Original Research Article

Maternal Hypothyroidism and Its Effect on Placenta and Newborn: A Morphometric and Histopathological Study

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Abstract

Placenta plays role in maintaining the environment for the growth of the fetus in the womb of mother. Some hormonal abnormalities of the mother also affect the morphology and histology of the placenta which further affect the growth of the fetus. The aim of this study was to evaluate the morphometric and histopathological changes of placenta of mother affected by thyroid disorder. For this study total 200 placentas were collected from the labour room and Operation Theater. Out of 200 placentas, 100 placenta were belonged to thyroid group (case group) and 100 placentas were of control uncomplicated group. The most common shape of the placenta in case group was circular (72%) followed by oval (21%) and irregular (7%) whereas in control group the shape of placenta was circular (61%), oval (27%), irregular (9%) and bilobed (3%). The mean weight of the placenta and thickness were lower in case group than the control group whereas area and number of cotyledon were higher in case group than the control group. The mean weight of the newborn was lower in case group than the control group. In histological examination some parameters such as fibrinoid necrosis, syncytial knot, hyalinization, calcification, medial coat proliferation of fetal blood vessels, exfoliated trophoblast, stromal fibrosis and cytotrophoblastic proliferation were seen and these parameters were higher in the case group than the control group. This study concluded that hormonal changes in mother affect the placenta than the fetus so early diagnosis and treatment may prevent the complications.

Keywords: Histopathology, Hypothyroid, Morphometric, Placenta.

Introduction

In pregnancy many hormonal and metabolic changes happened in mother that affects the thyroid gland and its functions[1]. During pregnancy the need of thyroid hormones increases with 50% and thyroid gland becomes enlarged with 10% of the size in normal pregnancy[2]. It happened because the HCG increases the stimulation of TSH receptors which further increases thyroid binding globulin and requirement of thyroid hormone in the body[3].Thyroid gland secrets 2 hormones named triiodothyronine (T3) and thyroxine (T4). Thyroid hormones regulates metabolic rate of body, heart rate, contraction of muscles and digestive functions[4]. Thyroid hormone of mother crosses the placenta and reaches to the developing fetus for their normal metabolic activities. Thyroid hormone regulates cell proliferation, differentiation and metabolism, so it affects all the cells of body[5].During pregnancy the dysfunction of the thyroid gland increases with approximate six times[1]. The most common thyroid disorder in pregnancy is hypothyroidism. The prevalence of hypothyroidism is approximately 2.5% in western population and 4.8-11% in Indian population[6]. Hypothyroidism in pregnancy increases the risk of fetal growth retardation, abortion, premature delivery,congenital anomalies,anemia,postpartum depression, cardiac dysfunction, neurological disorders, morbidity and mortality of mother and developing fetus[7-9]. Hypothyroidism during pregnancy increase the incidence of preeclampsia and together the risk of pre termlabour, antepartum hemorrhage and intrauterine growth retardation increases [10].Thyroid hormones helps in the development of nervous system of the fetus, so any kind of thyroid dysfunction in mother during pregnancy, may cause defect in the development of brain and leads to neurological disorders in the developing fetus[11-13]. Untreated hypothyroidism during pregnancy leads to low IQ level in the children[14].Placenta is a highly specialized organ and act as a connecting link between the mother and the developing fetus. It develops from maternal (decidua basalis) and fetal tissue (chorionic frondosum) in the womb of mother along with the fetus[15].It provides oxygen and nutrition to the fetus and also removes metabolic wastes from it[16].Placenta has the capacity to undergo considerable changes according to the blood supply from the mother and accommodate itself according to the environmental conditions [17]. So many morphological and histological changes happen in the placenta with complications in mother such as hypertension, diabetes mellitus and hypothyroidism etc. and these changes of the placenta affect the health of the developing fetus. In the present study we tried to observe the morphological and histopathological changes in the placenta of mother complicated with hypothyroidism and compared with the placenta of normal pregnancy.

