Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v30i17.2881

SUBCLINICAL HYPOTHYROIDISM IN INFERTILE WOMEN

Dr. Syeda Fariha Hussain[1]*, Dr. Shazia Aftab[2], Dr. Misbah Aziz[3], Dr. Zakia Bano[4], Dr. Erum Memon[5], Dr. Shagufta Naqvi[6]

[1]*Assistant Professor, Gynae and Obs department, Jinnah Medical and Dental College, Karachi
[2]Professor, Gynae and Obs department, Jinnah Medical and Dental College, Karachi
[3]Senior Registrar, Gynae and Obs department, Jinnah Medical and Dental College, Karachi
[4]Assistant Professor, Gynae and Obs department, Liaquat College of Medicine and Dentistry, Karachi
[5]Assistant Professor, Gynae and Obs department, Jinnah Medical and Dental College, Karachi
[6]Assistant Professor, Community Medicine department, Jinnah Medical and Dental College, Karachi

***Corresponding Author: -** Dr. Syeda Fariha Hussain
*Assistant Professor, Gynae and Obs department, Jinnah Medical and Dental College, Karachi,
Email: farihaikram.fh@gmail.com

ABSTRACT
Objective: To study the prevalence of subclinical hypothyroidism in infertile women.
Methodology: This cross sectional study was conducted on 151 married infertile women, attending the out-patient department of Jinnah Medical College hospital Karachi in duration of three months between March 1, 2021 and May 31, 2021.
Related history was taken; Serum TSH, T3 and T4 levels were calculated by using enzyme immune assay on ELISA reader. All information was recorded on a pre-designed data collection sheet. The normal ranges of our laboratory for TSH, T3 and T4 were taken as0.27-4.2 µIU/ml, 0.8-2 ng/dl and 4.8-12.7µg/dl respectively.
Results: The average age of the women was 29.13±6.20 years. The Prevalence of subclinical hypothyroidism in infertile women was found to be 34.81%. Higher prevalence was seen in cases with secondary infertility (59.5%) as compared to those with primary infertility (40.4%). Regarding thyroid profile, the mean serum T3 levels were found to be 1.56 ng/ml (with std of 0.870), mean T4 levels were 2.41µg/dl (with std of 1.003) and mean TSH levels were 2.89 µIU/ml (with std of 3.036). The correlation of BMI with subclinical hypothyroidism, it was seen that 74.5% of cases with subclinical hypothyroidism had BMI >25 kg/m^2.
Conclusion: - We found Sub-clinical hypothyroidism as an important cause of infertility. Women with infertility constitute a selected group of patients for whom systematic screening for thyroid disorders should be performed. When thyroid dysfunction is detected, treatment is able to restore normal fertility and reduce the likelihood of an Assisted Reproductive Technology procedure.

Key Words: Subclinical hypothyroidism, Infertility, Thyroid dysfunction

INTRODUCTION:

Infertility is the inability to conceive even after a year of unprotected intercourse. 10-15% of the couples all over the world are affected by infertility[1]. Studies have shown that 37% of infertile cases

are due to female factors[2]. Female endocrine disorders are an important cause of infertility and pregnancy related complications as they result in hypothalamic-pituitary dysfunction and thyroid disorders[3].

Thyroid hormones may have direct effects on the ovaries or indirectly interact with sex hormone binding protein and their disorders negatively affect the reproductive functions. Both hypo and hyperthyroidism can lead to menstrual irregularities, infertility and recurrent miscarriages.

Hypothyroidism leads to altered peripheral estrogen metabolism, hyperprolactinemia, and disturbances in gonadotrophin releasing hormone (GnRH) secretion that result in an abnormal pulsatile release of LH. The alterations in steroid metabolism are corrected if the euthyroid state is restored[4]. Various studies have reported the prevalence of hypothyroidism to be 2-4% [5.]

Subclinical hypothyroidism (SCH) is an elevated serum thyroid stimulating hormone (TSH) level above 4.5 mIU/l with normal serum-free thyroxine (FT4) levels. In the general population the prevalence of SH is estimated to be 4–8% and 0.9–40 % in infertile women [6.] In Subclinical hypothyroidism, there is a slightly raised thyroid stimulating hormone (TSH) signal which may represent an early or mild thyroid failure. There are differences in the prevalence of SCH depending upon age and ethnicity and it is observed to be increasing with age in addition to the presence of thyroid peroxidase antibody (TPOAb) which also increases with age[7].The adverse pregnancy and neonatal outcomes are also associated with SCH with possible risks of neurocognitive deficits in the newborn[7]. The association between subclinical hypothyroidism and infertility has been evaluated in different studies. The prevalence of subclinical hypothyroidism in Shalev et al study showed increased TSH levels in women with ovulatory dysfunction [8].

