Scholars LITERATURE

Journal of Womens Health Care and Management

Research Article

DOI: https://doi.org/10.47275/2692-0948-172
Volume 7 Issue 1

Thyroid Dysfunction Roles in Iraqi Women with Infertility: A Cross-sectional Study

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Abstract

Infertility is the inability of a couple to achieve pregnancy after one year of regular, unprotected sexual intercourse. Globally, infertility affects an estimated 60 - 80 million individuals. This study aimed to evaluate the impact of thyroid dysfunction on Iraqi females experiencing both infertility types. This cross-sectional study included 200 females with infertility (primary and secondary cases). This was confirmed by normal semen analysis parameters in their spouses, in accordance with standard reference values. For each participant, detailed demographic and clinical information was collected. A structured and predesigned proforma was used to systematically record relevant data, including age, duration and type of infertility (primary or secondary), and comprehensive menstrual history. This standardized data collection ensured consistency and accuracy in evaluating the association between thyroid dysfunction and infertility. Serum concentrations of thyroid hormones—thyroid-stimulating hormone (TSH), triiodothyronine (T3), and thyroxine (T4) - were measured using a chemiluminescence immunoassay (CLIA) analyzer (CLIA IIS, China). The assays were performed with commercially available kits (Autobio Diagnostics Co. Ltd., Zhengzhou, China), strictly following the manufacturer's protocols and procedures. Women experiencing secondary infertility were significantly older, with a mean age of 31.66 ± 8.13 years, compared to 25.89 ± 7.45 years in those with primary infertility ($p < 0.0001$). Serum T3 levels were also significantly higher in women with secondary infertility (1.46 ± 0.79 ng/mL) than in those with primary infertility (1.12 ± 0.54 ng/mL, $p < 0.0001$). Women with secondary infertility are significantly older and have higher serum T3 levels compared to those with primary infertility, while other thyroid parameters and menstrual patterns show no significant differences. These findings suggest that age and subtle thyroid hormone variations may influence secondary infertility, highlighting the importance of comprehensive hormonal evaluation in its management.

Keywords: Infertility, Hyperthyroidism, Hypothyroidism, Euthyroid, Thyroid-stimulating hormone, Triiodothyronine, Thyroxin

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Citation: Khalaf MK, Tufiak HMT, Al-Obaidi SAR (2026) Thyroid Dysfunction Roles in Iraqi Women with Infertility: A Cross-sectional Study. J Womens Health Care Manage, Volume 7:1. 172. DOI: https://doi.org/10.47275/2692-0948-172

Received: February 28, 2026; **Accepted:** June 23, 2026; **Published:** June 29, 2026

Introduction

The World Health Organization describes infertility as the inability of a couple to achieve pregnancy after one year of regular, unprotected sexual intercourse [1]. Globally, infertility affects an estimated 60 – 80 million individuals [2]. Primary infertility refers to a situation in which a couple has never been able to conceive, with reported rates ranging between 2% and 5%. In contrast, secondary infertility occurs when a couple who has previously conceived is unable to achieve another pregnancy, and it is estimated to affect approximately 20% of couples worldwide [2, 3].

Optimal hormonal balance and proper endocrine function are crucial for embryo implantation and the continuation of pregnancy. Thyroid hormones are closely linked with the reproductive system, although the exact mechanisms underlying this interaction are not yet fully clarified. Disorders of the thyroid gland are frequently associated with menstrual irregularities and reduced fertility. Thyroid hormones exert their effects by binding to specific receptors and activating transcription factors that are widely distributed across various tissues in the body. TSH regulates the production of thyroid hormones in the thyroid gland, but evidence suggests it also plays additional roles within the female reproductive system. Increased expression of thyroid hormone and TSH receptors in the receptive endometrium indicates their involvement in implantation, potentially through modulation of inflammatory mediators such as leukemia inhibitory factor, a key cytokine in female reproduction. The observed link between thyroid dysfunction and infertility suggests that thyroid hormones and TSH may influence both the endometrium and ovarian function through local (paracrine) mechanisms [4].