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Materials and Methods

The present study was done in the department of anatomy, Sawai Man Singh Medical College, Jaipur, Rajasthan in the year 2019-2020. It was an observational study. Ethical committee approval was obtained from the institutional ethical committee before proceeding with the study. Total 200 women were selected for the study. Selected women were examined with following parameters-

- Clinical examinations (height, weight, blood pressure, pulse and hemoglobin etc.)

- Medical history of any past illness, anemia, respiratory disorder, cardiovascular disorders, and psychiatric illness were recorded.
- Biochemical investigations (blood sugar, blood urea, blood creatinine, lipid profile, liver function test, thyroid profile and HIV test).
- Obstetric history – type of pregnancy (singleton or multiple), mode of previous delivery, complication if any in previous delivery, health of previous child were recorded.

Women belonged to the thyroid disorder during the pregnancy, were considered in case group and women with normal clinical parameters and normal uncomplicated pregnancy, were considered in control group.

Inclusion Criteria:

- Only fresh placenta were used
- Women complicated with thyroid disorder
- Thyroid complicated subjects with Pre term delivery
- In control group women who had no any complications during pregnancy and had normal biochemical tests were included

Exclusion criteria:

- Women who had experienced any other complication than thyroid disorder during pregnancy
- Damaged placenta
- Who denied for consent for sample collection

For this study freshly delivered placentas were collected from the Gynecology & obstetrics department of Mahila Chikitshalaya, Jaipur, Rajasthan. Informed consent was obtained from all the subjects and purpose of the study was explained before collecting the data. Socioeconomic status of the selected subjects were measure using modified Kuppuswamy scale (2019)[18].Subjects were classified into upper, upper middle, lower middle, upper lower and lower socioeconomic class based on education, occupation and income of head of family.

Placentas of the selected women were collected from the labor room or from the operation theater just after delivery. The placentas were washed under running tap water and their extra membranes were trimmed. Umbilical cord was cut around 2cm away from the attachment to the placenta.

Gross examination of each placenta was done which included weight, mean area, thickness at the center, attachment of the umbilical cord, number of cotyledon and shape of the placenta. Shape of the placenta was classified into 4 groups- oval, circular, irregular and lobulated. Weight of the placenta was measured using digital weighing machine. Area of the placenta was measured by below formula, using 2 diameters, which were highest and perpendicular to each other[19] (figure: 1).

$$Placental\ area = \pi \times \frac{Maximum\ diameter\ (cm)}{2} \times \frac{Minimum\ diameter\ (cm)}{2}$$

Thickness of the placenta was measured at the center using a needle. Umbilical cord attachment to the placenta was classified into centric, eccentric and marginal type (figure:2). Centric when umbilical cord attached. <2cm from the margins of the placenta, eccentric when umbilical cord attached >2cm from the margins of placenta and marginal when umbilical cord attached to the margins of placenta [20]. Each placenta was put on the flat surface with the maternal surface upwards. On the maternal surface elevations (cotyledons) were counted from left to right side than right to left side in a circular pattern.All the data were entered into the Microsoft excel and statistically significant difference was determined between case and control group. P-value less than 0.05 were considered as a statistically significant. For the histological examination the sections of the placenta were taken which include both basal and fetal plate and kept in 10% formalin. After tissue processing 5µm sections were cut using rotatory microtome. The slides were stained with haematoxyline and eosin stain and observed under light microscope.

The new born was examined for weight, height, Fetoplacental ratio and any clinical symptoms if any.

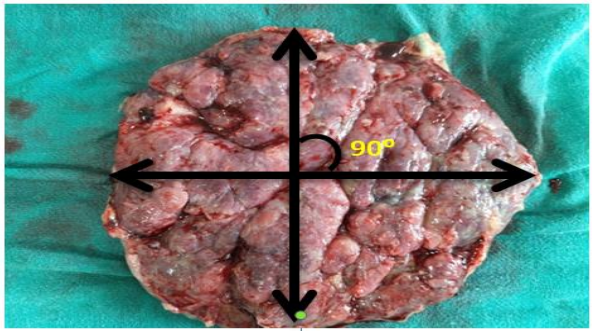


Fig. 1: Measurement of two maximum and perpendicular diameters of the placenta

Results-

In the present study total 200 women were included for the data collection out of which 100 were belonged to control group and 100 were belonged to thyroid disorder or case group. The two groups were well matched to each other in respect to age and socioeconomic status. The age of the selected subjects were ranging between 21-35years. Most of the selected women (70-75%) were belonged to upper middle class family (Table-1).Placentas of all the selected cases were examined for the shape, weight, area, thickness, number of cotyledon and attachment of the umbilical cord to the placenta.

