

Meta-Analysis

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Exploring the relationship between Hashimoto's thyroiditis and male fertility: A meta-analytic and meta-regression perspective on hormonal and seminal factors

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ABSTRACT

Objective: To explore the relationship between Hashimoto's autoimmune hypothyroidism (HT) and male fertility, focusing on hormonal and seminal factors.

Methods: A systematic literature search was conducted across databases such as PubMed, Web of Science, EMBASE, Scopus, Cochrane, and Google Scholar, covering studies published from January 2000 to March 2024. Studies investigating the impact of HT on semen quality parameters and reproductive hormones were included. Pooled effect estimates were calculated using standard mean difference (SMD) and 95% confidence intervals (CI).

Results: A total of 8 studies with 8965 participants were included. HT significantly affected semen quality and reproductive hormone levels. Specifically, there was a notable decrease in progressive morphology (SMD= -0.78; 95% CI: -1.40 to -0.17; $P=0.01$) and sperm motility (SMD= -1.151; 95% CI: -1.876 to -0.425; $P=0.002$). In addition, there were no significant changes in reproductive hormones, although there were elevated levels of luteinizing hormone (SMD=0.437; 95% CI: 0.000 to 0.874; $P=0.050$) and follicle-stimulating hormone (SMD=0.293; 95% CI: -0.171 to 0.758; $P=0.216$), with a slight impact on testosterone levels (SMD= -1.143; 95% CI: -2.487 to 0.200; $P=0.095$).

Conclusions: This systematic review and meta-analysis provides robust evidence of the detrimental effects of HT on semen quality and reproductive hormones, underscoring the necessity for thorough evaluation and management of thyroid function in male infertility assessments.

KEYWORDS: Hashimoto thyroiditis; Male fertility; Semen quality; Reproductive hormones; Meta-analysis; Meta-regression

1. Introduction

Hashimoto's thyroiditis (HT), an autoimmune disorder of the thyroid gland, is the most prevalent cause of hypothyroidism in regions with adequate iodine levels[1,2]. This condition is characterized by autoimmune-mediated inflammation and destruction of thyroid tissue, leading to decreased thyroid hormone production[3]. The biological hallmark of HT is the presence of antibodies against thyroid peroxidase (TPO-a) and thyroglobulin (TG-a), indicating a chronic autoimmune response against thyroid tissue. It is noteworthy that autoimmune thyroid disorders are more prevalent in women than men, likely due to hormonal differences. Consequently, Hashimoto's disease has received less attention regarding its impact on male reproductive health[4]. Furthermore, the specific effects of HT on male fertility, especially regarding reproductive hormones and semen quality parameters, have not yet been investigated in a comprehensive meta-analysis[4,5]. This knowledge gap is significant given the essential role of thyroid hormones in modulating the hypothalamic-pituitary-gonadal (HPG) axis and influencing spermatogenesis and steroidogenesis.

In the realm of HT, resultant hypothyroidism can profoundly disturb hormonal processes, posing potential risks to male

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reproductive capability. Specifically, hypothyroidism frequently correlates with variations in luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels, attributable to heightened secretion of thyrotropin-releasing hormone. This issue stimulates the pituitary gland, influencing the release of these crucial gonadotropins[6–8]. Furthermore, the dysfunction of the thyroid gland can indirectly impact testosterone levels as thyroid hormones play a vital role in the normal function of Leydig cells and steroidogenesis[9,10]. In addition, the impact of HT on semen quality is another crucial aspect of male fertility. Semen quality, encompassing parameters like sperm count, motility, and morphology, plays a fundamental role in facilitating the fertilization process[11–13]. Thyroid hormones regulate testicular temperature, antioxidant defense systems, and sperm maturation, suggesting that HT may lead to decreased sperm motility and increased abnormal sperm morphology. Although studies suggest a correlation between hypothyroidism caused by HT and male fertility issues, further research is required to definitively confirm this association[9,14].

This investigation aims to provide a comprehensive meta-analytic and meta-regression synthesis of the existing literature on the relationship between HT and male fertility, focusing on hormonal and seminal factors. This endeavor contributes to our understanding of the impact of HT on male fertility and underscores the importance of thyroid health in the broader context of reproductive function and fertility.

2. Methods

2.1. Protocol and registration

In order to uphold the highest standards of methodological rigor and transparency, this meta-analysis and systematic review on the effects of HT on male fertility follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Our study protocol is registered with PROSPERO, an international database for prospectively registered systematic reviews in health and social care, under the registration number CRD42024557738[15,16].

2.2. Eligibility criteria

Our study inclusion criteria were meticulously defined to capture the relevant literature assessing the relationship between HT and male fertility, focusing on semen quality parameters and reproductive hormones (LH, FSH, testosterone). Criteria included: (1) Observational studies exploring the link between HT and semen quality or reproductive hormone levels. Hashimoto's thyroiditis was classified by elevated anti-thyroid peroxidase (TPO) antibodies, along with corresponding changes in thyroid stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4). Also, we defined overt hypothyroidism using established thresholds:

increased TSH (>5.0 $\mu\text{IU/mL}$) with decreased FT4 (<0.89 ng/dL)[17]. (2) Research published from January 2000 to March 2024. (3) Studies that provided specific data on semen parameters like volume, motility, morphology, and hormone levels. (4) Human subject research published in English peer-reviewed journals. We excluded reviews, abstracts, non-human studies, and any research lacking primary data or adequate methodological detail.

2.3. Literature search

In order to conduct a comprehensive review of relevant literature, a meticulous search strategy was designed and executed across multiple prominent electronic databases including PubMed, Web of Science, EMBASE, Scopus, Cochrane Library, and Google Scholar. The search aimed to capture a wide array of studies published from January 2000 to March 2024, encompassing a span of over three decades to include seminal and contemporary research findings. A variety of keywords and medical subject headings (MeSH terms) were used to cover all potential studies related to HT and its implications for male fertility. Key search terms included "Hashimoto's thyroiditis," "hypothyroidism," "male fertility," "semen quality," "sperm quality," "semen parameters," "sperm concentration," and "sperm motility," as well as "reproductive hormones," "luteinizing hormone (LH)," "follicle-stimulating hormone (FSH)," and "testosterone". These terms were strategically combined using Boolean operators (AND, OR) to construct a nuanced and comprehensive search algorithm.

2.4. Study selection

Two independent reviewers (S.B., M.A.) conducted the initial literature screening, specifically focusing on titles and abstracts to identify relevant studies. Subsequently, they reviewed the full texts of the selected studies, ensuring that they met our predetermined inclusion criteria. Any discrepancies were resolved through discussion or, if necessary, with the involvement of a third party for adjudication (M.D.).

2.5. Data extraction

Data extraction from each relevant study was conducted methodically, employing a strategic approach aligned with a predefined data collection protocol previously established by our research team[18–20]. This included publication details (author, publication year, study location), study context, design specifics, participant demographics [sample size, age range, body mass index (BMI)], criteria for diagnosing overt hypothyroidism, assessed fertility parameters, and sperm quality outcomes (semen volume, morphology, progressive motility, total sperm count, sperm concentration), and other pertinent findings.

