

**PLACENTAL PATHOLOGY IN INTRA UTERINE GROWTH RETARDATION**P. Vijaya Sheela<sup>1</sup>, M. Sridevi<sup>2</sup>, R. Sujatha<sup>3</sup>, V. Saroja<sup>4</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT: INTRODUCTION:** The placental development is an essential step in developing effective strategies or the prediction of various maternal and fetal medical and developmental problems. Oxygen transfer and nutrients to the fetus will be actively regulated by the placenta. **AIM AND OBJECTIVE:** To study morphological changes of placenta in Intrauterine growth Retardation and to correlate morphological changes of placenta with fetal outcome. **MATERIALS AND METHODS:** Placental tissue samples were obtained from 50 pregnancies complicated by IUGR and 50 normal uncomplicated pregnancies with gestational age between 28 to 42 weeks attending King George hospital Visakhapatnam. **INCLUSIVE CRITERIA:** An IUGR fetuses whose estimated fetal weight less than those in 10<sup>th</sup> percentile are included in the study. Birth weight percentiles were determined by previously published normal curves. **EXCLUSIVE CRITERIA:** fetuses with known syndromes, chromosomal anomalies and twins. For all patients included in the data set gestational age was estimated from the last menstrual period or early ultra-sonogram before the 12<sup>th</sup> week of gestation. The final data set was composed of 50 pregnancies complicated by IUGR and APGAR scores. Because preeclampsia is an important maternal factor associated with IUGR, these cases were further divided into two subgroups according to presence of hypertension. Samples were taken both from vaginal deliveries and caesarean sections. All the placentas were examined by pathologists. The placentas were weighed. For each case one or two samples from the umbilical cords, extra placental membrane, and parenchyma were taken. Gross pathological findings were confirmed by histology. Histological data included are ischemic necrosis, decidual vascularity, acute chorioamnionitis, fibrinoid necrosis and choriangiomas. Appropriate statistical parameters were used. Chi-square test was conducted to compare placental pathological changes between case and control groups. **RESULTS:** In current study, 60% of the cases are with IUGR due to Hypertensive disorders and 40% are normotensives and 50 women with appropriate for gestational age in control group. Hypertensive IUGR cases were delivered at preterm than appropriate for gestational age and normotensive IUGR group. The birth weights are lower in hypertensive group compared to those of AGA and normotensive group [Pvalue 0.9] Most of the cases with IUGR are primi gravida. The fetal outcome in women with appropriate for gestational age is good whereas with IUGR the fetal outcome is poor. Incidence of intrauterine deaths, stillbirths, perinatal deaths and babies with low apgar are more in hypertensive group when compared normotensive IUGR group [p value 0.8]. 40% of the babies with hypertensive IUGR were delivered by caesarean operation [p value 0.147]. Mean placental weights were lower in IUGR group when compared to AGA group. But no significant change in thickness of placenta. Incidence of placental infarction and retroplacental haematoma was more in IUGR group when compared to AGA group [p value 0.2] Out of 19 cases of bad perinatal outcome 10 cases had feature of ischemic necrosis (pvalue-0.005) and placental infarcts (p value 0.0001) had significantly associated with bad perinatal outcome **CONCLUSION:** the abnormal uteroplacental vasculature, chronic uteroplacental insufficiency coagulation pathology in uteroplacental, intervillous and fetoplacental vasculature and

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chronic inflammatory lesions may be primary disease process related to the placental pathology of IUGR. Although the cause of IUGR in pregnancies is heterogenous, careful clinico-pathological correlations in individual cases are necessary for interpretation of placental lesions of IUGR.

**KEYWORDS:** intra uterine growth restriction, ischemic necrosis of placenta, chronic placental insufficiency, infarcts, fibrinoid necrosis.

