www.ThePharmaJournal.com

The Pharma Innovation

**ISSN: 2277- 7695**
TPI 2015; 4(7): 149-153

www.thepharmajournal.com
Received: 13-07-2015
Accepted: 18-08-2015

**Dr. SR Upadhye**
Department of Pathology KIMS, Karad, Maharashtra, India

**Dr. Dhirjkumar B Shukla**
Department of Pathology KIMS, Karad, Maharashtra, India

**Correspondence:**
**Dr. SR Upadhye**
Department of Pathology KIMS, Karad, Maharashtra, India

# Histopathological examination of placenta in second and third trimester of pregnancy in various clinical settings

**Dr. SR Upadhye and Dr. Dhirjkumar B Shukla**

**Abstract**
**Material and method:** 144 cases were obtained in a hospital based prospective study within a period of 2 years from May 2009 to April 2011 for descriptive and cross-sectional study. In 81.25% of cases the age group was 21-30 years, majority (73.6%) of cases were in the third trimester of pregnancy.
**Results:** Fetal disorders formed the major (48.6%) clinical presentation followed by maternal (39.6%) and placental disorders (11.8%). Overlapping of clinical features was observed. Fetal disorders included prematurity (43%), IUD (35.3%), fetal distress (12.4%), IUGR (11.7%), twin pregnancy (6.9%), and erythroblastosis fetalis (0.7%). There were 17 cases of disorders of placental disc and umbilical cord, which included abnormal cord insertion (35.3%), cord twists (23.6%), single umbilical artery (17.6%), placenta accreta and succenturate lobe (17.6%) and chorangioma (5.9%).Overall histopathological diagnoses included uteroplacental insufficiency (55.6%), chorioamnionitis and villitis (33.3%), chorangiosis (13.8%), lesions of cord (9%), amnion nodosum (2.8%), lesions of placental disc (2.8%) and erythroblastosis fetalis (0.7%). Overlapping of one or more features was observed.
**Conclusion:** Placental examination assists in timely management of mother and fetus. Diagnosis of placental lesions helps to improve the outcome of pregnancy. Hence placental pathology should be a routine component of obstetric and neonatal care.

**Keywords:** Chorioamnionitis and villitis, Erythroblastosis fetalis, Placenta

## Introduction
The placenta is a unique gestational organ which functions as the fount upon which the developing fetus derives its nutritional substance and obtains its metabolic and immunological requirements. Its strategic location at the fetomaternal interface provides a record of pregnancy in which the cumulative effects of pregnancy-related events and changes reflecting the intrauterine environment can be scrutinized in what is effectively a whole organ biopsy [1].
There are many instances in which information gained from placental evaluation will assist in the timely management of individual patients and may prove exceedingly valuable to the infant and mother. It helps to improve the pregnancies as in cases of repeated abortions [2]. As placental examination is a simple and noninvasive method which plays an important role in predicting and improving the outcome of pregnancy, we planned to do the histopathological study of placenta in 2nd and 3rd trimester of pregnancy in various clinical settings and to correlate the findings with relevant investigations and clinical information.

## Materials and Method
The present study is a two year hospital based prospective study of histopathological examination of placenta in 2nd and 3rd trimester pregnancy during a period of May 2009 to April 2011, which includes 144 cases. The study is a descriptive and cross-sectional, which is done in K.I.M.S. Karad having a tertiary care hospital. All the placentas received in our department in 2nd and 3rd trimester of pregnancy with various clinical settings like pregnancy induced hypertension (PIH), antepartum hemorrhage, intra uterine growth retardation (IUGR), intra uterine death (IUD), premature, post mature delivery, abortion, twin pregnancy, diabetes, maternal infections, hydramnios, oligohydramnios, fetal infections. The cases were from our hospital as well as from the outside hospital of the periphery were included except Placentas in first trimester of pregnancy and showing autolytic changes

### Collection of placentas
Placentas with attached membrane and umbilical cord were submitted to the pathology

department for examination, soon after delivery with requisition containing detailed clinical information. After receiving the specimen it was washed in running tap water, weighed and cut into vertical segments of 1-2 cms thickness from maternal to fetal surface to ensure proper fixation and then it was fixed in adequate volume of 10% formalin for 1 week [4]. The placentas were transferred in large, flat containers to maintain the placental shape.

