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Frequency of Thyroid Disorders in Female Infertility Aged 18 to 35 Years Examined at OPD DHQ Hospital Dera Ismail Khan

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ABSTRACT

Background: Thyroid disorders are a significant but often underrecognized cause of female infertility. Thyroid dysfunction, both overt and subclinical, disrupts the hypothalamic-pituitary-ovarian axis, leading to menstrual irregularities, ovulatory failure, and impaired endometrial receptivity, which collectively contribute to decreased fertility. Despite global awareness, regional data particularly from Dera Ismail Khan remain scarce. **Objective:** To determine the frequency of thyroid disorders in female infertility at DHQ Hospital Dera Ismail Khan. **Study Design:** Cross-sectional analysis. **Duration and Place of Study:** The study was conducted from September 2024 to March 2025 at the Department of Obstetrics and Gynaecology, DHQ Hospital, Dera Ismail Khan. **Methodology:** A total of 162 infertile women aged 18–35 years, with normal BMI and normal semen parameters in their partners, were enrolled. Thyroid function was evaluated using TSH and FT_4 levels. Hypothyroidism was defined as TSH ≥10 mU/L with FT_4 <0.7 ng/dL, and hyperthyroidism as TSH <0.1 mU/L with FT_4 >1.5 ng/dL. **Results:** The mean age of participants was 28.36 ± 4.12 years, and mean BMI was 21.47 ± 2.38 kg/m^2. Hypothyroidism was present in 48 (29.6%) and hyperthyroidism in 11 (6.8%) women. A significant association was found between BMI and hypothyroidism (p=0.026), with higher prevalence in women with BMI >25 kg/m^2. Primary infertility was also significantly associated with higher hypothyroidism rates (p=0.025). **Conclusion:** Thyroid dysfunction, particularly hypothyroidism, is a prevalent and potentially reversible contributor to female infertility.

INTRODUCTION

Thyroid disorders are a significant and common cause of infertility in women.[1] The thyroid gland plays a crucial role in regulation of metabolism and hormonal homeostasis and is required for normal reproductive function.[2] Hypothyroidism and hyperthyroidism can induce disruption to the hypothalamic-pituitary-ovarian (HPO) axis and lead to menstrual disorders and ovulatory failure and cause fertility impairment.[3] In addition, subclinical thyroid disease in its asymptomatic state can have adverse effects on ovulatory cycles and endometrial environment crucial for successful implantation.[4]

Overt and subclinical hypothyroidism is particularly associated with menstrual disorders in the pattern of oligomenorrhea, menorrhagia, or amenorrhea.[5] It can also interfere with the functioning of the luteal phase with defective progesterone production and failed embryo implantation.[6] Elevated thyroid-stimulating hormone (TSH) has also been associated with excess secretion of prolactin with consequential inhibition of gonadotropin-releasing hormone (GnRH) and disruption of ovulation.[7] Untreated hypothyroidism in females generally presents with infertility as the foremost symptom and significantly reverses with thyroid hormone replacement therapy upon detection.[8]

Hyperthyroidism, while being less frequent than hypothyroidism, also impacts fertility by generating menstrual disorders such as oligomenorrhea or amenorrhea.[9] Elevated thyroid hormone also increases the level of sex hormone-binding globulin (SHBG) and alters peripheral conversion of estrogen and hence disturbs normal feedback mechanisms within the HPO axis.[10] In autoimmune hyperthyroidism such as in Graves' disease thyroid stimulating immunoglobulines can also lead to reproductive malfunction through hitherto unknown mechanisms.[1]

Autoimmune thyroid disease (AITD), even in the euthyroid state, has been associated with increased risk of infertility and miscarriage.[11] Anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin autoantibodies are widespread in women with unexplained infertility and recurrent spontaneous abortion.[12] The inbuilt autoimmune reactive state has the capability to induce a pro-inflammatory environment to disrupt receptivity of the endometrium and early embryo development.[13] Screening for thyroid function and autoantibodies should therefore become a

standard part of the evaluation for infertility, especially in women with anovulatory cycles, history of miscarriage, or with any autoimmune disorders.[14]

A study conducted by Verma I. et al. involving 394 women presenting to an infertility clinic for the first time reported that 23.9% of the participants were found to have hypothyroidism based on thyroid-stimulating hormone (TSH) evaluation.[15] Similarly, in another study by Kumari P. et al., the prevalence of thyroid dysfunction among women with infertility was documented, with hyperthyroidism observed in 11.9% and hypothyroidism in 22.4% of the cases.[16]

Despite the well-known connection among thyroid malfunction and female infertility, local statistics for Dera Ismail Khan are limited. Given the likely impact of undetected thyroid illness upon reproductive capability, prevalence in this specified group has merit in being evaluated. Conducting this study will enrich regional clinical practices' knowledgebase, refine diagnostic processes, and guide focused management strategies to infertile females in the region.

