

Prevalence of Subclinical Hypothyroidism in Patients with Recurrent Miscarriages

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ABSTRACT

Background: Subclinical hypothyroidism poses a concealed threat to reproductive health. With evidence hinting at its prevalence in recurrent miscarriages, this study delves into unraveling the intricacies of this relationship for comprehensive understanding and improved clinical outcomes. **Objective:** To determine prevalence of subclinical hypothyroidism in patients with recurrent miscarriages. **Study Design:** Descriptive cross-sectional study. **Settings:** This study was conducted at the Department of Medicine, DHQ Teaching Hospital, KMU Institute of Medical Sciences, Kohat Pakistan. **Duration:** 6 months period from Jan-Jun, 2023. **Methods:** A total of 224 women meeting inclusion criteria were included in the study after taking informed written consent. Blood samples were taken as per standard hygiene protocol and send hospital lab for thyroid profile. Subclinical hypothyroidism was labeled when serum TSH level was ≥ 4.0 mIU/L and the patients didn't have clinical symptoms of hypothyroidism. All the data was collected in a predesigned format and data analysis was done using SPSS 27.0. **Results:** Mean age of the patients in this study was 29.01 ± 6.61 years wherein 58.0% (n=130) patients were in the age group of 18-30 years while remaining 42% (n=94) were in the age group of 31-40 years. As regards parity, 50.9% (n=114) patients were nulliparas, 28.1% (n=63) were primiparas and 21.0% (n=47) were multiparas. Mean BMI of the study sample was 24.87 ± 3.7 kg/m² wherein 52.7% (n=118) participants were normal weight, 37.9% (n=85) were overweight and only 9.4% (n=21) were obese. Previous number of miscarriages were almost same amount all the three groups as 3 miscarriages (33.5%), 4 miscarriages (35.7%) and 5 miscarriages (30.8%). Subclinical hypothyroidism was observed in 18.3% (n=41) patients. Frequency of mischarge was stratified on the basis of age, parity, BMI and previous number of miscarriage, it produced insignificant different for all the subgroups (p-value=0.05). **Conclusion:** In conclusion, our study highlights a consistent prevalence of subclinical hypothyroidism (18.3%) in women with recurrent miscarriage. This aligns with global findings, emphasizing the significance of thyroid dysfunction. These insights underscore the importance of routine thyroid screening in the management of recurrent miscarriage, guiding targeted interventions for improved reproductive outcomes.

Keywords: Recurrent Miscarriage, Subclinical Hypothyroidism, Thyroid Stimulating Hormone.

INTRODUCTION

Recurrent miscarriage, defined as the spontaneous loss of a pregnancy before the 20th week, presents a formidable challenge in reproductive medicine, affecting 8-15% of clinically recognized pregnancies and up to 30% of all pregnancies.¹ The intricate web of causative factors encompasses chromosomal abnormalities, uterine anomalies, hormonal imbalances, and maternal age.² Despite advancements in medical knowledge, a considerable percentage of cases remains unexplained.³

Among the array of factors contributing to recurrent miscarriages, hypothyroidism has emerged as a significant consideration. Studies by Uchida *et al.* (2017)⁴ and Negro *et al.* (2014)⁵ have shed light on the prevalence of hypothyroidism in the context of recurrent miscarriages, reporting rates of 17.7% and 14.6%, respectively. These findings underscore the substantial impact of hypothyroidism on reproductive health. However, the association between subclinical hypothyroidism characterized by elevated thyroid-stimulating hormone (TSH) within the normal thyroid

hormone range and recurrent miscarriages remains an insufficiently explored terrain.⁶ The subtle nature of subclinical hypothyroidism, often devoid of overt symptoms, makes it a potential yet covert contributor to adverse pregnancy outcomes.^{5,6}

Recognizing the critical need for a more comprehensive understanding, further research is imperative. The identified link between subclinical hypothyroidism and recurrent miscarriages, as illuminated by studies such as those conducted by Negro *et al* (2014)⁴ and Uchida *et al* (2017)⁵, emphasizes the necessity for systematic screening of pregnant women to detect thyroid dysfunction promptly.^{4,5} Early identification allows for interventions that may prevent recurrent miscarriages and promote healthier pregnancies.⁶

Pregnancy, being a physiologically intricate state, demands meticulous attention to thyroid function. Screening involves assessing TSH and, when indicated, free thyroxine (FT4) levels, with guidelines emphasizing the importance of maintaining TSH within specific ranges.⁷ The delicate balance of thyroid hormones plays a pivotal role in maternal and fetal well-being, influencing embryonic development and metabolic regulation.⁸ Management of hypothyroidism during pregnancy typically involves thyroid hormone replacement therapy, often with levothyroxine, aiming to restore thyroid hormone levels to the normal range. This approach is essential for minimizing complications and optimizing outcomes for both the mother and the developing fetus.^{9,10}