2.6. Quality assessment

Included studies were appraised using the Newcastle-Ottawa Scale to evaluate their quality and the risk of bias, focusing on the selection of study groups, comparability of groups, and ascertainment of either the exposure or outcome of interest[21]. Each study was independently reviewed by two team members, with discrepancies resolved through consensus or third-party adjudication.

2.7. Statistical analysis

The impact of HT on male fertility was quantitatively synthesized. Standardized mean differences (SMD), 95% confidence intervals (CI), and prediction intervals (PI) were calculated for each relevant outcome, including semen parameters and hormone levels[22]. Meta-regression and subgroup analyses were employed to investigate sources of heterogeneity and potential modifying effects. The I^2 statistic and Cochran's Q-test quantified heterogeneity among studies, while publication bias was assessed through Egger's test[23]. Given the considerable heterogeneity among the studies analyzed, a random-effects model was applied to better account for the variability across studies. Statistical analyses were executed using Comprehensive Meta-Analysis (CMA) v3 software, aiming to deliver a thorough and nuanced understanding of Hashimoto's impact on male reproductive health[22].

3. Results

3.1. Selection process and characteristics of the included studies

Our comprehensive literature search included multiple databases, yielding 819 studies relevant to HT and its impact on male fertility. After removing 191 duplicate records and excluding 571 articles based on title and abstract screening, we thoroughly evaluated 57 full-text articles. Ultimately, eight studies met our stringent inclusion criteria, encompassing a combined sample size of 8965 participants. During the full-text review, we excluded 49 articles for the following reasons: incorrect study design ($n=20$), inappropriate comparators ($n=18$), non-English language ($n=6$), and lack of full-text ($n=5$). The detailed selection process, from initial article retrieval to final study inclusion, is outlined in a flowchart (Figure 1), providing a comprehensive overview of our systematic review methodology. Table 1 shows the characteristics of eight studies included in the systematic review and meta-analysis.

3.2. Association and comparison details

The eight studies included in this analysis, involving a total of 8956 participants, primarily aimed to examine the relationship between HT and key indicators of male fertility. These indicators specifically include semen quality metrics and reproductive hormone levels. Furthermore, the studies included underwent assessment using the Newcastle-Ottawa scale to evaluate their quality and risk of bias, as shown in Table 2. Through our analyses, we identified potential variables contributing to outcome heterogeneity, such as BMI,

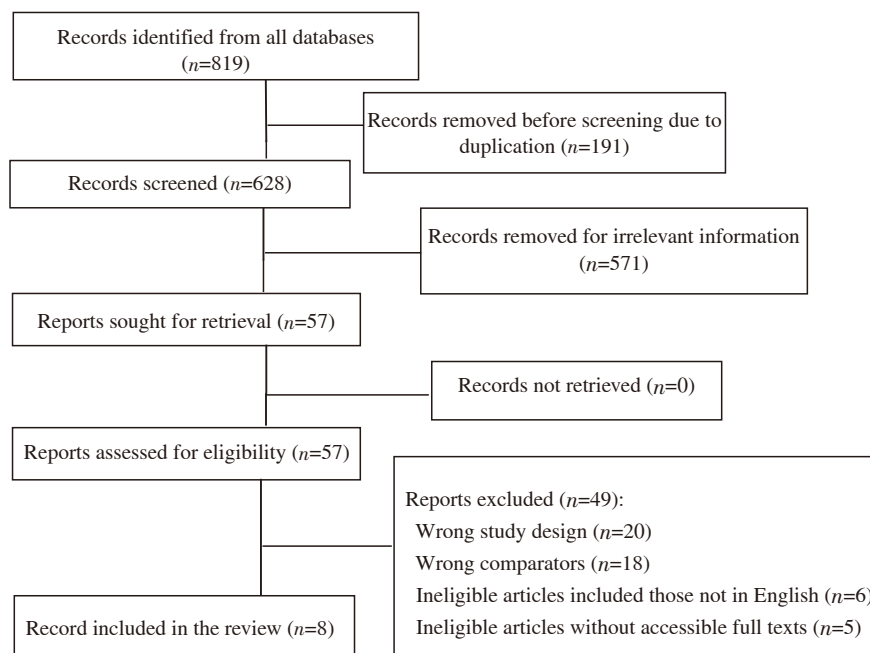


Figure 1. The flow diagram of the study selection.

Table 1. Characteristics of the studies included in the systematic review and meta-analysis.

Author	Year	Country	Ethnicity	Study design	No. of participants	Semen analysis method	Age (years)	BMI (kg/m ²)	Outcome
							Mean±SD (HT vs. Control)	Mean±SD (HT vs. Control)	
Vaghela <i>et al.</i> ,	2016	India	Asian	Case-control	351	WHO-guided semen analysis	33.22±0.90; 31.95±0.36	21.84±0.60; 22.15±0.23	Semen volume, sperm count, sperm viability, progressive motility, sperm morphology
Nikoobakht <i>et al.</i> ,	2012	Iran	Mixed	Case-control	72	CASA	43.1±11.6; 41.5±69.0	24.50±4.92; 2.46±4.14	Sperm total count, sperm motility, sperm morphology
Rao <i>et al.</i> ,	2021	China	Asian	Case-control	2511	WHO-guided semen analysis	36.0±56.8; 34.5±6.2	24.5±3.2; 24.2±3.3	Semen volume, sperm concentration, progressive motility, sperm morphology
Zhao <i>et al.</i> ,	2022	China	Asian	Cross-sectional	5401	CASA	35.35±6.48; 34.20±5.97	24.66±3.45; 24.34±3.48	Semen volume, sperm concentration, progressive sperm motility, total sperm count, normal sperm morphology
Rehman <i>et al.</i> ,	2020	Pakistan	Mixed	Cross-sectional	376	WHO-guided semen analysis	33.90±5.97; 37.65±6.12	26.78±3.58; 24.75±3.08	Sperm total count, sperm morphology
Lotti <i>et al.</i> ,	2016	Italy	European	Cross-sectional	157	WHO-guided semen analysis	39.1±5.5; 38.9±8.4	43.1±11.6; 41.5±69.0	Semen volume, sperm concentration, sperm total count, progressive motility, sperm morphology
Sarma <i>et al.</i> ,	2017	India	Asian	Cross-sectional	62	CASA	31.57±5.43; 33.59±4.48	24.13±1.10; 24.65±1.36	Semen volume, sperm count, total sperm motility
Krassas <i>et al.</i> ,	2008	Greece	European	Case-control	35	WHO-guided semen analysis	44.0±13.7; 41.8±12.3	NA	Sperm concentration, progressive motility, sperm morphology

Table 2. Quality assessment based on the Newcastle-Ottawa Scale of studies included in this meta-analysis.