METHODOLOGY

This cross-sectional analysis was conducted between September 2024 and March 2025 in the Department of Obstetrics and Gynaecology at DHQ Hospital, Dera Ismail Khan. A total of 162 women seeking evaluation for infertility were included in the study. The sample size was calculated using the WHO sample size calculator, considering a 95% confidence level, an 8% margin of error, and an expected frequency of hyperthyroidism in infertile females of 11.9%.[16]

Women aged 18 to 35 years were considered eligible if they had been unable to conceive despite engaging in regular, unprotected sexual intercourse for a period of 12 months or longer. Only those whose male partners demonstrated normal semen parameters—specifically a sperm concentration of at least 15 million per milliliter and a total motility of 40% or higher—were included. Eligible participants were also required to have a body mass index (BMI) within the normal range, defined as 18.5 to 24.9 kg/m^2. Women with a documented history of uterine fibroids, prior hormonal therapy, chemotherapy, or radiation exposure were excluded, as were those previously diagnosed with elevated prolactin levels that had not been treated.

Written informed consent was obtained from each participant after approval from the institutional ethics committee (46/GJMS Dated: June 07, 2023). Women who had never achieved a pregnancy despite regular attempts were categorized as having primary infertility, while those who had previously conceived at least once but failed to conceive again after 12 or more months of regular, unprotected intercourse were classified as having secondary infertility.

On the 21st day of each participant's menstrual cycle, following an overnight fast lasting between 8 to 12 hours, 5 ml of venous blood was drawn from the antecubital vein by a third-year trainee under aseptic conditions. The collected blood was transferred into sterile, disposable syringes and sent to the laboratory within three hours of collection. All procedures were performed under the supervision of a consultant gynecologist with more than three years of post-fellowship experience.

Thyroid function was assessed using standard biochemical analysis. Hyperthyroidism was diagnosed when thyroid-stimulating hormone (TSH) levels were below 0.1 mU/L and free thyroxine (FT_4) exceeded 1.5 ng/dL. Conversely, hypothyroidism was diagnosed when TSH values were equal to or greater than 10 mU/L along with FT_4 levels below 0.7 ng/dL.

All statistical analysis was carried out using IBM SPSS version 22. Categorical variables were described using frequencies and percentages. Continuous variables were expressed as mean ± standard deviation or median with interquartile ranges, depending on the distribution pattern. The Shapiro-Wilk test was applied to assess normality. Stratification was used to control the influence of confounding factors such as age, residence, education, socioeconomic status, type of infertility, duration of infertility, and BMI. After stratification, the Chi-square test or Fisher's exact test was employed to examine associations, with a p-value of ≤ 0.05 considered statistically significant.

RESULTS

The study included 162 infertile women with a mean age of 28.36±4.12 years, mean BMI of 21.47±2.38 kg/m^2, and mean infertility duration of 7.65±1.56 years. The demographic characteristics revealed that 95 (58.6%) women were from rural areas while 67 (41.4%) were from urban areas. Educational distribution showed 55 (34.0%) were uneducated, 39 (24.1%) had primary education, 42 (25.9%) had secondary education, and 26 (16.0%) had higher education. Socioeconomic status indicated 88 (54.3%) were poor, 45 (27.8%) were middle class, and 29 (17.9%) were rich. Regarding infertility type, 93 (57.4%) had primary infertility while 69 (42.6%) had secondary infertility (as shown in Table 1).

