https://doi.org/10.37939/jrmc.v28i3.2558

Connecting The Dots: The Impact Of Subclinical Hypothyroidism On Female Subfertility And Obesity

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Abstract

Objective: To find the frequency of subclinical hypothyroidism in females with subfertility
Methods: This was a descriptive cross-sectional study Department of Obstetrics and Gynecology, CMH Hospital Kharan, for 6 months (1st Jan 2023 to 30th June 2023).
A total of 159 females meeting inclusion criteria were included after taking informed consent. Females were enquired about infertility status and their thyroid status was measured in terms of thyroid stimulating hormone (TSH) and free thyroxine (FT4). Mean and Standard Deviation were used for quantitative variables whereas frequency and percentages were used for categorical variables.
Results: The mean age of females in this study was 27.86±7.58 years. The mean weight, height and BMI were 72.87 ± 13.31 kg, 1.64 ± 0.06 m, and 27.23 ± 4.90 respectively.
Fifty-three (33.33%) females were obese and 106(66.67%) females were non-obese. The mean level of TSH was found to be 2.51 ± 2.29 mIU/mL with huge variation as the minimum TSH level was 0.1 and the maximum was 7.90 mIU/mL. The mean FT4 was 1.29±0.4 ng/dl with a minimum and maximum FT4 level of 0.70 and 1.90 ng/dl respectively. There were 43 (27%) females with subclinical hypothyroidism whereas, 116 (73%) did not have subclinical hypothyroidism. There was an association between subclinical hypothyroidism and obesity, p-value < 0.05.
Conclusion: This study concludes that the prevalence of subclinical hypothyroidism was found to be greater in infertile women and hence routine screening of subclinical hypothyroidism among females with subfertility should be practiced. We also found an association of SCH with obesity in these females.
MeSH Keywords: Subfertility, hypothyroidism, infertility, TSH, pregnancy.

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Cite this Article: Ashfaq N, Hussain W, Hussain M, Saba N, Muddasir A, Liaqat J. Connecting The Dots: The Impact Of Subclinical Hypothyroidism On Female Subfertility And Obesity. JRMC. 2024 Sep. 27;28(3).455-459. https://doi.org/10.37939/jrmc.v28i3.2558.
Received January 19, 2023; accepted July 31, 2023; published online September 26, 2024

1. Introduction

Subfertility is a prevalent and critical health problem affecting around 8-10% of couples globally.[1] Subfertility has an inevitable role in the relationship of couples, not merely from a public health perspective, but it affects mental health, quality of life, societal stigma, economic distress and other marital issues as well.[2,3] According to 2023 estimates of subfertility among women published by the World Health Organization (WHO), almost 1 in 6 women have experienced subfertility with a lifetime prevalence of 17.6% and a period prevalence i.e. population with subfertility in a given period of current or past time in life, of 12.6%.[4] The prevalence of primary subfertility has been reported to be 18.3% and that of second subfertility is 2.5%.[5] Several etiological, biological, environmental and other risk factors have been reported to be responsible for female subfertility. Some of these are modifiable, and hence, identification and elimination of such factors may significantly reduce the burden of subfertility.[6]

One of the potential risk factors of female subfertility is considered to be hypothyroidism.[7] Since women have a 4 to 5 times higher prevalence of thyroid dysfunction compared to males, researchers have made their interests in its possible involvement in female subfertility.[8] The global prevalence of hypothyroidism during the average fertile age lies between 2-4%.[9,10] Any abnormality in thyroid level may have a profound effect on the estrogen levels causing several abnormalities in the menstrual cycle and fertility status of women. Some of these abnormalities include delay in the onset of periods, irregular periods, anovulatory menstrual cycle, sub-fertility, complications during pregnancy and even miscarriage.[11] Therefore, Thyroid tests are usually indicated for women with problems conceiving, especially for longer than a year, with multiple abortions, irregular periods and other such issues.[12]
Recent literature has suggested an increased frequency of subclinical hypothyroidism among infertile women.[13] Clinically Subclinical Hypothyroidism (SCH) has been defined as mildly raised levels of Thyroid Stimulating Hormones (TSH) with normal

readings of free thyroxine (fT4).[14] Several studies have reported the prevalence of subclinical TSH among infertile women and have published it between 0.7% to as much as 43%.[15, 16] Despite of alarmingly high prevalence, disparity in studies have been found. Moreover, local evidence is particularly scarce in this area. Therefore, this study was designed to find the prevalence of subclinical hypothyroidism among patients with patients with subfertility.

