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An Observational Study to Assess Thyroid Function Tests in First Trimester of Pregnancy

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Abstract: ***Introduction: Miscarriage is a common occurrence in early pregnancy, defined as the loss of a nonviable intrauterine pregnancy within the first 12 weeks. Various maternal and fetal factors contribute to miscarriage, with maternal thyroid dysfunction playing a significant role. Thyroid disorders, particularly hypothyroidism, are prevalent in reproductive - age women and can lead to complications such as miscarriage, preterm birth, and fetal developmental issues. Objective: This study aims to assess the relationship between thyroid function and the risk of miscarriage by comparing thyroid hormone levels, including thyroid - stimulating hormone (TSH), T3, T4, and thyroid peroxidase antibodies (TPO - Ab), in women with early pregnancy loss versus those with viable pregnancies. Materials and Methods: A comparative observational study was conducted at the Department of Obstetrics and Gynecology, SMS Medical College, Jaipur, over one year, starting in November 2022. The study included 50 cases of women with first - trimester miscarriage and 50 controls with viable pregnancies. Thyroid function tests, including serum TSH, T3, T4, and TPO - Ab levels, were performed. Continuous variables were analyzed using an unpaired t - test, and categorical variables were analyzed using the chi - square or Fisher exact test, with a p - value <0.05 considered statistically significant. Results: The mean age was 27.64 years in the case group and 26.78 years in the control group. The mean TSH level was significantly higher in the case group (2.56) compared to the control group (1.14), with a p - value of 0.001. The presence of TPO antibodies (≥35 U/ml) was observed in 9 cases versus none in controls, which was statistically significant (p - value 0.007). Conclusion: Hypothyroidism is associated with an increased risk of early pregnancy loss. Routine thyroid function screening is crucial for early diagnosis and management to improve pregnancy outcomes.***

Keywords: Miscarriage, thyroid dysfunction, hypothyroidism, TSH, pregnancy, thyroid peroxidase antibodies

1. Introduction

Miscarriage is a common occurrence in early pregnancy, defined as a nonviable intrauterine pregnancy within the first 12 weeks of gestation. The term "spontaneous abortion" encompasses various forms, including threatened, inevitable, incomplete, complete, and missed abortions.1 The causes can be either fetal, such as chromosomal abnormalities, or maternal, including advanced age, infections, medications, uterine defects, and endocrine disorders like diabetes and thyroid diseases.[1]

Thyroid function plays a crucial role in pregnancy, particularly in fetal development during the first trimester when the fetus relies entirely on maternal thyroxine until its thyroid becomes functional around 16 weeks of gestation.[2] Thyroid disorders, the second most prevalent endocrine conditions among reproductive - age women, affect 2 - 3% of pregnant women. Gestational hypothyroidism is more common than hyperthyroidism, posing risks such as miscarriage, preterm birth, and developmental issues in the child. In India, the prevalence of hypothyroidism during pregnancy ranges widely from 1.2% to 67%, often due to iodine deficiency or autoimmune conditions like Hashimoto's thyroiditis.[3]

Thyroid disorders during pregnancy are categorized as subclinical or overt. Subclinical hypothyroidism presents with elevated serum thyroid - stimulating hormone (TSH) but normal thyroxine levels, while overt hypothyroidism involves high TSH and low thyroxine levels.6 Thyroid dysfunction, especially hypothyroidism, increases the risk of pregnancy complications, such as placental abruption, low IQ, and cretinism.[4]

During pregnancy, thyroid function undergoes significant changes, including increased production of thyroid hormones due to higher metabolic demands. These changes are driven by rising levels of human chorionic gonadotropin (hCG), which stimulate the maternal thyroid, particularly in the first trimester. Regular thyroid function tests, including TSH, T3, T4, and testing for thyroid peroxidase antibodies (TPO - Ab), are essential for detecting thyroid abnormalities and managing pre - existing thyroid conditions during pregnancy.[5]

Iodine deficiency is the leading cause of hypothyroidism in pregnant women in India, while autoimmune conditions, such as Graves' disease, account for most cases of hyperthyroidism.10 Screening for thyroid dysfunction during pregnancy is crucial, as it can prevent adverse outcomes for both the mother and child. Current guidelines recommend screening for TSH and TPO - Ab levels, especially for women at high risk or those with a history of miscarriage, as early detection and treatment can prevent complications.[6] This study aims to analyze thyroid function during pregnancy and its association with the risk of miscarriage.