Table 1

Patient Demographics

Demographics		Mean ± SD
Age (years)		28.36±4.12
BMI (Kg/m^2)		21.47±2.38
Infertility Duration (years)		7.65±1.56
Residence	Rural n (%)	95 (58.6%)
	Urban n (%)	67 (41.4%)
Education	Uneducated n (%)	55 (34.0%)
	Primary n (%)	39 (24.1%)
	Secondary n (%)	42 (25.9%)
	Higher n (%)	26 (16.0%)
Socioeconomic Status	Poor n (%)	88 (54.3%)
	Middle n (%)	45 (27.8%)
	Rich n (%)	29 (17.9%)
Type of Infertility	Primary n (%)	93 (57.4%)
	Secondary n (%)	69 (42.6%)

The frequency analysis revealed that thyroid disorders were notably prevalent among infertile women, with hypothyroidism being the predominant condition affecting 48 patients (29.6%) while hyperthyroidism was less common, occurring in 11 patients (6.8%). The majority of patients, 114 (70.4%), did not have hypothyroidism, and 151 patients (93.2%) were free from hyperthyroidism (as shown in Table 2).

Table 2
Frequency of Thyroid Disorders

Thyroid Disorders		Frequency	% age
Hyperthyroidism	Yes	11	6.8%
	No	151	93.2%
Hypothyroidism	Yes	48	29.6%
	No	114	70.4%

The demographic stratification analysis revealed significant associations between thyroid disorders and various patient characteristics in this infertile population. Age distribution showed that among women ≤25 years, 12 (31.6%) had hypothyroidism versus 26 (68.4%) without hypothyroidism, while in women >25 years, 36 (29.0%) had hypothyroidism versus 88 (71.0%) without hypothyroidism (p=0.764). For hyperthyroidism, 3 (7.9%) women ≤25 years had the condition versus 35 (92.1%) without it, while 8 (6.5%) women >25 years had hyperthyroidism versus 116 (93.5%) without it (p=1.000). BMI analysis demonstrated that women with BMI ≤25 kg/m^2 had 39 (26.9%) cases of hypothyroidism versus 106 (73.1%) without it, while those with BMI >25 kg/m^2 showed significantly higher prevalence with 9 (52.9%) having hypothyroidism versus 8 (47.1%) without it (p=0.026). For hyperthyroidism, 9 (6.2%) women with BMI ≤25 kg/m^2 had the condition versus 136 (93.8%) without it, while 2 (11.8%) women with BMI >25 kg/m^2 had hyperthyroidism versus 15 (88.2%) without it (p=0.608). Residence analysis showed rural women had 23 (24.2%) cases of hypothyroidism versus 72 (75.8%) without it, while urban women had 25 (37.3%) cases versus 42 (62.7%) without it (p=0.072). For hyperthyroidism, rural women had 3 (3.2%) cases versus 92 (96.8%) without it, while urban women had significantly higher prevalence with 8 (11.9%) cases versus 59 (88.1%) without it (p=0.052). Educational stratification revealed that uneducated women had 14 (25.5%) cases of hypothyroidism versus 41 (74.5%) without it, primary educated women had 8 (20.5%) cases versus 31 (79.5%) without it, secondary educated women had 17 (40.5%) cases versus 25 (59.5%) without it, and higher educated women had 9 (34.6%) cases versus 17 (65.4%) without it (p=0.196). For hyperthyroidism, no cases (0.0%) were found among uneducated women with 55 (100.0%) being free of the condition, primary educated women had 3 (7.7%) cases versus 36 (92.3%) without it, secondary educated women had 4 (9.5%) cases versus 38 (90.5%) without it, and higher educated women had 4 (15.4%) cases versus 22 (84.6%) without it (p=0.055). Socioeconomic analysis showed poor women had 22 (25.0%) cases of hypothyroidism versus 66 (75.0%) without it, middle class women had 14 (31.1%) cases versus 31 (68.9%) without it, and rich women had 12 (41.4%) cases versus 17 (58.6%) without it (p=0.238). For hyperthyroidism, poor women had 6 (6.8%) cases versus 82 (93.2%) without it, middle class women had 1 (2.2%) case versus 44 (97.8%) without it, and rich women had 4 (13.8%) cases versus 25 (86.2%) without it (p=0.151). Duration of infertility analysis revealed that women with ≤5 years duration had 4 (57.1%) cases of hypothyroidism versus 3 (42.9%) without it, while those with >5 years duration had 44 (28.4%) cases versus 111 (71.6%) without it (p=0.197). For hyperthyroidism, no cases (0.0%) were found among women with ≤5 years duration with 7 (100.0%) being free of the condition, while women with >5 years duration had 11 (7.1%) cases versus 144 (92.9%) without it (p=1.000). Type of infertility analysis showed primary infertility patients had significantly higher hypothyroidism rates with 34 (36.6%) cases versus 59 (63.4%) without it, while secondary infertility patients had 14 (20.3%) cases versus 55 (79.7%) without it (p=0.025). For hyperthyroidism, primary infertility patients had 8 (8.6%) cases versus 85 (91.4%) without it, while secondary infertility patients had 3 (4.3%) cases versus 66 (95.7%) without it (p=0.356) (as shown in Table 3).