**Methods of examination and sampling**

The placentas were examined for abnormal colour and configuration. The gross examination of the placenta was done with careful review of the umbilical cord, placental membranes, fetal and maternal surfaces, and villous tissue [3]. All significant changes and lesions were described and measured, and their locations within the placenta were noted. Estimate of the percentage of villous tissue or surface involved was made. The fetal membranes were placed in their usual anatomic position (maternal side outward), and a brief assessment of the membranes, cord, and fetal and maternal surfaces was made.

Examination of the umbilical cord with measurement of its length and diameter was done. Alterations in the diameter of the cord may reflect edema, vascular abnormalities, or a lack of Wharton's jelly. The site of the cord insertion in the placental disc was noted; whether centrally or eccentrically, at the margin, or in the membranes (velamentous). The length and intactness of any velamentous vessels in the membranes was evaluated and noted. Aberrations such as excessive twisting or strictures identified and noted. The presence and tightness of true cord knots noted. The number of umbilical vessels is ascertained in the cord at least 3 to 5 cm above the chorionic plate, as the two arteries may fuse near the insertion. At least two sections of the umbilical cord were taken, one near the placental end and one closer to the fetus [3].

The extra placental membrane inspected for colour, opacity and mode of attachment to the placenta which can be at the margin, circummarginate, or circumvallate. The preparation of the peripheral membranes for histologic sectioning was done via a membrane roll. The fetal surface was inspected for color, opacity, subchorionic fibrin and the presence of lesions such as cysts, large subchorionic hematomas and amnion nodosum. The vessels of the chorionic surface were examined for thrombi and calcification. The maternal surface was inspected for intactness and the presence of hematomas and/or depressions. The cut slices were examined for the presence of focal lesions such as infarcts, thrombi, hemorrhages and excessive fibrin [5].

Sections of the villous parenchyma were taken to include the full thickness of the placenta, extending from the fetal to the maternal surface, including both amnion and decidua. These sections were from the central region, rather than from the margin, which is often non representative. Small lesions were individually measured and described. When such processes were extensive or multifocal, an estimate of the percentage of placental involvement was made. If no focal lesions are present, a minimum of three such sections were taken from different locations of normal-appearing villous tissue If focal lesions (e.g., large infarcts, hematomas) are present, sections of these with a margin of adjoining uninvolved placenta were taken in addition.

Examination of placentas of multiple gestations included a ―T‖ section from dividing membrane for chorionicity and studies for vascular anastomoses. The number of discs and the character of their dividing membranes were identified to establish chorionicity [2].

**Histopathological processing**

The bits taken were subjected to routine processing. The paraffin embedded tissue blocks were cut at 4-6 micron thickness and de-paraffinised sections were stained with H and E stain. Special stains like gram stain, Periodic Acid Schiff (PAS) stains were done whenever necessary.

**Results and Discussion**

Total 144 cases were obtained within a period of 2 years from May 2009 to April 2011, in a hospital based prospective and cross-sectional study. 81.25% cases were between 21 to 30 years of age group which is most common reproductive period. Most of the cases (73.63%) were in 3rd trimester of pregnancy. Overlapping of the clinical and microscopic features was seen in most of the cases. Fetal disorders contributed the major clinical presentation (48.6%) followed by maternal disorders (39.6%) and placental disorders (11.8%). Fetal disorders were prematurity (43%), intrauterine death (IUD) (35.3%), fetal distress (12.4%), intrauterine growth retardation (IUGR) (11.7%), twin (6.9%) and erythroblastosis fetalis (0.7%).Maternal disorders included pregnancy induced hypertension (19.4%), anaemia (9.5%), polyhydramnios (4.2%), oligohydramnios (3.5%) and premature rupture of membranes (2.4%).

