Association between Thyroid Dysfunction during Early Pregnancy and its Correlation with Lipid Abnormalities - A Cross-Sectional Study

Krishna Kumari[1], Siyavar Sharan[2], Rajendra Kumar[3]

ABSTRACT

Introduction: Thyroid disease is the second most common endocrine disorder affecting women of reproductive age and when left untreated during pregnancy is seen with an adverse risk of placental abruption, anaemia in pregnancy, miscarriages, hypertensive disorders and growth restriction. During pregnancy, thyroid gland regulates the production of hormones called triiodothyronine (T3) and thyroxine (T4) which plays an important function in the development of the brain and nervous system of the foetus. The aim of the present study is to assess the association between maternal lipid profile and thyroid stimulating hormone in pregnancy.

Materials and methods: The present study was performed in department of physiology. Out of which 100 antenatal cases from October, 2015 to October 2017 were enrolled after taking an informed written consent. The venous blood sample was collected from all subjects for measurement of lipid profile and thyroid hormones in the 16th week and 32nd week of gestation for analysis.

Results: It was observed that T3, T4, TSH were increased significantly among healthy pregnant women. Significant positive correlation was seen between TSH and Triglycerides and also between T3 and Cholesterol.

Conclusion: Screening for lipid profile and thyroid hormone in pregnant women is essential to prevent medical complications during pregnancy.

Keywords: Lipid Profile, Pregnancy, Thyroid Dysfunction, T3, T4

INTRODUCTION

Pregnancy is a time of various hormonal changes and metabolic demands which result in complex effects on thyroid function. It is commonly known that thyroid function undergoes many significant changes during pregnancy. Thyroid dysfunction is relatively a common disease which affects individuals, irrespective of their age and gender. Hypothyroidism is a common metabolic disorder which is existent in the general population. Thyroid hormones have important functions in embryogenesis and foetal development.[1]

Two pregnancy -related hormones- Beta human chorionic gonadotropin (Beta- hCG) and estrogen – cause increased thyroid hormone levels in blood. Beta hCG is similar to TSH and mildly stimulates the thyroid to produce more thyroid hormone. Increased estrogen produces higher levels of thyroid-binding globulin, a protein that transports thyroid hormone in the blood.[2] Thyroid disorders is the second most commonly found endocrine disorder affecting women of reproductive age, and obstetricians usually care for patients who have been previously diagnosed with alterations in the thyroid gland function.

These disorders can affect fertility, foetal growth and development. The physiological changes mostly seen during pregnancy such as increase in cardiac output, oxygen consumption and heat production may mimic mild thyrotoxicosis, and may exacerbate or improve underlying thyroid disorder.[3] Thyroid hormone causes increased cholesterol synthesis and degradation as well as increased lipolysis. This results in a lowering of serum cholesterol. In the first trimester of pregnancy, the foetus is completely dependent upon their mother for thyroid hormones. During the second and final trimesters of pregnancy, developing foetus continues to rely upon their mothers for some hormones. Problems related to brain development takes place when either the mother is unable to provide for the foetus' needs in the first trimester, or neither the mother nor the foetus can fulfil foetal needs during the remainder of pregnancy.[4]

Controlled hyper-stimulation of the ovaries with exogenous gonadotropins (for in vitro fertilization) resulted in a rise of serum Thyroid Binding Globulin (TBG), Thyroxine (T4), and triiodothyronine (T3) concentrations while there was a fall in serum free T4 concentration, and a small rise in serum TSH concentrations (usually within the normal range). The serum TBG concentration usually raises two fold in pregnancy because of estrogen which both increases TBG production and sialylation; the latter generally reduces the clearance of TBG. Excess quantity of TBG leads to an increment in both serum T3 and T4 concentrations, but not the serum free T3 and T4 concentrations. Thus, total T3 and T4 concentrations usually, show rise during the first half of pregnancy.[5]

[1]Associate Professor, Department of Physiology, [2]Associate Professor, Department of Microbiology, [3]Tutor, Department of Physiology, Patliputra Medical College Dhanbad, Jharkhand, India

Corresponding author: Dr. Siyavar Sharan, Associate Professor, Department of Microbiology, Patliputra Medical College Dhanbad, Jharkhand, India

How to cite this article: Krishna Kumari, Siyavar Sharan, Rajendra Kumar. Association between thyroid dysfunction during early pregnancy and its correlation with lipid abnormalities - a cross-sectional study. International Journal of Contemporary Medical Research 2018;5(6):F4-F7.