**INTRODUCTION:** The development of placenta is an essential step in developing effective strategies or the prediction of various maternal and fetal medical and developmental problems and possible treatment of growth restricted fetus. Oxygen transfer and nutrients to the fetus will be actively regulated by the placenta. Particularly aminoacids which are precursor for protein synthesis from the maternal circulation into the placenta in the microvillous membrane and basement membrane. Depending upon the ultrasound measurements of HC and AC ratio IUGR is classified as asymmetrical (proportionally small) and symmetrical<sup>1</sup> (disproportionally lagging abdominal girth). About 3-10 percent of infants are growth restricted.<sup>2</sup> Another classification small for gestational age infants as those whose weights were below the 10<sup>th</sup> percentile for their gestational age.<sup>3</sup> Fetal growth restriction is associated with substantial perinatal mortality and morbidity, fetal demise, birth asphyxia, meconium aspiration, neonatal hypoglycaemia, and hypothermia. Postnatal growth and development of growth restricted fetus depends on the cause of restriction, nutrition in infancy and social environment. Infants with growth restriction due to congenital, viral, chromosomal or maternal constitutional factors remain small throughout life. But those infants with intrauterine growth restriction due to placental insufficiency will often have catch up growth after birth. In general any disease complicated by severe maternal hypoxia is likely to lead to intrauterine growth restriction usually due to defective uteroplacental circulation. Eg: Heart disease, Respiratory diseases, chronic renal diseases, endocrinal diseases, connective tissue diseases etc.

**AIM AND OBJECTIVE:** To study morphological changes of placenta in Intrauterine growth. Restriction and to correlate morphological changes of placenta with fetal outcome.

**MATERIALS AND METHODS:** Placental tissue samples were obtained from 50 pregnancies complicated by intra uterine growth restriction and 50 normal uncomplicated pregnancies with gestational age between 28 to 42 weeks attending King George hospital Visakhapatnam. Inclusive criteria: An IUGR fetuses whose estimated fetal weight less than those in 10<sup>th</sup> percentile are included in the study. Birth weight percentiles were determined by previously published normal curves. Exclusive criteria: fetuses with known syndromes, chromosomal anomalies and twins. For all patients included in the data gestational age was estimated from the last menstrual period or early ultrasound before the 12<sup>th</sup> weeks gestation. The final data was composed of 50 pregnancies complicated by IUGR and APGAR scores. Because preeclampsia is an important maternal factor associated with IUGR, these cases were further divided into two subgroups according to presence of hypertension. Samples were taken both from vaginal deliveries and caesarean sections. All the placentas were examined by pathologists. The placentas were weighed. For each case one or two samples from umbilical cords, extra placental membranes and parenchyma were taken. Gross pathologic findings were confirmed by histology. Histological data included are ischemic necrosis, decidual vasculopathy, acute chorioamnionitis, fibrinoid necrosis and choriangiomas. Appropriate

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statistical parameters were used. Chi-square test was conducted to compare placental pathological changes between case and control groups.

**RESULTS:** In current study, 60% of the cases are with IUGR due to Hypertensive disorders and 40% cases are normotensives among total 50 cases where as 50 women with appropriate with gestational age in control group. Mean ages of the mothers are not significantly different in both groups.

Appropriate for GA	50
IUGR with Hypertension	30
IUGR without Hypertension	20

**Table 1: Distribution of cases and controls**

	Term	Preterm	Total
AGA	40 (80%)	10 (20%)	50 (100%)
Hypertensive	13 (26%)	17 (34%)	30 (60%)
Normotensive	15 (30%)	5 (10%)	20 (40%)

**Table 2: Distribution of the cases and controls according to gestational age at presentation**

Most of the IUGR cases both hypertensive and normotensive associated with primi gravida. Hypertensive IUGR cases were relatively delivered earlier than appropriate for gestational age and normotensive IUGR group. The birth weights are lower in the hypertensive group compared to those of AGA and normotensive group [Pvalue 0.9]. The fetal outcome in women with appropriate for gestational age is good whereas with IUGR the fetal outcome is poor. Incidence of intrauterine deaths, stillbirths, perinatal deaths and babies with low apgar are more in hypertensive group when compared normotensive IUGR group [p value0.8].