Thyroid hormones play a central role in regulating growth, metabolism, and overall cellular activity. In addition to gonadotropins such as Follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin, they contribute significantly to the proper functioning

of the female reproductive system and the maintenance of fertility [5-7]. Both hypothyroidism and hyperthyroidism are well recognized for their association with menstrual disturbances, which can subsequently impair fertility. Abnormal thyroid function is a major contributor to menstrual disorders such as oligomenorrhea, amenorrhea, polymenorrhea, and menorrhagia. These disturbances are largely attributed to alterations in the hormonal milieu, including imbalances in estrogen, prolactin, and Gonadotropin-releasing hormone (GnRH), as well as disruptions in the normal pulsatile secretion of LH [8].

Thyroid hormones exert a direct influence on oocyte development, and maintaining normal thyroid function is essential for optimal fertilization outcomes. Evidence supports this relationship, as treatment of hypothyroid women with infertility has been shown to restore prolactin concentrations and normalize the LH response to GnRH. These hormonal corrections often reduce menstrual irregularities and improve the likelihood of natural conception. In women undergoing *in vitro* fertilization, serum levels of TSH may also serve as a predictive marker for treatment success or failure [9, 10].

In cases of thyrotoxicosis, menstrual disturbances such as oligomenorrhea and amenorrhea are frequently observed. Although circulating reproductive hormone levels may be elevated, ovulatory cycles can still occur in some women. The rise in LH, FSH, and estrogen metabolism is thought to result from increased activity of GnRH [11]. However, the characteristic mid-cycle LH surge may be diminished or entirely absent [12]. Additionally, studies have reported a marked increase in LH secretion—without a corresponding rise in FSH—following administration of thyrotropin-releasing hormone [13].

In women with thyrotoxicosis, levels of sex hormone–binding globulin are typically elevated, which alters the availability of circulating sex steroids [14]. Additionally, the metabolic clearance rates of testosterone and estradiol are reduced, leading to changes in their serum concentrations [15]. Some patients also exhibit enhanced peripheral aromatization of androgens to estrogens, further contributing to hormonal imbalance [16, 17].

This study aimed to evaluate the impact of thyroid dysfunction on Iraqi females experiencing both infertility types.

Methods

Study design and setting

This cross-sectional study included 200 females with infertility (primary and secondary cases), who were referred to infertility clinics between 12th June 2023 and 25th July 2025.

Data collection

All women who attended the infertility clinic for comprehensive evaluation were considered eligible for inclusion in the study, provided that male factor infertility had been excluded. This was confirmed by normal semen analysis parameters in their spouses, in accordance with standard reference values. By limiting inclusion to cases with normal male partner findings, the study focused specifically on female-related factors contributing to infertility.

Women were excluded if they had a known history of thyroid dysfunction, were currently receiving treatment for any thyroid disorder, or had previously undergone thyroidectomy. These exclusion criteria were applied to avoid confounding effects from pre-existing or treated thyroid conditions.

For each participant, detailed demographic and clinical information was collected. A structured and predesigned proforma was used to systematically record relevant data, including age, duration and type of infertility (primary or secondary), medical and obstetric history, and comprehensive menstrual history. Menstrual details included cycle regularity, frequency, duration, and the presence of abnormalities such as oligomenorrhea, amenorrhea, polymenorrhea, or menorrhagia. This standardized data collection ensured consistency and accuracy in evaluating the association between thyroid dysfunction and infertility.

Thyroid function assessment

Serum concentrations of thyroid hormones-TSH, T3, and T4 were measured using a CLIA analyzer (CLIA IIS, China). The assays were performed with commercially available kits (Autobio Diagnostics Co. Ltd., Zhengzhou, China), strictly following the manufacturer's protocols and procedures. The reference ranges used to assess thyroid function were as follows:

- TSH: 0.35 - 5.3 μIU/mL
- T4: 5.0 - 13.0 μg/dL
- T3: 0.8 - 1.9 ng/mL

Statistics

Statistical analyses were conducted using SPSS version 24. Continuous variables were expressed as mean ± standard deviation (SD). Comparisons between women with primary and secondary infertility were performed using the Chi-square test to assess statistical significance. A p-value < 0.05 was considered indicative of a statistically significant difference.