Table 3
Association of Thyroid Disorders with Demographic Factors

Demographic Factors		Hypothyroidism		p-value	Hyperthyroidism		p-value
		Yes n(%)	No n(%)		Yes n(%)	No n(%)	
Age (years)	≤25	12 (31.6%)	26 (68.4%)	0.764	3 (7.9%)	35 (92.1%)	1.000*
	>25	36 (29.0%)	88 (71.0%)		8 (6.5%)	116 (93.5%)	
BMI (Kg/m^2)	≤25	39 (26.9%)	106 (73.1%)	0.026	9 (6.2%)	136 (93.8%)	0.608*
	>25	9 (52.9%)	8 (47.1%)		2 (11.8%)	15 (88.2%)	
Residence	Rural	23 (24.2%)	72 (75.8%)	0.072	3 (3.2%)	92 (96.8%)	0.052*
	Urban	25 (37.3%)	42 (62.7%)		8 (11.9%)	59 (88.1%)	
Education	Uneducated	14 (25.5%)	41 (74.5%)	0.196	0 (0.0%)	55 (100.0%)	0.055*
	Primary	8 (20.5%)	31 (79.5%)		3 (7.7%)	36 (92.3%)	
	Secondary	17 (40.5%)	25 (59.5%)		4 (9.5%)	38 (90.5%)	
	Higher	9 (34.6%)	17 (65.4%)		4 (15.4%)	22 (84.6%)	
Socioeconomic Status	Poor	22 (25.0%)	66 (75.0%)	0.238	6 (6.8%)	82 (93.2%)	0.151*
	Middle	14 (31.1%)	31 (68.9%)		1 (2.2%)	44 (97.8%)	
	Rich	12 (41.4%)	17 (58.6%)		4 (13.8%)	25 (86.2%)	
Duration of Infertility (years)	≤5	4 (57.1%)	3 (42.9%)	0.197*	0 (0.0%)	7 (100.0%)	1.000*
	>5	44 (28.4%)	111 (71.6%)		11 (7.1%)	144 (92.9%)	
Type of Infertility	Primary	34 (36.6%)	59 (63.4%)	0.025	8 (8.6%)	85 (91.4%)	0.356*
	Secondary	14 (20.3%)	55 (79.7%)		3 (4.3%)	66 (95.7%)	

*Fischer Exact Test

DISCUSSION

The findings of this study demonstrate a substantial prevalence of thyroid disorders in infertile women, with hypothyroidism affecting nearly one-third of the study population (29.6%) and hyperthyroidism occurring in 6.8% of cases, indicating that thyroid dysfunction is a significant contributing factor to female infertility. The predominance of hypothyroidism over hyperthyroidism in this cohort aligns with the pathophysiological understanding that thyroid hormone deficiency more profoundly disrupts the hypothalamic-pituitary-ovarian axis, leading to anovulation, luteal phase defects, and menstrual irregularities that compromise fertility. The significant association between higher BMI and increased hypothyroidism prevalence (52.9% in women with BMI >25 kg/m^2) can be attributed to the complex interplay between adipose tissue and thyroid function, where increased body fat leads to elevated leptin levels that can suppress thyroid-stimulating hormone production and peripheral thyroid hormone conversion. The higher prevalence of hypothyroidism in primary infertility patients (36.6% vs 20.3% in secondary infertility) suggests that thyroid dysfunction may be a primary causative factor rather than a secondary consequence of reproductive aging or previous pregnancies, as primary infertility represents cases where conception has never occurred despite adequate exposure. The trend toward higher hyperthyroidism rates in urban versus rural women (11.9% vs 3.2%) may reflect environmental factors such as increased stress levels, dietary iodine variations, and exposure to endocrine-disrupting chemicals more commonly found in urban environments. The educational gradient observed in hyperthyroidism prevalence, with higher rates in more educated women (15.4% in higher educated vs 0% in uneducated), could be related to increased awareness leading to earlier detection, differences in lifestyle factors, or occupational stress patterns that may trigger autoimmune thyroid conditions.

