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Gynecology

THYROID HORMONE AS A RISK FACTOR FOR MISCARRIAGE!!

Dr Yashi Srivastava	Junior Resident Department of Obst and Gynae MLN Medical College, Prayagraj, Uttar Pradesh, India
Dr Urvashi Barman Singh*	Associate Professor Department of Obs and Gynae MLN Medical College Prayagraj, Uttar Pradesh India. *Corresponding Author
Dr Meena Dayal	Professor Department of Obs and Gynae MLN Medical College Prayagraj, Uttar Pradesh India.
Dr Shakti Jain	Assistant Professor Department of Obs and Gynae MLN Medical College Prayagraj, Uttar Pradesh, India.

ABSTRACT ***Aim:*** Abnormal thyroid hormone levels could give rise to increased placentation defects that underlies the association between maternal thyroid dysfunction and adverse pregnancy outcomes. This study was designed to analyze the thyroid hormone profile in the study groups and its possible association with the risk of abortion during pregnancy.

***Methodology*:** This was a analytical observational cohort study conducted over a time period of 1 year, on 120 women attending the antenatal clinic in Department of Obstetrics and Gynaecology, Swaroop Rani Nehru Hospital, Prayagraj. The patients were divided into two groups, Group 1 ($n = 80$) included women with previous history of abortions and group 2 ($n = 40$,control group) included women with no history of abortions. $S.T_3$, $S.T_4$ and TSH levels were estimated and compared in both the groups.

Result: In the present study, the abortion rate was higher in the hypothyroid group as compared to euthyroid group ($p < 0.05$). TSH was found to be strongly associated with abortion in the cases ($p \leq 0.001$). TSH levels were significantly higher in women who had an history of previous pregnancy loss than the women who had successful continuation of pregnancy.

Conclusion: S.TSH was found to be strongly associated with abortions, mainly in the first trimester, in both the groups. Thus, screening of thyroid dysfunction in early pregnancy has clinical significance and adequate T_4 replacement therapy if given in cases of hypothyroidism would help to reduce the risk of miscarriage in these women.

KEYWORDS :

INTRODUCTION

Recurrent Miscarriage is defined as three or more failed clinical pregnancies at less than 20 weeks of gestation or fetal weight less than 500 grams, that ends spontaneously prior the fetus can survive.(1) The World Health Organization (WHO) defines this unsurvivable state as a fetus weighing 500gm or less, which typically corresponds to a fetal age of 20-22 weeks. The estimated incidence of recurrent miscarriage is reported as between 1% and 5% of woman of reproductive age.(1) Known causes of miscarriage include chromosomal abnormalities, Infectious diseases, endocrinological abnormalities, antiphospholipid antibodies, uterine anomalies.(2,3,4,5) Several endocrinological abnormalities may include thyroid disease, uncontrolled diabetes and decreased ovarian reserve that may be implicated as etiologic factors for recurrent pregnancy loss.

Following implantation, the maintenance of the pregnancy is dependent on a multitude of endocrinological events that will eventually aid in the successful growth and development of the fetus. It is estimated that approximately 8-12% of all pregnancy losses are the result of endocrine factors.(6)Thyroid disturbances are common in women during their reproductive years. Thyroid dysfunction interferes with human reproductive physiology, reduces the likelihood of pregnancy and adversely affects pregnancy outcome, thus becoming relevant in the algorithm of reproductive dysfunction.(7)

Autoimmune thyroid disease is present in around 4% of young females and up to 15% are at risk because they are thyroid antibody-positive. There is a strong relationship between thyroid immunity on one hand and infertility, miscarriage, and thyroid disturbances in pregnancy and postpartum, on the other hand. Even minimal hypothyroidism can increase rates of miscarriage and may also have adverse effects on later cognitive development of the offspring.(7) Pregnant women with subclinical hypothyroidism or thyroid antibodies have an increased risk of complications, especially pre-eclampsia, perinatal mortality, and miscarriage.(6)

AIMS AND OBJECTIVES

To determine the thyroid hormones (total T4, T3 and TSH) in women with history of recurrent miscarriage and compare the pregnancy outcomes in euthyroid and hypothyroid women.

MATERIAL AND METHODS

- Prospective observational case-control study
- Among pregnant women attending the antenatal clinic of Swaroop Rani Nehru hospital, Prayagraj.
- Study duration: June 2018- June 2019

Criteria for selection of cases-

1). Women who have definite history of spontaneous pregnancy losses/implantation failure, non pregnant and pregnant.
2). Normal pregnant and non pregnant women.