Author, & year	Quality indicators			Total quality scores
	Selection	Comparability	Outcome/ exposure	
Krassas <i>et al.</i> , 2008	***	*	**	6
Nikoobakht <i>et al.</i> , 2012	***	*	**	6
Lotti <i>et al.</i> , 2016	*****	**	**	8
Vaghela <i>et al.</i> , 2016	***	*	***	7
Sarma <i>et al.</i> , 2017	*****	**	***	9
Rehman <i>et al.</i> , 2020	*****	*	**	7
Rao <i>et al.</i> , 2021	***	**	**	8
Zhao <i>et al.</i> , 2022	*****	*	**	7

geographic location, study quality, and participant health status. This thorough examination offered deeper insights into the multifaceted relationship between thyroid dysfunction and male reproductive health.

3.3. A meta-analysis of the relationship between Hashimoto's thyroiditis and male fertility

3.3.1. Assessing the effect of HT on reproductive hormones

Further analysis revealed that men with HT experience significant changes in their reproductive hormone profiles. Specifically, there

were significant increases in LH (SMD=0.437; 95% CI: 0.000 to 0.874; $P=0.050$; PI: -1.149 to 2.023) and FSH (SMD=0.293; 95% CI: -0.171 to 0.758; $P=0.216$; PI: -1.415 to 2.002). Additionally, there is an unexpected decrease in testosterone levels (SMD=-1.143; 95% CI: -2.487 to 0.200; $P=0.095$; PI: -6.433 to 4.146) compared to the control groups (Figure 2).

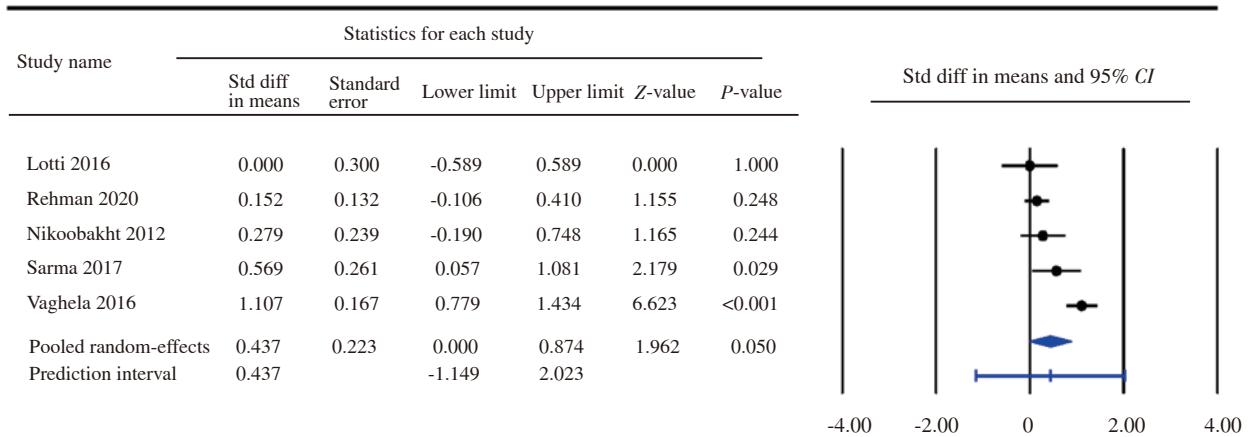
3.3.2. Assessing the effect of HT on semen quality parameters

Our meta-analytic findings demonstrated significant associations between HT and various semen quality parameters. Affected individuals showed reductions in semen volume (SMD=-0.221; 95% CI: -0.527 to 0.084; $P=0.155$; PI: -1.301 to 0.858), total sperm count (SMD = -0.499; 95% CI: -1.127 to 0.130; $P=0.120$; PI: -2.919 to 1.922), and progressive motility (SMD = -1.151; 95% CI: -1.876 to -0.425; $P=0.002$; PI: -3.807 to 1.506). Sperm morphology was also adversely affected (SMD = -0.78; 95% CI: -1.40 to -0.17; $P=0.01$; PI: -2.97 to 1.41). These pivotal results are visually summarized in forest plots for more transparent comprehension (Figure 3).

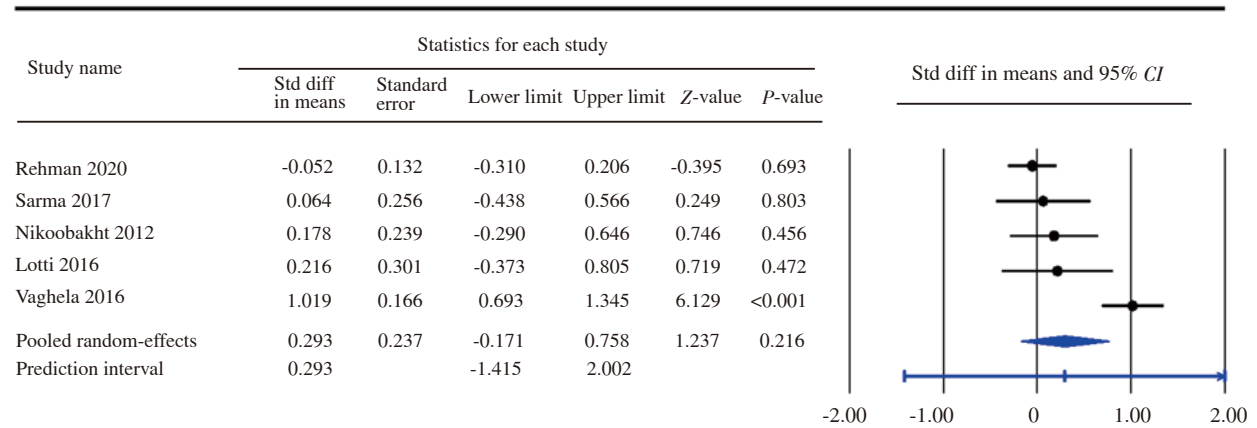
3.4. Meta-regression analysis

In the meta-regression analysis section of our study, we meticulously examined several potential moderators that could

