VOLUME - 9, ISSUE - 7, JULY - 2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Pathology

HISTOPATHOLOGICAL STUDY OF PLACENTA IN ASSOCIATION WITH THYROID DYSFUNCTION, IN VIEW OF PRE-ECLAMPSIA/ECLAMPSIA: A CASE CONTROL STUDY

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ABSTRACT **Objectives** To study the histo-morphology of placenta in association with thyroid dysfunction in Pre-eclampsia / Eclampsia patients, in relation to the birth weight of the baby. **Methods** Study was conducted in the dept. of Pathology over a period of 1 month. Cases and controls were defined on the basis of 3rd trimester TSH level of the ANC patients. Patients with TSH outside the normal range for 3rd trimester (0.3-3.1 mIU/L) were considered as cases. 17 cases and 33 controls were defined out of a total study population of 50. Histopathology report of the resected placenta specimens were obtained. Clinical details like diagnosis of mother and birth weight of baby were obtained. Finally, the placental histo-morphology, mother's diagnosis and baby birth weight were correlated. **Results** Among the cases, 10 patients (59%) were diagnosed pre-eclampsia, as compared to 5 (15%) among controls. With respect to histology, hemorrhage in the placenta was seen more among cases (15/17; 88%) as compared to controls (51%). Calcification was more among controls (51% vs 29%). No significant differences were noted among other characteristics like placental weight, infarction, chorangiosis, syncytial knots and villitis. 65% (11/17) babies born to cases had Low birth weight (<2.5 kg) compared to 36% in controls. **Conclusion**The incidence of pre-eclampsia is high among mothers with thyroid dysfunction. This is subsequently reflected in the increased incidence of low birth weight babies. So, we strongly emphasize the importance of thyroid screening in all ANC patients.

KEYWORDS :

INTRODUCTION

Fetal growth is dependent upon a number of endocrine, paracrine, and autocrine events within the fetoplacental unit. Thyroid status is one of the several factors that have been postulated to play a critical role in the pathogenesis of morbidity in the fetus, especially with respect to the growth and development of the central nervous system[1].

Thyroid hormones play a crucial role in controlling trophoblast growth and development. Trophoblast has a high binding capacity of T3, and it has been suggested that placenta is a thyroid hormone dependent tissue. Studies have reported stimulation by thyroid hormones of trophoblast endocrine function, with enhanced production of human placental lactogen and human chorionic gonadotrophin. It has been also shown that T3 enhances the production of epidermal growth factor, a potent trophoblast mitogen. Thyroid hormones thus play an important role in villous development and placentation[2].

TH also regulates secretion of several growth factors and cytokines that are critical for Endovascular trophoblast (EVT) invasion and angiogenesis of maternal and fetal placental vessels, including angiogenin, angiopoietin 2 (Ang-2), vascular endothelial growth factor (VEGF), Interleukin 10 and TNF. Furthermore, it also attenuates trophoblast proliferation, motility and invasion[3].

We aim to study the histomorphological features of placenta and correlate it with TSH levels, and birth weight of baby in 3rd trimester mothers especially with disorders like eclampsia/pre-eclampsia.

Materials and Methods

Study was conducted in the Department of pathology over a period of two months. Study population was 3rd trimester mothers undergoing labour. Placenta specimens were received in containers with 10% formalin. They were adequately examined and sectioned serially and fixed in a fresh preparation of 10% formalin. They were allowed to fix for 24 hours. Grossing is done the next day wherein crucial parameters were noted down like weight and dimensions of the placental disc, length and diameter of the umbilical cord and distance of cord from disc margin. Then representative sections were obtained from the four quadrants of the placental disc, the central area and the area of cord insertion. Sections from the umbilical cord and placental membrane were also obtained. The sections are processed in an automatic tissue processor. The paraffin block was obtained at the end from which thin sections were cut using a microtome. The sections were then subjected to routine H&E staining.

Other relevant reports of the patients were obtained from the central laboratory. Thyroid function tests are conducted on the VITROS 5600. TSH level of 0.3-3.1 mIU/L were considered as the normal range for 3rd trimester mothers according to ICMR guidelines. Clinical details like baby's birth weight and clinical diagnosis of the mother were obtained from the master register in the labor room. Total sample size was 50 out of which cases and controls were divided on the basis of TSH levels, yielding 33 controls and 17 cases. Cases being those with TSH level outside the normal range. Correlation between the placental morphology, TSH levels, and birth weight of baby was done, the results were tabulated and percentage values obtained.