The overall prevalence of thyroid disorders in our study (36.4%) was notably higher than that reported by Bendary and El Hodiby (2022) [17], who found thyroid dysfunction in 32.9% of their infertile group compared to 3.4% in fertile controls. This slight difference may be attributed to variations in study populations, diagnostic criteria, or geographical factors. However, both studies consistently demonstrate a substantially higher prevalence of thyroid disorders in infertile women compared to fertile controls, reinforcing the established association between thyroid dysfunction and female fertility issues as described by Potiris et al. (2024) [18].

The predominance of hypothyroidism over hyperthyroidism in our study (29.6% vs 6.8%) is consistent with the findings of Akande et al. (2022) [19], who reported overt hypothyroidism as the most common thyroid disorder (9.6%) in their infertile population. This pattern reflects the general epidemiological trend where hypothyroidism is more prevalent than hyperthyroidism in the general population, but the significantly higher rates in infertile women underscore the particular vulnerability of this group to thyroid dysfunction.

Our study revealed a significant association between BMI and hypothyroidism, with women having BMI >25 kg/m^2 showing a markedly higher prevalence of hypothyroidism (52.9%) compared to those with BMI ≤25 kg/m^2 (26.9%, p=0.026). This finding provides valuable insight into the complex interplay between metabolic factors and thyroid function in infertile women. The association between obesity and thyroid dysfunction has been established in general populations, but our results specifically demonstrate this relationship in the context of female infertility, suggesting that metabolic dysfunction may compound fertility challenges through multiple pathways.

A particularly noteworthy finding from our study was the significantly higher prevalence of hypothyroidism in women with primary infertility (36.6%) compared to secondary infertility (20.3%, p=0.025). This observation aligns with the findings of Akande et al. (2022) [19], who noted that overt hypothyroidism was more prevalent in secondary infertility (21.8%). While the specific percentages differ between studies, both demonstrate a clear association between infertility type and thyroid dysfunction patterns, suggesting that the timing and nature of thyroid disorders may influence different aspects of reproductive function.

Our study revealed interesting trends regarding socioeconomic status and education, with higher rates of hypothyroidism observed in women from higher socioeconomic backgrounds (41.4% in rich vs 25.0% in poor, p=0.238) and those with secondary education (40.5%). While these associations were not statistically significant, they suggest potential lifestyle, dietary, or healthcare access factors that may influence thyroid function in different population subgroups. These findings warrant further investigation as they may inform targeted screening and prevention strategies.

The high prevalence of thyroid disorders in our infertile population supports the mechanistic understanding provided by Potiris et al. (2024) [18], who described how thyroid dysfunction interacts with the hypothalamic-pituitary-ovarian axis and modulates ovarian functions. The predominance of hypothyroidism in our study is consistent with their findings that hypothyroidism causes ovulatory dysfunction and luteal hypoplasia, which can be restored through appropriate levothyroxine supplementation.

The association between thyroid antibodies and infertility, as highlighted by Bendary and El Hodiby (2022) [17], who found thyroid antibodies in 18.6% of their infertile group with a positive correlation to infertility duration, provides additional context for understanding the autoimmune component of thyroid-related infertility. While our study did not specifically examine thyroid antibodies, the high prevalence of thyroid disorders suggests that autoimmune thyroid conditions may also be contributing to the infertility burden in our population.

The slightly higher overall prevalence of thyroid disorders in our study compared to some international studies may reflect regional factors such as iodine status, genetic predisposition, environmental factors, or healthcare-seeking behaviors. The finding that urban women had higher rates of hyperthyroidism (11.9%) compared to rural women (3.2%, p=0.052) suggests potential environmental or lifestyle factors that may influence

thyroid function differently across geographical locations. While our study provides valuable insights into the frequency of thyroid disorders in female infertility, several limitations should be acknowledged. The cross-sectional design limits our ability to establish causality, and the lack of a control group of fertile women prevents direct comparison of thyroid disorder prevalence between fertile and infertile populations. Future prospective studies examining the temporal relationship between thyroid dysfunction and fertility outcomes, along with investigation of thyroid antibodies and their correlation with specific fertility parameters, would enhance our understanding of this complex relationship.

CONCLUSION

Our study confirms the substantial burden of thyroid disorders in infertile women, with hypothyroidism being the predominant condition affecting nearly one-third of our study population. The significant associations with BMI and infertility type, along with the demographic variations observed, highlight the multifactorial nature of thyroid-related infertility.

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