A



B



C

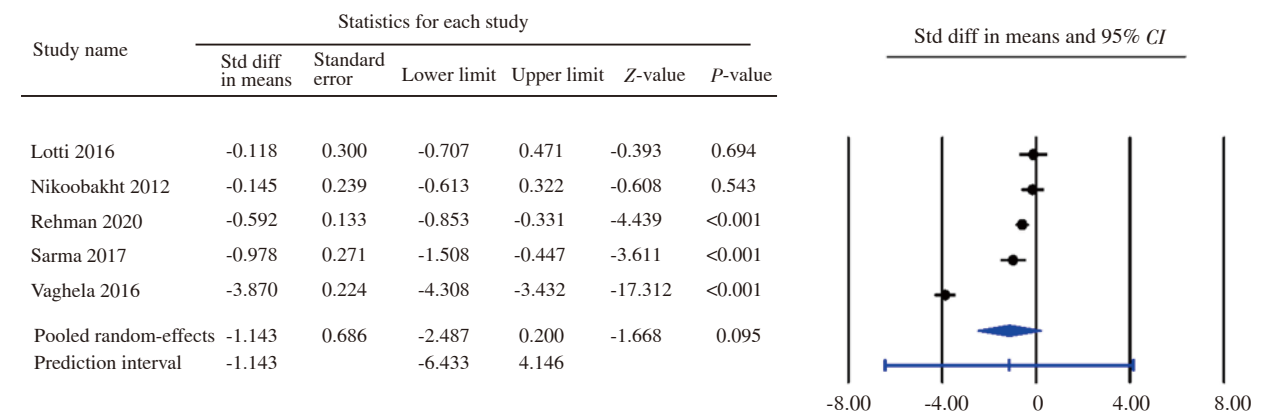
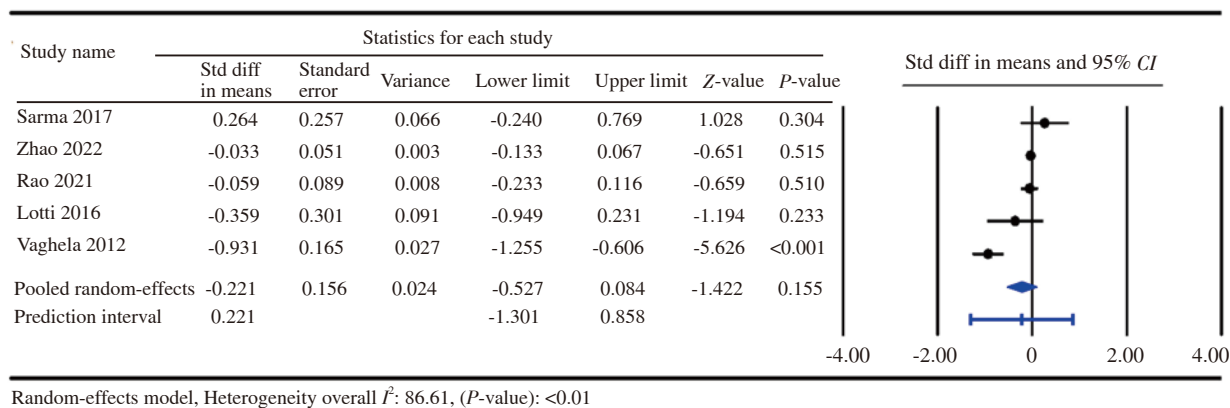
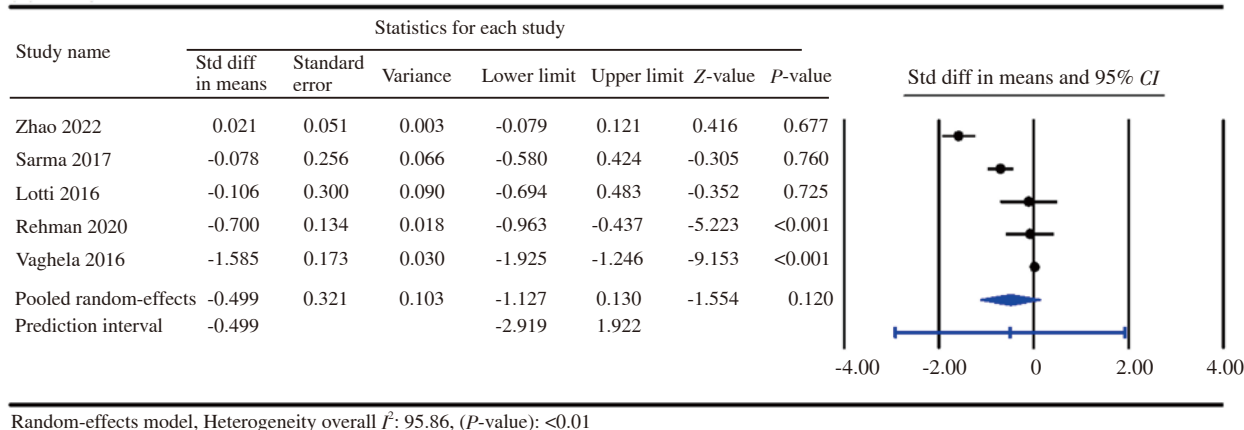


Figure 2. Forest plots demonstrating the effects of Hashimoto's thyroiditis (HT) on male reproductive hormones, including A) luteinizing hormone (LH), B) follicle-stimulating hormone (FSH), and C) testosterone levels.

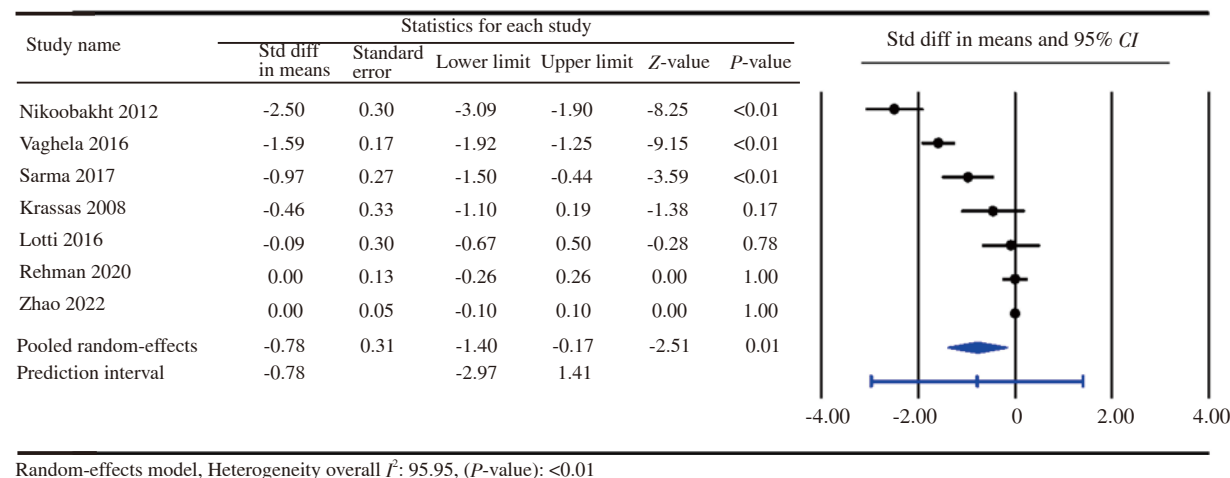
A



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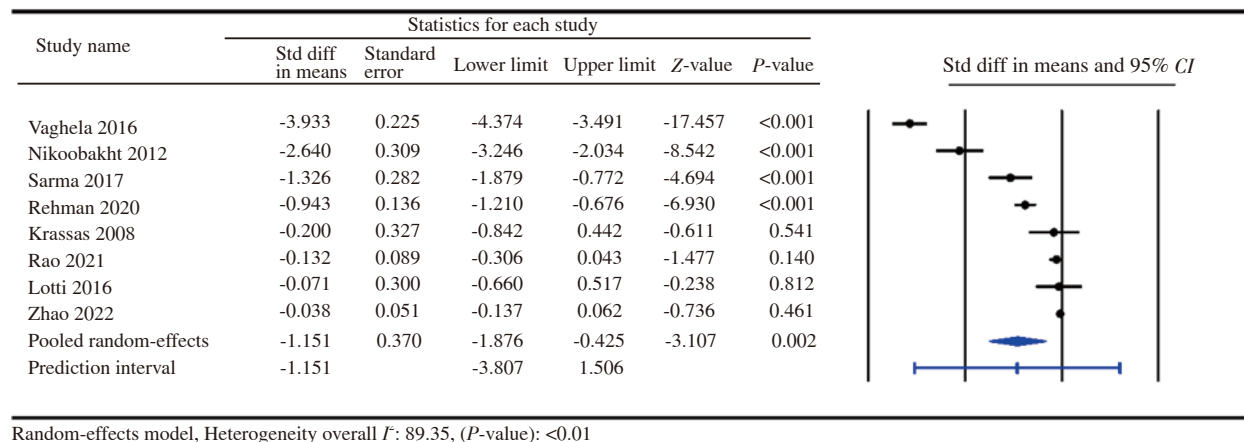