DOI: http://dx.doi.org/10.21276/ijcmr.2018.5.6.17

Thyroid dysfunction without any primary thyroid disease may result in various qualitative or quantitative changes of triglycerides, phospholipids, cholesterol, and other lipoproteins. Dyslipidemia, a consequence of thyroid dysfunction, generally increases the risk for cardiovascular disease. Some studies have shown that thyroid stimulating hormone (TSH), free thyroxine (FT4) and free triiodothyronine (FT3) are found to be significantly associated with lipid profile in the euthyroid population, regardless of gender.[6]

The action of thyroid stimulating hormone on lipid profile has been assumed to be mediated indirectly, through its effect on thyroid hormones. However, additional evidence suggests that this association is partially contributed by the direct extra-thyroidal effect of TSH on lipid profile. Normal pregnancy is associated with expected changes in lipid metabolism and rise in lipid concentration as gestation progresses. However, these changes are considered to be generally non-atherogenic, and fall sharply to pre-pregnancy levels following delivery.[7] Understanding the physiology of thyroid stimulating hormone in normal pregnancy has highlighted the importance of the consequences of abnormal function on obstetric outcome and foetal well-being. As to how modification in thyroid stimulating hormone modulates changes in lipid profile is yet to be ascertained in an Indian population. Hence estimation of lipid profile is strongly recommended during pregnancy to prevent deleterious effect of hyperlipidaemia associated with pregnancy.[8] Therefore, the aim of the current study is to determine the association between thyroid stimulating hormone and lipid profile in pregnant women.

MATERIAL AND METHODS

The present study was conducted in department of physiology. Out of which 100 antenatal cases from October, 2015 to October 2017 were enrolled after taking an informed written consent. The venous blood sample was collected from all the study subjects for measurement of lipid profile and thyroid hormones in the 16th week and 32nd week of gestation for analysis.

All pregnant women with a singleton pregnancy with a gestational age of 13-28 weeks, irrespective of parity and gravida were included. Pregnant women in whom hypertension was detected before 14 weeks and those with diseases or complications like chronic hypertension, obstetric and foetal Complications like hydrops foetalis, congenital foetal anomalies, Diabetes, Renal Disorders and Thyroid Disorders were excluded from the study.

Ten millilitres of blood was taken from pregnant women at each trimester then centrifuged (at 2500 round/min for 10 min) to get the serum, which is stored at (-20oc) unless used immediately. This part was divided to two part some of serum used to measured thyroid hormone (T3,T4,TSH) and others for measuring the lipid profile (cholesterol, triglycerides, HDL and LDL).

Serum samples were analysed for the following parameters by different methods. TSH, T_3 and T_4 by Chemiluminescence immunoassay, Triglyceride by Glycerol 3- Phosphate Oxidase method, Total cholesterol by Cholesterol oxidase – peroxidase method, HDL – Cholesterol by Phosphotungstic acid method, and LDL-Cholesterol level was Calculated by using Friedewald formula.

STATISTICAL ANALYSIS

It was performed using SPSS Version 21. Mean and Standard deviation was calculated and confidence intervals were calculated at the 95% level. The data was presented using frequencies, percentages, descriptive statistics followed by charts and graphs. Level of significance was set at 5%.

RESULTS

The mean Triglycerides, Cholesterol, High density lipoproteins, low density lipoproteins and TSH are depicted in the Table no. 1. It was found that serum cholesterol and serum triglycerides were increased from second to third trimester followed by decrease in the high density lipoprotein. It was also seen that low density lipoprotein and TSH was also found to be raised with increased gestational age among study subjects.

During second trimester, it was observed that there was positive correlation between TSH levels and lipid profile (Table 2). TSH was negatively correlated with cholesterol

Parameters	Second trimester	Third Trimester
Serum Cholesterol {mg/dl}	114.295 ± 10.163	142.324± 12.137
Serum Triglycerides {mg/dl}	108.28 ± 14.874	128.18± 14.274
HDL-Cholesterol {mg/dl}	39.115 ± 4.147	32.064± 2.124
LDL-Cholesterol {mg/dl}	82.410 ±12.938	114.214± 10.454
TSH Level {mIU/L}	2.528±0.0434	3.694±0.296

Table-1: Showing differences in mean values of lipid profile and thyroid hormones in second and third trimester of pregnancy

TSH	TSH	Cholesterol	Triglycerides	HDL	LDL
Cholesterol	-0.018				
Triglycerides	-0.140	0.094			
HDL	-0.040	0.021	0.078		
LDL	0.054	-0.071	-0.002	0.010	0.010

Table-2: Showing correlations between TSH and Lipid Profile parameters in 2nd trimester (correlation is significant at the 0.01 level and 0.05 level)

TSH	TSH	Cholesterol	Triglycerides	HDL	LDL
Cholesterol	-.314				
Triglycerides	.079	.075			
HDL	-.006	.090	.190		
LDL	.086	.136	-.059	-.059	-.052

