

ORIGINAL ARTICLE

Study of Hypothyroidism in Pregnancy and its Association to Development of Pre-Eclampsia

Dr. A.U. Mehta*, Dr. Foram P. Shah**

*Professor and Head in Obstetrics & Gynecology Department, **MS 3rd year resident
B.J. Medical College, Civil Hospital, Ahmedabad

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ABSTRACT

AIMS: To study association of development of pre-eclampsia in hypothyroid cases. To study outcome and infertility association in hypothyroid cases. **SUBJECTS AND METHODS** : It is an observational study of 87 antenatal hypothyroid patients. Association of hypothyroidism to infertility noted. Patients were followed for the development of pre-eclampsia and outcome. **RESULTS** : There is 13.79% development of pre-eclampsia in hypothyroid cases, more so in patients with S.TSH level >8mIU/L. Hypothyroidism is also associated with infertility. **CONCLUSION** : The Odd's Ratio for development of pre-eclampsia in hypothyroid cases with S.TSH level >8mIU/L is 1.94 showing positive correlation between hypothyroidism and development of pre-eclampsia.

INTRODUCTION

Over the past twenty years there has been a major expansion of our knowledge regarding thyroid disorders associated with pregnancy. The impact of iodine deficiency on the mother and developing fetus and the adverse effects of maternal hypothyroidism on other aspects of maternal health and fetal mental status have been under evaluation for years⁽¹⁾. Pregnancy may affect the course of thyroid disorder and conversely thyroid disorders may affect the course of pregnancy.

There is still a raging debate regarding the thyroid functional changes in pre-eclampsia. Alterations in thyroid gland function have been correlated with the severity of pre-eclampsia by some and totally rejected by others. Kumar et al showed that odds ratio corresponding to TSH levels >5mIU/L in the pre-eclampsia group compared to the normotensive controls was 4.85 and concluded that TSH is a strong associating factor for pre-eclampsia⁽²⁾. However, a report from Jordan in 2003 found no significant difference in the levels of serum FT4, FT3 and TSH in pre-eclamptic patients and various healthy controls in different gestational age subgroups⁽³⁾. Other reports found a significant correlation between hormones, especially elevated serum TSH and pre-eclampsia^(4,5,6). The most consistent finding from different studies is the link between biochemical hypothyroidism and pre-eclampsia.

A large Colorado study showed a continuous graded increase in serum cholesterol over a range of serum TSH values from <0.3 to >60mIU/L⁽⁷⁾. It has been noted that mild thyroid failure can significantly increase systemic vascular resistance and impair cardiac systolic and diastolic function⁽⁸⁾. Subclinical hypothyroidism or mild thyroid failure was shown to be an independent risk factor for both myocardial infarction and radiologically visible aortic atherosclerosis in a Dutch study⁽⁹⁾. The finding of impaired flow-mediated endothelium dependent vasodilatation even in subjects with borderline hypothyroidism or high-normal serum TSH values⁽¹⁰⁾ is of potential importance; with the postulation that serum TSH elevation may directly cause endothelial dysfunction which is a proposed core pathogenic mechanism in pre-eclampsia and eclampsia. Other evidence suggests that high levels of exposure to anti-angiogenic factors as in pre-eclampsia may be associated with increased risk for reduced thyroid function during after pregnancy^(11,12,13). The meta-analysis of the relevant studies and their references are shown in subsequent sections.

AIMS AND OBJECTIVES

- 1) To study development of pre-eclampsia in patients with sub-clinical or overt hypothyroidism.

Correspondence Address : Dr. A.U.Mehta
A-33, Sharnam-8, Near Super Society, Satellite, Ahmedabad – 380015
E-mail : the_amiya@yahoo.co.in

2) To study association between known hypothyroid cases and infertility as well as history of 2 or more abortions

3) To study outcome in pre-eclamptic hypothyroid cases

MATERIALS AND METHOD

My study is an observational single centre study. There is no control group.

This study is carried out in out-patient and in-patient Department of Obstetrics and Gynaecology, Civil Hospital, Ahmedabad.

The study spans over a period of 2 years starting from November 2015 to October 2017.

SELECTION CRITERIA

INCLUSION CRITERIA :

- All Hypothyroid pregnant women and those with elevated S.TSH level in patients before 20 weeks of gestation.

EXCLUSION CRITERIA :

- All euthyroid pregnant women and those with hypertension before pregnancy or detected in first trimester.
- All pregnant patients with other medical disorders like Diabetes Mellitus, renal diseases.

