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Original Article

Frequency of Subclinical Hypothyroidism in Patients with First-Trimester Pregnancy Loss

Saleha Hassan, Rabiya Akbar, Uzma Urooj, Sadaf Zohra, Nusrat Noor
Department of Obs & Gynae, Combined Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

***Objectives*:** To determine the frequency of subclinical Hypothyroidism in women with first-trimester pregnancy loss.
***Study Design*:** Cross-sectional study.
***Place and Duration of Study*:** Gynaecology & Obstetrics Department, Combined Military Hospital, Rawalpindi Pakistan, from Jun 2018 to Dec 2018.
***Methodology*:** The study included 130 women aged 18-40 years who had first-trimester pregnancy loss. Patients with chronic renal failure, known thyroid disorders and taking medication that can affect thyroid functions were excluded. Venous blood samples were taken to analyse thyroid function tests, and subclinical Hypothyroidism was noted.
***Results*:** The mean age of the women was 28.68±4.80 years. Most patients 77(59.23%), were between 18 and 30 years old. The mean BMI was 29.42±2.50 kg/m2. 16(12.31%) women with first-trimester miscarriage had subclinical Hypothyroidism.
***Conclusion*:** This study concluded that the frequency of subclinical Hypothyroidism in women with first-trimester pregnancy loss was significant. Proper management protocol for early recognition and management of subclinical Hypothyroidism in women can improve pregnancy outcomes.

Keywords: Early pregnancy loss, Miscarriages, Thyroid disorders.

How to Cite This Article: *Hassan S, Akbar R, Urooj U, Zohra S, Noor N. Frequency of Subclinical Hypothyroidism in Patients with First-Trimester Pregnancy Loss. Pak Armed Forces Med J 2023; 73(5): 1404-1406. DOI: https://doi.org/10.51253/pafmj.v73i5.7432*

INTRODUCTION

Early pregnancy miscarriages occur in 20% of all diagnosed pregnancies; on average, one out of four women experiences at least one miscarriage during their lifetime.[1] In third-world low-resource countries, miscarriages result in excessive vaginal bleeding and infection, leading to increased maternal morbidity and even mortality, leading to increased concerns.[2] Moreover, depression and anxiety associated with miscarriages also add to mental morbidity. Hypothyroidism is mostly asymptomatic in pregnancy, especially when it is subclinical.[3] There are multi-factorial etiologies of first-trimester miscarriages, which often remain unknown, but there are few risk factors which increase the likelihood of miscarriages.[4]

The incidence of developing Hypothyroidism is 4.1/1000 in women and 0.6/1000 in men during their lifetime.[5] One of the most common endocrinological disorders is thyroid disorders, requiring 3% of the population to undergo life-long treatment or prolonged thyroid replacement therapy. Many studies have shown that undiagnosed and untreated thyroid disorders can lead to recurrent pregnancy loss and sub-fertility.[6,7] One of the most common thyroid gland dysfunctions in pregnancy is Hypothyroidism, with prevalence of 1.5%-4.4%.[8]

Correspondence: Dr Uzma Urooj, Department of Obs & Gynae, Combined Military Hospital, Rawalpindi Pakistan
Received: 26 Sep 2021; revision received: 20 Mar 2023; accepted: 29 Mar 2023

The role of subclinical Hypothyroidism in increasing miscarriages is still under investigation. Few studies found no correlation between subclinical Hypothyroidism and miscarriage, as well as any other adverse outcomes in pregnant women.[9,10] Moreover, it is known that the prevalence of thyroid disorders during pregnancy varies in different regions, so the purpose significance of this study was to evaluate the frequency of subclinical Hypothyroidism in women with first-trimester pregnancy loss in our local population. Thyroid functions are not done routinely in pregnancy. Failure to recognize the presence of abnormal thyroid hormone levels in pregnancy may be a primary cause of recurrent as well as first-trimester pregnancy loss, therefore the results of this study will not only provide the magnitude of the local population but also help the clinicians to design a proper management protocol for early recognition and management of subclinical Hypothyroidism in females to improve the pregnancy outcome and decrease the first-trimester pregnancy loss.

METHODOLOGY

The study was carried out at the Gynaecology and Obstetrics Department, CMH Rawalpindi from June to December 2018 after approval from the Ethical Review Committee (ERB/270/1). The sample size was calculated with prevalence of subclinical Hypothyroidism of 11.45% in women with first-trimester pregnancy loss.[11]

Inclusion Criteria: Women aged 18-40 years who had first-trimester pregnancy loss were included.

Exclusion Criteria: Patients with chronic renal failure (assessed on history and s/creatinine >1.5 mg/dl), patients with known thyroid disorders assessed on history and medical record and Patients taking medication that can affect thyroid functions (dopamine antagonists, antiepileptics, lithium, glucocorticoids).