Table-3: Showing correlations between TSH and Lipid Profile parameters in 3rd Trimester (Correlation is significant at the 0.01 level ad 0.05 level)

Parameters	r-value	p-value	Significance
TSH V/S Triglycerides	0.387	0.04	S
T3 V/S LDL	0.477	0.005	S
T4 V/S Total cholesterol	0.229	0.227	NS

Table-4: Showing correlation between lipid profile and thyroid profile in pregnant subjects

(r= -0.214, $p < 0.01$). With increase in TSH level, cholesterol levels decreases. However, they are still within normal range (Table 3). In third trimester TSH was correlated with Cholesterol (r= -0.214, $p < 0.01$). When TSH level increases, cholesterol levels decreases.

The Pearson correlation between lipid profile and thyroid is also applied which is shown in table no.4. It was found that positive correlation was found between thyroid stimulating hormone and triglycerides and also between T3 and low density lipoprotein which was also statistically significant. On the other hand, negative association was seen among T4 and Total Cholesterol which was statistically not significant.

DISCUSSION

Changes in lipid profile have been shown to occur during pregnancy to ensure a continuous supply of nutrients to the growing foetus, despite the frequently maternal food intake. Some previous studies showed that the most dramatic damage found is in the lipid and lipoprotein profile in pregnancy is serum triglyceridemia, which may be as high as two or three folds in the third trimester. It is commonly known that thyroid hormone has formidable effects on the transport of the plasma lipoproteins.[9]

According to Duntas increase of TC and LDL-C can be due to the effect of thyroid hormone on expression of LDL receptors. A significant rise in serum triglycerides level in our study is in agreement with the studies done by Aboul-Khair et al, Herrera et al. This increase might be due to the decreased formation of lipoprotein lipase which is responsible for the clearance of triglyceride rich lipoproteins.[10,11,12]

It was seen that positive correlation was found between TSH and TG, T3 and LDL-C and negative correlation was found between T4 and TC which is in concordance with the studies done by Thorkild et al. Earlier studies also reported that the striking changes in the lipid profile in normal pregnancy are serum hypertriglyceridemia, which may be as high as two to three folds in the last trimester over the levels when compared to non-pregnant women. In our study also this observation holds relevance and the increase in serum triglycerides was statistically significant. It was also found from studies that assessment of triglyceride level between 28 and 32 weeks could be suggestive of preeclampsia.[13]

Various studies have reported that hypertriglyceridemia could be related in the mechanism of hypertensive disorders during pregnancy. They also found a significant and positive association between proteinuria and triglyceride levels. These findings suggest that these lipids may be involved in the endothelial damage observed in preeclampsia patients. Subclinical thyroid dysfunction is probably more prevalent and frequently remains undiagnosed unless specific screening programs are initiated to disclose thyroid function abnormalities in early gestation period and if left untreated might result in hypothyroidism in many cases.[14,15,16]

A study was done to compare increased TG levels (>195 mg/dl) with decreased TG levels <195mg/dl among pregnant women. It was concluded that the most important outcome measures were the incidence of preterm birth, gestational diabetes, pre-eclampsia and uterine artery pulsatility index. Eight women with increased triglyceride levels had preeclampsia (17.8% v. 3.7% in the control group, $p<0.004$), preterm birth occurred in 24.4% and 5.9% in the increased triglyceride group and the control group, respectively (OR 5.1, 95% CI 1.9-13.8, $p<0.0001$).[17]

Triglycerides greater than 195mg/dl in second trimester and 236mg/dl in third trimester predispose pregnant females to develop preeclampsia. Triglycerides greater than 199mg/dl in second trimester and 216mg/dl in third trimester predispose pregnant females to develop Gestational Diabetes. Triglycerides greater than 203mg/dl in second trimester and greater than 233mg/dl in third trimester predispose pregnant females to have preterm deliveries. Hence estimation of lipid profile is strongly recommended as part of the laboratory investigation during pregnancy so as to institute prompt management strategies to prevent deleterious effect of hyperlipidaemia associated with pregnancy.[18]

The principle mechanism behind hypertriglyceridemia is hyperoestrogenemia that induces hepatic biosynthesis of triglycerides. Estrogens stimulate expression of TBG (thyroid binding globulin) in liver, and the normal rise in estrogen during pregnancy induces roughly a doubling in serum TBG concentrations. In the present study the result shows that T4 and T3 and TSH are significantly increased in healthy pregnant women compared to the value of healthy non pregnant women which is found to be similar to the study done by Rahman et.al. It is well established that there is much increase in concentration of thyroid binding globulin during pregnancy due to influence of high levels of circulating estrogens.[19,20]

Endothelial cells are disturbed directly or indirectly and vasoconstriction occurs all throughout the body. In our study it has been found that total cholesterol and triglycerides,

are significantly raised in healthy pregnant women with increased gestational age.[20] Further studies are required to check the association of thyroid profile with lipid profile with a larger sample size.