2. Materials & Methods

This cross-sectional study was conducted at the Department of Obs and Gynae at CMH Hospital, Kharian, for 6 months (1st Jan 2023 to 30th June 2023). The data was collected using non-probability consecutive sampling from 159 females. The sample size is calculated using the proportion of subclinical hypothyroidism in subfertility as 11.7%[17], at 5% margin of level and 95% confidence level. All females aged 18-45 years, any parity, and type of infertility were included in the study. Whilst, females on medical of thyroid disorders and females with known cardiovascular disease and diabetes mellitus were excluded. The participants were informed of the purpose of the research and were requested to sign an informed consent that ensured their anonymity and covered other ethical aspects. After taking demographic information, the information about the subfertility and the level of thyroid (TSH and FT4) were measured. Subclinical hypothyroidism was defined as if the TSH level is between 4.6–8.0 mIU/mL[17] with normal Ft4 (0.7 to 1.9 ng/dl). All data was entered in SPSS version 26, mean ± S. D was used for quantitative data, and frequency and % were used for categorical data.

3. Results

A total of 159 females were included in this study having a mean age of 27.86±7.58 years with minimum and maximum ages of 18-45 years respectively. The mean weight, height and BMI were 72.87 ± 13.31 kg, 1.64 ± 0.06 m, and 27.23 ± 4.90 respectively. (Table -1) There were 53(33.33%) females were obese and 106(66.67%) females were non-obese. (Figure-1)

The mean level of TSH was found to be 2.51 ± 2.29 mIU/mL with huge variation as the minimum TSH level was 0.1 and the maximum was 7.90 mIU/mL. The mean FT4 was 1.29±0.4 ng/dl with a minimum and maximum FT4 level of 0.70 and 1.90 ng/dl respectively. (Table 1). There were 43 (27%) females with subclinical hypothyroidism whereas, 116 (73%) did not have subclinical hypothyroidism. (Figure-2)

In the current study we found that among females with subclinical hypothyroidism, there were 32(74.4%) obese and 11(25.6%) were non-obese and in females who had no subclinical hypothyroidism, there were 21(18.1%) obese and 95(81.9%) non-obese females. There was an association between subclinical hypothyroidism and obesity, p-value < 0.05. (Table -2).

Table 1: Descriptive Analysis of Age (years), weight (kg), Height (m), BMI, TSH (mIU/mL) level and FT4 (ng/dl) level

	Mean	S.D	Range	Minimum	Maximum
Age (years)	27.86	7.58	27	18	45
Weight (kg)	72.87	13.31	53.00	47.00	100.00
Height (m)	1.64	0.06	.20	1.52	1.72
BMI	27.23	4.90	18.92	19.03	37.95
TSH	2.51	2.29	7.80	.10	7.90
FT4	1.29	0.40	1.20	.70	1.90

S.D| Standard deviation, BMI| Body mass index, TSH| Thyroid stimulating hormone, FT4| Free thyroxine

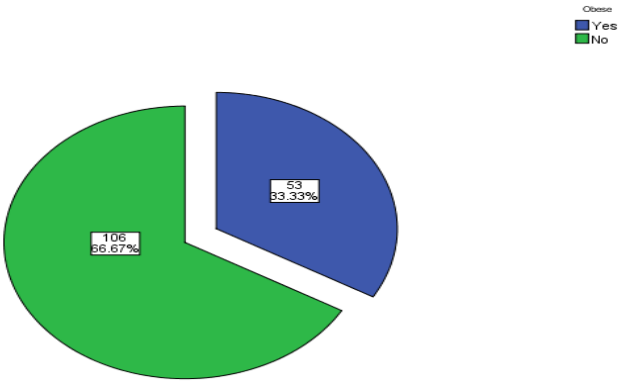

Figure 1: Distribution of obesity

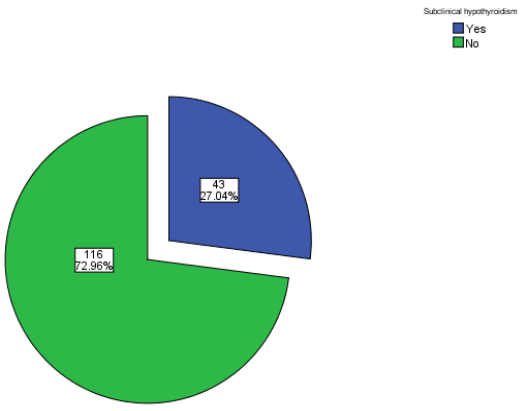

Figure 2: Status of Subclinical Hypothyroidism among Females with Subfertility

Table 2: Association of Subclinical Hypothyroidism and Obesity

		Subclinical Hypothyroidism		
		Yes	No	Total
Obese	Yes	32(74.4%)	21(18.1%)	53(33.3%)
	No	11(25.6%)	95(81.9%)	106(66.7%)
Total		43(100.0%)	116(100.0%)	159(100%)

