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Prevalence of Hypothyroidism in Infertile Women and Evaluation of Treatment Response for Hypothyroidism on Infertility

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(Received: 04 February 2024 Revised: 11 March 2024 Accepted: 08 April 2024) **ABSTRACT:** Introduction: According to the World Health Organization (WHO), the prevalence of **KEYWORDS** primary infertility in India ranges from 3.5% to 16.8%. Thyroid disorders are more prevalent Infertility, in females, occurring at a rate of 4-5 times higher than in males. Both hyperthyroidism and Hypothyroidism, hypothyroidism can significantly influence estrogen and androgen metabolism, menstrual Thyroxine, function, and fertility. This study aimed to investigate the prevalence of hypothyroidism Thyroid Function among women experiencing infertility and to assess the efficacy of hypothyroidism Tests treatment on infertility outcomes. Materials and Methods: 123 infertile women underwent thyroid stimulating hormone (TSH) assessment. Infertile women diagnosed with clinical or subclinical hypothyroidism received thyroxine doses ranging from 25 to 150 µg. Results: Among the 123 infertile women studied, 53.65% exhibited hypothyroidism (TSH > 4.6 µIU/ml). Following thyroxine treatment, 34% of subclinical hypothyroid women achieved conception within a period ranging from 6 weeks to 2 years. The average time to conception was 14.65 ± 4.38 months. Conclusion: In the evaluation of infertility, assessing thyroid function is crucial. Even in cases where TSH levels are within the normal range but thyroid antibodies are detected, treatment with levothyroxine is recommended.

Introduction

Infertility presents a global health challenge affecting approximately 8–10% of couples worldwide. The World Health Organization (WHO) estimates the prevalence of primary infertility in India to be within the range of 3.5– 16.8%. Thyroid dysfunction is notably more prevalent in females, occurring at rates 4–5 times higher than in males. Hyperthyroidism and hypothyroidism significantly impact estrogen and androgen metabolism, menstrual function, and fertility [1-3]. These conditions can manifest in delayed puberty onset, menstrual irregularities, anovulatory cycles, miscarriages, and infertility. If left untreated, thyroid disorders can contribute to sub-fertility and infertility. It's recommended to evaluate thyroid function in women seeking conception with a family history of thyroid issues, irregular menstrual cycles, more than two abortions, or unsuccessful attempts at conception after a year of unprotected intercourse [4,5].

The prevalence of hypothyroidism among women of reproductive age ranges from 2% to 4%. Detecting hypothyroidism is straightforward through serum thyroid stimulating hormone (TSH) level assessment. Slight elevations in TSH with normal T3 and T4 levels suggest

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subclinical hypothyroidism, while elevated TSH with low T3 and T4 levels indicate clinical hypothyroidism. Increased thyrotropin-releasing hormone levels due to hypothyroidism often correlate with higher prolactin (PRL) levels and a delayed LH response to GnRH. It's advised to prioritize treating hypothyroidism in the presence of elevated PRL levels before exploring other potential causes [6-8].

Given the scarcity of population-based studies on infertile women with subclinical or clinical hypothyroidism, we aimed to investigate the prevalence of hypothyroidism among infertile women and evaluate their response to hypothyroidism treatment.



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Material and Methods

The research was conducted at Index Medical College Hospital and Research Centre, Indore, India. Participants were recruited from the outpatient department (OPD) and after obtaining informed consent. Thyroid profile assessments, including serum TSH, T3, T4 levels, thyroid peroxidase antibody, thyroglobulin antibody were conducted during the initial visit for all participants. Following the criteria outlined in the National Health and Nutrition Examination Survey III (2002) [9], participants were categorized into three groups:

- Group 1 (euthyroid): Infertile women with normal TSH levels (0.39–4.6 mIU/ml).

- Group 2 (subclinical hypothyroidism): Infertile women with elevated TSH levels ranging from 4.6–20 mIU/ml and normal T3, T4 levels.

- Group 3 (overt hypothyroidism): Infertile women with TSH levels exceeding 20 mIU/ml and low T3,T4 levels. Hyperprolactinemia, as per WHO guidelines, was defined as a PRL level exceeding 25 μ g/l [10]. Serum samples were collected for the assessment of TSH, T3, and T4 levels using a chemiluminescence assay method. The immulite 1000 machine, equipped with assay-specific coated beads serving as reaction vessels, was utilized for chemiluminescence testing.

