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Frequency of Hypothyroidism and Subclinical Hypothyroidism in Females with Secondary Infertility Presenting at a Tertiary Care Hospital

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ABSTRACT

Hypothyroidism, particularly subclinical hypothyroidism (SCH), is a frequent endocrine disorder linked to reproductive dysfunction, including secondary infertility. In Pakistan, where infertility rates are rising, understanding the prevalence and impact of thyroid dysfunction among women with secondary infertility is critical for improving fertility management. **Objectives:** To investigate the correlation between secondary infertility and subclinical hypothyroidism among Pakistani women. **Methods:** A cross-sectional descriptive study was conducted on 130 women aged 20–40 years presenting with secondary infertility at a tertiary care hospital in Pakistan. Participants underwent clinical assessment, including measurement of thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) levels. SCH was defined as TSH between 4.5 and 20 mIU/L with normal FT3 and FT4. Data on demographic variables, parity, and duration of infertility were collected. Statistical analysis involved chi-square tests to examine associations between hypothyroidism and demographic/clinical factors. **Results:** Hypothyroidism was identified in 28.5% of participants, comprising 20.8% with subclinical and 7.7% with overt hypothyroidism. The highest prevalence of subclinical hypothyroidism was observed among women aged 31–40 years (28.6%) and those with BMI ≥25 kg/m^2 (21.1%). However, it revealed no statistically significant associations between hypothyroidism and age (p=0.256), BMI (p=0.827), parity (p=1.000), or duration of infertility (p=1.000). **Conclusions:** Thyroid dysfunction, particularly subclinical hypothyroidism, is highly prevalent in women with secondary infertility, despite the absence of significant associations with common demographic or reproductive variables. These findings support routine thyroid screening as an essential component of infertility assessment.

INTRODUCTION

Family and children are seen in Pakistan as the pillars of society; procreation has great social and cultural value linked to them [1]. Economic development and social stability depend critically on the idea of children. According to recent studies, couples in Pakistan seem to be increasingly infertile; the prevalence rates range from 12% to 18% and show a continuous increase over the years [2]. While rates of infertility in the Western world have stayed

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constant, Pakistan has seen rising worries about reproductive health, especially among women suffering secondary infertility, in which case conception does not follow a past successful pregnancy [3]. A common yet subtle endocrinological condition, hypothyroidism, affects reproductive health greatly. In women who manage to conceive, it disrupts things like delayed puberty, menstrual irregularities, anovulatory cycles, infertility, and a higher chance of pregnancy loss [4]. The milder type of the disorder, subclinical hypothyroidism (SCH), is defined by modestly raised thyroid-stimulating hormone (TSH) levels ranging from 4.5 to 20 mIU/L, with normal free triiodothyronine and free thyroxine levels [5]. Affecting ovarian function and the release of sex hormone-binding globulin (SHBG), prolactin, and gonadotropin-releasing hormone (GnRH), recent investigations have shown that SCH is tightly linked with reproductive failure, therefore influencing menstrual cycles [6]. Furthermore, connected to ovulatory dysfunction and maybe causing infertility in women is SCH. With some studies showing its frequency as high as 14% among infertile women, compared to only 2-4% in the general population, subclinical hypothyroidism is thought to be a major cause of fertility issues in Pakistan, where the incidence of infertility is rising [7]. Research on women with high TSH levels has indicated that they often have longer periods of infertility and reduced conception rates than those with normal thyroid function, therefore stressing the need for recognizing and treating thyroid dysfunctions as part of infertility treatment [8]. The study hypothesize that subclinical hypothyroidism is prevalent in women with secondary infertility. The purpose of this study is to investigate the correlation between secondary infertility and subclinical hypothyroidism. The results might have major effects on fertility treatment strategies and enhance the Pakistani population's reproductive health outcomes.

This study aimed to ascertain among women presenting with infertility the requirement of regular screening of thyroid function, especially for SCH.