In this study, I have taken the permission of the ethics committee and the Head of Department of Obstetrics and Gynaecology, civil hospital, Ahmedabad and have attended the patients coming to outpatient department of obstetrics and gynaecology, labour room, wards. The antenatal patients fulfilling the inclusion criteria were included in the study. Their baseline data like demographic details, clinical history, laboratory investigations are recorded in a predefined proforma. All the patients were followed up throughout pregnancy to see for development of preeclampsia and pregnancy outcome. The data of patients was recorded and analysed by using appropriate statistical tests.

Clinical parameters used for diagnosis of hypothyroidism and hypertension :

S.TSH value used for diagnosis of hypothyroidism was measured by ARCHITECT TSH machine(which is calibrated periodically) by Chemiluminescent Microparticle Immunoassay (CMIA). Blood pressure, urine albumin and pedal edema were used for diagnosis of gestational hypertension, pre-eclampsia.

Definitions :

Subclinical Hypothyroidism – Normal free T4 level with increased S.TSH level between 2.5 and 8mIU/L. Overt Hypothyroidism – Low free T4 Level with increased

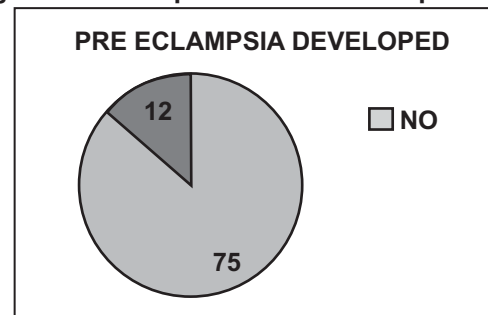
S.TSH level OR S.TSH >8mIU/L irrespective of free T4 level.

Gestational hypertension – BP >140/90mmHg without proteinuria detected first time during pregnancy after 20 weeks of pregnancy. Pre-eclampsia – BP >140/90 mmHg with proteinuria detected first time during pregnancy after 20 weeks of pregnancy.

OBSERVATIONS AND DISCUSSION

Out of 87 hypothyroid patients of the study, association of development of pre-eclampsia and other outcome related observations are as follows :

Figure 1 : Development of Pre-Eclampsia



Out of 87 hypothyroid patients of the cohort, 12 (13.79%) developed pre-eclampsia during pregnancy.

Table 1: Total number of patients distribution according to Subclinical and Overt hypothyroidism

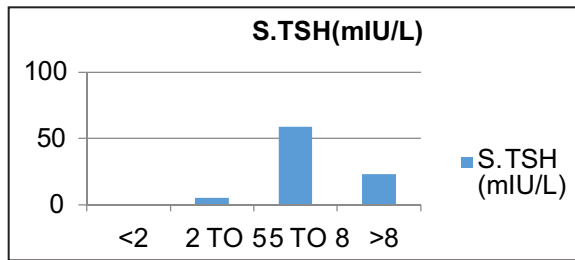
S.TSH level (mIU/L)	No. of total patients
2 TO 5	5(5.74%)
5 TO 8	59(67.81%)
>8	23(26.43%)

Table 2: Strength of association between S.TSH level and development of Pre-eclampsia :

S.TSH level (mIU/L)	PREECLAMPSIA PRESENT	PREECLAMPSIA ABSENT	TOTAL
>8	5	18	23
<8	8	56	64
	13	74	87

From the data as shown in the above table, the Odd's Ratio comes out to be 1.94 which is suggestive that the chances of development of pre-eclampsia in the hypothyroid patients with S.TSH level >8mIU/L is 1.94 times higher than the those with S. TSH level <8 mIU/L.

Figure 2 :

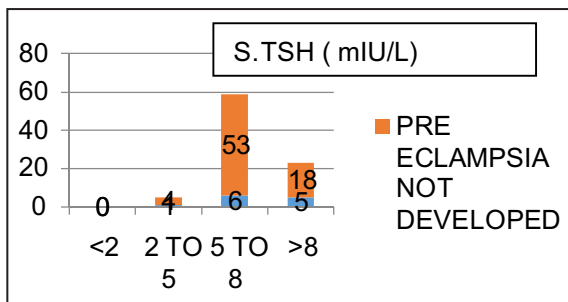


In this study, 73.56% patients had subclinical hypothyroidism and 26.44% patients had overt hypothyroidism.