The most common shape of the placenta in case group was circular (72%) followed by oval (21%) and irregular (7%) whereas in control group the shape of placenta was circular (61%), oval (27%), irregular (9%) and bilobed (3%). The shape of the placenta was statistically non-significant in these 2 groups.The mean placental weight in case group was 409.7gm± 79.76gm and in control group was 443.9gm± 64.05gm. The mean thickness at the center of the placenta was 1.16 ± 0.29 in case group and 2.56 ± 0.59 in control group. The mean weight and thickness of the placentas were higher in control group than the case group and statistically significant difference was observed. Mean area of the placenta and number of cotyledon were shown slight significant difference between case and control group.

The mean weight of the new born babies was 2.36kg ± 0.473kg in case group and 2.8kg ± 0.442kg in control group. The weights of the new born baby were significantly lower in case group than the control group. The ratio of new born baby weight and placental weight (Fetoplacental ratio) was significantly lower in case group when compared with control group (Table-2).

Histological examination- In the microscopic study of placenta showed presence of syncytial knots, fibrinoid necrosis, hyalinized villi, calcification, and exfoliated trophoblast in the intervillous space, stromal fibrosis, cytotrophoblastic cellular proliferation and proliferation of medial coat in fetal vessels (Figure- 3,4,5& 6). Peripheral and central sections of placenta were examined in low power field for microscopic parameters. All the microscopic parameters were shown increase in number in thyroid group when compared with control group and showed statically significant difference between the groups (Table-3). The occurrences of pathological changes in placenta were more numerous in the peripheral section of the placenta than the section towards the attachment of umbilical cord to the placenta and the data showed significant difference (Table-4).

Table 1:Comparison of socioeconomic status of two groups

Characteristics		Control group(n = 100)	Thyroid group(n = 100)	Chi -square test	P - Value	Significance
Socio economic status	Upper Lower	1	-	0.3351	0.9533	Not Significant
	Lower Middle	6	8			
	Upper Middle	72	74			
	Upper	21	18			
	Still Birth	2	6			

Table 2:Comparative result of placental morphometry and new born

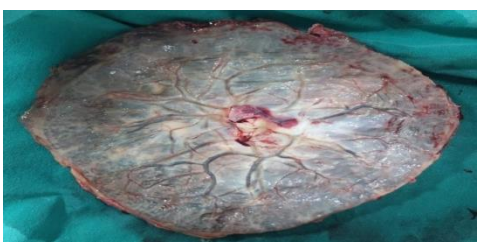
Characteristics	Control group (n = 100)	Thyroid group (n = 100)	t - test	P - Value	Significance
Baby weight	2830.8 ± 442.1	2360.5 ± 473.8	7.257338	0.00000	Highly significant
Height(cm)	29.35 ± 2.15	29.4 ± 2.77	-0.14259	0.88676	Not significant
Placenta weight	443.9 ± 64.1	409.7 ± 79.77	3.342027	0.00099	Highly significant
Area	285.6 ± 59.13	306.7 ± 47.84	-2.77415	0.00606	Significant
Thickness	2.56 ± 0.59	1.16 ± 0.29	21.29539	0.00000	Highly significant
No. of cotyledon	20 ± 6.11	22.9 ± 7.96	-2.88999	0.00428	Significant
fetoplacental ratio	6.5 ± 1.33	5.86 ± 1.18	3.599541	0.00040	Highly significant