Placental disorders were abnormal cord insertion (35.3%), umbilical cord twist (23.6%), single umbilical artery (17.6%), placenta accreta and succenturate lobe (17.6%) and chorangioma (5.9%). Same indications are quoted in various studies [2].

**Histopathological diagnosis of placental lesions**

With overlapping of the diagnosis, most frequent histopathological diagnosis was, uteroplacental insufficiency in 55.6%, followed by chorioamnionitis and villitis in 33.3%, chorangiosis in (13.8%), lesions of cord in 9%, amnion nodosum and lesions of placental disc 2.8% each and erythroblastosis fetalis 0.7%. Though study of overall lesions of placenta in different clinical situations as a whole has not been carried out, we compared the frequency with individual studies wherever possible.

**Uteroplacental insufficiency**

Total 55.6% showed uteroplacental insufficiency, out of which 27.5% presented as PIH, 16.2% with IUD, 15% as prematurity, 12.5% as IUGR, IUD with PIH 11.2%, 7.5% with twin gestation, 7.5% with umbilical cord pathology, and 1.3% each of PROM and oligohydramnios. Amongst these, there were 8 cases of anaemia showing overlapping of clinical presentation. Weight of placenta was lower than expected in 37% cases, as quoted in literature by Sheppard and Bonnar [6].

**Chorioamnionitis and Villitis**

Fourty eight cases (33%) revealed chorioamnionitis (Fig.1A) and villitis which matches with the finding as quoted by Kraus FT, and colleagues [7]. Choriomnionitis and villitis was seen in 71% cases which revealed high morbidity and mortality (71%) in the form of IUD, still birth (SB), IUGR and fetal distress.18.7% cases had history of repeated abortion, which reflects infections as direct cause. One case was positive for TORCH titre having history of previous abortion and microscopy (Fig.1B) revealed features of chronic villitis.

Detailed microbiological study was advised but could not be carried out as mothers were already discharged.

**Fig 1:** A) Gross photograph of thick whitish membranes in chorioamnionitis;
B) Photomicrograph showing acute chorioamnionitis (H&E stain: 100x)

**Chorangiosis**

Chorangiosis was seen in 20 cases (13.9%). Cases of chorangiosis were associated with overlapping of clinical features like IUD, IUGR, PIH, still birth, prematurity, twin pregnancy and oligohydramnios. Full term and preterm deliveries were 10 (50%) cases, though in literature it is mainly associated after 32 weeks of gestation. Weight of placenta was more than expected in 7 (35%). Four cases (20%) cases were twin pregnancies and 3 (15%) cases of PIH, which suggests hypoxia.

**Pregnancy induced hypertension**

Present study included 28 (19.4%) cases of PIH. They were classified into two subgroups as mild and severe PIH. Out of 28 cases, 11 (39%) patients were of mild PIH and 17 (60%) cases revealed severe PIH. Placentas are smaller in PIH, large multifocal infarcts 12 (42.85%) cases being commonest pathology, followed by retroplacental clot – 8 (28.5%) cases, abruption 6 (21.42%) cases and calcification 2 (7%) cases. Infarcts were seen at the base and edge and were extensive. Infarcts were seen in 10 cases (58.8%) of severe PIH and 2 cases (18.2%) of mild PIH.

Amongst severe PIH cases, 13 placentas (76.4%) showed low placental weight, while in mild PIH only 2 cases (18.2%) showed low placental weight for expected gestational age. It revealed that low placental weight was significantly associated with PIH (Chi-square=6.930 and P value 0.08).

Uteroplacental insufficiency (UPI) contributed the major pathological diagnosis in 78.6% cases as documented in literature [8].

**Anaemia**

There were 14 (9.7%) cases of anaemia. 7 (50%) cases presented with preterm deliveries. 42.8% placentas revealed low placental weight. It revealed that low placental weight was significantly associated with anaemia (Chi-square= 3.871 and P value 0.04).While 64.3% of babies showed low birth weight. Microscopic changes reflect the uteroplacental insufficiency and infections.