Results

Table 1: Baseline demographic variables of study participants

Variable	Euthyroidism (n=57)		Subclinical	Overt	
	TabNegative (n=52)	Tab Positive (n=5)	hypothyroidism (n=62)	hypothyroidism (n=4)	P Value
Age (years); Mean ± SD	26.55 ± 3.84	28.88 ± 5.56	27.59 ± 4.52	24.39 ± 5.73	0.75
BMI (kg/m ²); Mean ± SD	21.77 ± 2.73	21.28 ± 2.66	24.58 ± 4.54	30.79 ± 3.41	< 0.05

Table 2: Baseline clinical parameters of study participants

	Euthyroidis	sm (n=57)	Subclinical	Overt
Variable	Tab	Tab	hypothyroidism	hypothyroidism
	Negative (n=52)	Positive (n=5)	(n=62)	(n=4)
Primary infertility (%)	100	100	46	100
Secondary infertility (%)	-	-	54	-
Menstrual cycles (%)				
Regular	100	86	78	-
Oligomenorrhea	-	8	17	-
Menorrhagia	-	-	3	-
Hypomenorrhea	-	6		

Table 3: Thyroid and	l prolactin	parameters in	study	participants
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Variable	Euthyroidism (n=57)		Subclinical	Overt	
	Tab	Tab	hypothyroidism	hypothyroidism	P Value
	Negative (n=52)	Positive (n=5)	(n=62)	(n=4)	
Mean TSH (mIU/L)	2.67 ± 0.95	2.60 ± 0.99	8.49 ± 3.07	32.94 ± 3.67	< 0.05

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Mean T4 (nmol/L)	103.55 ± 17.27	102.25 ± 16.57	112.16 ± 22.61	11.33 ± 6.11	-
Mean Prolactin (µg/L)	6.69 ± 2.69	6.66 ± 2.59	15.16 ± 10.15	15.47 ± 8.97	-
Hyperprolactinemi a (%)	Nil	Nil	22.9	Nil	-
TPOAb (%)	-	100	100	-	-
TgAb (%)	-	47.5	64.62	-	-
Mean TSH (mIU/L)	2.67 ± 0.95	2.60 ± 0.99	8.49 ± 3.07	32.94 ± 3.67	

Discussion

The prevalence of subclinical hypothyroidism was more common than overt hypothyroidism in this investigation, aligning with findings from Verma et al. [11], Biradar et al. [12], and Rijal et al. [13]. Age did not significantly differ among the various groups based on thyroid status (P > 0.05). However, a notable difference in body mass index was observed in infertile women with hypothyroidism compared to those with normal thyroid levels (P < 0.01), consistent with Rahman et al. [14].

The majority of the study's participants experienced primary infertility, and most women across all groups had regular menstrual cycles [Table 1]. The average time to conception (approximately 14 months) exceeded that reported by Raber et al. [6]. Elevated TSH levels were linked to a lower conception rate, in line with Raber et al. [6] and Gerhard et al. [15].

Among hypothyroid infertile women who conceived with levothyroxine's assistance, 32% experienced abortions, with 80% of these women testing positive for thyroid antibodies. This study recorded a higher abortion rate compared to Raber et al. [6] and Rahman et al. [14]. However, due to the small sample size, the association between thyroid antibodies and abortions couldn't be definitively established. For euthyroid women positive for antithyroid antibodies, 50% achieved conception following levothyroxine treatment. Among them, 50% experienced a miscarriage, while the remaining 50% continued with their pregnancies. This finding contrasts with Negro et al. [16], who reported no impact on pregnancy rates due to antithyroid antibodies or levothyroxine treatment.

Conclusion

Hypothyroidism is increasingly recognized as a significant contributor to female infertility. Therefore, the decision to commence levothyroxine treatment in cases of subclinical hypothyroidism among infertile women is justifiable, particularly when identified at an early stage. Our findings also indicate that infertile women with normal TSH levels but positive thyroid antibodies should receive levothyroxine therapy. In the context of fertility planning, screening for serum TSH, T3, T4, and thyroid antibodies, specifically thyroid peroxidase antibody and thyroglobulin antibodies, should be included in the infertility assessment.

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