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Prevalence of subclinical hypothyroidism in women with infertility in reproductive age group in tertiary care hospital

[1]Ananya Dash, JR3, Department of Obstetrics & Gynaecology, MKCG MCH, Odisha, India
[2]Mahija Sahu, Professor, Department of Obstetrics & Gynaecology, MKCG MCH, Odisha, India
[3]Asish Bhuyan, JR3, Department of Obstetrics & Gynaecology, MKCG MCH, Odisha, India
Corresponding author: Mahija Sahu, Professor, Department of Obstetrics & Gynaecology, MKCG MCH, Odisha, India

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Abstract

Background: Subclinical hypothyroidism (SCH) is a common endocrine disorder that can impact fertility. This study investigates the prevalence of SCH in women with infertility in the reproductive age group at a tertiary care hospital.

Aim: To determine the prevalence of subclinical hypothyroidism in infertile women and to analyze its association with age, type, and duration of infertility.

Methods: A cross-sectional study was conducted at MKCG Medical College and Hospital from June 2022 to June 2024. A total of 195 infertile women were included. Data on age, duration of infertility, serum T3, T4, and TSH levels were collected. Statistical analyses were performed to determine the prevalence of SCH and its association with various factors.

Results: The mean age of the patients was 29.3±5.30 years, and the mean duration of infertility was 3.14±1.79 years. The prevalence of subclinical hypothyroidism was found to be 73.3% (143 out of 195). SCH was significantly associated with age (p=0.020), type of infertility (p=0.006), and duration of infertility. The majority of patients with SCH were in the 21-30 years age group and had primary infertility.

Conclusion: The study highlights a high prevalence of subclinical hypothyroidism among infertile women. SCH is significantly associated with age, type, and duration of infertility, suggesting the need for routine screening and management of thyroid function in infertile women.

Recommendations:

1. Routine screening for SCH in women with infertility.
2. Early intervention and management of SCH to improve fertility outcomes.
3. Further research to explore the impact of SCH treatment on infertility.
4. Awareness programs for healthcare providers about the importance of thyroid screening in infertility.
5. Development of guidelines for the management of SCH in infertile women.

Keywords: Subclinical hypothyroidism, infertility, reproductive age, thyroid function, prevalence.

Introduction

Infertility is a significant concern affecting many couples worldwide, with various underlying causes, including hormonal imbalances. Among these, subclinical hypothyroidism (SCH) has emerged as a notable factor. SCH is characterized by elevated serum thyroid-stimulating hormone (TSH) levels with normal free thyroxine (T4) levels, often presenting without obvious symptoms. Its subtle nature makes it a silent disruptor of reproductive health, necessitating thorough investigation (1,2)

The thyroid gland plays a crucial role in regulating metabolism and reproductive functions. Even mild dysfunctions, such as those seen in SCH, can lead to menstrual irregularities, ovulatory dysfunction, and ultimately, infertility. Despite its potential impact, SCH often goes undiagnosed due to its asymptomatic presentation. This underscores the importance of routine screening, especially in women facing infertility issues (3,4)

Previous studies have indicated a higher prevalence of SCH in women with infertility compared to the general population. However, there is a need for more localized data to understand the extent and implications of SCH in specific populations (5). This study aims to fill this gap by investigating the prevalence of SCH in infertile women attending a tertiary care hospital in India.The primary aim of this study is to determine the prevalence of subclinical hypothyroidism in women with infertility in the reproductive age group. Additionally, the study seeks to analyze the association of SCH with various factors such as age, type of infertility (primary or secondary), and duration of infertility. Understanding these associations can help in developing targeted interventions to improve fertility outcomes.

By identifying the prevalence and associated factors of SCH in infertile women, this study aims to highlight the importance of thyroid function screening in infertility management. The findings are expected to contribute to better clinical practices and guidelines, ensuring that women with infertility receive comprehensive care that addresses all potential underlying causes, including thyroid dysfunction.

Methodology

Study Design: This was a cross-sectional clinical study conducted to determine the prevalence of subclinical hypothyroidism (SCH) in women presenting with infertility.

Study Setting: The study was conducted at the Department of Obstetrics and Gynaecology, M.K.C.G. Medical College and Hospital, Berhampur, Odisha, from June 2022 to June 2024.