**Oligohydramnios**

We observed total 5 cases (3.5%) of oligohydramnios, of which 2 (40%) cases were intrauterine death and 1 (20%) case each of intrauterine growth retardation, still birth and fetal distress. Premature rupture of membrane was seen in 3 cases (60%). One case presented with renal cystic disease and 1 case with twin transfusion syndrome. All these features correlate with the studies done by Shenker Land colleagues [9]. In 3 cases (60%), gross findings were thick, opaque, whitish membranes. Microscopy revealed amnion nodosum in 4 cases (80%), chorioamnionitis all 5 cases (100%). These findings correlate with the authers Joshi V31, Shenker L and collegues [9].

**Polyhydramnios**

There were 6 cases of (4.17%) polyhydramnios. Clinical presentation was intrauterine death in 2 cases (33.34%), 1 case each of twin transfusion syndrome, anencephaly, still birth and chorangioma. Weight of placenta was higher than expected in 3 cases (50%). The cause was obvious in twin transfusion syndrome anencephaly and chorangioma as documented by Joshi V [8]

**Premature rupture of membranes**

We obtained 4 cases (2.7%) of PROM, out of which 3 cases (75%) were associated with chorioamnionitis. The association documented by Salafia CM *et al.* [10]

**Prematurity**

There were 62 (43%) cases of prematurity and remaining 82 (57%) were term deliveries. There was no case of post maturity observed in our study. The weight of placenta in 36 cases (58%) of the preterm deliveries were less than expected. Out of the total preterm cases, IUD (50%) and PIH (30.6%) were most common clinical diagnoses other clinical diagnoses were multiple gestation, still birth, fetal distress, IUGR, retained placenta and PROM. Similar clinical presentation was observed by Minesh Khashu *et al.* [11] in our study 19 cases (30.64%) were PIH, which is comparable with the literature.

Microscopically chorioamnionitis was observed in 14 cases (22.6%) cases in present study which correlates well with study done by Hameed C. *et al.* (1984) 95, who observed 15% cases of chorioamnionitis. D. Ogunyemi [12] found chorioamnionitis in 45% in preterm labour.

**Intrauterine death**

Total 51 cases (35.4%) cases were presented with intrauterine death. Majority of cases- 31 (60.7%) were preterm, while 20 cases (39.3%) were full term. Most of the cases (55%) presented with abdominal pain or loss of fetal movements.

Bad obstetric history was seen in 6 (11.7%) cases, similar to Mphahlele M in his study of 75 cases found incidence to be 14.6%. 97 Five cases (9.8%) of IUD had congenital malformations, which included anencephaly, encephalocele, neural tube defect, pulmonary artery hypoplasia with renal cyst and single umbilical artery with pulmonary artery hypoplasia 1 case each. Incidence of congenital abnormalities in IUD cases is varible in studies done by different authors.

In 13 cases (86.6%) weight of placenta and baby were less

than expected weight for gestational age.64, 65 Dominant clinical features were anaemia 33.3% followed by PIH in 26%. The cause was uteroplacental insufficiency in 66% cases followed by infection (46.6%). These findings match with those mentioned in the literature [13, 14].

**Multiple gestation**

Total 10 cases (7%) presented as twin pregnancy. We obtained more cases of twin pregnancy because ours is a tertiary care hospital and twin is a high risk pregnancy being refered to our hospital. Majority (70%) of these cases were preterm deliveries [15]. Commonest clinical presentation was IUD in 6 cases (60%), PIH in 3 cases (30%) followed by still birth in I case. In 60% of cases birth weight of babies was less than expected gestational age [16]. These features match with those mentioned in literature [17]. In 60% cases uteroplacental insufficiency was the pathology followed by chorangiosis in 40%.