Table 3:Comparative result of histopathological study

Characteristics	Control group (n = 100)	Thyroid group (n = 100)	t-test	P - Value	Significance
Fibrinoidnecrosis	4.45 ± 2.6	41.05 ± 12.6	-28.448	0.00000	Highly significance
Syncytial knot	8.01 ± 2.61	11.69 ± 5.2	-6.325	0.00000	
Stromal fibrosis	3.86 ± 2.61	16.25 ± 6.06	-18.778	0.00000	
Hyalinization	3.26 ± 2.29	12.24 ± 9.03	-9.639	0.00000	
Calcification	1.18 ± 0.23	4.66 ± 2.09	-16.551	0.00000	
Medial coat cell proliferation of fetal capillaries	3.76 ± 0.26	2.99 ± 1.42	5.334	0.00000	
Cytotrophoblasticcellular proliferation	6.63 ± 1.53	6.94 ± 3.14	-0.888	0.37588	Not Significance
Exfoliated trophoblast	4.47 ± 1.92	6.81 ± 2.18	-8.055	0.00000	Highly significance

Table 4:Comparative result of histopathological study in different sections of thyroid group

Characteristics	Histo periphery (n = 100)	Histo center (n = 100)	t-test	P - Value	Significance
Fibrinoidnecrosis	41.05 ± 12.6	34.77 ± 11.37	3.700	0.00028	Highly significant
Syncytial knot	11.69 ± 5.2	9.35 ± 4.77	3.316	0.00109	Significant
Stromal fibrosis	16.25 ± 6.06	13.44 ± 5.91	3.320	0.00107	
Hyalinization	12.24 ± 9.03	9.78 ± 7.79	2.063	0.04044	
Calcification	4.66 ± 2.09	3.45 ± 1.82	4.366	0.00002	Highly significant
Medial coat cell proliferationof fetal capillaries	2.99 ± 1.42	2.32 ± 1.1	3.730	0.00025	
Cytotrophoblasticcellular proliferation	6.94 ± 3.14	5.13 ± 2.96	4.194	0.00004	
Exfoliated trophoblast	6.81 ± 2.18	4.98 ± 2.25	5.841	0.00000	



a

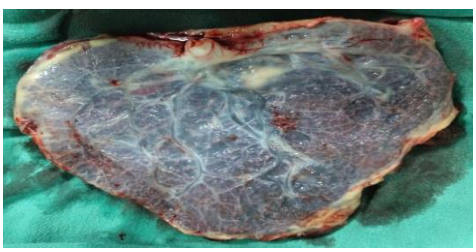


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Fig. 2:Showing different type of insertion of umbilical cord to the placenta- a. Central b. marginal and c. eccentric

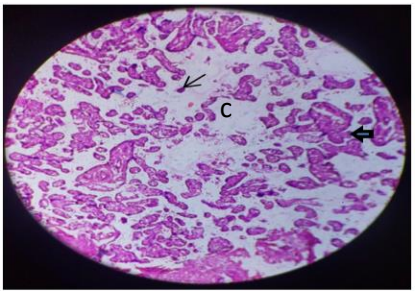

Fig. 3:Photograph of thyroid villi, syncytial knot (thin arrow) and exfoliated trophoblast (thick arrow)

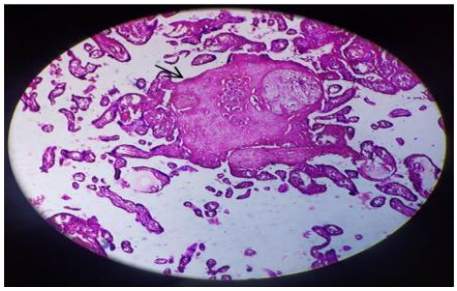

Fig. 4:Photograph of thyroid villi with hyalinization (thin arrow)

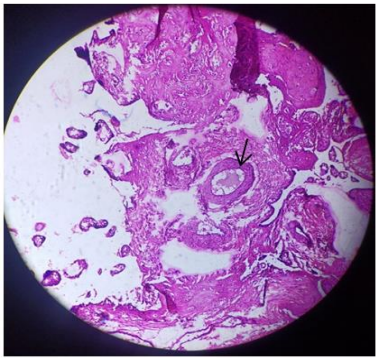

Fig. 5: Photograph showing increased thickness of medial coat of fetal blood vessels (thin arrow) in thyroid group