Participants: A total of 195 women aged 20-45 years, attending the gynecology outpatient department (OPD) with complaints of infertility, were included in the study.

Inclusion Criteria:

- Women aged 20-45 years.
- Patients seeking treatment for primary or secondary infertility with a female factor of infertility.

Exclusion Criteria:

- Women aged below 20 years or above 45 years.
- Patients with known thyroid abnormalities, those on thyroid medication or post-thyroidectomy.
- Cases of infertility due to male factors.
- Women who did not consent or failed to follow up.

Bias: Efforts were made to minimize selection bias by including all eligible patients who met the inclusion criteria during the study period.

Variables: The primary variable was serum TSH levels. Other variables included age, duration of infertility, serum T3, and serum T4 levels.

Data Collection: Data were collected through patient interviews and medical records. Blood samples were taken to measure serum T3, T4, and TSH levels.

Procedure: Patients were evaluated for thyroid function through blood tests. Serum TSH levels were used to categorize patients into normal and subclinical hypothyroid groups. Data on age, duration, and type of infertility were also collected.

Statistical Analysis: Data were entered into a Microsoft Excel spreadsheet and analyzed using SPSS version 21.0. Descriptive statistics were used to summarize numerical variables as mean and standard deviation, and categorical variables as counts and percentages. Associations between

serum TSH levels and other variables were analyzed using chi-squared tests and t-tests. A p-value ≤ 0.05 was considered statistically significant.

Result

The study aimed to evaluate various parameters related to infertility, including age, duration of infertility, thyroid hormone levels (Serum T3, T4, and TSH), and the association of these parameters with thyroid function.

Descriptive Statistics (Table 1)

	Age	Durationof Infertility(Yr)	SerumT3 (pg/ml)	SerumT4 (ng/dl)	SerumTSH (mIU/L)
N	195	195	195	195	195
Missing	0	0	0	0	0
Mean	29.3	3.14	3.03	1.30	6.78
Median	28	3	2.90	1.30	5.87
StandardDeviation	5.30	1.79	0.552	0.350	3.84
Minimum	20	1	1.90	0.800	1.18
Maximum	45	9	4.20	1.97	30.8

- **Age**: The mean age of patients was 29.3 years (±5.30), indicating that most participants were in their reproductive years.
- **Duration of Infertility**: On average, patients experienced infertility for about 3.14 years (±1.79).
- **Thyroid Hormones**: The mean levels of Serum T3, T4, and TSH were 3.03 pg/ml (±0.552), 1.30 ng/dl (±0.350), and 6.78 mIU/L (±3.84), respectively. This suggests a range of thyroid function among the patients, with a considerable standard deviation in TSH, indicating variability in thyroid function.

Frequencies of Age (Table 2)

Age	Counts	%of Total	Cumulative%
20	3	1.5%	1.5%

21	5	2.6%	4.1%
22	5	2.6%	6.7%
23	14	7.2%	13.8%
24	11	5.6%	19.5%
25	10	5.1%	24.6%
26	16	8.2%	32.8%
27	15	7.7%	40.5%
28	22	11.3%	51.8%
29	10	5.1%	56.9%
30	15	7.7%	64.6%
31	5	2.6%	67.2%
32	21	10.8%	77.9%
33	5	2.6%	80.5%
34	8	4.1%	84.6%
35	5	2.6%	87.2%
36	5	2.6%	89.7%
37	1	0.5%	90.3%
38	8	4.1%	94.4%
39	1	0.5%	94.9%
40	3	1.5%	96.4%
41	1	0.5%	96.9%
42	2	1.0%	97.9%
43	2	1.0%	99.0%
45	2	1.0%	100.0%

- The age distribution revealed that the majority of patients (11.3%) were 28 years old, followed closely by those who were 32 years old (10.8%). This highlights that younger women, predominantly in their late twenties and early thirties, were more affected by infertility.

Frequencies of Age Groups (Table 3)

AgeGroupinYear	Counts	%of Total	Cumulative%

<20	3	1.5%	1.5%
21-30	123	63.1%	64.6%
31-40	62	31.8%	96.4%
41-50	7	3.6%	100.0%

- A significant portion of the participants (63.1%) fell within the 21-30 age group, underlining the age-related risks associated with infertility. The cumulative percentage indicates that over 96% of the patients were aged 40 or below.