Total of 130 women with first-trimester pregnancy loss were included in the study after taking written informed consent. The sampling was done by non-probability, consecutive sampling. The venous blood sample was taken and sent to the laboratory for analysis of thyroid function tests and subclinical Hypothyroidism (i.e., TSH >5.2 mIU/L, T3=1.4-4.2 pg/ml, and T4=0.8-2.0 nmol/l) was noted. All the data (age, BMI, place of living, history of pregnancy loss and subclinical Hypothyroidism) obtained from patients were recorded on the proforma.

Statistical Package for Social Sciences (SPSS) version 22.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to explore the inferential statistics. The *p*-value of ≤0.05 was set as the cut-off value for significance.

RESULTS

This study included 130 women aged 18 to 40 years, with a mean age of 28.68±4.80 years, shown in Table-I.

Table-I: Age Distribution of Patients (n=130)

Age (In Years)	No. of Patients	%Age
18-30	77	59.23
31-40	53	40.77
Total	130	100.0

Table-II: Association of subclinical hypothyroidism with different parameters (n=130)

Parameters	Subclinical Hypothyroidism		*p*-value
BMI (kg/m2)	Yes	No	
≤27	09(6.9%)	31(23.8%)	0.018
>27	07(5.3%)	83(63.8%)	
Previous history of Pregnancy Loss			
Yes	08(6.1%)	32(24.6%)	0.075
No	08(6.1%)	82(63%)	
Place of Living			
Rural	06(4.6%)	51(39.2%)	0.585
Urban	10(7.6%)	63(48.4%)	

The mean BMI was 29.42±2.50 kg/m^2. The study included 90(69.23%) with no history of previous miscarriage and 40(30.77%) with a previous history of pregnancy loss. The rural population was 57(43.85%), and 73(56.15%) of the study group lived in urban areas. The frequency of subclinical Hypothyroidism in women with first-trimester miscarriage was found in 16(12.31%) women, and 114(87.69%) had no sub-clinical history. Association of sub-clinical thyroid with different parameters is shown in the Table-II.

DISCUSSION

Thyroid physiology is perceptibly modified during normal pregnancy, and these alterations take place to cope with the increased metabolic demands of pregnancy. Untreated or uncontrolled Hypothyroidism leads to preterm birth, low birth weight and respiratory distress in neonates. Spontaneous miscarriage is the most common complication of the first trimester and occurs within the first 12 weeks of gestation to more than 80%.[11] Fetal or parental are the main causes leading to abortion. Reversible changes in thyroid function are also linked with pregnancy. Proper maternal thyroid function is critical for both mother and fetus during pregnancy.[12] An increased risk of preterm birth, placental abruption, fetal death, and impaired neurological development in the child is related to elevated maternal thyroid stimulating hormone (TSH).93-95 Miscarriage risks are manifold in the presence of antibodies to thyroid peroxidase (TPO-Ab).[13] Prevalence of elevated TSH ranging from 4% to 9% while TPO-Ab from 11.3% to 18% is observed in pregnant women.[14]

Subfertility in women is related to Hypothyroidism, and if they conceive, it will escalate manifold risks, including miscarriage, gestational hypertension, anaemia, abruption of the placenta and postpartum haemorrhage.[15,16] A study by Stagnaro-Green *et al.* concluded that the impact on female reproductive organs and embryos by local action of thyroid hormones seemed critical for a successful pregnancy. Early pregnancy and preg-nancy loss are associated with changes in the highly regulated local thyroid activity.[17] Canaris *et al.*[18] concluded that a higher miscarriage rate is related to untreated Hypothyroidism, subclinical or overt at the time of conception, as compared to patients with normal thyroid levels. Hollowell *et al.*[19] in a study, showed a significant association between low mater-nal free thyroxine (FT4) during the first trimester and fetal loss in pregnancies complicated by subclinical Hypothyroidism.

This study reflected women with first-trimester miscarriage having a frequency of subclinical Hypothyroidism of 16(12.31%). Several large-scale studies validated risk of first-trimester miscarriage as significantly increased by subclinical Hypothyroidism.[20,21] Moreover, the elevation of the serum TSH level also increases the risk of miscarriage, which is consistent with the results of a study by

Ashoor *et al*. In a study, 11.45% of women with first-trimester pregnancy loss had subclinical Hypothyroidism.[22] Systemic review and meta-analysis undertaken by Thagiratinam *et al*. reflected miscarriage in women with thyroid antibodies at an incidence of 17-33%.[23]

CONCLUSION

Maternal Hypothyroidism is a disorder with great potential to affect maternal and fetal outcomes adversely. Sub-clinical Hypothyroidism is associated with early pregnancy loss. Therefore, proper management protocol for early recognition and management of subclinical Hypothyroidism in women with first-trimester miscarriage should be done to decrease the rate of first-trimester miscarriages.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

SH: & RA: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

UU: & SZ: Study design, drafting the manuscript, critical review, approval of the final version to be published.

NN: Concpet, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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