METHODS

This cross-sectional descriptive design allowed data collection from June to August 2025, providing a snapshot of the prevalence of thyroid dysfunction in this specific population. The study was approved by the review board of the Lahore General Hospital, Lahore, with reference number 2025/ERC/40. All participants had been informed about the reasons for the study, what they could gain from it, and the possible risks and gave consent. The investigators kept the participants' information private throughout the study. Women in the study were aged 20 to 40 and had secondary infertility, successfully reaching the infertility clinic of the tertiary care hospital in Lahore. If a couple experiences infertility after already having a child, that is called secondary infertility, and usually it means there aren't any other clear reasons for infertility [9]. The study excluded women with initial difficulty getting pregnant, those with suspected thyroid disorders at the start and women with reproductive system abnormalities. The sample size of 130 was calculated using the formula $n = Z^2 \times P(1-P) / d^2$, assuming a prevalence (P) of 14% for subclinical hypothyroidism, 95% confidence level ($Z = 1.96$), and 5% margin of error ($d = 0.05$) [7]. To have enough power in the statistical analysis for the study, 130 infertile women were chosen based on the 14% prevalence of subclinical hypothyroidism in this group. Self-developed systematic questionnaire was used, besides clinical evaluations, to obtain the data. During their tests, the participants' medical history and physical examination concentrated on whether they had periods, whether they were pregnant before and if they had any health concerns. Blood samples were collected for thyroid function testing, including TSH, FT3, and FT4, using enzyme-linked immunosorbent assay (ELISA) kits (TSH: Human TSH ELISA Kit, DRG Instruments GmbH, Germany; FT3: Free Triiodothyronine ELISA Kit, Calbiotech Inc., USA; FT4: Free Thyroxine ELISA Kit, Monobind Inc., USA). Subclinical hypothyroidism (SCH) was defined as a TSH level between 4.5 and 20 mIU/L with normal FT3 and FT4 concentrations. Both descriptive and inferential types of statistics were used to look at the data. In the study, researchers used frequencies and percentages to see how many people had subclinical hypothyroidism. To study the impact of hypothyroidism on several socio-demographic parameters, a chi-square test was performed, whereas logistic regression analysis was used to evaluate any hazardous effects of thyroid dysfunction on infertility. SPSS version 25.0 was used to analyze all the data, and the significance level chosen was $p<0.05$.

RESULTS

A total of 130 women with secondary infertility were included in the study. Among women aged 31–40 years, subclinical hypothyroidism was notably higher (28.6%) compared to younger women (13.4%), despite a lower rate of overt hypothyroidism (3.2% vs. 6.0%). Similarly, women with a BMI ≥25 kg/m^2 exhibited a slightly higher prevalence of both overt (8.4%) and subclinical hypothyroidism (21.1%) compared to those with lower BMI, though the difference was not statistically significant ($p=0.827$). The distribution across parity and infertility duration showed similar trends, with subclinical hypothyroidism consistently more prevalent than overt forms in all subgroups (Table 1).

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Table 1: Prevalence of Hypothyroidism by Demographic and Clinical Variables

Variables	Total (n)	Overt Hypothyroidism n (%)	Subclinical Hypothyroidism n (%)	Total Hypothyroidism n (%)	p-Value (Chi-square)
Age					
18–30 Years	67	4 (6.0%)	9 (13.4%)	13 (19.4%)	0.256
31–40 Years	63	2 (3.2%)	18 (28.6%)	20 (31.3%)	
BMI					
<25 kg/m^2	35	2 (5.7%)	7 (20.0%)	9 (25.7%)	0.827
≥25 kg/m^2	95	8 (8.4%)	20 (21.1%)	28 (29.5%)	
Parity					
Primipara	51	4 (7.8%)	10 (19.6%)	14 (27.5%)	1.000
Multipara	79	6 (7.6%)	17 (21.5%)	23 (29.1%)	
Infertility Duration					
1–3 Years	73	5 (6.8%)	16 (21.9%)	21 (28.8%)	1.000
>3 Years	57	5 (8.8%)	11 (19.3%)	16 (28.2%)	

