STUDY OF THYROID PROFILE IN DIFFERENT TRIMESTERS OF PREGNANCY

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ABSTRACT

Background: Thyroid disorders and dyslipidemia are frequent during pregnancy, which are associated with complications for both the mother and the fetus. Hence, this study aims to evaluate thyroid function test and its association with dyslipidemia in pregnancy.

Method: This laboratory-based cross-sectional study was carried out in Manmohan Memorial Teaching Hospital, Kathmandu, Nepal. A total of 200 participants; where 100 pregnant and 100 non pregnant women were included in the study. Pregnant women were further subdivided into 1st, 2nd and 3rd trimester groups. Thyroid Profile and Lipid profile were estimated. Student t-test, one way ANOVA, and Pearson's correlation were applied.

Findings: The findings of the study revealed that the level of TSH was significantly ($p<0.001$) lower, TG, TC and VLDL were significantly ($p<0.001$) higher and HDL was significantly ($p<0.001$) lower in pregnant women as compared to non-pregnant women. In different trimester of pregnancy TG ($p<0.001$), TC ($p<0.05$) and VLDL ($p<0.001$) were found to be significantly increased with increasing trimester of pregnancy.

Conclusion: In medical interventions, screening of thyroid hormones, lipid profile and adjustment of TSH level according to trimester specific range in different trimesters should be implemented to improve lipid indices to decrease pregnancy complications outcomes.

Key words: Pregnancy, Thyroid hormones, Trimester specific TSH level, Dyslipidemia

INTRODUCTION

Thyroid hormone regulates metabolic processes essential for normal growth and body[1-3]. Thyroid problems are frequent during pregnancy due to changes in synthesis and metabolism, which is associated with the risk for both the mother and the fetus[4]. Thyroid hormone plays a significant role in baby's brain development during pregnancy. It is apparent that overt hypothyroidism, especially at the beginning of pregnancy, might damage the baby's brain development or cause to other problems with the pregnancy[5]. Since the fetal thyroid gland starts functioning in the second trimester of pregnancy, fetal thyroxin is mainly acquired from maternal sources during the first trimester of pregnancy[6]. Pregnancy produces an arrangement of significant physiologic change within the mother that have a critical influence on maternal thyroid hormone. These changes may lead to dysregulate maternal thyroid function test [7]. During early pregnancy, there is rise in serum estrogen and progesterone levels. In addition, there is hyperinsulinemia leading to increased peripheral utilization of glucose, increased glycogen accumulation in the liver as well as increased storage of lipids and decreased lipid breakdown[8]**.** Controlled hyper stimulation of the ovaries during pregnancy causes a rise in serum TBG, T_4 and T_3 concentrations as well as a decline in serum free T_4 concentration and a slight increase in serum TSH concentrations (within the normal range)[9]. Additionally, due to extremely high levels of human chorionic gonadotropin (HCG) in the first half of pregnancy, particularly in the first trimester, TSH levels are often repressed. Triglycerides, cholesterol, and other lipoproteins can change qualitatively or quantitatively as a result of thyroid dysfunction without any underlying thyroid disease resulting in cardiovascular disease risk[10].

Prevalence of thyroid dysfunction in pregnant women is 2 - 3 % globally. Hyperthyroidism occurs in 0.2–0.4% and incidence of hypothyroidism in pregnancy is 0.5–3.5%[11]. The prevalence of thyroid disorder in pregnancy was found to be 24.62% in Nepal[12]. The consequences in pregnancy such as abortion, anemia, pregnancy-induced hypertension, preeclampsia, postpartum hemorrhage, premature birth, low birth weight, intrauterine fetal death, increased neonatal respiratory distress, and infant neuro-developmental dysfunction were associated to overt hypothyroidism[13]. Hence, this study aims to find the association between thyroid hormone and lipid indices in pregnant women.

MATERIAL AND METHODS

This laboratory-based cross-sectional study was conducted in Manmohan Memorial Medical College and Teaching Hospital (MMTH), Kathmandu, Nepal, and Manmohan Memorial Institute of Health Sciences, Kathmandu, Nepal, from October 2022 to March 2023. Ethical approval (Regn no: MMIHS-IRC 878) was taken from Institutional Review Committee, MMIHS, Soalteemode, Kathmandu.

Inclusion and Exclusion Criteria: Females with history of thyroid disorders and metabolic complications like DM, dyslipidemia, hepatic disease, and, patients under medication were excluded from the study. A total of 200 participants attending MMTH were included in the study, out of which 100 were pregnant women and 100 were non pregnant healthy females.

Informed consent: The female participants in the study provided written informed consent after being fully informed on the procedures in Nepali.

Experimental protocol: 5ml fasting (8-12 hours) blood sample was collected by venipuncture method in a serum separator tube (BD Vacutainer® SST™ Tubes), and separated serum through centrifugation process. The lipid profile test such as total cholesterol (TC), Triglyceride (TG), High-density lipoprotein cholesterol (HDL-C), and Low-density lipoprotein cholesterol (LDL-C) were performed using a fully automated chemistry analyzer (VITROS® 350 Chemistry System, USA). Thyroid profiles – FT_3, FT_4, and TSH – were assessed using a fully automated MAGLUMI® 800, Chemiluminescence Immunoassay (CLIA) System (SNIBE, China). All the lipid profile parameters were measured in mg/dl, FT_3 and FT_4 were measured in pg/ml, and TSH in µIU/ml.