	IUD	Stillborn	Low APGAR	Perinatal death
AGA	---	---	---	---
Hypertensive	5 (10%)	2 (4%)	3 (6%)	3 (6%)
Normotensive	---	4 (8%)	2 (4%)	---

**Table 3: Distribution of cases and controls according to fetal out come**

Weight	AGA	Normotensive	Hypertensiv
Mean placental	475G	307G	304G

**Table 4: Distribution of the cases and controls according to the mean placental weight**

40% of the babies with hypertensive IUGR delivered by caesarean operation. (p value 0.147). Mean placental weights were lower in IUGR group when compared to AGA group. But the thickness of placenta is not varied significantly. Incidence of placental infarction was more in IUGR group when compared to AGA group (p value 0. 2).

Incidence of retroplacental hematoma was higher in IUGR group.

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Out of 19 cases of bad perinatal outcome 10 cases had the common feature of ischemic necrosis (p-value 0. 005) and placental infarcts (p value 0. 0001) had significantly associated with bad perinatal outcome.

	AGA	Normotensives	Hypertensive	P. value
Ischemic necrosis	2 (4%)	5 (10%)	15 (30%)	<0. 05
Inflammatory cells	7 (14%)	7 (14%)	9 (18%)	>0. 05
Fibrosed villi	6 (12%)	12 (24%)	18 (36%)	>0. 05
Syncitial knots	7 (14%)	7 (14%)	7 (14%)	>0. 05
Fibrinoid necrosis	6 (12%)	4 (8%)	4 (8%)	>0. 05

**Table 5: Distribution of the cases and according to histopathological features of placenta**

	Ischemic necrosis	Placental infarcts	Inflammatory cells	Fibrosed villi	Syncitial knots
Still births	4 (4%)	1 (1%)	1 (1%)	---	---
IUD	2 (2%)	3 (3%)	4 (4%)	1 (1%)	1 (1%)
Perinatal deaths	3 (3%)	2 (2%)	---	3 (3%)	---
Low APGAR	1 (1%)	---	2 (2%)	1 (1%)	2 (2%)

**Table 6: Correlation between placental pathology and fetal outcome**

**DISCUSSION:** IUGR is related to a variety of clinic-pathologic factors including maternal, uterine and fetal factors. Although some studies showed that there are no consistent histological abnormalities in placentas of IUGR pregnancies, recent studies provide evidence for occurrence of distinctive structural and histological abnormalities in the placentas complicated by IUGR.

The current study demonstrate several different placental histopathologic lesions in IUGR-related placenta. Average placental weights were 307gms, 304 and 475gms in the normotensive, hypertensive IUGR and AGA groups respectively (P=0. 000). Maulik et al (2006) found placental weights were 631g in control group and 409 g in the IUGR group with the differences being statistically significant.<sup>4</sup>

Macara et al worked on the structural analysis of placental terminal villi from growth restricted pregnancies with umbilical artery wave forms. They found that the terminal villi from IUGR cases are smaller in diameter than the controls and had increased syncitial nuclei, reduced cytotrophoblastic nuclei, thickened basal lamina, and increased stromal deposition of collagen and laminins. In the current study, the observed findings of the placental lesions are ischemic necrosis, increased syncitial knots, inflammatory cell collections, excessive fibrinoid necrosis, placental infarcts. Since there are certain overt maternal factors that may lead to inadequate fetal growth placental lesions of IUGR group are examined according to the presence or absence of maternal hypertension. In the hypertensive IUGR group, the observed histo pathological findings were similar to those previous studies on preeclampsia. Uteroplacental vascular insufficiency may compromise placental growth, and it may lead to infarct. The overall incidences of infarction increased in IUGR

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group. Similar incidences were observed in study 16% in IUGR group and only 2% in AGA group. In our study incidence of fibrosed villi is more in normotensive group and incidence of ischemic necrosis is more in hypertensive IUGR.

In studies conducted by Benischke, Faye Petersen, Maulik and Salafia et al circumvallate placenta, circummarginate, velamentous insertion of the cord and placenta previa were suggested as possible causes of IUGR.<sup>5</sup> In their study, these types of placenta were not found in cases. It is recommended that types of placental shapes be studied based on etiology of IUGR.