Study conducted by M. Arshad from Pakistan revealed that subclinical hypothyroidism was present in 12% of infertile women [2] while Jamila et al. conducted a study in Peshawar including 320 infertile women and found that subclinical hypothyroidism was present in 2.1% of cases [9.] Pushpagiri et al. found that SCH was present in 27.62% of primary infertile group and 14.65% among the secondary infertile group [10.]

A few studies have also found an association between SCH and unexplained infertility and according to American society of reproductive medicine it is found to be 5%[6.]

As sub clinical hypothyroidism is a treatable cause of subfertility, assessment of thyroid dysfunction should be considered as an important component in the workup of infertile women. The guideline of the American Endocrine society and American association of clinical endocrinologists and American thyroid association recommend treatment with thyroxine (T4) for patients with SCH who wants to have children. The study aims at determining the prevalence of subclinical hypothyroidism in infertile women.

Methodology:

This cross sectional study was conducted on 151 married infertile women, attending the out-patient department of Jinnah Medical College hospital Karachi in duration of three months between March 1, 2021 and May 31, 2021.

Females selected were between the ages of 18-45 years and duration of marriage was more than one year, either with primary or secondary infertility.

A detailed history of patients was recorded on a pre designed questionnaire after taking verbal consent. This included information about patient's demographic profile, height, weight, BMI, duration of infertility, type of infertility, past medical and surgical history, drug history, menstrual history, any symptoms and signs of thyroid dysfunction etc. Peripheral venous blood samples were collected aseptically with patient's consent and assayed for thyroid function tests using ELISA reader. The normal ranges of our laboratory for TSH, T3 and T4 were taken as0.27-4.2 µIU/ml, 0.8-2 ng/dl and 4.8-12.7µg/dl respectively.

Exclusion criteria: Infertile females with any congenital anomaly of the urogenital tract, any pathology in the fallopian tubes, ovary or uterus, any male infertility factor and any history of thyroid disorder, past thyroid surgery or those on thyroid medications were excluded.
Data was analyzed using SPSS 17. Mean and standard deviation was calculated for age, duration of infertility and BMI. Frequency and percentage was calculated for type of infertility and subclinical hypothyroidism. Stratification with respect to age, duration of infertility, type of infertility and BMI was done. Post stratification chi-square test was applied. The p-value of <0.05 was considered to be significant.
Ethical approval was taken from the relevant ethical review committee of Jinnah Medical and Dental College hospital Karachi prior to conducting the study (Ref#JMC.ERC.00087/21). Non probability, consecutive sampling technique was used.

Operational definition: The study population was categorized as EUTHYROID when the value of TSH was within the normal range i-e; 0.5-.7mIU/L
HYPERTHYROID: is diagnosed if serum TSH was <0.1mIU/L.
HYPOTHYROID: is diagnosed if serum TSH was >4mIU/L.
SUBCLINICAL HYPOTHYROIDISM: A condition where serum TSH is above the upper limit of normal range, despite normal level of free thyroxine (T3)

Results:
During the three months study period, a total of 151 infertile women were included in the study. All cases were within the reproductive age limit (18 to 45 years), majority of participants being in the age range of 26-35 years (51.11%) where as 31.11% participants were 18-25 years old and 17.78% were of age more than 35 years. The mean age of the participants was 29.13±6.20 years. Most of the patients belonged to low socioeconomic status with monthly income < Rs15000 (79.1%). Regarding the educational status of the patients, 34.8% of the women had received primary education, 23.7% were educated till middle class, 20.74% participants studied till secondary classes and 8.15% had received higher education. Out of the total participants 12.59% were uneducated. The socio-demographic profile of the study population is shown in table 1.

48.15% of women were with primary infertility and 51.85% had secondary infertility. Regarding thyroid profile, the mean serum T3 levels were found to be 1.56 ng/ml (with std of 0.870), mean T4 levels were 2.41µg/dl (with std of 1.003) and mean TSH levels were 2.89 µIU/ml (with std of 3.036).

In the study we found that 34.81% of all infertile women had subclinical hypothyroidism and the incidence of subclinical hypothyroidism was more in the cases with secondary infertility i.e. 59.5% as compared to those with primary infertility i.e. 40.4%

The prevalence of Subclinical hypothyroidism was significantly found to be higher in the age group of 18 to 25 years i-e 44.6%, while 12.8% of cases with subclinical hypothyroidism belonged to the age group of >35 years. In Figure 1, the correlation of subclinical hypothyroidism with age is shown.

Our study showed that 74.1% of the patients were overweight, with BMI of 25kg/m^2-29.9kg/m^2, whereas 18.5% had normal BMI 18.5 – 24.9Kg/m^2. Upon analyzing the correlation of BMI with subclinical hypothyroidism, it was seen that 74.5% of cases with subclinical hypothyroidism had BMI >25 kg/m^2 which is shown in Table 2.