Table 3: Association of Pre-eclampsia development in hypothyroid cases according to S.TSH level

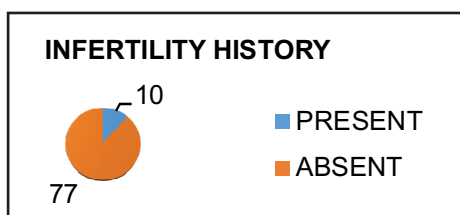
HYPOTHYROIDISM LEVEL (mIU/L)	PERCENTAGE OF PRE-ECLAMPSIA DEVELOPMENT
2 TO 5	20%
5 TO 8	10.16%
>8	21.73%

Figure 3 :



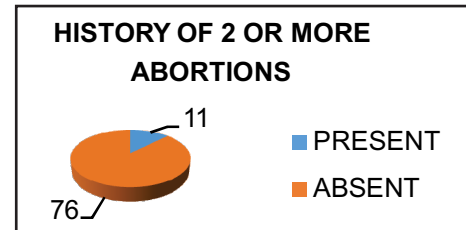
As shown in above table and figure, overall, overt hypothyroid patients are maximum in number in the cohort as compared to subclinical hypothyroidism. And as the S.TSH level increases, there are more chances to develop pre-eclampsia showing significant association between the level of S.TSH and development of pre-eclampsia during pregnancy.

Figure 4: Association between known hypothyroid cases and history of infertility



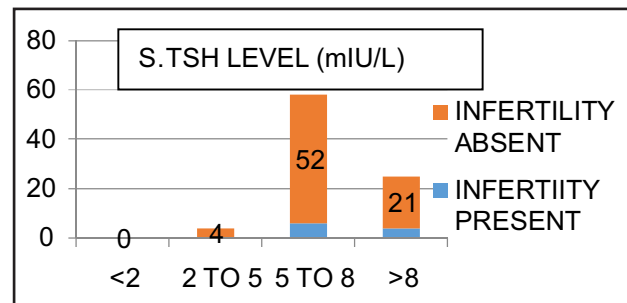
As shown in the above pie chart; out of 87 hypothyroid cases of the cohort, 10 patients had the previous history of infertility making 11.49%. This shows the association between high S.TSH level and infertility.

Figure 5: Association between known hypothyroid cases and history of 2 or more abortions



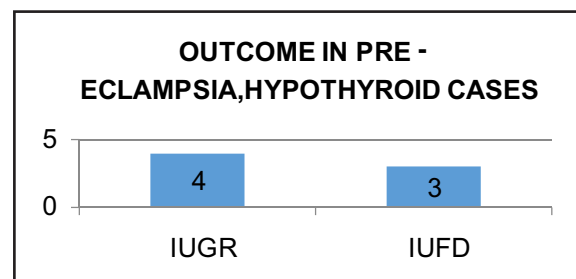
As shown in the above pie chart; out of 87 hypothyroid cases of the cohort, 11 patients had the previous history of recurrent abortions(2 or more in number) making 12.64%. This shows the association between high S.TSH level and bad obstetric history in the form of more numbers of abortions.

Figure 6: Association between subclinical & overt hypothyroidism and infertility



As shown in this bar-chart, the percentage of infertility in patients increases with higher serum levels of TSH. In this study there no cases of infertility in subclinical hypothyroid cases.

Figure 7: Outcome in pre-eclamptic hypothyroid cases



In my study, out of total 87cases and out of the cases having hypothyroidism with development of pre-eclampsia, in 4 cases the neonatal outcome was IUGR and in 3 cases the neonatal outcome was stillborn.

CONCLUSION

- My study concludes that, there is 13.79% development of pre-eclampsia in known hypothyroid cases indicating significant association of hypothyroidism and pre-eclampsia.
- The Odd's Ratio for development of pre-eclampsia in hypothyroid cases with S.TSH level >8mIU/L is 1.94 showing positive correlation between hypothyroidism and development of pre-eclampsia. This study implies a further research in the linkage and causality between overt hypothyroidism and development of pre-eclampsia.
- The study shows more prevalence of patients with S.TSH level between 5 and 8 among all cases of hypothyroidism.
- The study also shows that development of pre-eclampsia is more prevalent in overt hypothyroid cases with S.TSH level >8 mIU/L.
- Hypothyroidism in pregnancy is also associated with history of infertility and recurrent abortion.

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