were eclampsia (29.8%) and preeclampsia (26.3%) (Figure 2). If hypertension related co-morbidity is considered (i.e. eclampsia, pre-eclampsia and pregnancy induced hypertension) it was the most common co-morbidity (63.15%).

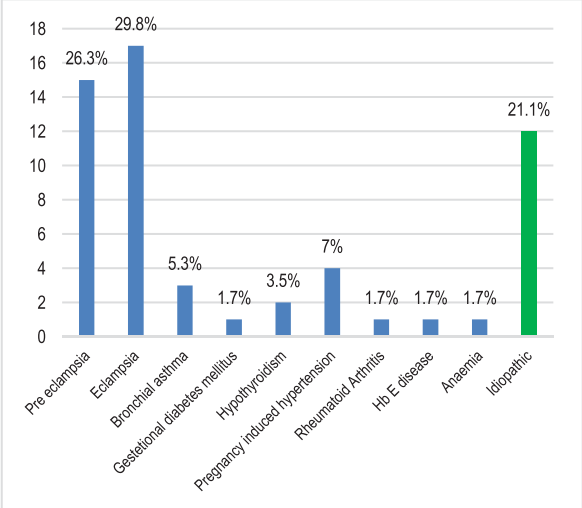


Figure 2: Co-morbidities found in the study population.

Table I explains birth weight of babies ranged between 1.4 kg to 2.5 kg with a mean 2.04±0.23 kg. They were divided into three weight groups. Maximum number of babies 29(50.9%) were in 2.0 to 2.5 kg. In the weight group between 1.5 - 2.0 kg were 25(43.9%) babies and in the weight group between 1.0 – 1.5 kg were 3(5.3%) babies.

Table I: Distribution of birth weight of the babies (n=57)

Weight in kg	Number of subject (%)
1.0 - 1.5	3(5.3)
1.5 – 2.0	25(43.9)
2.0 - 2.5	29(50.9)
Total	57(100)
Mean ± SD	2.04 ± 0.23
Range	1.4 – 2.5

SD=standard deviation.

The mean baby weight in hypertensive and non-hypertensive mothers was 1.99kg and 2.14 kg respectively. There was significant ($p<0.05$) difference in mean baby weight among the hypertensive and non-hypertensive mothers (Table II).

Table II: Distribution of the mean baby weight in hypertensive and non-hypertensive mothers (n=57)

	Mean baby weight(kg)
Hypertensive mother	1.99±0.22
Non Hypertensive mother	2.14±0.21
p value	<0.05[s]

s = Significance (when p value <0.05)
p value reached from t- test.

Among the study samples histopathological changes were found in 94.7% ($p<0.05$) (Figure 3). The histopathological changes found in this study were perivillous fibrin (63.2%), syncitial knot (70.1%), fibrinoid necrosis (33.3%), infarct (33.3%), calcification (31.6%), chronic inflammation (19.3%), stromal fibrosis (17.5%), intervillous haemorrhage (10.5%), avascular villi (10.5%) and acute inflammation (7%) (Figure 4).

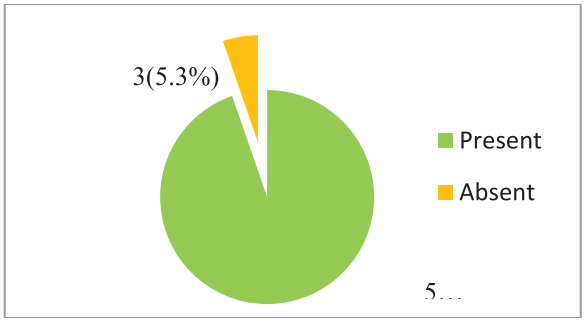


Figure 3: Distribution of the study samples by histopathological changes (n=57)

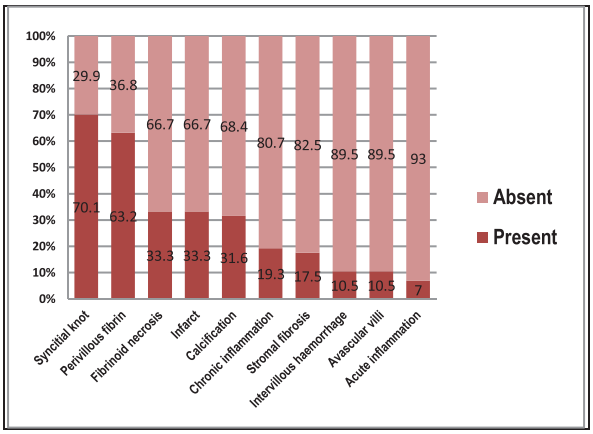


Figure 4: Bar diagram showing the histopathological changes found in the study samples

Regarding the birth weight of the babies, weight group between 1.0-1.5 kg, histopathological changes were found in 100% cases. Birth weight of babies between 1.5-2.0 kg, 96% placentas showed histopathological changes and 93% placentas in weight group between 2.0-2.5 kg (Table III).

Table III: Distribution of the histopathological changes according to birth weight of babies (n=57).

Birth weight of babies (kg)	Histopathological changes	
	Present n (%)	Absent n (%)
1.0 – 1.5	3(100)	0
1.5 – 2.0	24(96)	1(4)
2.0 – 2.5	27(93)	2(7)

Histopathological changes were found in all cases of preeclampsia, bronchial asthma, GDM, hypothyroidism, Hb E disease and anemia. All

the idiopathic cases also had microscopic changes (Table IV).