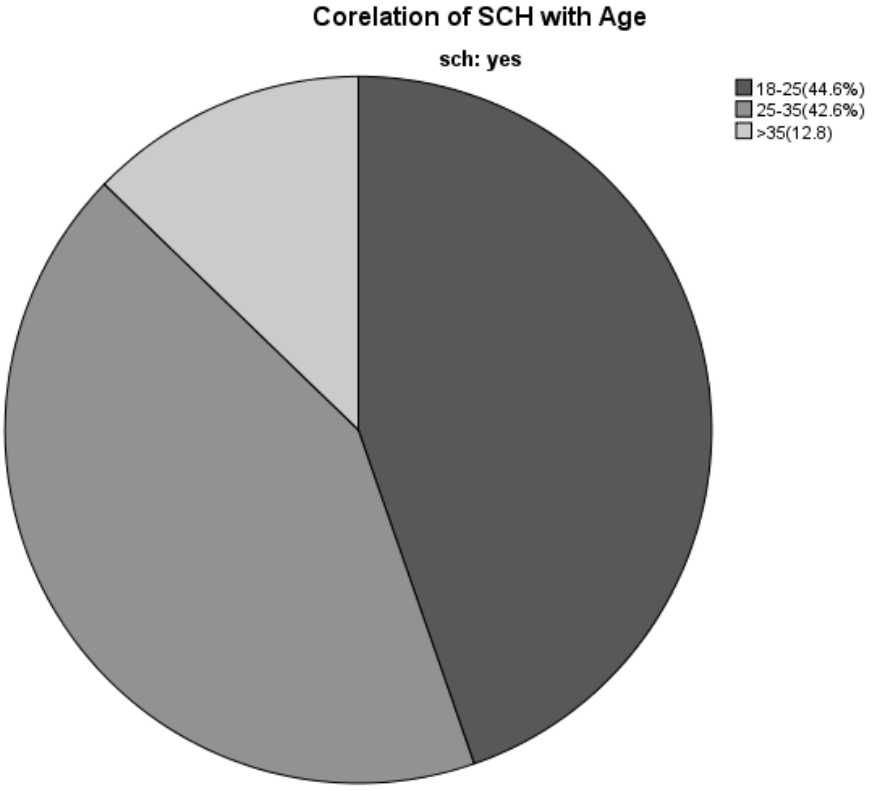
TABLE 1: Socio-demographic profile of the study population

Variables	Mean	SD	Median	IQR
Age (Years)	29.13	6.20	30	10
Weight (kg)	63.09	6.56	62	8
Height (cm)	152.81	5.77	154	7
BMI (kg/m^2)	27.05	2.94	26.67	3.7
Duration of Infertility (years)	3.84	1.134	4	2

TABLE 2: Prevalence of Subclinical Hypothyroidism in infertile Women with Respect To BMI n=151

BMI	Subclinical Hypothyroidism	
	Yes	NO
Normal ($18.5– 24.9kg/m^2$)	25.5%	14.8%
Over weight ($25-29.9\ kg/m^2$)	74.5%	73.9%
Obese ($>30\ kg/m^2$)	0%	11.4%

FIGURE 1: Correlation of SCH with Age:



Discussion:

Thyroid hormone levels and reproductive functions are closely related to each other. Reproductive and pregnancy outcomes depend upon normal thyroid hormone levels. The prevalence of hypothyroidism in women in the reproductive age varies between 4% and 8% [11.] In our study, the prevalence of subclinical hypothyroidism was found to be 34.8% while a study conducted by Raber's W which followed infertile females over a period of five years, similar results were found and 34% of infertile women had SCH[12]. On the contrary, Verma et al found different result and the prevalence of subclinical hypothyroidism in their study was 14.97%[11], whereas Rojina et al and

Bohnet et al found subclinical hypothyroidism in 3.8% and 1.8% of infertile women respectively in their studies, which is lesser as compared to our results[12, 13.]

It is notable that, in our study higher number of cases with subclinical hypothyroidism were seen in women with secondary infertility (59.9%) in comparison to those with primary infertility (40.4%).

In a cross sectional study conducted in Bangladesh by Akhter et al. obtained similar results with prevalence of sub-clinical hypothyroidism was more (15%)in secondary infertility and less (6.5%) in cases with primary infertility[14].

There were contradictory results from the study conducted by Rojina et al. where almost equal number of cases with primary and secondary infertility had subclinical hypothyroidism i-e 3.9% and 3.7 % respectively [12].

Increasing age is generally considered as a risk factor for infertility. In our study, mean age of the infertile women was found to be 29.13 years, which is similar to the mean age of infertile women in study conducted by Arjoki et al. i-e 30 years [15].