Figure 3. Forest plots illustrating the impact of Hashimoto's thyroiditis (HT) on semen quality parameters in men, including A) semen volume, B) total sperm count, C) morphology, and D) progressive motility.

influence the relationship between HT and key male fertility parameters, including hormonal levels (LH, FSH, testosterone) and seminal quality indicators. The meta-regression was structured to discern the effects of variables such as BMI, semen analysis methods, Newcastle-Ottawa Scale (NOS) quality score, and total sample size on the outcomes of interest (Table 3).

The meta-regression results based on BMI > 25 kg/m² revealed nuanced relationships with the fertility parameters. Specifically, we observed that higher testosterone levels were positively correlated with increasing BMI (meta-regression coefficient: 1.3093; 95% CI: -1.671 to 4.290; $P=0.038$). Conversely, sperm volume demonstrated a negative correlation with higher BMI values (meta-regression coefficient: -0.1592; 95% CI: -1.073 to 0.754; $P=0.043$). Analyzing other seminal parameters like sperm concentration and total sperm count also exhibited negative but less pronounced correlations with BMI. Regarding the meta-regression analysis focused on the semen analysis method based on global health guidelines, we found that the progressive motility of sperm exhibited a negative association with the methodology employed (meta-regression coefficient: -0.0461; 95% CI: -1.888 to 1.787; $P=0.096$). This finding was intriguing, particularly when juxtaposed with the positive correlation observed between the semen analysis method and sperm morphology (meta-regression coefficient: 0.0031; 95% CI: -1.702 to 1.708; $P=0.060$). In terms of the NOS quality score meta-regression results, both progressive sperm motility and morphology demonstrated negative correlations (progressive motility meta-regression coefficient: -0.1241; 95% CI: -1.304 to 1.056; $P=0.83$); morphology meta-regression coefficient: -0.3201; 95% CI: -1.899 to 0.221; $P=0.27$). These outcomes suggest that studies of higher methodological quality reported more detrimental effects of HT on these parameters.

Lastly, the meta-regression analysis based on the total sample size indicated positive correlations for both progressive sperm motility (meta-regression coefficient: 0.002; 95% CI: -0.001 to 0.006; $P=0.22$) and morphology (meta-regression coefficient: 0.035; 95% CI: -0.011 to 0.027; $P=0.31$). These findings suggest that more extensive studies tend to report more significant associations between HT and improvements in these seminal parameters.

These nuanced findings from our meta-regression analyses provide deeper insights into the multifactorial nature of male fertility in the context of overt Hashimoto's thyroiditis, underscoring the significance of individual and study-related factors in interpreting the associations observed across the literature.

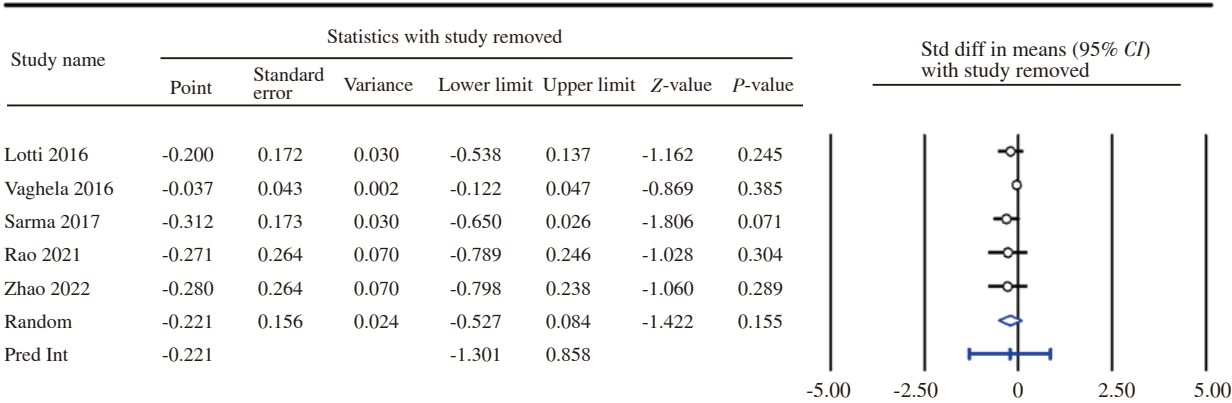
3.5. Sensitivity analysis and publication bias

A sensitivity analysis was rigorously performed to ensure the robustness and consistency of our meta-analytic findings. Methodically removing individual studies from the pooled analysis did not significantly alter the core conclusions, affirming the meta-analysis's stability and reliability. Such findings are graphically represented in Figure 4. The investigation into publication bias involved applying Egger's test, complemented by a thorough examination of the funnel plot for asymmetry. Results from Egger's test indicated no significant evidence of publication bias in the studies examining the relationship between HT and male fertility parameters. The symmetrical distribution observed in the funnel plot is detailed in Figure 5.

Table 3. Meta-regression analysis for the potential variables between studies.