CONCLUSION

In the present study, it was observed that T3, T4 and TSH levels were raised due to the effect of estrogen, HCG, TBG and altered renal function. Among all parameters of lipid profile, Total Cholesterol, Triglycerides, LDL were found to be significantly increased due to endothelial dysfunction. There was a significant positive correlation found between TSH levels and cholesterol. Hence, TSH levels should be checked in early trimesters of pregnancy to prevent fatal, neonatal, and maternal complications.

REFERENCES

1. Muzamil Hassan, Sheema, Kouser Sideeq, S.M Saleem Khan. Prevalence of hypothyroidism in pregnant females of block hazratbal, Kashmir. International Journal of Contemporary Medical Research 2016;3:2841-2843.
2. Erem C., Kavgaci, H., Karahan,C., Mocan M. Z.and Telatar, M. Thyroid function tests in pregnant women with and without goiter in the eastern Black Searegion. Gynecol. Endocrinol 2001;15:293-297.
3. Osde, Balat, O Kuskay, S. Plasma lipid and lipoprotein concentrations in pregnancy induced hypertension. Clin. Biochem 2003;36:575-8.
4. Mulder JE. Thyroid diseases in women. Med Clin N Am. 1998; 82:103-125.
5. Guillaume J, Schussler GC, Goldman J. Components of the total serum thyroid hormone concentrations during pregnancy: High free thyroxine and blunted thyrotropin (TSH) response to TSH-releasing hormone in the first trimester. J Clin Endocrinol Metab. 1985; 60:678-884.
6. Lacka K, Lakoma H. Thyroid gland and pregnancy: Physiology and pathology. Wiad Lek. 2002;55:450-462.
7. Lazarus JH. Thyroid function in pregnancy. Brit Med Bull. 2011; 97:137-148.
8. Roos A, Bakker SJL, Links TP, Gans ROB, Wolffenbuttel BHR. Thyroid function is associated with components of the metabolic syndrome in euthyroid subjects. J Clin Endocrinol Metab. 2007; 92:491-496.
9. Wang F, Tan Y, Wang C, Zhang X, Zhao Y, Song X, et al. Thyroid-stimulating Hormone levels within the reference range are associated with serum lipid profiles independent of thyroid hormones. J Clin Endocrinol Metab. 2012; 97:2724-31.
10. Duntas LH, Brenta G. The effect of thyroid disorders on lipid levels and metabolism. Med Clin North Am 2012; 96: 269-281.
11. Aboul-Khair SA, Crooks J, Turnbull AC, Hytten FE. The physiological changes in thyroid function during pregnancy. Clin Sci. 1964; 27:195–207.
12. Herrera E, Gomez DC, Lasuncion MA. Lipid metabolism in pregnancy. Biol Neonate. 1987; 51:70-7.
13. Pusukuru, R., Shenoi, A. S., Kyada, P. K., Ghodke, B., Mehta, V., Bhuta, K., and Bhatia, A. Evaluation of Lipid Profile in Second and Third Trimester of Pregnancy. JCDR 216;10:QC12–QC16.
14. Suhad abdulaziz Ibrahem and Salman A. Ahmed. Study of association between lipid profile and thyroid hormones in Pregnancy. Journal of Al-Nahrain University. 2013; 16:37-45.
15. Desoye G, Schweditsch MO, Pfeiffer KP, Zechner I, and Kostner GM. Correlation of hormones with lipid and lipoprotein levels during normal pregnancy and post-partum. J Clin Endocrinol Metab PP 64:704-12. 1999.
16. Thorkild F, Laurids PR. Serum lipids in hyper and hypothyroidism before and after treatment." Clin. Chem. Acta. 1987; 162: 155-163.
17. Belo L, Caslake M, Gaffney D, et al. Changes in LDL size and HDL concentration in normal and preeclamptic pregnancies. Atherosclerosis. 2002; 162:425-32.
18. Glinoer D. The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology. Endocr Rev. 1997;18:404-33.
19. Rahman MH, Chowdhury MA, Alam MT. Serum thyroxine and triiodothyronine levels in normal pregnancy and pre-eclampsia. TAJ. 2007; 20:06-10.
20. Savita Rathore, Amita Parmar, Meena Varma. A relevance of lipid changes in hypothyroidism patients as- sociated with and without metabolic syndrome. International Journal of Contemporary Medical Research 2016;3:585-590.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 23-05-2018; **Accepted:** 25-06-2018; **Published:** 06-07-2018