The observed prevalence of subclinical hypothyroidism in patients with recurrent miscarriages, as highlighted by specific studies, accentuates the necessity for meticulous research and heightened awareness within the medical community. Early screening for thyroid dysfunction during pregnancy, informed by prevalence rates provided by research such as that conducted by Uchida *et al.* (2017)⁴ and Shrestha *et al.* (2014)⁸, serves as a pivotal step toward effective interventions, potentially averting recurrent miscarriages and promoting optimal maternal and fetal health. Understanding the role of hypothyroidism in recurrent miscarriages is essential in advancing our knowledge of reproductive health and improving outcomes for expectant mothers.

METHODS

This descriptive cross sectional study was conducted at the Department of Medicine, DHQ Teaching Hospital, KMU Institute of Medical Sciences, Kohat. A sample size of 224 cases was calculated at 80% power of test and 5% level of significance, and expected frequency of hypothyroidism in women with recurrent miscarriages to be 17.7%.⁴ Inclusion criteria was women with age

between 18-40 years, from any parity, having recurrent miscarriages and those who gave written informed consent. However, women taking thyroxin or anti-thyroid drugs or who conceived through IVF were excluded. Blood samples were taken as per standard hygiene protocol and send hospital lab for thyroid profile. Subclinical hypothyroidism was labeled when serum TSH level was ≥ 4.0 mIU/L and the patients didn't have clinical symptoms of hypothyroidism. All the patients were managed as per standard protocol of the department. All the data was collected in a predesigned format and data analysis was done using SPSS 27.0.

RESULTS

Mean age of the patients in this study was 29.01 ± 6.61 years wherein 58.0% (n=130) patients were in the age group of 18-30 years while remaining 42% (n=94) were in the age group of 31-40 years. As regards parity, 50.9% (n=114) patients were nulliparas, 28.1% (n=63) were primiparas and 21.0% (n=47) were multiparas. Mean BMI of the study sample was 24.87 ± 3.7 kg/m² wherein 52.7% (n=118) participants were normal weight, 37.9% (n=85) were overweight and only 9.4% (n=21) were obese. Previous number of miscarriages were almost same amount all the three groups as 3 miscarriages (33.5%), 4 miscarriages (35.7%) and 5 miscarriages (30.8%). Data is given in Table 1. Subclinical hypothyroidism was observed in 18.3% (n=41) patients. Data is given in Table 2. Frequency of mischarge was stratified on the basis of age, parity, BMI and previous number of miscarriage, it produced insignificant different for all the subgroups (p-value=0.05).

Table 1: Baseline characteristics of the study sample

Variables	Participants (n=224)	
Age (18-40 years)	18-30 years	130 (58.0%)
	31-40 years	94 (42.0%)
Parity	Nulliparas	114 (50.9%)
	Primiparas	63 (28.1%)
	Multiparas	47 (21.0%)
BMI (Kg/m ²)	Normal	118 (52.7%)
	Overweight	85 (37.9%)
	Obese	21 (9.4%)
Previous Miscarriages	3	75 (33.5%)
	4	80 (35.7%)
	5	69 (30.8%)

Table 2: Frequency of subclinical hypothyroidism in women with recurrent miscarriages

Subclinical Hypothyroidism	Frequency (n)	Percent (%)
Yes	41	18.3%
No	183	81.7%
Total	224	100.0%

Table 3: Frequency of subclinical hypothyroidism stratified for age, parity, BMI and previous miscarriage

Variables		Subclinical Hypothyroidism		P-value
		Yes	No	
Age	18-30 years	21 (51.2%)	109 (59.6%)	0.328
	31-40 years	20 (48.8%)	74 (40.4%)	
Parity	Nulliparas	19 (16.7%)	95 (83.3%)	0.637
	Primiparas	14 (22.2%)	49 (77.8%)	
	Multiparas	8 (17.0%)	39 (83.0%)	
BMI (Kg/m ²)	Normal	21 (17.8%)	97 (82.2%)	0.429
	Overweight	14 (16.5%)	71 (83.5%)	
	Obese	6 (28.6%)	15 (71.4%)	
Previous Miscarriages	3	13 (17.3%)	62 (82.7%)	0.421
	4	12 (15.0%)	68 (85.0%)	
	5	16 (23.2%)	53 (76.8%)	

Chi-square test, p-value ≤ 0.05 was to be considered as statistically significant

DISCUSSION

The association between recurrent miscarriages and subclinical hypothyroidism is gaining attention in reproductive health. Subclinical hypothyroidism, characterized by elevated thyroid-stimulating hormone (TSH) within the normal thyroid hormone range, has been implicated as a potential contributor to recurrent pregnancy loss.^{1,2} The nuanced and often asymptomatic nature of subclinical hypothyroidism highlights the need for heightened awareness and comprehensive screening in pregnant individuals. This study was planned with the aim to establish more evidence, recognizing the critical importance of understanding this association for early intervention and the potential prevention of recurrent miscarriages, contributing to improved maternal and fetal outcomes.