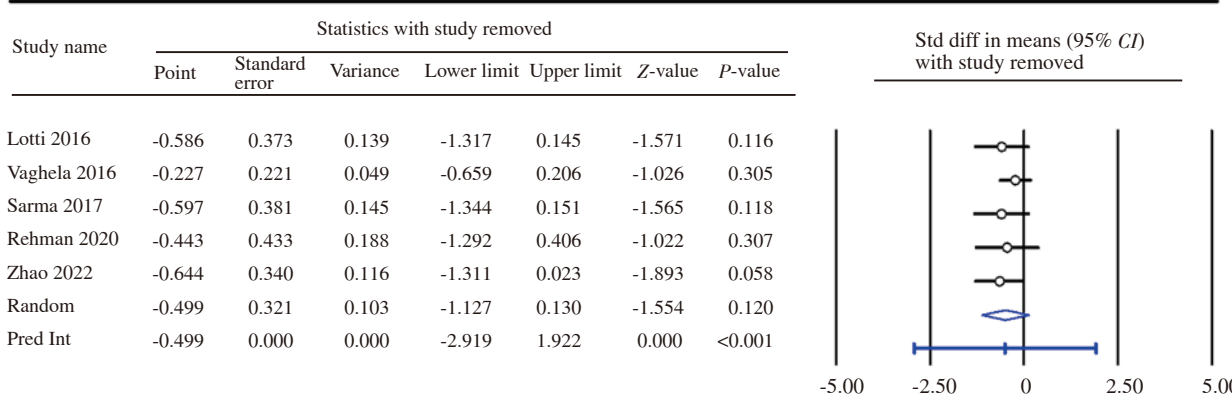
Variables	No. studies	Coefficient	Standard error	<i>P</i>	95% CI
BMI > 25 kg/m ²					
Luteinizing hormone	5	-0.5921	0.351	0.091	-1.2807 to 0.0966
Follicle-stimulating hormone	5	-1.2036	1.55	0.437	-4.2441 to 1.8370
Testosterone levels	5	1.3093	1.52	0.038	-1.671 to 4.290
Semen volume	6	-0.1592	0.46	0.043	-1.073 to 0.754
Semen analysis method					
Semen morphology	7	0.0031	0.07	0.060	-1.702 to 1.708
Semen progressive motility	7	-0.0461	0.93	0.096	-1.888 to 1.787
NOS quality score					
Semen morphology	7	-0.3201	0.33	0.27	-1.899 to 0.221
Semen progressive motility	7	-0.1241	0.60	0.83	-1.304 to 1.056
Luteinizing hormone	5	0.4273	0.13	0.001	0.157 to 0.679
Follicle-stimulating hormone	5	0.4677	0.12	0.002	0.221 to 0.714
Testosterone levels	5	-1.524	0.57	<0.001	-2.653 to -0.396
Total sample size					
Semen morphology	7	0.035	0.07	0.31	-0.011 to 0.027
Semen progressive motility	7	0.002	0.00	0.22	-0.001 to 0.006
Luteinizing hormone	5	0.0021	0.01	0.36	-0.02 to 0.006
Follicle-stimulating hormone	5	0.0004	0.00	0.86	-0.005 to 0.006
Testosterone levels	5	-0.004	0.00	0.53	-0.018 to 0.009

A



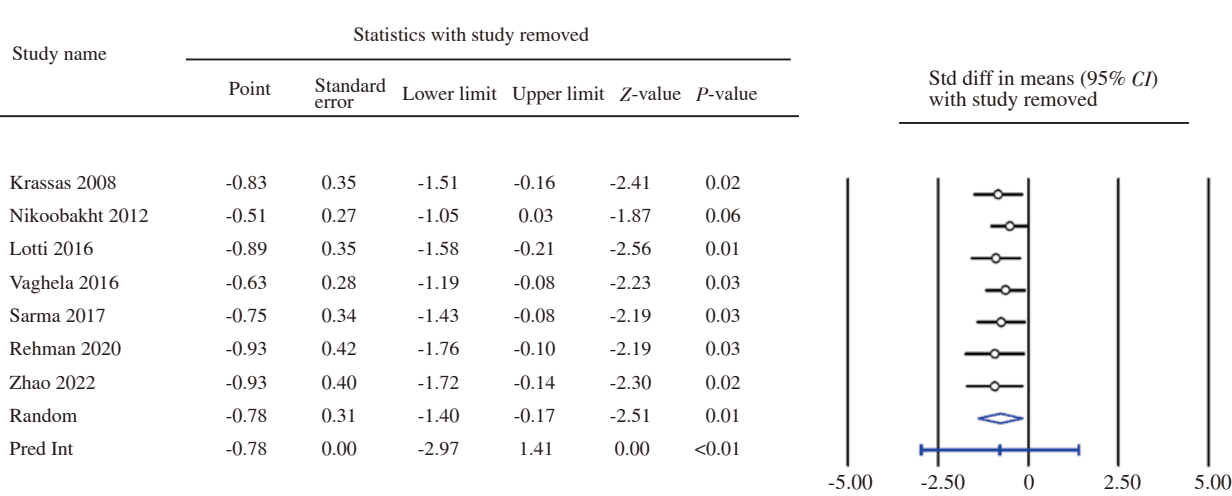
Sensitivity analysis

B



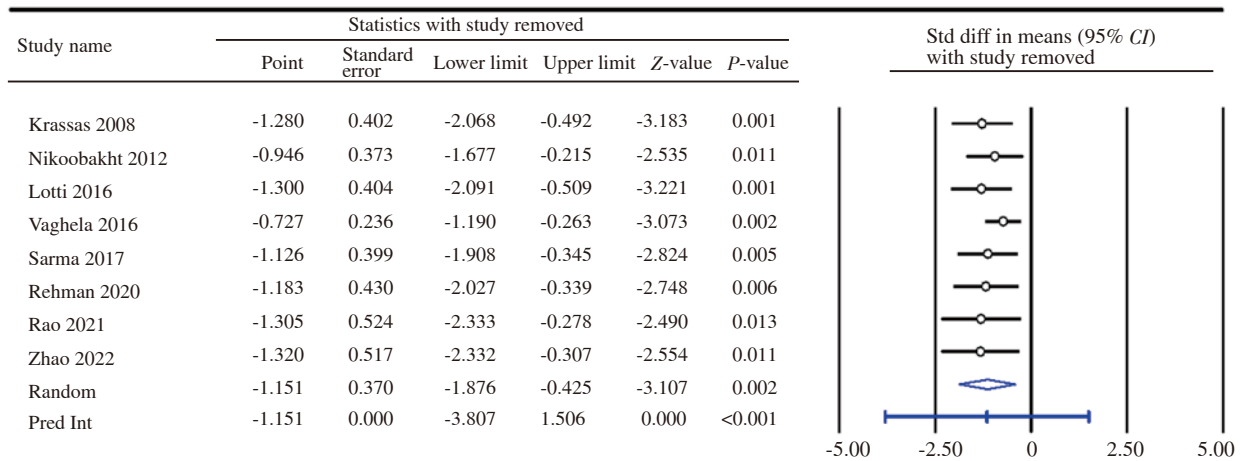
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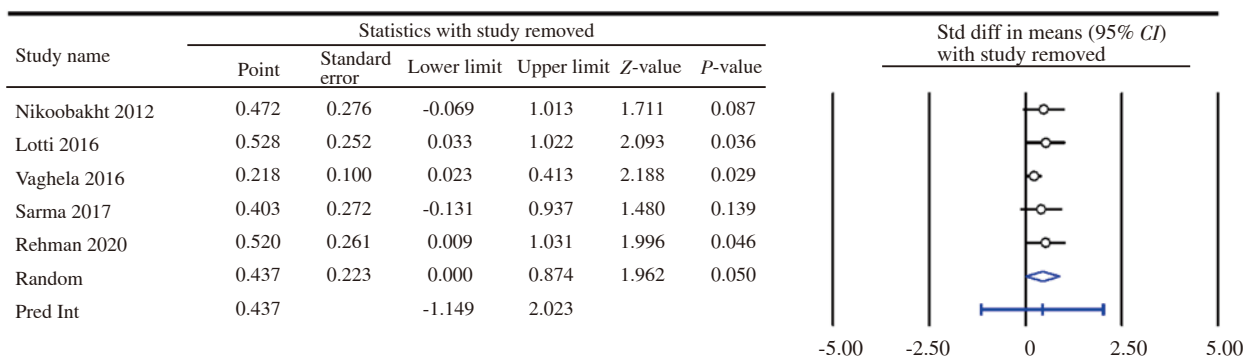
Sensitivity analysis