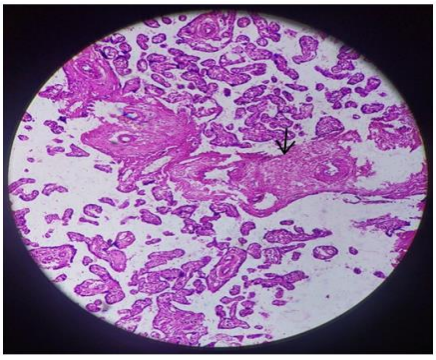

Fig. 6: Photograph of thyroid villi with fibrinoid necrosis (thin arrow)

Discussion

Development, metabolism and differentiation of fetal cells depend of the maternal thyroid hormone till onset of its own thyroid hormone production. Maternal thyroid hormone crosses the placenta and directly acts on fetal tissues. Maternal thyroid hormone attaches to the thyroid receptor of the placental tissue and modulate the metabolism and development of the placenta[21]. Thyroid hormones have their importance in maintaining the fertility and pregnancy in human. Hypothyroidism alters the morphology of decidua of uterus and increase the rate of still birth, miscarriage and fetal growth retardation[22,23].The shape of the placenta in normal pregnancy is oval to circular in shape. Placental insufficiency may lead to alter the shape of the placenta to lobulated, irregular, bidiscoidal and circumvallate etc. In the present study 72% of the placentas were of circular shaped followed by oval shaped (21%) and 7% were of irregular shaped. The study done by Kumari S (2016)[24] reported 66% circular shaped and 10% irregular shaped placenta. In both the studies there was no alterations found in the shape of placenta between case and control group.In the present study the average weight of placenta was 409.7 ± 79.77 in case group and 443.9 ± 64.1 in control group, which shows significant difference between 2 groups. The study done by Kumari S[24] also reported reducing of placental weight in thyroid group (408±89.45) than control group (430.75±86.18). It was reported that in hypothyroid cases, expression of vasculo-endothelial growth factor reduces in trophoblast cells, which impairs the normal vascular development. Hypothyroidism also increases apoptosis, which cause reduction of weight of placenta[25,26].The thickness at the center of placenta in the present study was less in thyroid group (1.16 ± 0.29)than in control group (2.56 ± 0.59), which correlate with the study of Kumari S[24] (1.91±0.47 in case group and 2.29±0.54 in control group).in this study number of cotyledons and area of the placenta significantly increased in case group than the control group and it correlate with the study done by Kumari S.In the present study, histological study of the placenta of control and case group showed significantly increased number of syncytial knots, fibrinoid necrosis, stromal fibrosis, thickening of medial coat of fetal blood vessels, hyalinization, calcification and exfoliated trophoblast in case group than control group. Number of cytotrophoblastic proliferation was also increased in case group than the control group but the difference was not significant between two groups. Ozogul C et al[27] in 2010 did immunohistochemical study and reported significantly increased

number of syncytial knots, stromal fibrosis and hyalinization in case group, whereas the thickening of medial sized blood vessels was decreased in case group than the control group. The formation of syncytial knots increases with hypoxia, hyperoxia or reactive oxygen species[28].Reduced blood flow and toxemia are responsible for the early aging of the villi and increase the number of stromal fibrosis and fibrinoid necrosis.

Conclusion

During pregnancy uncontrolled thyroid disorder in woman affects the health of the placenta and the developing fetus. Hypothyroidism significantly affects the weight of the placenta and the developing fetus, Fetoplacental ration, thickness of the placenta and diameter of the placenta. Histologically all the parameters such as fibrinoid necrosis, syncytial knot, stromal fibrosis, hyalinization, calcification, medial coat proliferation of fetal blood vessels and exfoliated trophoblast. This indicates early diagnosis and treatment of the patient to reduces the developmental anomalies of the developing fetus, morbidity and mortality

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