In a study by Sharma and Mardi (2003) placental infarction on macroscopic and microscopic surfaces as well as ischemic necrosis was higher in the IUGR placenta compared to those normal.<sup>6</sup> Curtin (2007) compared IUGR and normal placenta. He found an association between the vascular reduction of fetoplacental unit and loss of functional placental tissue with the lesions like macroscopic and microscopic infarction, thickness of placental membranes, avascular villi and tissue ischemia which are significant.<sup>7</sup> The infarctions are associated with IUGR, miscarriage, preterm labor and intrauterine fetal death. Pathophysiological mechanisms appear to be caused by maternal platelet aggregation and placental thrombosis.<sup>8,9</sup> Sometimes it recurs in next pregnancy may be associated with maternal thrombophilia

Intervillous fibrinoid deposition of less than 5% was observed more frequently in the control group. But intervillous fibrinoid deposition of more than 10% seen in study group. Therefore, high amount of intervillous fibrinoid deposition is a pathological finding in IUGR-related placenta<sup>6</sup> confirms our study (James High risk pregnancy).

In another study suggested the association between chronic villitis and growth restriction.<sup>10</sup> In the present study incidence of chronic villitis was 14% in AGA group and 32% in IUGR group. In the present study, the placentas were significantly smaller in IUGR group than AGA group. Our subject of interest was ischemic placental disease which consists of maternal disease -preeclampsia, fetal disease consists of IUGR, placental disease-abruption or combination of the three. Maternal disease is confirmed by the presence of accelerated villous maturation or infarct. Fetal disease is confirmed by extensive avascular villi, obliterative endarteritis, hemorrhagic endovasculitis vascular thrombi. The present study unable to identify these features because of small sample size. Extensive studies are needed in this aspect and it would be very much clinically helpful as the disease process tend to recur in pregnancies.

Similar studies Danburry hospital Connecticut, they examined 128 placentas from IUGR cases, 179 from AGA as controls they found that there was higher frequency of IUGR cases when there is prior h/o IUGR, one or more lesions were found in 71 out of 128 cases In IUGR cases, 53% had chronic villitis, 63% had infarcts, 59% vasculitis. And also they found that decreased birth weight was associated with infarct.<sup>11</sup>

Mardik, Sharma j Indira Gandhi Medical Hospital, SHIMLA they found that infarction fibrosed villi are more in IUGR cases. American Pediatric Society 1996 concluded lesions causing placental insufficiency are more common in IUGR, infarction 44%, inflammatory lesions 26%, vasculitis 8%, vascular thrombosis 14%.

Study was carried out at military hospital Rawalpindi from Jan 2002 to June 2002. Ten placenta of normal and 30 placentae of known IUGR cases were used in this cross sectional comparative study. Concluded terminal villi, syncytial knots and capillaries of the IUGR cases were more in the central region as compared to n the peripheral region. The quantitative difference

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between syncytial knots and capillaries in IUGR and control group were statistically significant ( $p < 0.05$ ).

**CONCLUSION:** that abnormal uteroplacental vasculature and chronic uteroplacental insufficiency, coagulation related pathology in the uteroplacental, intervillous and fetoplacental vasculature and chronic inflammatory lesions may be primary disease processes related to the placental pathology of IUGR. Although the cause of IUGR pregnancies is heterogenous, careful clinicopathological correlations in individual cases are necessary in the interpretation of placental lesions of IUGR.

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**AUTHORS:**

1. P. Vijaya Sheela
2. M. Sridevi
3. R. Sujatha
4. V. Saroja

**PARTICULARS OF CONTRIBUTORS:**

1. Assistant Professor, Department of Obstetrics & Gynaecology, King George Hospital, Andhra Medical College, Visakhapatnam, Andhra Pradesh.
2. Assistant Professor, Department of Obstetrics & Gynaecology, King George Hospital, Andhra Medical College, Visakhapatnam, Andhra Pradesh.

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3. Assistant Professor, Department of Obstetrics & Gynaecology, King George Hospital, Andhra Medical College, Visakhapatnam, Andhra Pradesh.
4. Senior Resident, Department of Obstetrics & Gynaecology, King George Hospital, Andhra Medical College, Visakhapatnam, Andhra Pradesh.

**NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:**

Dr. P. Vijaya Sheela,  
Door No. 18-238, Plot No. 30,  
Adarsh Nagar Colony, HB Colony,  
Visakhapatnam-530022,  
Andhra Pradesh, India.  
E-mail: pvsheela195@gmail.com

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