Results

In this study comparing women with primary and secondary infertility (Table 1), significant differences were observed in both age and serum T3 levels. Women experiencing secondary infertility were significantly older, with a mean age of 31.66 ± 8.13 years, compared

Table 1: Comparative analysis of thyroid function and demographics in infertile Iraqi women.

Variables/parameters		Infertility		p-value
		Primary (n = 126)	Secondary (n = 74)	
		Mean ± SD/no. (%)		
Age, years		25.89 ± 7.45	31.66 ± 8.13	< 0.0001
Menstrual cycle	Irregular	36 (18)	21 (10.5)	0.99
	Regular	90 (45)	53 (26.5)	
TSH (μIU/mL)		1.89 ± 0.85	1.94 ± 0.98	0.71
T3 (ng/mL)		1.12 ± 0.54	1.46 ± 0.79	< 0.0001
T4 (μg/dL)		10.35 ± 4.72	11.09 ± 5.65	0.32
Thyroid status	Hypo	2 (1)	3 (1.5)	0.1
	Hyper	21 (10.5)	20 (10)	
	Euthyroid	103 (51.5)	51 (25.5)	

to 25.89 ± 7.45 years in those with primary infertility ($p < 0.0001$). This age difference may reflect the natural decline in fertility with increasing age, as well as the cumulative impact of prior pregnancies and reproductive health changes over time. Serum T3 levels were also significantly higher in women with secondary infertility (1.46 ± 0.79 ng/mL) than in those with primary infertility (1.12 ± 0.54 ng/mL, $p < 0.0001$), suggesting a possible association between thyroid hormone activity and the etiology of secondary infertility. In contrast, no significant differences were observed in TSH and T4 levels ($p = 0.71$ and 0.32, respectively), indicating that overall thyroid function, as reflected by these parameters, may not differ substantially between the two groups. Menstrual cycle regularity also did not differ significantly, with 18% of women with primary infertility and 10.5% with secondary infertility reporting irregular cycles ($p = 0.99$). Furthermore, thyroid status, categorized as hypothyroid, hyperthyroid, or euthyroid, showed no statistically significant differences between the groups ($p = 0.1$), with the majority of women in both groups being euthyroid. These findings suggest that while age and T3 levels may play a role in secondary infertility, other thyroid parameters and menstrual patterns appear comparable between women with primary and secondary infertility, highlighting the multifactorial nature of infertility and the need for comprehensive hormonal evaluation.

Discussion

The present analysis highlights notable differences between women with primary and secondary infertility, particularly in age and serum T3 levels. Women with secondary infertility were significantly older than those with primary infertility, consistent with the well-established decline in female fertility with age. Elevated T3 levels in the secondary infertility group may indicate subtle alterations in thyroid hormone metabolism or regulation, although overall thyroid function, as reflected by TSH, T4, and categorical thyroid status, did not differ significantly. Menstrual cycle patterns were also comparable between the groups, suggesting that cycle regularity is not a distinguishing factor in the type of infertility. These findings underscore that secondary infertility may be influenced by age-related reproductive changes and specific hormonal variations rather than broad thyroid dysfunction. Clinically, this emphasizes the importance of evaluating age and thyroid hormone profiles, particularly T3, when assessing women with secondary infertility. Future studies with larger cohorts and additional hormonal or metabolic markers could help clarify the mechanistic role of T3 in secondary infertility.

The data on infertility in this study are comparable to the research conducted in India, which reported primary infertility at 73.31% and secondary infertility at 26.68% [18]. In contrast, the study by Ghazi et al. [19] found 54.5% of cases were primary infertility and 45.6% were secondary. Similar findings have been reported by Schmidt [20] and Kasius et al. [21]. However, the work of Girish and Manjunath [22] indicated a higher proportion of primary infertility (80%) and a lower proportion of secondary infertility (17.8%).

Regarding thyroid disorders, the prevalence observed in this study aligns closely with findings from a local tertiary care hospital, which reported a prevalence of 16% [23]. Other investigations have documented higher rates of hyperthyroidism, such as 26% by Biradar et al. [24] and 23% by Binita et al. [25]. Conversely, some studies have reported much lower prevalence rates of 2.1% [26], 2.2% [27], 3.1% [28], and 4.2% [29], suggesting that regional variations may influence these differences.

