









ASSOCIATION BETWEEN TSH STATUS AND PREVALENCE OF
MISCARRIAGES AND STILLBIRTH

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Abstract

Thyroid hormones play a significant role in normal human body growth. Abnormalities in thyroid stimulating hormone (TSH) levels can result in pregnancy loss due to miscarriages and intrauterine death (IUD). The objective of the study was to assess the levels of association of thyroid stimulating hormone with miscarriages and IUD. The descriptive study involving 110 samples between 18-40 years of age fulfilling inclusion criteria were sampled for TSH testing (2ml blood) after attaining their written informed consent. The mean age of participants was 29.49±4.26 year. The prevalence of hypothyroidism and hyperthyroidism was 3.64% and 2.73%, respectively. Complications like gestational hypertension, depression and oligomenorrhea were found prevalent in these females. Majority of females were taking high/low iodine than recommended iodine level (150mcg). This work shows that there is a significant association between pregnancy loss and disturbed TSH levels among pregnant females.

Keywords: Hypo-/hyperthyroidism. Iodine Intake. IUD. Pregnant Females. TSH.

1. Introduction

Thyroidal hormones especially thyroid stimulating hormone (TSH) has its utmost importance in regulating normal pregnancy outcomes by managing iodine uptake by blood cells. The activity of the thyroid increases during pregnancy, and the maximum limit of TSH during pregnancy is 2.5 mU/l in the first trimester and 3.0 mU/l in the second or third trimester, which is used for diagnosis of subclinical and overt hypothyroidism (Korevaar 2018). Lower verbal IQ has been observed in children with mothers with hypothyroidism in early pregnancy (Andersen et al. 2018) and hyperthyroidism can result in early and late pregnancy loss due to IUD, miscarriages, stillbirth or spontaneous abortions (Brent 2012; Andersen et al. 2014). Until the 17 weeks of gestation fetus relies on mother's thyroid hormones for its growth. Disturbed TSH level (hypo-/hyperthyroidism) may cause elevated chance of pregnancy loss (5% in total population), lifelong hypertension, postpartum thyroiditis, impaired child growth and depression (Feki et al. 2008). Gestational hypothyroidism is prevalent up to 2-3% in subclinical cases and 0.3-0.5% for overt hypothyroidism. Rate of hyperthyroidism is estimated as almost 0.2-0.4% in total pregnancies (Khalid et al. 2013). Although CT scan are required in severe cases of thyroidal dysfunction like diagnosis and detection of thyroid cancer, the simplest and easiest method for initial screening of hypo- and hyperthyroidism are TSH,

free thyroxine (free T4), and anti-thyroid peroxidase antibodies (anti-TPO Abs) T4 (Koulouri et al. 2013; Sheehan 2016).

Low iodine intake in developing countries is one of the major reasons of iodine deficiency (Biban and Lichiardopol 2017). This may lead to a disturbed TSH in pregnant mothers. In this study TSH levels are measured in pregnant females, which suggest a relation between irregularity of TSH and spontaneous abortion/IUD exists.

2. Material and Methods

This study was conducted after approval from Ethical review board, Department of Biotechnology, Lahore College for Women University, Lahore and Institutional Review Board of Sheikh Zayed Medical Complex, Lahore. 110 females aged between 18 to 40 years was registered in the outpatient department of Sheikh Zayed Hospital with earlier miscarriage or IUD. Patients with autoimmune infections, history of either clinically related diseases, cousin marriages, late marriages and congenital thyroidal disorders were excluded from this study. The sample size of 110 was estimated by using 95% confidence level 5% margin of error with expected prevalence of thyroidal disorders among females with recent history of miscarriages/stillbirth as 5%.

A well-structured questionnaire was filled by each patient after taking written informed consent. The questionnaire included patient's clinical history, miscarriage history, thyroidal history, BMI and dietary chart (relating to iodine intake). Each patient was registered to give 2 ml blood for serum TSH analysis. Blood samples were stored at -20°C until analysis by using human TSH ELISA kit (Calbiotech, USA). The quality control pools were used with each sample run. The analytical sensitivity of test was 0.5uLU/ml. The cut-off value for TSH was 0.4-4.2 uLU/ml.

Data was analyzed by using statistical package for social sciences (SPSS) version 21.0. Frequencies of variables were calculated by using chi square test. Quantitative variables were analyzed by T-test ($p < 0.005$ was considered significant) and their standard deviation, mean and median was calculated. Association between TSH and miscarriages/IUD was analyzed by using ANOVA.