Chi-square test = 44.77
p-value < 0.0001 (highly significant)

4. Discussion

A difficult and multifaceted challenge is presented by the interaction of subfertility and the high frequency of subclinical hypothyroidism in females who are struggling with infertility.[18] Subclinical hypothyroidism, a disease where thyroid hormone levels are somewhat low and can go unnoticed without obvious clinical symptoms,[19] can increase subfertility, which is defined by protracted periods of unsuccessful efforts at conception.[20] This interaction may result in irregular menstrual periods, ovulatory dysfunction, and poor embryo implantation by upsetting the delicate hormonal balance required for healthy reproduction.[21] In addition, untreated subclinical hypothyroidism may raise the risk of miscarriages and pregnancy problems.[22] Understanding and treating this coexisting disease is essential for maximizing reproductive results and emphasizes the value of complete, multidisciplinary care for women who are having trouble getting pregnant.[23] Despite global attention on this aspect, local literature is scarce and hence latest statistics in this area are urgently needed for future medical strategies.

This study, thus, aimed to find the prevalence of subclinical hypothyroidism among females with subfertility. The 159 female participants in this study ranged in age from 18 to 45 years, with a mean age of 27.86 ±7.58. Another study with similar objectives reported that infertile females with subclinical hypothyroidism had a mean age of 28.37±4.76 years. [8] Yet, one more study reported that the mean age of females with any type of infertility was 30±4.78 years and that TSH levels were abnormal in 22 of 255 women (9.8%). Anti-TPO antibodies were found in 44 (17.3%) of the participants, while anti-TG antibodies were found in 26 (10.2%). TSH levels were higher than 4.5 mIU/L in 70 individuals (27.5%). There was no significant difference in TSH or antithyroid antibodies between different causes of infertility. In group B, there was a positive connection between the frequency of both positive anti-TG and secondary infertility. [24]

The average TSH level in our study was determined to be 2.51 ± 2.29 mIU/mL. The minimum and maximum FT4 levels were 0.70 and 1.90, respectively, with a mean FT4 of 1.29±0.4 ng/dl. One other study found that among a total of 495 studied patients, 38.8% (192/495) had infertility. Infertile women in the study had a prevalence of Subclinical Hypothyroidism (SCH) of 11.7% (7/60). A statistically significant difference in average serum TSH levels (3.19 ± 4.38mIU / Lvs 1.60 ± 1.22 mIU /L) as well as in FT3 and the FT4 level (0.29 ± 0. 074 ng / dlvs. 0.95 ± 0 .16 ng /dl & 0.33 ± 0.071 ng /dlvs 1.09 ± 0. 19 ng /dl) was also reported.[25] Additionally, research that originally included 6426 women was changed to include 4126 women after applying exclusion criteria. From 21.09 to 11.91% and 28.57 to 10.67%, respectively, the prevalence of subclinical hypothyroidism significantly decreased with age and sampling duration (*p-value* = 0.001). The average blood levels of TSH, FT3, and FT4 decreased with age (*p-value* = 0.017, *p-value* = 0.001, and *p-value* = 0.001, respectively). TSH levels from the morning were much higher (*p-value* 0.001), even though FT4 and FT3 levels varied little across groups (*p-value* = 0.258 and *p-value* = 0.300, respectively).[26]

All these studies agree with our results and report that the risk of SCH is high among females with subfertility and hence the women visiting healthcare professionals seeking infertility treatment should be routinely screened for thyroid testing.

Females who are diagnosed with subclinical hypothyroidism have been linked or associated with obesity or weight gain,[27] and hence recently it was reported in a study that obese females should be screened for Subclinical Hypothyroidism.[28] In the current study association between subclinical hypothyroidism and obesity is established, p-value < 0.05. Hence, by targeting weight reduction, these females may be prevented from prospective complications.

5. Conclusion

This study concludes that the prevalence of subclinical hypothyroidism was found to be greater in infertile women and hence routine screening of SCH among females with subfertility should be practised. We also found an association of SCH with obesity in these females.

INSTITUTIONAL REVIEW BOARD

00291116MMANA Dated 30-11-2016

CONFLICTS OF INTEREST- None

Financial support: None to report.
Potential competing interests: None to report
Contributions:
N.A, W.H, A.M, - Conception of study
- Experimentation/Study Conduction
M.H, N.S, J.L - Analysis/Interpretation/Discussion
N.A, W.H, - Manuscript Writing
M.H, N.S, A.M, J.L - Critical Review

All authors approved the final version to be published & agreed to be accountable for all aspects of the work.

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