Results

Table 1: Distribution of controls and cases

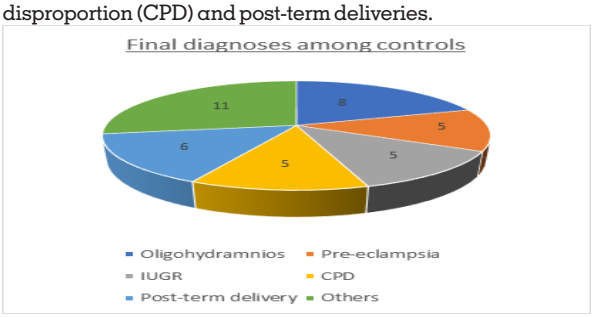
TSH Level	Controls (TSH = 0.3-3.1 mIU/L)	Cases (TSH > 3.1)
No. n=50	33 [67%]	17 [33%]

Table 2: Final clinical diagnosis of the mother.

Final Diagnosis of Mother	Controls	Cases
Pre-eclampsia/Eclampsia	5 [15.1%]	10 [58.8%]
Oligohydramnios	8	1
IUGR	5	1
Previous LSCS	4	4
Contracted Pelvis/CPD	5	0

Anemia	3	3
Placenta Previa	0	1
HELLP Syndrome	1	0
Post-Term Delivery	6	0
IUD	1	0
Others	2	2

Among the cases, 10 patients (58.8%) were diagnosed as pre-eclampsia, as compared to 5 (15.1%) among controls. Other common disorders among the controls were oligohydramnios, Intra-uterine growth retardation (IUGR), cephalopelvic disproportion (CPD) and post-term deliveries.



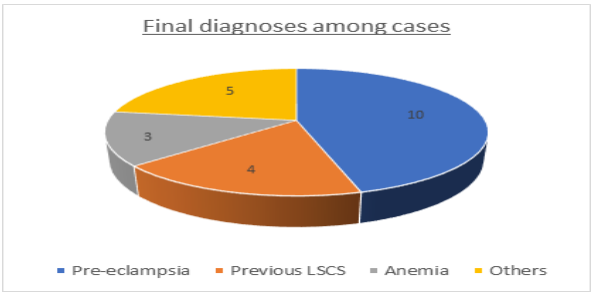


Table 3: Placental Weight

Weight (gms)	Controls	Cases
<100	1	0
100-200	1	0
200-300	8	2
300-400	13 (39%)	6 (35%)
400-500	7 (21%)	6 (35%)
500-600	3 (9%)	3 (18%)
Total	33	17

With respect to the placental weight, 88% of the cases had a placental weight of over 300 gm. Whereas among the controls 69% had weight over 300 gm.

Table 4: Histomorphology of placenta

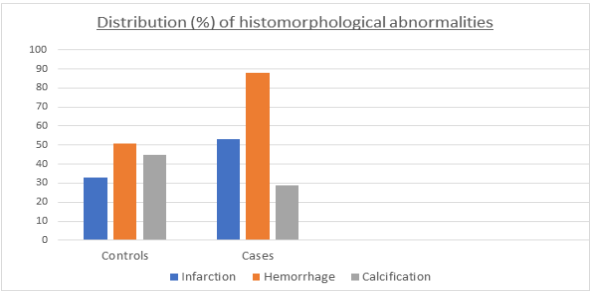
Feature		Controls	Cases
Infarction		11 (33%)	9 (53%)
Syncytial knots	Type-1	17	32
	Type-2a	5	9
	Type-2b	2	1
Chorangiosis		15 (45%)	7 (41%)
Haemorrhage		17 (51%)	15 (88%)
Calcification		15 (45%)	5 (29%)

With respect to histology, hemorrhage in the placenta was seen more among cases (15/17; 88%) as compared to controls (51%). Infarction was noted more among the cases (53%) compared to the controls (33%). Calcification was more among controls (51% vs 29%). No significant differences were noted among other characteristics like chorangiosis, syncytial knots and villitis100.

Table 5: Birth Weight Of Baby:

Birth Wt (Kg)	Cases	Controls
<1.5	1	4
1.5-2.5	10	8
2.5-3.5	5	18
>3.5	1	2
Total =	17	33

Low Birth Weight (<2.5 kg): Cases- 11/17: **64.7%** Controls- 12/33: 36.4% 64.7 % (11/17) babies born to cases had Low birth weight (<2.5 kg) compared to only 36.4 % among the controls.



DISCUSSION

Our study differentiates cases and controls on the basis of their third trimester TSH levels. That yielded 17 cases and 33 controls. Among the cases, 10 patients (59%) were diagnosed as pre-eclampsia, as compared to only 5 (15%) among controls.

This is in line with the study conducted at Regional Institute of Medical Sciences, Imphal, Manipur which concluded severe preeclampsia was seen in 64.3% of the patients with thyroid dysfunction compared with 39.6% in euthyroid patients[4].

In a similar study at the Wenzhou Medical University, China, compared with euthyroid status, subclinical hypothyroidism (SCH) was associated with higher rates of Gestational hypertension (1.819% vs. 3.504%, P = 0.020)[5].