3. Results

In this study a total number of 110 females (age 18-40 years) having a history of pregnancy loss fulfilling inclusion criteria and attending Sheikh Zayed Medical Complex, Lahore in the period of six months were enrolled. The mean age of these participants was 29.49 ± 4.26 years.

The prevalence of hypothyroidism and hyperthyroidism was quite low in total number of pregnant females with pregnancy loss (Table 1).

Table 1. Frequency of TSH status in pregnant females (N=110).

Thyroid status	Percentage (%)
Hypothyroidism	3.64
Hyperthyroidism	2.73
Euthyroid	93.63

Majority of participants suffered from miscarriages or IUD either complained fatigue followed by depression and constipation or heat sensitivity and alopecia in addition to other related complications. These results showed that depression, fatigue and constipation were the major complications playing a role in participants suffered from miscarriages or IUD (Figure 1).

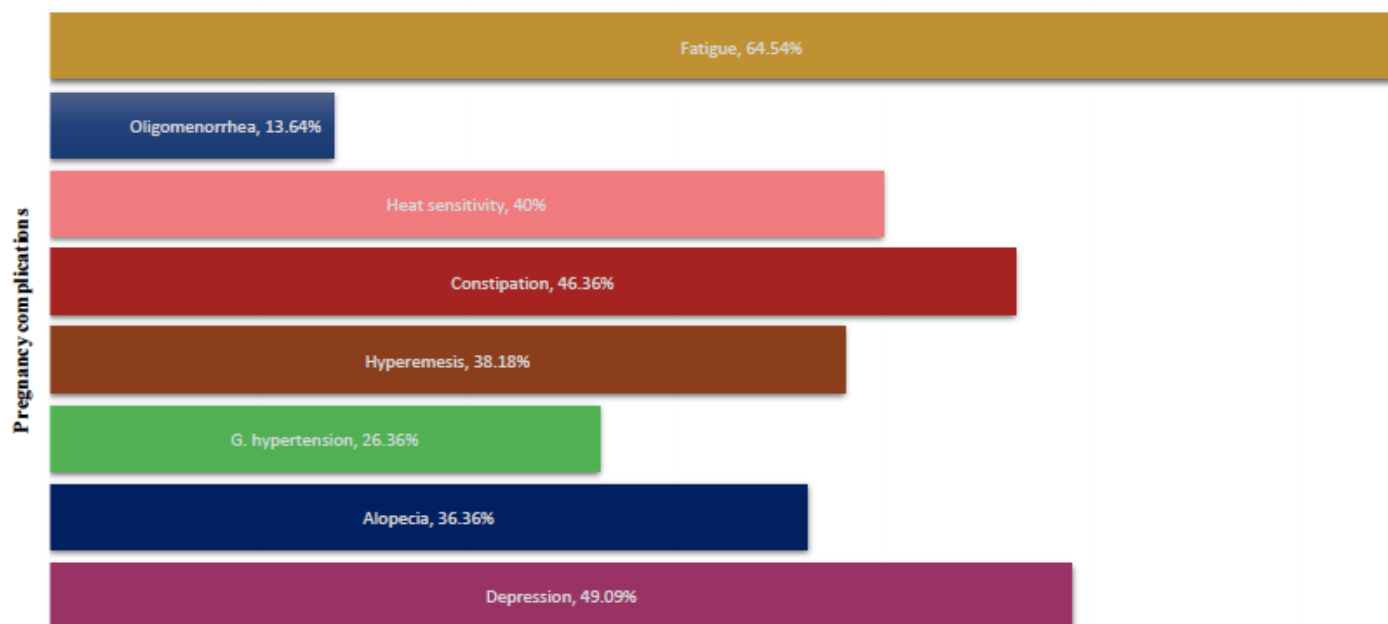


Figure 1. Comparison of fatigue, oligomenorrhea, heat sensitivity, constipation, hyperemesis, G. hypertension, alopecia and depression with miscarriages/IUD within total number of participants (N=110).

Gestational hypertension was present in 2 participants who were hypothyroid and 1 who was hyperthyroid (Table 2).

Table 2. Association of thyroid disorders and gestational hypertension.

Thyroid Disorder	Normal (N)	Gestational Hypertensive (N)
Hypothyroidism	2	2
Hyperthyroidism	2	1

In all three participants who were hyperthyroid, their iodine intake from food was above (>235 mcg) normal level, whereas the hypothyroid patients 2 had a low and 2 had a normal iodine level (Table 3).

Table 3. Association of iodine intake with hypo and hyperthyroidism (N=110).