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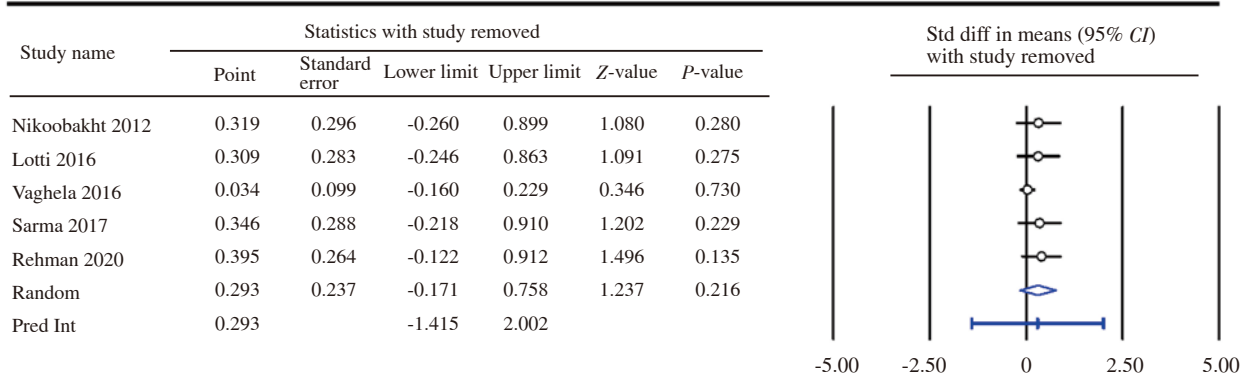
Sensitivity analysis

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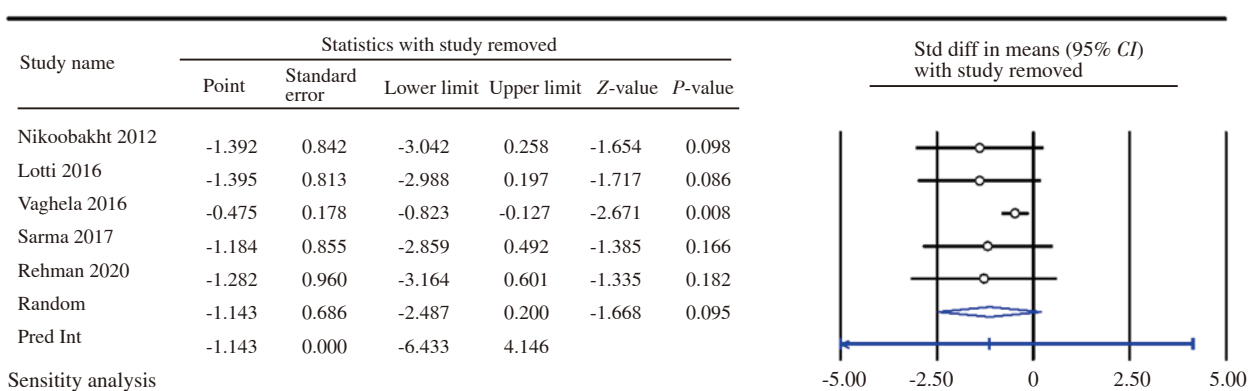
Sensitivity analysis

F



Sensitivity analysis

G



Sensitivity analysis

Figure 4. Sensitivity analysis and male fertility parameters, including A) semen volume, B) total sperm count, C) morphology, D) progressive motility, E) luteinizing hormone (LH), F) follicle-stimulating hormone (FSH), and G) testosterone levels. Pred Int: prediction interval.

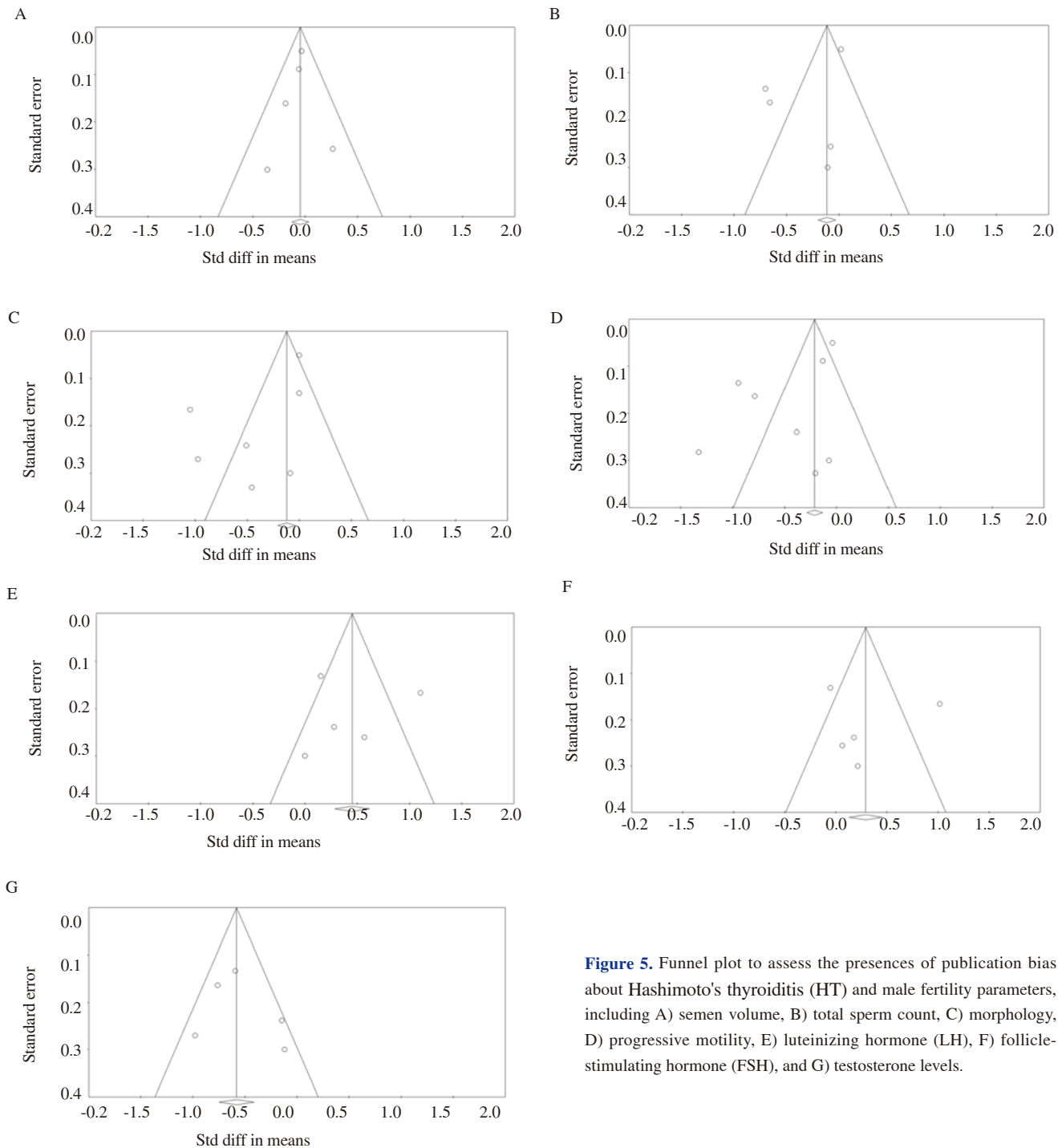


Figure 5. Funnel plot to assess the presences of publication bias about Hashimoto's thyroiditis (HT) and male fertility parameters, including A) semen volume, B) total sperm count, C) morphology, D) progressive motility, E) luteinizing hormone (LH), F) follicle-stimulating hormone (FSH), and G) testosterone levels.