Menstrual irregularities in this study were similar to those described by Yadav et al. [30], whereas the research conducted by Binita et al. [25] reported 60% of cases with menstrual disturbances. The higher incidence in Binita et al. [25] study was attributed to a specific referral pattern, where patients suspected of having thyroid disorders were more likely to be included.

Petta et al. [31] and Rahman et al. [32] reported hyperthyroidism in infertile women of reproductive age as 3.2% and 3.3%, respectively. Although these figures are slightly higher than the prevalence observed in the current study, information regarding hypothyroidism was not provided.

Furthermore, Gude [33] found a significant association between hyperthyroidism and menstrual irregularities in infertile women. Their study suggested that infertile patients with abnormal thyroid profiles and menstrual disturbances faced a higher risk of infertility compared to euthyroid individuals.

Clinical Implications

The significantly higher age in women with secondary infertility highlights the need for early evaluation and intervention, as reproductive potential declines with increasing age. Clinicians should consider age-related fertility decline when counseling women on family planning and treatment options. Elevated T3 levels in secondary infertility suggest that even subtle variations in thyroid hormones may influence reproductive outcomes. Routine assessment of thyroid function, including T3, in infertile women may help identify those at risk and guide individualized management. Since menstrual cycle regularity and overall thyroid status did not differ significantly, clinicians should adopt a holistic approach that considers other hormonal, metabolic, and lifestyle factors rather than relying solely on cycle pattern or broad thyroid categories. These findings support tailoring fertility interventions according to age and specific hormonal profiles, which may improve diagnostic accuracy and optimize treatment outcomes in women with secondary infertility. Women with secondary infertility, particularly those with elevated T3, may benefit from closer follow-up during fertility treatments to detect subtle endocrine changes that could impact treatment success.

Limitations

The study included a relatively small number of participants ($n = 200$) and was conducted at a single center, which may limit the generalizability of the findings. The study design was cross-sectional, preventing conclusions about causal relationships between thyroid hormones, age, and infertility type. Only basic thyroid parameters (TSH, T3, T4) were measured. Other reproductive hormones, such as FSH, LH, anti-mullerian hormone (AMH), or prolactin, were not assessed, which could provide additional insights into infertility mechanisms. Factors such as lifestyle, BMI, metabolic conditions, previous pregnancies, or environmental exposures were not controlled, which may influence infertility outcomes. Thyroid hormones were measured at a single time point; fluctuations over the menstrual cycle or seasonal variations were not accounted for. The study did not follow participants to evaluate actual fertility treatment outcomes or pregnancy success, limiting the clinical predictive value of the findings.

Conclusion

Women with secondary infertility are significantly older and have higher serum T3 levels compared to those with primary infertility, while other thyroid parameters and menstrual patterns show no significant differences. These findings suggest that age and subtle

thyroid hormone variations may influence secondary infertility, highlighting the importance of comprehensive hormonal evaluation in its management.

Future Recommendations

1. Larger, multicenter studies: Conduct studies with larger and more diverse populations to validate the association between T3 levels, age, and secondary infertility, and to ensure findings are generalizable across different demographics.

2. Longitudinal research: Follow women over time to assess how changes in thyroid hormones, particularly T3, influence fertility outcomes, conception rates, and response to treatments.

3. Comprehensive hormonal profiling: Include additional reproductive and metabolic hormones (e.g., FSH, LH, prolactin, AMH, insulin) to better understand the interplay between thyroid function and infertility.

4. Interventional trials: Investigate whether correcting subtle thyroid hormone imbalances, especially elevated T3, can improve fertility outcomes in women with secondary infertility.

5. Integration of lifestyle and environmental factors: Examine the role of diet, stress, obesity, and environmental exposures alongside hormonal changes to develop a holistic model for predicting and managing secondary infertility.

6. Clinical guidelines: Use findings to inform updated clinical guidelines on routine evaluation of thyroid hormones—including T3—during infertility workups, particularly in women presenting with secondary infertility.

Acknowledgements

None.

Conflicts of interest

None.

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