Amongst the other ailments that affected the cases, anemia (18%) was the commonest, followed by Oligohydramnios, placenta previa and IUGR. Among the controls there was a high incidence of oligohydramnios (24%), post-dated delivery (18%), cephalon-pelvic disproportion (15%) and IUGR (15%). One baby born to a woman from control suffered from intrauterine death (IUD). Four from either side had history of previous LSCS.

With respect to the placental weight, 88% of the cases had a placental weight of over 300 gm. Whereas among the controls 70% had weight over 300 gm.

In histology, the incidence of placental hemorrhage was significantly higher among the cases (88%) as compared to controls (51%). Similar trend was seen for placental infarction as well. 53% of the cases showed infarction compared to only 33% among the controls.

In women with pre-eclampsia, the mean luminal diameter of uterine spiral arterioles is less than one-third of the diameter of similar vessels in an uncomplicated pregnancy. Consequently there is reduced uteroplacental perfusion leading to ischemic changes and fetal hypoxia. Also the villous surface area, the villi diameters and the density of fetal blood vessels in the terminal villi is reduced in a pre-eclamptic patient[1].

Calcification was more among controls (51% vs 29%). This is probably due to increased incidence of post-dated pregnancies seen among the controls. Among other histologic criteria like syncytial knots and chorangiosis, significant differences were not seen between both groups.

As far as birth weight of baby is concerned, 64.7% (11/17)

babies born to cases had Low birth weight (<2.5 kg) compared to only 36.4% (12/33) in controls.

This is in accordance with the study conducted at the Wenzhou Medical University, China, where more LBW infants were delivered in the subclinical hypothyroidism (SCH) group than in the euthyroid group (4.582% vs. 1.885%, P,0.001)5.

In another study conducted at Institute of Obstetrics & Gynecology, Chennai, the gestational age at birth was significantly decreased and cesarean rate was significantly high in preeclampsia. Low birth weight was significant in preeclampsia[6].

Similar study done at Regional Institute of Medical Sciences, Imphal, Manipur concluded Complications like abruption, intrauterine fetal death (IUD), intrauterine growth restriction (IUGR), oligohydramnios, preterm deliveries, postpartum hemorrhage (PPH), low birth weight babies, birth asphyxia in babies and subsequent neonatal intensive care unit (NICU) admissions were significantly higher (p <0.05) in the preeclampsia patients with thyroid dysfunction in comparison with euthyroid ones[4].

In another study conducted at Narayana medical college, Nellore, the morphology of stem and terminal villi (TV) was studied, and the surface area and diameter of TV and capillaries were measured. The gross placental morphometrical study revealed that the mean placental weight, thickness, diameter, and surface area were significantly lower in placentas with PE than in controls. The histomorphometrical findings of the villous surface area and diameter were lower in placentas with PE, whereas the TV density was higher in placentas with PE than in controls, and the differences were significant (P<0.0001)[7].

In another study conducted at Navodaya medical college, Raichur on the maternal thyroid profile in pre-eclampsia, there was no significant difference in the thyroxine (T4) and tri-iodothyronine (T3) levels in two groups, but there was a significant increase in thyroid stimulating-hormone (TSH) levels in pre-eclampsia patients (7.22 ± 1.3) compared to normal pregnancy (2.48 ± 1.05) (p = 0.0001)[8].

Another study done in the US by various contributors aimed to discern if stillbirth with preeclampsia and gestational hypertension (PE/GH) has a particular phenotype by comparing stillbirths with and without PE/GH. Among PE/GH pregnancies, stillbirths had increased maternal and fetal vascular lesions, including retroplacental hematoma, parenchymal infarction, fibrin deposition, fetal vascular thrombi, and avascular villi. Stillbirth pregnancies are overwhelmingly associated with placental lesions. Parenchymal infarctions are more common in PE/GH preterm stillbirths[9]

Another study conducted in Universiti Kebangsaan Malaysia medical center, Kaula Lampur showed an increased syncytial knot formation in the placenta of hypertensive mothers. Vascular endothelial growth factor (VEGF) expression was seen in syncytiotrophoblasts of 14 of the hypertensive cases (14/15, 93.3%), while only two of the normotensive cases were positive (2/15, 13.3%)[10].

This study showed an increased number of syncytial knots is a consistent histological finding in the placenta of patient with hypertensive disorder of pregnancy (HDP). VEGF expression was significantly increased in syncytiotrophoblasts in placenta of hypertensive group, and it could be used as a biomarker for hypertension.

CONCLUSION

In our study the incidence of pre-eclampsia was high among mothers with thyroid dysfunction. This can cause placental insufficiency in the form of increased hemorrhage, infarction and reduced placental weight. This is subsequently reflected in the increased incidence of Low birth weight babies.

So screening for hypothyroidism in pregnancy is recommended in all antenatal females and replacement of thyroid hormones in indicated women will improve the obstetric outcome in future.

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