There was 1 case of twin transfusion syndrome (TTS) diagnosed on clinical suspicion and antenatal ultrasonography done at 25 weeks of gestation. Placental examination confirmed the diagnosis of TTS. Placenta was diamniotic and monochorionic. Donor and recipient portion were fused and revealed significant difference in size and thickness of umbilical cords with velamentous cord insertion. All findings matched with Terence Zach.18

**Erythroblastosis fetalis (Ef)**

One case presented with erythroblastosis fetalis who was a Rh negative mother with previous history of abortion. Baby was Rh positive showing features of fetal hydrops. Grossly placenta was pale, edematous with increased weight (800 gram). Microscopy revealed edematous premature villi with nucleated RBCs and Hofbauer cells. These findings are consistent with those documented by Rebecca [19]

**Miscellaneous lesions of placenta**

This category included 4 cases, 2 cases of placenta accreta, 1 caseeach of succenturate lobe of placenta and chorangioma. A case of chorangioma presented with polyhydramnios and preterm vaginal delivery. The association has been documented by Kraus FT [20]

**Lesions of umbilical cord**

Lesions of umbilical cord included 13 cases (9%) which included single umbilical artery, marginal insertion, velamentous insertion and umbilical cord twists.

Commonest clinical feature was IUD in 62% cases. One case of twin transfusion syndrome showed velamentous insertion of cord. The cases of cord twists showed worst fetal outcome in the form of IUGR 2 cases and fetal distress and IUD in two cases. Two cases of single umbilical artery revealed congenital malformations in the form of renal cyst and pulmonary artery hypoplasia. Amongst 3 cases of marginal insertion the outcome was IUD in 2 cases where PIH was the direct cause of mortality and fetal distress in 1 case which was related to cord rupture. As mentioned by Cunningham *et al.* [21]

**Conclusion**

Clinical history and investigations of a mother and baby play essential role while making a histopathological diagnosis of placental lesions. Fetal disorders form the major clinical presentation in our study followed by maternal disorders and lesions of placental disc and umbilical cord. Prematurity and IUD were commonest fetal disorders followed by fetal distress, IUGR, twin pregnancy, and erythroblastosis fetalis. Maternal disorders presented as PIH, anaemia, polyhydramnios oligohydramnios, and PROM. Frequent histopathological diagnoses were uteroplacental insufficiency, chorioamnionitis and villitis and chorangiosis.

The cases of chorangiosis were associated with fetal hypoxia. Pathology of placenta reveal changes of uteroplacental insufficiency like large multifocal infarcts, syncytial knots, basement membrane thickening, stromal fibrosis of villi and calcification. Preterm deliveries are more common in cases of anaemia and the clinical presentation was IUD, IUGR, fetal distress, retained placenta and premature rupture of membranes. Placental examination assists in timely management of mother and fetus. Diagnosis of placental lesions helps to improve the outcome of pregnancy. Hence placental pathology should be a routine component of obstetric and neonatal care.