2. Material and Method

This observational comparative study was conducted at the Department of Obstetrics and Gynecology, SMS Medical College and Associated Hospitals, Jaipur. The data collection spanned one year, starting from November 2022. The study population included women with singleton pregnancies in their first trimester attending the outpatient department (OPD). Cases comprised women with clinically or sonographically diagnosed first trimester pregnancy loss, while controls were viable first trimester pregnancies. A total of 50 cases and 50 controls were included, with the sample size calculated based on previous studies, ensuring 80% power and a 0.05 α error for TSH levels.

Inclusion Criteria:
This study included women with early pregnancy loss confirmed either clinically or through sonographic diagnosis. Additionally, women with viable pregnancies in the first trimester were included as controls. All participants were required to provide informed consent and should not have been involved in any other concurrent study.

Exclusion Criteria:
Women with pre - existing medical conditions such as diagnosed thyroid disorders, diabetes, pregnancy - induced hypertension (PIH), renal disease, or hypertension were excluded. Other exclusion factors included consanguineous marriage, known uterine abnormalities, and pregnancies conceived through assisted reproductive techniques.

3. Methodology

After applying inclusion and exclusion criteria, informed consent was obtained from all participants. The study group was divided into two: cases (women with early pregnancy loss) and controls (women with viable first - trimester pregnancies). A complete medical history was taken, and physical examinations were performed. Thyroid function tests, including serum TSH, T3, T4, and anti - TPO antibodies, were conducted for all participants.

Statistical Analysis: Continuous variables were summarized as means and analyzed using an unpaired t - test, while categorical variables were summarized as proportions and analyzed using the chi - square or Fisher exact test. A p - value of <0.05 was considered statistically significant.

4. Results and Observations

In the present study we included 50 women each in cases and control. Among the case group majority (44%) of women were married since 1 - 5yrs. In the control group, majority (52%) were married for 1 - 5yrs. In the case group, 33 patients were from urban areas, and 17 were from rural areas. In the control group, 26 patients resided in urban areas, while 24 were from rural areas.

Table 1: Distribution of women according to age

Age group	Cases		Controls	
	No. of patients	Percentage	No. of patients	Percentage
19 - 20 years	3	6	3	6
21 - 25 years	14	28	18	36
26 - 30 years	18	36	17	34
31 - 35 years	15	30	12	24
Total	50	100	50	100
Mean ± SD	27.64±44.38		26.78±4.56	
P - value	0.3			

This table shows that among the case group majority (36%) patients were in age group 26 - 30yrs. Among the control group, majority (36%) patients were in 21 - 25yrs group. The distribution among cases and controls was not found statitstically significant (p - value 0.3) according to age.

Table 2: Distribution of women according to period of amenorrhea

Period of amenorrhea (In months)	Case Group		Control Group	
	No. of patients	Percentage	No. of patients	Percentage
One	11	22	14	28
Two	21	42	25	50
Three	18	36	11	22
Total	50	100	50	100
Mean±SD	2.14±0.75		1.94±0.71	
p - value	0.17			

We found that mean period of amenorrhea in cases of early pregnancy loss is 2.14 months. Among the controls the mean period of amenorrhea at presentation is 1.94 months. This distribution is not statistically significant (p value - 0.17).

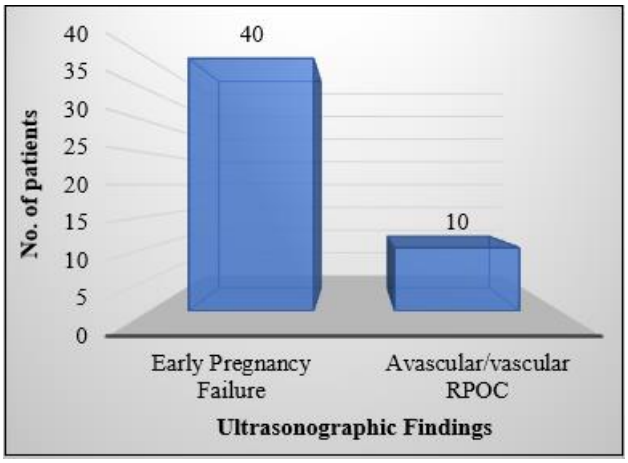

Figure 1: Distribution of women according to ultrasonographic findings.

In the case group, ultrasonographic findings revealed 80% instances of early pregnancy failure, 20% cases of avascular or vascular retained products of conception (RPOC).