Statistical analysis: A database was constructed using Microsoft Excel 2013 and analyzed by SPSS version 18 (IBM corporation, Armonk, NY, USA). Independent t-test, Spearman's Correlation, one-way ANOVA and Post-hoc analysis was applied in SPSS. The data were presented in mean and standard deviation during mean comparison. Spearman's correlation was applied between thyroid profile test and lipid panels. Statistical significance was set at a p-value less than 0.05.

RESULTS

Among 200 study population, whereas 50% pregnant women (26.5% in 1st trimester, 13% in 2nd trimester and 10.5% in 3rd trimester) and 50% non- pregnant women, which is represented in table 1.

Table 1: Demographic data of Study Populations

Subjects	Sub Groups	Frequency (n)	Percentage (%)	Total
Cases	1st Trimester	53	26.5%	100
	2nd Trimester	26	13%	
	3rd Trimester	21	10.5%	
Control		100	50%	100
Total		200	100%	200

There was significant increase in FT_4 ($p < 0.001$), TSH ($p < 0.001$), TG ($p < 0.001$), and VLDL ($p < 0.001$) in pregnant women, whereas significant decrease in HDL ($p < 0.001$) in pregnant women as compared to non-pregnant women (Table 2).

Table 2: Comparison of Biochemical Parameters between pregnant and non- pregnant women

Variables	Groups	Mean ± SD	*p*- value
FT_3 (pg/ml)	Non- pregnant	3.35±0.38	0.063
	Pregnant	3.26±0.28	
FT_4 (pg/ml)	Non- pregnant	8.56±1.74	**<0.001**
	Pregnant	12.16±1.49	
TSH (µIU/ml)	Non- pregnant	3.15±2.25	**<0.001**
	Pregnant	2.00±1.38	
TG(mg/dl)	Non- pregnant	102.20±54.10	**<0.001**
	Pregnant	145.74±71.40	
T. Chol (mg/dl)	Non- pregnant	167.70±34.77	0.05
	Pregnant	179.43±49.30	
HDL(mg/dl)	Non- pregnant	46.03±10.05	**<0.001**
	Pregnant	40.74±4.97	
LDL(mg/dl)	Non- pregnant	104.13±25.31	0.323
	Pregnant	109.65±49.57	
VLDL(mg/dl)	Non- pregnant	20.44±10.82	**<0.001**
	Pregnant	29.15±14.28	

Table no. 3 shows the comparison of Thyroid profile and Lipid profile with different trimesters of pregnancy by using one way ANOVA. TG ($p < 0.001$), T. Cholesterol ($p = 0.029$), and VLDL ($p < 0.001$) are significantly increased in 3rd trimester as compared to 1st and 2nd trimester of pregnancy.

Table 3: Comparison of Thyroid profile and Lipid profile with different trimesters of pregnancy (ANOVA)

Variables	Trimesters	Mean± S.D	*p*- value
AGE	First	27.09±4.16	
	Second	27.88±5.42	0.372
	Third	28.76±4.94	
FT_3	First	3.2525±0.29	
	Second	3.2850±0.29	0.890
	Third	3.2538±0.27	
FT_4	First	12.4787±1.50	
	Second	11.9146±1.16	0.076
	Third	11.6967±1.71	
TSH	First	2.1783±1.60	
	Second	1.5962±1.11	0.207
	Third	2.0752±0.95	
TG	First	124.23±62.24	
	Second	150.88±69.66	**0.000**
	Third	193.67±73.68	
T. CHOL	First	167.585±41.47	
	Second	188.365±44.70	**0.029**
	Third	198.286±64.92	
HDL	First	41.60±5.04	
	Second	39.27±4.62	0.137
	Third	40.38±4.98	
LDL	First	101.13±41.72	
	Second	119.34±45.89	0.190
	Third	119.17±67.79	
VLDL	First	24.85±12.44	
	Second	30.18±13.93	**0.000**
	Third	38.73±14.73	

Table no. 4 shows Post hoc analysis of different significant variable such as FT_4 (first and third), TG (first and third & second and third), T. Cholesterol (first and third) and VLDL (first and third & second and third).

Table 4: Post hoc analysis of different significant variable

Variables	Trimesters	95% Confidence Interval		Sig.
		Lower Bound	Upper Bound	
FT_4	First & Third	.0292	1.5349	0.042
TG	First & Third	-103.570	-35.310	0.000
	Second & Third	-81.610	-3.950	0.031
T.CHOL	First & Third	-55.278	-6.123	0.015
VLDL	First & Third	-20.710	-7.059	0.000
	Second & Third	-16.323	-0.790	0.031

The FT_3 value has significant negative correlation with HDL (r= -0.33**, p<0.01). Similarly, FT_4 value has significant negative correlation with TG (r= -0.22*, p<0.05) and VLDL (r= -0.22*, p<0.05) as shown in Table No. 5.