**Conflict of interest:** No Conflict of interest

**Acknowledgement:** KIMSDU, Karad

**Funding:** KIMSDU, Karad.

**References**

1. Chang KTE. Pathological examination of placenta: Raison d'etre. Clinical relevance and medicolegal utility. Singapore Med J. 2009; 50(12):1123-1132.
2. Langston, Claire, Kaplan, Cynthia, Macpherson, Trevor, *Et al*. Practice guideline for examination of the placenta: developed by the Placental Pathology Practice Guideline Development Task Force of the College of American Pathologists. Arch Pathol Lab Med. 1997; 121:449-76.
3. Benirschke K, Kaufmann P. Pathology of the Human Placenta. 3rd ed. New York: Springer-Verlag, 1995.
4. Hall JG, Froster-Iskenius UG, Allanson JE. Handbook of Normal Physical Measurements. New York, NY: Oxford University Press, 1989, 432.
5. Rebecca N. Baergen. Neoplasms. Manual of Benirschke and Kaufmann's Pathology of the Human Placenta. New York. Springer Science, 2005: Chapter 22, 405-415.
6. Sheppard BL, Bonnar J. Uteroplacental arteries and hypertensive pregnancy. In: Bonnar J, MacGillivray I, Symonds EM, eds. Pregnancy hypertension. Lancaster: MTP Press, 1980, 213-9.
7. Frederick Kraus T, Raymond Redline W, Deborah Gersell J, Michael Nelson D, Jeffrey Dicke M. – Inflammation and infection. In: Donald West King, editor–Atlas of nontumor pathology, Placental pathology. AFIP ARP First Series Fascicle 3. Washington DC: American Registry of Pathology. 2004, 75-116.
8. Joshi V. Handbook of placental pathology. New York. Igaku-Shoin Medical Pub, 1994, 81-92.
9. Shenker L, Reed KL, Anderson CF, Borjon NA. Significance of oligohydramnios complicating pregnancy. Am J Obstet Gynecol. 1991; 164(6 Pt 1):1597-1600.
10. Salafia CM *et al*. Placental surface shape, function, and effects of maternal and fetal vascular pathology, Placenta (2010), j placenta. 2010.09.005
11. Khashu M, Narayanan M, Bhargava S, Osiovich H. Perinatal Outcomes Associated With Preterm Birth at 33 to 36 Weeks 131 Gestation: A Population-Based Cohort Study. Pediatrics. 2009; 123(1):109 -113.

12. Ogunyemi D, Murillo M, Jackson U, Hunter N, Alperson B. The relationship between placental histopathology findings and perinatal outcome in preterm infants. Journal of Maternal-Fetal and Neonatal Medicine. 2003; 13(2):102-109.
13. Rebecca Baergen N. Manual of Benirschke and Kaufmann's Pathology of the Human Placenta. New York. Springer Science; 2005: Chapter 20, Placental Abnormalities in Fetal Conditions, 371-391.
14. Frederick Kraus T, Raymond Redline W, Deborah Gersell J, Michael Nelson D, Jeffrey Dicke M. – Clinical Syndromes and Their Pathologic Correlates in the Placenta. In: Donald West King, editor– Atlas of nontumor pathology, Placental pathology. AFIP ARP First Series Fascicle 3. Washington DC: American Registry of Pathology, 2004, 33-46.
15. Crane JM, Van den Hof M, Armson BA, Liston R. Transvaginal Ultrasound in the Prediction of Preterm Delivery: Singleton and Twin Gestations. Obstetrics and Gynecology. September 1997; 90(3):357-363
16. Thanawala U, Khopkar K. Intrauterine growth restriction, Diagnosis and management. In: Desai P, Malhotra, Shah-editors. Principles 127 and Practice of Obstetrics and gynecology. 3rd Ed. Jaypee brothers. New Delhi, 2008, 204.
17. Cunningham F, Leveno K, Bloom S, Hauth J, Rouse D, Spong C. Williams Obstetrics: 23rd Ed. United States. McGraw-Hill; 2010, Chapter 39, Multifetal Gestation. 862-889.
18. Terence Zach. Micheal Barsoom. Twin to Twin Transfusion syndrome. [internet] 2010 [updated 2010 Jan 29; cited 2010 SEP 24]
19. Bruner JP, Rosemond RL. Twin-to-twin transfusion syndrome: a subset of the twin oligohydramnios-polyhydramnios sequence. Am J Obstet Gynecol. 1993; 169(4):925-30.
20. Frederick Kraus T, Raymond Redline W, Deborah Gersell J, Michael Nelson D, Jeffrey Dicke M. Tumor-like Lesions and Metastatic Neoplasms. In: Donald West King, editor–Atlas of nontumor pathology, Placental pathology. AFIP ARP First Series Fascicle 3.Washington DC: American Registry of Pathology, 2004, 239-248
21. Cunningham F, Leveno K, Bloom S, Hauth J, Rouse D, Spong C. Williams Obstetrics: 23rd Ed. United States. McGraw-Hill; 2010: Chapter 27, Abnormalities of the Placenta, Umbilical Cord, and Membranes, 577-587.