4. Discussion

The interplay between HT and male fertility is a complex and multifaceted issue that has garnered significant attention in endocrinological and reproductive medical research[24,25]. Our meta-analysis included eight studies and 8965 participants from January 2000 to March 2024, providing compelling insight into this crucial issue. Meta-analytic and meta-regression analyses offer substantive evidence regarding the adverse effects of HT on both seminal quality and reproductive hormone profiles in affected males, highlighting the critical impact of this autoimmune thyroid disorder on male reproductive health. Our meta-analysis result revealed

significant negative associations between HT and important semen quality parameters. In particular, a reduction in semen volume, total sperm count, and progressive motility, as well as impaired sperm morphology were observed. These results suggest that HT impairs spermatogenesis and sperm function through its influence on thyroid hormone levels and possibly associated autoimmune or inflammatory processes[26]. These results are consistent with previous studies, as shown by Vaghela and his colleagues[27]. The reduction in semen volume and sperm count in HT may be due to the direct and indirect effects of thyroid hormone imbalance on the seminiferous tubules and Sertoli cells, which are critical for spermatogenesis[28,29]. Thyroid hormones have been shown to regulate gene expression and

protein synthesis in Sertoli cells, and their dysregulation may impair the support these cells provide to developing spermatozoa[30,31]. In addition, autoimmunity of the thyroid gland can have adverse effects through systemic inflammation or specific autoimmune responses targeting the testes[32]. Also, these results are consistent with previous studies, as shown by Zhao *et al*[33]. The observed decrease in progressive sperm motility and morphology further emphasizes the potential impact of HT on the functional aspects of sperm[34]. In addition, thyroid hormones are known to affect mitochondrial energy metabolism, which is paramount for sperm motility. An imbalance in thyroid hormone levels may disrupt the energy supply of sperm, consequently impacting their motility and fertilization potential[35,36]. The significant changes in LH, FSH, and testosterone levels in men with HT indicate a disruption of the HPG axis[37,38]. Elevated LH and FSH levels may reflect a compensatory response to decreased testicular function, while decreased testosterone levels indicate impaired Leydig cell activity[38,39].

Conversely, the observed decline in testosterone levels is particularly concerning as it plays a central role in spermatogenesis, libido, and overall male reproductive health[39,40]. These hormonal changes could be due to the direct effects of thyroid hormone imbalance on the HPG axis or the broader systemic effects of chronic autoimmune inflammation associated with HT. This topic has been thoroughly investigated in prior studies, such as those conducted by Sharma *et al*[39].

Our meta-regression analyses provided further deepened our understanding of the associations between HT and male fertility parameters and have shown how these associations may vary depending on specific moderators. The association between higher BMI and altered fertility parameters underscores the complex interplay between metabolic health and reproductive function[41,42]. The positive correlation between BMI and testosterone levels may reflect an adaptive response to increased adiposity, while the negative correlations with semen volume and other parameters suggest that metabolic factors associated with higher BMI may exacerbate the reproductive effects of HT[43,44]. These results are consistent with previous studies, as demonstrated by Krasas and his colleagues[45]. The results of the methodology of semen analysis underline the importance of standardization and quality in assessing reproductive health[46,47]. The negative correlation with progressive motility suggests that methodological differences may influence the observed effects of HT on this parameter. Conversely, the positive correlation with sperm morphology suggests that certain analytical methods may be more sensitive to morphological changes associated with the disease. Finally, the NOS quality score meta-regression results suggest that higher-quality studies tend to have stronger negative associations between HT and key sperm parameters, adding credibility to these findings[48,49]. This meta-analysis on the relationship between HT and male fertility boasts several strengths, bolstering the reliability and relevance of its findings. Firstly, the rigorous search methodology employed ensured the inclusion of a comprehensive and representative sample of studies

encompassing diverse populations and settings. This extensive data pool, comprising 8965 participants across multiple studies, enhances the generalizability of the results, making them applicable to a broader demographic. The utilization of meta-regression techniques is a significant strength, as it allows for the exploration of potential moderators and confounders that could influence the observed associations. By systematically examining variables such as age, assay technique, and BMI, the analysis provides nuanced insights into how different factors might modulate the impact of HT on male reproductive health. This approach not only strengthens the interpretation of the results but also helps identify specific subgroups that might be more vulnerable to the detrimental effects of HT. Another notable strength is the focus on both hormonal and seminal parameters. This dual approach provides a holistic understanding of how HT affects male fertility, addressing both endocrine and gametogenic aspects.

Despite these strengths, several limitations must be acknowledged to provide a balanced perspective. One significant limitation is the heterogeneity among the included studies. Variations in study design, diagnostic criteria for HT, and methods for assessing reproductive parameters contribute to substantial heterogeneity (all $I^2=75\%$). This variability can influence the robustness of the pooled estimates and suggests that the impact of HT on male fertility may differ across populations and contexts. Future studies should strive for standardization in diagnostic and assessment methodologies to mitigate this issue. Additionally, the influence of confounding factors such as concomitant medical conditions, medications, and lifestyle variables was not uniformly accounted for across studies[50,51]. For instance, conditions like obesity and diabetes, which are prevalent in HT patients, can independently affect reproductive health[52]. The lack of consistent adjustment for these confounders may skew the observed associations. Detailed reporting and control of these variables in future research will enhance the accuracy of the findings. Lastly, while the study provides valuable insights into the impact of HT on male fertility, it does not extensively explore the underlying biological mechanisms. Future studies should delve deeper into these mechanisms, using advanced molecular and genetic techniques to unravel the precise biological underpinnings.

In conclusion, according to a meta-analytic investigation involving 8965 individuals, male fertility parameters such as seminal factors and reproductive hormones are linked to HT in men. The analysis, which covers various studies and involves data from a significant number of participants, highlights the potential negative impacts of HT on semen quality parameters and reproductive hormone profiles. These findings underscore the importance of clinicians considering the assessment of thyroid function as an integral part of strategies for evaluating and treating male infertility.

Conflict of interest statement

The authors declare no competing interests.

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Data availability

The datasets analyzed during the current study are available in the main text, tables, and figures.

Authors' contributions

Seyed Sobhan Bahreiny conducted the data analysis and was primarily responsible for drafting the initial manuscript. Mojtaba Aghaei, Mohammad Reza Dabbagh, and Mahdi Amraei were instrumental in the conceptualization, design, and oversight of the study. These authors also played key roles in writing the final version, critically reviewing, and substantially editing the manuscript to ensure the validity and accuracy of the results. All authors meticulously reviewed the final manuscript, provided essential feedback, and approved it before submission for publication.

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