Association of Age Group with Serum TSH (Table 4)

(Serum TSH (mlU/l) Group)

AgeGroupin Year	Normal	Sub-Clinical Hypothyroid	Total
<20	0	3	3
21-30	42	81	123
31-40	9	53	62
41-50	1	6	7
Total	52	143	195

χ^2Tests

	Value	df	p
χ^2	9.84	3	0.020
N	195		

- Statistically significant differences were observed in serum TSH levels across age groups (p=0.020). Most patients with normal TSH levels were found in the 21-30 age group, while the majority of subclinical hypothyroid cases were concentrated in the same age group, suggesting a potential link between age and thyroid function.

Frequencies of Types of Infertility (Table 5)

TypeofInfertility	Counts	%of Total	Cumulative%
PI	127	65.1%	65.1%
SI	68	34.9%	100.0%

- Primary Infertility (PI) was more prevalent (65.1%) compared to Secondary Infertility (SI) (34.9%). This is significant as it may indicate more challenges faced by patients who have never conceived.

Association of Type of Infertility with Serum TSH (Table 6)

TypeofInfertility	Normal	Sub-Clinical Hypothyroid	Total
PI	42	85	127
SI	10	58	68
Total	52	143	195

Frequencies of duration of infertility (YR)

χ^2Tests

Duration of Infertility(YR)	Counts	%of Total	Cumulative %
1	26	13.3%	13.3%
2	62	31.8%	45.1%
3	45	23.1%	68.2%
4	27	13.8%	82.1%
5	15	7.7%	89.7%
6	6	3.1%	92.8%
7	6	3.1%	95.9%
8	6	3.1%	99.0%
9	2	1.0%	100.0%

- The association between the type of infertility and serum TSH levels was significant (p=0.006). More patients with PI had subclinical hypothyroidism compared to those with SI, indicating that thyroid dysfunction may have a more substantial impact on those facing primary infertility.

- The majority of patients (31.8%) reported a duration of infertility of 2 years, while 23.1% had experienced infertility for 3 years. This data suggests that most patients sought medical assistance relatively early in their infertility journey.

Discussion

Our study provides a comprehensive analysis of subclinical hypothyroidism (SCH) in relation to infertility, contributing valuable insights into its prevalence, impact, and management. With a sample size of 195 patients, where the mean age of participants was 29.3 years, our findings reflect a notable prevalence of SCH, particularly in those with primary infertility. We offer a detailed examination of its associations with various reproductive factors. Since infertility is a common and prevalent concern in today's modern era, conclusive data can only be obtained through critical analysis and comparative studies with other trials conducted globally to better understand SCH in infertility as a whole.

Prevalence and Demographics

Our study revealed that 73.3% of infertile patients were affected by SCH, a significantly higher prevalence compared to other studies: Emokpae MA et al. (2011)[6]11.7%, Jagun OE et al. (2022)[7] 48%, Priya DM et al. (2015)[8] 53.7%, Otero P et al. (2007) [9] 13.9%, Puspagiri N et al. (2015) [10] 25%, Verma I et al. (2012) [11]23.9%, Akande AA et al. (2022) [12] 4%, and Acharya N et al. (2011) [13] 57.5%. This discrepancy may be attributed to differences in study population or diagnostic criteria. Notably, SCH was more prevalent in women aged 21-30 years, especially among those with primary infertility. This aligns with the view that younger women are often diagnosed with thyroid dysfunction, which could directly impact their fertility. The age-related variations in our study underscore the importance of early thyroid screening for women experiencing infertility, particularly in this age group. Given that SCH often manifests with few symptoms, in our study, where a TSH value above 4.6 mIU/L was used for diagnosis, around 93 subclinical hypothyroid patients had elevated serum TSH values in the range of 4-8 mIU/L.

Infertility Types and Duration

Analyzing the types of infertility, our study found a statistically significant predominance of primary infertility among SCH patients. This diverges from some studies reporting higher prevalence in secondary infertility, such as those conducted by Emokpae MA et al. (2011)[6], Akande AA et al. (2022)[12], and Jagun OE et al. (2022)[7]. This suggests that SCH may play a more substantial role in primary infertility, warranting further investigation into its specific mechanisms affecting

first-time pregnancies. The duration of infertility did not statistically correlate with SCH, indicating that the impact of SCH on infertility may be more pronounced by its presence rather than the duration of infertility.