Criteria for exclusion of cases-

1). Women with documented:
- uterine anomalies
- abnormal karyotype
- polycystic ovarian syndrome
- endometriosis

2). Women with:
- chronic disease or
- with chronic ongoing treatment
- thrombophilia
- documented endocrinopathies.

All women of 20-40 years of age after taking detailed history and thorough clinical examination were subjected to routine investigations. Women were followed up to see the conception rate and the outcome of pregnancy, in particular, miscarriage rate. The t-test for continuous variables and chi-square test for categorical variables were applied and correlation between these factors for evaluation of miscarriage in patients with low ovarian reserve was seen. For all statistical analysis p-value <0.05 was considered as significant.

OBSERVATION

Table 1: Distribution of cases under study (n=120)

Group	Criteria	No. of cases
I	Cases- with history of miscarriages	80
II	Control- without history of miscarriages	40

The total numbers of patients under study were divided into two major

groups (table 1). Patients with history of miscarriages were categorized as Group I which included 80 out of 120 women and patients with no history of miscarriages were categorized as Group II which included 40 out of 120 women.

Table 2: Distribution based on demographic variables. (n=120)

Characteristics		Number of cases (n=120)	Percentage
Age(years)	<30 yrs ≥30 yrs	88 32	73.33% 26.66%
Literacy	Illiterate literate	39 81	32.50% 67.50%
Residential area	Rural Urban	65 55	54.17% 45.83%
Age at marriage	<30 yrs ≥30 yrs	83 37	69.16% 30.83%

In the study population, it was observed that 88(73.33%) cases were of age group <30yrs and 32(26.66%) were above 30 yrs. Majority of the cases 81(61.50%) were literate. More than half i.e. 65(54.17%) cases belonged to rural area and 55(45.83%) were from urban area. 83(69.16%) cases were married before 30 years of age and 37(30.83%) after 30 yrs of age (table 2).

Table 3: S.T3, T4 and S.TSH levels in euthyroid and hypothyroid women with recurrent pregnancy loss (group I)

S.no.	Thyroid status	No. of cases (n=80)	%	Mean T3 levels (pg/dl)	Mean T4 levels (ng/dl)	Mean S.TSH(µIU/ml)± SD
1	Euthyroid	24	30%	3.25	1.81	2.38±0.688
2	Hypothyroid	56	70%	2.17	1.35	10.94±2.83

In group I, out of 80 women, more than half i.e. 56(70%) had hypothyroidism with mean S.TSH value of 10.94 µIU/ml and 24(30%) were euthyroid with mean S.TSH of 2.38 µIU/ml (table 3).

Table 4: S.T3, T4 and S.TSH levels in euthyroid and hypothyroid women in control group (group II)

S. no.	Thyroid status	No. of cases (n=40)	%	Mean T3 levels (ng/dl)	Mean T4 levels (µg/dl)	Mean S.TSH levels (µIU/ml) ±SD
1	Euthyroid	25	62.5%	1.89	1.49	2.70±0.788
2	Hypothyroid (S.TSH≥4µIU/ml)	15	37.5%	2.17	0.49	7.43±1.41

In group II, 25(62.5%) women, out of 40, were euthyroid and mean S.TSH of 2.70 µIU/ml, 15(37.5%) women had hypothyroidism and mean S.TSH of 7.43 µIU/ml (table 4).

Table 5: Comparison of S.TSH levels in the two groups

Groups	S.TSH(µIU/ml)			p-value
	EUTHYROID	HYPOTHYROID	Mean±SD	P value
I(n=80)	24(30%)	56(70%)	8.38±4.59	<0.0001
II(n=40)	25(62.5%)	15(37.5%)	4.47±2.52	

On evaluating and comparing the mean S.TSH levels in both groups, it was observed that in group I, the high S.TSH levels (mean value of 8.38µIU/ml) were seen with majority of the cases being hypothyroid. Whereas in group II, the S.TSH values were comparatively lower (mean value of 4.47µIU/ml) and maximum cases in group II were euthyroid. This correlation between recurrent abortions and S.TSH levels was seen to be statistically significant with p value<0.0001(table 5).

Table 6: Outcome of pregnancy and correlation with S.TSH in group I

Outcome	Group I(n=80)		S.TSH values(µIU /ml)	
	No. of cases	%	Range	Mean±SD
Aborted before 20 weeks	21	61.76 %	7.24-15.43	12.20±2.08
Pregnancy beyond 20 weeks	13	38.23%	1.35-3.60	2.43±0.761
Total	**34**	**100%**	**p-value:<0.0001**	

Out of 80 women in group I, 34 conceived during the study period and it was seen that 21(61.76%) who aborted before 20 weeks had high S.TSH levels with a mean value of 7.24µIU /ml and those who continued pregnancy beyond 20 weeks had a lower mean S.TSH levels of 2.43µIU /ml. the difference observed was found to be statistically significant (p-<0.0001) (table 6).