Table 5: Correlation between Thyroid profile (T3, T4 TSH) and Lipid profile in pregnant women

Variables		TG	T. Chol	HDL	LDL	VLDL
FT_3	**r**	0.15	-0.05	-0.33**	-0.06	0.15
	***p*-value**	0.14	0.62	**0.001**	0.53	0.14
FT_4	**r**	-0.22*	-0.13	0.08	-0.07	-0.22*
	***p*-value**	**0.02**	0.18	0.39	0.43	**0.02**
TSH	**r**	-0.15	-0.09	-0.05	-0.04	-0.14
	***p*-value**	0.14	0.34	0.59	0.62	0.14

Pearson Correlation: *Correlation is significant at the 0.05 level; **Correlation is significant at the 0.01 level

DISCUSSION

This study evaluates the significance of monitoring lipid levels and performing thyroid function tests throughout pregnancy to reduce the risk of problems for both the mother and the fetus. Pregnant females had higher level of FT_4 and Low TSH levels as compared to non-pregnant females; however, FT_3 level were not found to be significantly changed. The finding of this study is in accordance with the study of Zarghami N and Khandakar[14-15]. Serum HCG in pregnancy which binds to the TSH receptor on the thyroid cell membrane which is a weak stimulator, resulting in increased secretion of FT_4 and FT_3 and partial suppression of TSH. On other hand, fetus is absolutely dependent on maternal thyroid hormones for normal neurological development especially in first trimester since fetal thyroid gland reaches maturity by week 11-12, close to the end of the first trimester and begins to secrete thyroid hormones by about 16 weeks. In this study FT_3 was not significantly changed in different trimester, which is in support with the study of Yeasmin et al.[16]; however, some findings showed the increased synthesis of FT_3[17-18]. Deiodination of maternal FT_4 by the fetus results in local fetal production of triiodothyronine (FT_3). Maternal FT_3 does not cross the placenta so may appear to be normal reflecting the normal adaptation.

Dyslipidemia is commonly associated with pregnancy with the increased risk of pregnancy complications like preeclampsia. In this study TG and VLDL were significantly increased and HDL was significantly decreased in pregnant as compared to non-pregnant. The finding is supported by similar studies performed by Haddow et al. and Parveen et al., [19-20] whereas some of the studies conducted by Wiznitzer et al., Piechota et al., Herrera et al. and McElduff et al. have different findings [21-24].

The pattern of dyslipidemia is higher with increasing trimester of pregnancy. The increase is more in third trimester, when compared to second which is in support with other studies[19, 25-26]. This could be due to the metabolic changes that occur during pregnancy to support fetal growth and development. The rise in triglyceride is in parallel with the rise in estrogen levels in the pregnancy. The rise in triglyceride rich VLDL particles during pregnancy is dependent more on an increased rate of synthesis caused by estrogens than on a decrease in the rate of removal. These physiological changes support the metabolic adaptations required for fetal development and maternal energy needs. However, the elevated lipid levels during pregnancy are necessary for close monitoring to identify potential risks and manage any associated complications. The large rise in triglycerides is due to two factors, increased hepatic lipase activity, leading to enhanced hepatic triglyceride synthesis and reduced lipoprotein lipase activity, resulting in decreased catabolism of adipose tissue [20]. Dyslipidemia during pregnancy may contribute to an increased risk of cardiovascular diseases and impact both maternal and fetal health.

American Thyroid Association guideline has established the trimester specific TSH ranges as 0.1-2.5 µIU/ml in first trimester, 0.2-3.0 µIU/ml in second trimester and 0.3-3.0 µIU/ml in third trimester even 5.5 µIU/ml is the upper cutoffs of normal range. In this study euthyroid pregnant females of different trimesters were categorized into two groups, pregnant with trimester specific TSH range and pregnant with beyond trimester specific TSH range to find out any associations of variables between these groups. In first trimester pregnant females with TSH level >2.5-5.5 µIU/ml had significant higher level of FT_4 and LDL levels as compared to pregnant females with trimester specific TSH range (0.1-2.5 µIU/ml). In this study majority of pregnant female in second trimester and third trimester had TSH level within the

trimester specific range therefore further categorization was not done. Since the fetus dependent on maternal thyroid hormones and its high demand of thyroid and increased synthesis of HCG in first trimester of pregnancy results in derangement of TSH level. Therefore, screening of thyroid profile especially in first trimester is required. It is better to maintain TSH level within the trimester specific range with levothyroxine supplement for needed. Similarly screening for lipid profile is also important as dyslipidemia is seen in majority pregnancies to decrease adverse pregnancy outcomes.

This study has some limitations. It was conducted in a small number of sample sizes in different sub groups. We could not observe the same group of pregnant women from different trimesters. Due to limited time frame study of pregnancy outcomes was not done**.**

CONCLUSION

In medical interventions, screening of thyroid hormones, lipid profile and adjustment of TSH level according to trimester specific range in different trimesters should be implemented to improve lipid levels and decrease adverse pregnancy outcomes.

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