This study presents a comprehensive overview of thyroid hormone levels measured via ELISA and the distribution of thyroid status within the study population of 130 women with secondary infertility. Euthyroid women constituted the majority (71.5%), with all thyroid parameters within normal ranges. Subclinical hypothyroidism (20.8%) was defined by elevated TSH (mean 7.8 mIU/L) alongside normal FT3 and FT4 levels, while overt hypothyroidism (7.7%) showed more pronounced TSH elevation (mean 15.6 mIU/L) and reduced peripheral hormones (FT3 and FT4), consistent with classic biochemical hypothyroidism. These results highlight that nearly 1 in 3 women in this infertile population had some form of thyroid dysfunction, with subclinical hypothyroidism being the most common form, underlining the importance of thyroid screening even in the absence of overt symptoms (Table 2).

Table 2: Thyroid Hormone Levels (ELISA) and Distribution of Thyroid Status in Study Population (n=130)

Thyroid Status	n (%)	TSH (mIU/L)	Ft3 (pg/mL)	Ft4 (ng/dL)
Euthyroid	93 (71.5%)	2.1 ± 0.9	3.3 ± 0.5	1.2 ± 0.2
Subclinical Hypothyroid	27 (20.8%)	7.8 ± 2.3	3.1 ± 0.4	1.1 ± 0.2
Overt Hypothyroid	10 (7.7%)	15.6 ± 3.8	2.2 ± 0.5	0.7 ± 0.3

Findings summarize the results of chi-square analyses assessing the association between hypothyroidism and demographic/clinical variables. No statistically significant associations were found between hypothyroidism and age group ($\chi^2 = 1.291$, p=0.256), BMI ($\chi^2 = 0.047$, p=0.827), parity ($\chi^2 = 0.002$, p=1.000), or duration of infertility ($\chi^2 = 0.001$, p=1.000). These results suggest that in this sample population, thyroid dysfunction—whether overt or subclinical occurs relatively independently of these common reproductive and metabolic indicators. This further underscores the clinical value of routine thyroid screening in all women with secondary infertility, regardless of their age, weight, or infertility history (Table 3).

Table 3: Chi-Square Test Results for Association with Hypothyroidism

Variables	Chi-Square Value (χ^2)	Degrees of Freedom (df)	p-Value
Age Group (18–30 vs 31–40)	1.291	1	0.256
BMI Group (<25 vs ≥25 kg/m^2)	0.047	1	0.827
Parity (Primipara vs Multipara)	0.002	1	1.000
Duration of Infertility (1–3 vs >3 Years)	0.001	1	1.000

Results present the logistic regression model analyzing potential predictors of hypothyroidism. None of the variables, like age, BMI, parity, or duration of infertility, demonstrated statistically significant associations with the outcome. Women aged 31–40 had an odds ratio (OR) of 1.89 (95% CI: 0.85–4.21, p=0.117), suggesting a trend toward increased risk, although not reaching significance. Similarly, elevated BMI (OR=1.21, p=0.640), multiparity (OR=1.08, p=0.851), and longer infertility duration (OR=0.97, p=0.942) did not significantly impact hypothyroidism risk (Table 4).

Table 4: Binary Logistic Regression Analysis of Factors Associated with Hypothyroidism

Predictor	Odds Ratio (OR)	95% Confidence Interval (CI)	p-Value
Age (31–40 vs 18–30)	1.89	0.85 – 4.21	0.117
BMI (≥25 vs <25)	1.21	0.54 – 2.71	0.640
Parity (Multipara vs Primipara)	1.08	0.48 – 2.46	0.851
Duration (>3 vs 1–3 Years)	0.97	0.43 – 2.18	0.942