Table 7: Outcome of pregnancy and correlation with S.TSH in group II

Outcome	Group II(n=40)		S.TSH values(µIU /ml)	
	No. of cases	%	Range	Mean±SD
Aborted before 20 weeks	4	15.38%	5.64-9.76	7.68±1.53
Pregnancy beyond 20 weeks	22	84.61%	1.09-4.456	2.78±0.87
Total	**26**	**100%**	**p-value:<0.0001**	

Similar to the results observed in group I, out of 40 women in group II, 26 conceived during the study period and it was seen that 4(15.38%) who aborted before 20 weeks had high S.TSH levels with a mean value of 7.68 µIU /ml and those who continued pregnancy beyond 20 weeks had a lower mean S.TSH levels of 2.78 µIU /ml. The difference observed was found to be statistically significant (p-<0.0001) (table 7).

DISCUSSION

The present study was conducted on 120 women over a time period of one year. The patients were divided into two groups based on the history of previous miscarriages. 80 women with history of previous abortions were taken as the cases and 40 with no history of previous pregnancy losses were included as the control group (table 1). The main objective of the study was to assess the predictive potential of serum thyroid hormones in pregnancy outcome, particularly miscarriage rates. The patients were evaluated for levels of thyroid hormone profile, with the aim to identify their role as a risk factor for miscarriages and to see S.TSH as a predictor of miscarriage.

Maximum number of cases i.e. 59(73.75%) in group I and 29(72.50%) in group II, including more than half of the study population were in the age group 21-30yrs of age (table 2). In the current study it was observed that the risk of miscarriage increased with increasing serum TSH levels and the correlation seen was statistically significant (p<0.05) (table 5). On analyzing the thyroid profile of women who conceived in group I, mean S.TSH value of 12.20 was observed in women who aborted before 20 weeks as compared to a value of 2.43 in women who continued their pregnancy beyond 20 weeks. Similar observations were made in group II, where a mean S.TSH level of 7.68 was seen in women who aborted before 20 weeks and 2.78 in those who continued beyond 20 weeks (table 6 and 7). The association between S.TSH and outcome of pregnancy i.e. increased rate of miscarriage was seen to have a significant correlation with a p value of <0.001.

Taylor et al (2015)(8) also observed best pregnancy outcomes in women with target TSH levels, and a strong risk of miscarriage at TSH levels exceeding 4.5 mU/L. Women with S.TSH levels between 4.5-10 mU/L or TSH greater than 10 mU/L had an increased risk of miscarriage of 1.8 or 3.95 times respectively, compared to women who had a normal TSH (0.2-2.5mU/L) during early pregnancy. Women with a TSH between 2.51-4.5mU/L did not appear to have an increased risk of miscarriage. Sarkar et al (2012)(6) also observed that pregnant women with subclinical hypothyroidism or thyroid antibodies have an increased risk of complications, especially pre-eclampsia, perinatal mortality, and miscarriage.In contrast to this, Hirsch et al(2013)(9) found no statistically significant differences in the rate of pregnancy complications between the study and control groups. Negro et al (2010)(10) reported 6% pregnancy loss in pregnant women with very mild subclinical hypothyroidism (TSH level 2.5–5.0 mIU/l) and negative thyroid auto antibodies. Casey et al (2006)(11) reported no significant increase of placenta abruption, preterm labor and spontaneous abortions in pregnancy complicated by subclinical hyperthyroidism in comparison with euthyroid ones.

CONCLUSION

Recurrent pregnancy loss (RPL) is a challenging disorder for both patients and clinicians. The present study was designed to evaluate the serum thyroid hormone profile in the study groups and analyze its possible association with the risk of abortion during pregnancy.

In the present study it was observed that the risk of miscarriage increased with increasing TSH and this was seen to have significant positive correlation (p<0.05). It was observed that in women who

aborted before 20 weeks of pregnancy, a higher S.TSH was seen i.e. poor pregnancy outcome particularly miscarriage was associated with high S.TSH levels with a statistically significant difference ($p<0.05$). Although it is well documented that overt hypothyroidism and overt hyperthyroidism have deleterious impacts on pregnancy and childhood outcomes, there is however no consensus on the potential impact of subclinical hypothyroidism and subclinical hyperthyroidism on maternal and fetal health. Furthermore in women who suffered from thyroid dysfunction prior to pregnancy, the hormonal changes are magnified, leading to possibly adverse pregnancy outcomes, if not treated appropriately.

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