Table 3: TPO Antibodies.

	No. of patients	Percentage	No. of patients	Percentage	
<35 U/ml	41	82	50	100	0.007
≥ 35 U/ml	9	18	0	0	
Total	50	100	50	100	

In the case group, 41 patients had TPO antibodies levels less than 35 U/ml, while 9 patients had TPO antibodies levels equal to or greater than 35 U/ml. In control group, 50 patients had TPO Antibodies levels less than 35 U/ml. This distribution of TPO antibodies among cases and controls was not statistically significant (p value - 0.007).

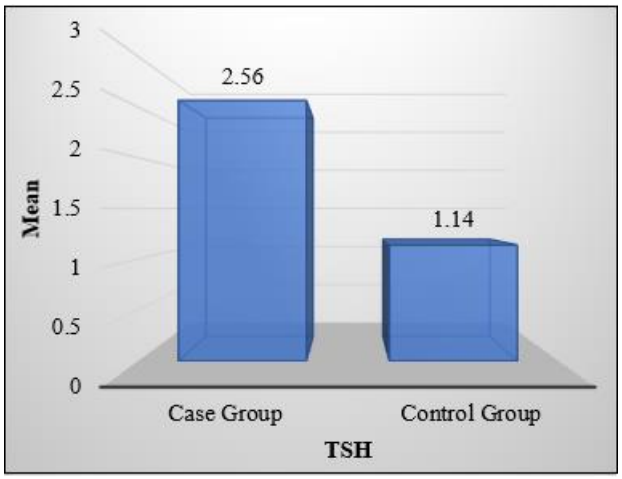

Figure 2: Mean TSH Levels

The mean TSH level in the case group was 2.56, while in the control group, it was 1.14. The difference in mean TSH levels was statistically significant in cases and controls (p value - 0.001).

5. Discussion

Pregnant women often experience clinical and subclinical hypothyroidism, which is linked to various complications such as miscarriage, preterm birth, placental abruption, and developmental problems in the child, including lower IQ and cretinism. Additionally, the presence of thyroid autoantibodies in many pregnant women may signal subtle thyroid dysfunction that can affect both maternal and fetal health. Effective management of thyroid dysfunction during pregnancy has been shown to improve outcomes for both the mother and the child, highlighting the importance of early detection and treatment.[7]

Our study found that the mean age of patients in the case group was 27.64 years, while in the control group it was 26.78 years. **Mainalia S et al.**[8] reported that most patients were aged between 24 and 49 years (n = 79, 49.4%), with the average age being 25.83 years. This is consistent with findings from **Altomare et al.**[9]

In our study, mean TSH levels were 2.56 in the case group and 1.14 in the control group. Primigravida had TSH levels of 2.99 in the case group versus 1.85 in the control group, while multigravida had 2.68 versus 1.03, respectively. **Kumar R et al.**[10] reported TSH levels of 1.88 ± 0.66 mIU/ml for euthyroid, 9.06 ± 3.12 mIU/ml for overt hypothyroidism, 3.99 ± 0.92 mIU/ml for subclinical hypothyroidism, and 0.04 ± 0.02 mIU/ml for overt hyperthyroidism. **Thanuja PM et al.**[11] observed a lower prevalence of 0.7%, while **Singh KP et al.** reported a higher prevalence of 18%.[12]

In our study, 41 patients in the case group had TPO antibody levels below 35 U/ml, and 9 had levels of 35 U/ml or higher. In the control group, 50 patients had TPO antibody levels below 35 U/ml. **Karakosta et al.**[13]identified that TPO antibodies ≥ 35 IU/ml, along with anti - thyroglobulin antibodies > 40 IU/ml, indicate thyroid dysfunction. **Hollowell JG**[14]reported that detectable serum TPO antibodies are found in up to 17% of adult women in the US.

6. Conclusion

Hypothyroidism is common in pregnancy and requires careful management due to its impact on maternal and fetal health. Thyroid dysfunction can lead to complications such as preterm birth, low birth weight, and developmental delays. Untreated thyroid issues may also increase the risk of pre - eclampsia and other adverse outcomes. Early screening for thyroid peroxidase antibodies (TPO - Ab) is crucial for timely identification and treatment of thyroid dysfunction, reducing complications. Routine thyroid function tests during pregnancy are recommended to detect and manage thyroid disorders early, helping to prevent pre - eclampsia and improve outcomes for both mother and baby.

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