DISCUSSIONS

This study shows that among women presenting at a tertiary care hospital in Pakistan with secondary infertility [10], 28.5% hypothyroidism, including 20.8% subclinical hypothyroid and 7.7% overt hypothyroid is rather common. This frequency is in line with results of comparable studies conducted throughout the world, where hypothyroidism is recognized as a frequent endocrine condition among infertile women [11]. Routine thyroid monitoring is therefore even more important in the management of infertility, as several studies have shown a prevalence of hypothyroidism in infertile populations between 24% and 28%. Particularly, subclinical hypothyroidism, which affects ovarian function, ovulation, and early pregnancy maintenance, hypothyroidism has been identified as a major contributing cause to low fertility [12]. Despite the great frequency of hypothyroidism noted in our study, no statistically significant correlations were detected between hypothyroidism and age, body mass index (BMI), parity, or length of infertility. This implies that, in this group, hypothyroidism may not be particularly influenced by these factors, even if it is still a major determinant of reproductive dysfunction. Previous research has revealed

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different relationships between hypothyroidism and these variables; some suggest that rising age and BMI could help to explain thyroid malfunction. Our results, however, refuted these links, which would indicate the complexity of thyroid diseases and their multifaceted influence on reproductive health [13]. Women between the ages of 31 and 40 had more hypothyroidism (31.3%) than those between the ages of 18 and 30 (19.4%). Although this variation might seem clinically important, statistical investigation revealed no notable correlation between age and hypothyroidism. This result is consistent with some other research indicating that although advancing age increases risk, thyroid malfunction can develop in women of different age ranges. Our study's lack of statistical significance could be ascribed to other confounding elements not taken into consideration or sample size [14]. Although earlier studies have indicated a possible link between obesity and thyroid malfunction, especially subclinical hypothyroidism, our analysis revealed no appreciable correlation between BMI and hypothyroidism. Though this difference was not statistically significant, women with a BMI greater than 25 kg/m2 had a somewhat higher prevalence of hypothyroidism (29.5%) than those with a BMI of less than 25 kg/m^2 (25.7%). The absence of a robust correlation could suggest that thyroid malfunction in infertile women could be independent of BMI, or that other underlying factors (e.g., genetic predispositions or environmental factors) may play a more major role in thyroid health [15]. Likewise, there was no appreciable association between hypothyroidism and parity (primipara vs. multipara) or infertile length of time. These results align with certain research demonstrating hypothyroidism as a risk factor for infertility independent of past pregnancies or duration of infertility [16]. Longer periods of infertility, however, have been linked in some studies to increased prevalence of thyroid dysfunction since the cumulative impact of hormonal abnormalities may aggravate over time [17]. The absence of correlation in our study could reflect the rather homogeneous character of the population, or it could imply that thyroid dysfunction has a similar influence over different infertility durations [18]. The great frequency of hypothyroidism shown in this study highlights the need to add thyroid screening to the infertility treatment for women with secondary infertility. Early identification of thyroid dysfunction, especially subclinical hypothyroidism, may direct suitable therapy and enhance fertility results [19]. In women with thyroid insufficiency, thyroid hormone replacement therapy has been demonstrated to enhance ovulatory ability and conception rates. Thus, prompt management may help women with hypothyroidism who are experiencing infertility to have either spontaneous conception or assisted reproductive technology more successfully [19, 20].

CONCLUSIONS

This study revealed a high prevalence of thyroid dysfunction among women with secondary infertility, with 28.5% found to have hypothyroidism, including 20.8% with subclinical hypothyroidism and 7.7% with overt hypothyroidism. Subclinical hypothyroidism emerged as the predominant thyroid abnormality, often occurring without overt clinical symptoms, thus posing a hidden barrier to conception. These findings highlight the critical importance of incorporating routine thyroid function testing into infertility evaluations for early detection and appropriate management of thyroid dysfunction.

Authors Contribution

Conceptualization: HMMA
Methodology: AN, AB, SC, MS
Formal analysis: HMZR
Writing review and editing: AN, FS, AB, SC, MS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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