Table IV: Distribution of the study subjects according to co-morbidity of mother and histopathological changes (n=57)

Comorbidity	Histopathologic changes		
	Total	Present	Absent
Preeclampsia	15	15(100)	0
Eclampsia	17	16(94.1)	1(5.9)
Bronchial asthma	3	3(100)	0
GDM	1	1(100)	0
Hypothyroidism	2	2(100)	0
PIH	4	3(75)	1(25)
RA	1	0	1(100)
Hb E disease	1	1(100)	0
Anemia	1	1(100)	0
Idiopathic	12	12(100)	0
Total	57	54(94.7)	3(5.3)

GDM=Gestational diabetes mellitus
PIH=Pregnancy induced hypertension
RA=Rheumatoid arthritis

Discussion:

Intrauterine growth retardation (IUGR) is related to a variety of clinicopathological factors including maternal, uterine and fetal factors. Many recent studies provide good evidence for the occurrence of distinctive structural and histological abnormalities in the placentas complicated by IUGR[11,12].

In the current study 79% mothers had co-morbidities. The co-morbidities were eclampsia (29.8%), preeclampsia (26.3%), bronchial asthma (5.3%), pregnancy induced hypertension(7%), hypothyroidism (3.5%), rheumatoid arthritis (1.7%), Hb E disease (1.7%), anemia (1.7%) and 21.1% cases were idiopathic. In another study revealed the following co-morbidity were PET & eclampsia (18%), hypertension (16%), anemia (14%), antepartum haemorrhage (6%), urinary tract infection (2%) and idiopathic (34%)[13]. In another study by Gupta and Khajuria[14] found two major co-morbidities i.e. PIH (37%) and anemia (40%). In their study 20% cases were idiopathic.

This study revealed mean weight of baby was 2.04±0.23 kg ranged between 1.4 to 2.5 kg. Among them 29(50.9%) babies had their weight between 2.0 to 2.5 kg. Other study revealed similar findings[15].

In this study most common co-morbidity was related to hypertension (63.15%). The mean baby weight in hypertensive and non-hypertensive mothers were 1.99 kg and 2.14kg respectively. There was significant ($p<0.05$) difference in mean baby weight among the hypertensive and non-hypertensive mothers. Other study found the mean baby weight 1.8±.43kg in hypertensive mothers were significantly lower than non-hypertensive mother where the mean baby weight 2.17±.38kg respectively ($p<0.05$)[16].

Among the study samples significant histopathological changes were found in 94.7% of cases. Oliveira, Xavier and Lana[10] found at least one histopathological change was present in 95% of the cases which is almost same to this study.The histopathological changes found in this study were syncitial knot (70.1%), perivillous fibrin (63.2%), fibrinoid necrosis (33.3%), infarct (33.3%), calcification (31.6%), chronic inflammation (19.3%), stromal fibrosis (17.5%), intervillous haemorrhage (10.5%), avascular villi (10.5%) and acute inflammation (7%). Singh, Pemmaraju and Nema[15] found placental infarction in 63.33%, calcification in 46.66%, perivillous fibrin in 86.66% and intervillous haemorrhage in 83.33% cases. İskender-Mazmanet al[17] revealed infarct in 33%, perivillous fibrin in 16%, calcification in 8%, acute inflammation in 12.5% cases. The study of Veena et al[13] showed increased syncitial knot in 90%, infarction in 58%, fibrinoid necrosis in 30%, inflammatory cells in villi in 26% and perivillous fibrin deposition in 20% cases. The findings of these studies are similar to this present study.

Mardi and Negi[18] found several major histologic changes in IUGR placentas. These changes include intervillous fibrin deposition (64% cases), increased syncytial knot-ting (64% cases), stromal fibrosis (56% cases), cytotrophoblastic hyperplasia (44% cases) and basement membrane thickening (40% cases). In addition, hypovascular villi and infraction were present in 32% and 28% of placentas of IUGR pregnancies.

Regarding the birth weight of the babies, this study showed histopathological changes were present in 100% cases among the babies with

birth weight between 1.0-1.5 kg, 96% cases between 1.5-2.0kg and 93% cases between 2.0-2.5 kg. Mardi and Negi[18] showed more the microscopic changes in placenta of babies with less birth weight.

In this study out of 57 cases histopathological changes were found in 54(94.7%) cases. Histopathological changes were found in all cases of preeclampsia, bronchial asthma, GDM, hypothyroidism, Hb E disease and anemia. All the idiopathic cases also had histopathological changes. The study of Sheela et al[19] had found similar findings.

Conclusion:

This study showed the histopathological changes in the placenta of IUGR newborn were syncitial knot, perivillous fibrin, fibrinoid necrosis, infarct, calcification, acute inflammation andchronic inflammation, stromal fibrosis, intervillous haemorrhage and avascular villi. These findings suggest that chronic ischemia and associated secondary changes probably lead to improper perfusion and IUGR. Therefore, all pregnancies diagnosed with IUGR antenatally must be suspected or ruled out for etiology of placental changes unless proved otherwise. Such IUGR fetuses must be considered at risk for poor placental circulation and hypoxia along with compromised nutrition. The histopathological findings of a placenta are more objective and seem to offer a good way to get proper information about IUGR.

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