Iodine intake (mcg)	Hypothyroidism N (%)	Hyperthyroidism N (%)
53-113	2 (1.82%)	0 (00)
114-174	2 (1.82%)	0 (00)
175-235	0 (00)	3 (2.73%)
Total	4 (3.64%)	3 (2.73%)

Table 4. Comparison of foetus age with miscarriages and IUD (N=110).

Pregnancy loss	Foetus age (N)			Total (N)
	1st trimester	2nd trimester	3rd trimester	
Miscarriages	65	5	0	70
IUD	0 (00)	39	1	40
Total	65	44	1	110

In the present study 92.72% were unaware of their thyroidal status at the time of their miscarriages and IUD. Only eight participants (5 with miscarriages and 3 having IUD) were aware of their thyroidal status. Out of those females who were not aware of their TSH status, 3 were later found to be hyperthyroid and 2 were hypothyroid. Out of the aware group only 2 had some knowledge about their thyroidal history. In Table 4 the number miscarriages and IUD in different trimesters is tabulated, showing highest number of miscarriages and IUDs in first and second trimester, respectively.

4. Discussion

Thyroid disorders (hypothyroidism and hyperthyroidism) are amongst the most common endocrinological disorders. During pregnancy hypothyroidism is not uncommon. But unfortunately, the symptoms such as tiredness and weight gain, which is normal during pregnancy can be overlooked, which may pose a risk for both mother and baby, if left untreated.

Worldwide thyroid disorders can lead to pregnancy complications, which may result in fetal loss. This study was conducted to find prevalence and association of hypothyroidism and hyperthyroidism with pregnancy loss in females. The present study included participants between the age group of 18-40 years with the mean age of 29.49 years. In a similar study, it was reported that most of the females with high rate of miscarriages suffering from hypo/hyper thyroid consequences were nearly 29 years old (Negro et al. 2016).

In present study it was found that majority females suffering from pregnancy loss were having a normal range of TSH during their gestational period. Only few participants were identified with high or low TSH levels during their pregnancy. A similar study conducted on Tunisian females reported that 3.2% and 1.3% of pregnant females suffered from hypo- and hyperthyroidism, respectively (Feki et al. 2008). In Indian pregnant females the prevalence of hypothyroidism was reported as 4%, whereas of hyperthyroidism was 0.3%. The prevalence ratio of hypothyroidism during conception is greater than hyperthyroidism (Nambiar et al. 2011), which is similar to findings of the current study. Furthermore, gestational hypertension is more prevalent in hypothyroid females as compared to euthyroid and hyperthyroid females (Wilson et al. 2012), which is why it is important to monitor females suffering from preeclampsia (Gui et al. 2020).

A study conducted in Zurich institute reported that the recommended iodine intake during pregnancy to be 150mcg per day. Any disturbance in the iodine level had a risk of thyroidal disorders, which can result in pregnancy loss. Moreover, imbalanced maternal iodine level can effect fetal growth and development (Zimmermann and Boelaert 2015; Huang et al. 2020). The present study is in accordance with these findings. It was noted that most of the females with pregnancy loss were unaware of their thyroidal status. In a research by Wang and co-workers it was reported that only 4-6% females out of total females suffering from pregnancy loss were aware of their TSH levels (Wang et al. 2011). Awareness of thyroid profile could reduce the risk of pregnancy loss, which is also recommended in present study (Wang et al. 2011).

Miscarriages were mostly carried out in first trimester whereas, IUD cases were more common in second or third trimester. A study briefed that 60% of miscarriages occurred during first trimester (Poppe and Glinoeer 2003; Jiashu et al. 2019). Another study reported that IUDs occurred at or after 20 weeks of gestation (Black et al. 2008). In the US, an assessment was conducted to evaluate the effectiveness of thyroid hormone treatment among pregnant women with subclinical hypothyroidism (Maraka et al. 2017), and in an earlier study it was found that untreated subclinical hyperthyroidic pregnant female with are at higher risk for pregnancy loss and neonatal death compared with euthyroid women (Maraka et al. 2016). In Australia, the presence of thyroid autoantibodies (18%) was determined in an unselected population of women in their late first trimester (Mcelduff and Morris 2008). Overall, it was concluded that hypo- (3.64%) and hyperthyroidism (2.73%) is more prevalent in South Asian pregnant females in their middle fertility age. These results suggest that more work should be done to prevent pregnancy complications due to hypo- or hyperthyroidism.

5. Conclusions

Low iodine intake in developing countries is one of the major reasons of iodine deficiency, which leads to disturbance in TSH level in pregnant females. In this study it is found that a relation between irregularity of TSH and spontaneous abortion/IUD exist. Therefore, it suggested that testing of TSH in early stage of pregnancy should be done to prevent miscarriages.

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