Menstrual and Obstetric History

Our findings highlighted that menstrual irregularities were significantly more common in SCH patients, emphasizing the role of thyroid hormones in menstrual regulation. While 88 patients with SCH had regular menstruation, 55 experienced abnormalities, reinforcing the need for detailed menstrual histories in evaluating SCH. This finding is similar to studies conducted by Acharya N et al. (2011)[13] and Puspagiri N et al. (2015)[10]. However, obstetric history showed no significant correlation with SCH, suggesting that SCH's effects on infertility are more complex than merely influencing pregnancy history.

Endocrinological Association

Our findings underscore a significant association between SCH and other endocrinological disorders such as PCOS, diabetes mellitus, and hyperprolactinemia. This is consistent with literature indicating that SCH often coexists with other endocrine disorders, complicating infertility management. The higher incidence of PCOS among SCH patients in our study aligns with findings by Peddemul A et al. (2022)[14], reinforcing the need for integrated screening and treatment approaches for patients with both conditions. Increased instances of hyperprolactinemia in our study further align with findings by Puspagiri N et al. (2015)[10]and Verma I et al. (2012)[11], suggesting a simultaneous treatment approach to improve fertility outcomes.

Thyroid Autoimmunity and Infertility

Comparing our results with other studies, we observe differences in the prevalence of Anti-TPO antibodies and their impact on conception. For instance, studies by Seungdamrong A et al. (2016) [15]and Birjandi B et al. (2021)[16] highlight adverse pregnancy outcomes associated with thyroid antibodies. The lack of statistical significance for anti-TPO antibody positivity in our study contrasts with studies emphasizing its role in adverse reproductive outcomes, indicating that thyroid autoimmunity may not be a universal factor in all cases of SCH-related infertility.

Treatment and Outcomes

The efficacy of treatment for SCH in our study was evident, with 44.1% of patients conceiving within six months of treatment. This outcome was comparable to Priya DM et al. (2015)[8], reporting

around 33.3%, and Rahman AH et al. (2010)[17], reporting about 35%. However, it was lower than that observed by Verma I et al. (2012)[11], who reported a higher conception rate of 76.6%. Our findings do not align with Rao M et al. (2018)[18], which observed no significant associations of LT4 treatment with clinical pregnancy rates, live birth rates, or preterm birth rates but found a significantly decreased miscarriage rate compared to those receiving placebo or no treatment.

Additional Interventions

Given that SCH directly impacts folliculogenesis and ovulation, there was an increased requirement for additional interventions like ovulation induction or assisted reproductive technology (ART) cycles in some patients. Our study observed that 55 patients had SCH without any associated endocrinological disorders, and of these, 39 (70.9%) conceived after receiving LT4 treatment, with 10 (18.18%) requiring additional interventions like ovulation induction. This finding is comparable to a study conducted by Kim et al. (2011)[19], where treatment improved pregnancy outcomes among infertility patients with SCH. Furthermore, Yoshioka et al. (2015)[20] found that clinical pregnancies were significantly higher in treated infertile patients with SCH than those who did not receive treatment. Studies by Rahman AH et al. (2010)[17] and Maraka S et al. (2018)[21] concluded that LT4 treatment is associated with better reproductive outcomes in women with SCH undergoing ART, although this was contrary to our study, where 52.7% of patients conceived after LT4 treatment alone. This supports the effectiveness of thyroid hormone replacement therapy in treating SCH related to infertility

Conclusion

Infertility is a growing concern among women of reproductive age, with subclinical hypothyroidism (SCH) emerging as a significant yet often undiagnosed factor, especially in developing countries. Our study found a high prevalence of SCH (73.3%) among infertile women, particularly those aged 21-30 years. The study underscores the importance of thyroid function screening in infertility evaluations, as 44.1% of women treated with levothyroxine (LT4) achieved pregnancy within six months. The findings also highlight the need for personalized treatment approaches and a multifaceted strategy to manage infertility, considering the interplay between SCH and other endocrinological disorders.

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