In the current investigation, the mean age of women experiencing recurrent pregnancy loss was determined to be 29.01±6.61 years. Comparative assessments from existing studies reveal a consistency in reported mean ages. Ahmad *et al.* (2020)¹¹ in Pakistan documented a mean age of 28.2±4.2 years, while Chakraborty *et al.* (2013)¹² observed a mean age of 28.9±4.3 years among Indian women with recurrent pregnancy loss. Studies

conducted by Yuksel *et al.* (2014)¹³ in Turkey reported mean ages of 28±5 years, among women with recurrent miscarriage. Our findings align with those of Ali *et al.* (2020), Zahran *et al.* (2015)¹⁴, and Shaaban *et al.* (2017)¹⁵, who reported comparable mean ages of 27.8±2.2 years, 27.9±5.7 years, and 26.6±3.2 years, respectively, among Egyptian women experiencing recurrent pregnancy loss. Implications of these findings extend beyond demographic comparisons, offering insights into the consistent age patterns among women facing recurrent pregnancy loss across diverse geographic locations. Understanding the mean age in this context is crucial for tailoring effective interventions and support mechanisms, considering the potential impact of age-related factors on recurrent pregnancy loss. These findings contribute to the broader landscape of reproductive health research, guiding healthcare providers in formulating targeted strategies for managing recurrent pregnancy loss in diverse populations.

Our investigation revealed that a significant majority of women (50.9%) experiencing recurrent pregnancy loss were nulliparas. This observation aligns with the findings of Kashif *et al.* (2015)¹⁶, who reported a nullipara frequency of 57.1%. Similarly, Shaaban *et al.* (2017)¹⁵ reported a comparable incidence of nulliparas, noting it to be 52.7% among Egyptian women with recurrent pregnancy loss. This consistent pattern emphasizes the noteworthy representation of nulliparas among women facing recurrent pregnancy loss. Understanding the prevalence of nulliparity in this context has implications for clinical management and counseling strategies, as the reproductive experiences of nulliparous women may differ from those who have previously carried a pregnancy to term.

In our current study, the mean body mass index (BMI) of women experiencing recurrent miscarriage was determined to be 24.87±3.7 kg/m². This observation aligns closely with the findings of Ahmad *et al.* (2020)¹¹, who reported a similar mean BMI of 24.7±3.1 kg/m². Chakraborty *et al.* (2013)¹² reported a comparable mean BMI of 25.7±2.7 kg/m². Consistent patterns are evident in studies conducted by Emarah *et al.* (2020)¹⁷ who observed a mean BMI of 24.9±4.8 kg/m² in Egypt. These findings highlight a commonality in mean BMI among women experiencing recurrent miscarriage across diverse geographic locations. Understanding the consistent BMI patterns in this context is crucial for assessing potential associations between body weight and recurrent miscarriage.

We observed that 18.3% of women experiencing recurrent miscarriage had subclinical hypothyroidism. This prevalence aligns closely with the findings of Uchida *et al.* (2017)⁴, who reported a frequency of 17.7% in Japanese

women. Similarly, Negro *et al.* (2010)⁵ documented a slightly lower frequency of 15.6% in Italian women with recurrent miscarriage. It is noteworthy that the frequency of hypothyroidism observed in our study remained consistent across various subgroups. These observations underscore the global nature of subclinical hypothyroidism as a factor in recurrent miscarriage. The prevalence aligns with previous research across different populations, emphasizing the relevance of thyroid dysfunction in the context of recurrent pregnancy loss.

CONCLUSION

In conclusion, our study highlights a consistent prevalence of subclinical hypothyroidism (18.3%) in women with recurrent miscarriage. This aligns with global findings, emphasizing the significance of thyroid dysfunction. These insights underscore the importance of routine thyroid screening in the management of recurrent miscarriage, guiding targeted interventions for improved reproductive outcomes.

LIMITATIONS

Limitations include potential regional variations and the absence of prospective data, warranting cautious generalization. Nonetheless, the study contributes valuable insights to inform further research and clinical considerations.

SUGGESTIONS / RECOMMENDATIONS

Future research should adopt longitudinal designs, assess regional variations, and evaluate targeted interventions' efficacy for subclinical hypothyroidism in recurrent miscarriage. Exploring molecular and genetic aspects is essential for advancements.

CONFLICT OF INTEREST / DISCLOSURE

Respondents are well-informed, with assured confidentiality. No conflicts of interest exist among the authors conducting the study.

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