Whereas in similar studies performed by Grassi et al and Raber et al [16, 17] mean age was 32 years. In our study 87.2% of infertile women with Subclinical hypothyroidism were in the age group of less than 35 years which is similar to study conducted in India by Bhoyar et al. on 150 infertile women, where 66% of hypothyroid cases were seen in age group 25-30 years[1].

Most of the patients in our study population were overweight having BMI range of 25-30 kg/m^2 (74%) regardless of the type of infertility and presence or absence of subclinical hypothyroidism, with mean BMI of 27.04 kg/m. Similar study was done in Bangladesh with a sample size of 128 infertile females and average BMI was found to be 25.2 kg/m^2[2, 18.]

In non-pregnant females of reproductive age, the upper limit of thyroid stimulating hormone is usually 4.2 to 4.5 μIU/ml, though there is still debate among endocrinologists over the appropriate upper limit for normal levels of serum TSH [19].

In our study mean T3, T4, and TSH levels were found to be 1.56ng/ml, 2.41μg/dl and 2.91mIU/ml respectively whereas M Arshad, in his study found mean values of T3, T4 and TSH to be 1.6ng/ml, 9.7μg/dl and 1.5μIU/ml respectively which are unrelated to our study[2].

The results of our study indicate that thyroid evaluation should not be over looked in infertile women who otherwise show no symptoms of hypothyroidism and assessment of thyroid hormones should be a part of infertility work up.

Recommendations: we recommend that further studies based on a larger sample size along with treatment and long term follow up should also be planned, in which we can assess the effect of treatment in infertile patients with subclinical hypothyroidism.

CONCLUSION:

Sub-clinical hypothyroidism is a problem which is mostly overlooked and is an important cause of infertility associated with anovulation. We found Sub-clinical hypothyroidism as an important cause of infertility. Women with infertility constitute a selected group of patients for whom systematic screening for thyroid disorders should be performed in order to achieve maximum conception rate despite the fact that definitive proof of a beneficial impact of treatment remains debatable. As screening and treatment of subclinical hypothyroidism is simple and cost effective it should be done especially in women with unexplained infertility or women with unexplained anovulation in order to prevent and decrease the number of artificial reproductive techniques performed for these indications.

Limitations of study: This study is not without limitations as it is a hospital-based study so limiting the other areas of the community and may not present the actual prevalence in the community so further studies maybe needed for more elaboration.

Conflict of interest: None

Funding source: None

REFERENCES

1. B Rupeshri, R Soumya,M Srushti, K Swadha. Screening for thyroid disorders in infertile women. Int. J. Clin. Obstet.2020; 4(2): 209-212
2. A Muhammad, N Shafaq, Z Shah. Association of thyroid dysfunction with female infertility. JGDMS, 2014-15 1 (1): 3-8
3. Emokpae, MA, Osadolor HB, Omole Ohonsi. Sub-clinical hypothyroidism in infertile Nigerian women with hyperprolactinaemia. Niger J Physiol Sci. 2011; 26(1):35-38
4. Bharti G, Singh K, Kumari R et al. Prevalence of hypothyroidism in subfertile women in a tertiary care centre in North India. Int J Res Med Sci. 2017;5(5):1777-1780
5. Orazulike NC, Odum EP. Evaluation of thyroid function in infertile female patients in Port Harcourt, Nigeria. TropJObstetGynaecol 2018; 35:38-43.
6. American Society for Reproductive Medicine Subclinical hypothyroidism in the infertile female population: A guideline. Fertil. Steril. 2015;104:545–553. doi: 10.1016/j.fertnstert.2015.05.028.
7. Feldthusen AD, Pedersen PL, Larsen J, Toft Kristensen T, Ellervik C, Kvetny J. Impaired fertility associated with subclinical hypothyroidism and thyroid autoimmunity: the Danish general suburban population study. J Pregnancy. 2015;2015:132718
8. Shalev E, Eliyahu S, Ziv M, Ben-Ami M. Routine thyroid function tests in infertile women: are they necessary? Am J Obstet Gynecol. 1994;171:1191–2
9. M N Jamila, S F Syeda, N Talat, H K Ejaz. Frequency of TSH derangement in subfertility workup. J. Med. Sci.2014; 22(4):182-184
10. Pushpagiri N et al. Int J Reprod Contracept Obstet Gynecol. 2015 Dec;4(6):1733-1738
11. Verma I, Sood R, Juneja S, KaurInt S. Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility. Int J Appl Basic Med Res. 2012 Jan-Jun:2(1):179
12. M Rojina, L M Bekha, S Jyoti. Thyroid profile in infertile. Nepal Med J 2018;01(01):5-10
13. Bohnet HG, Fiedler K, Leidenberger FA. Subclinical hypothyroidism and infertility. The Lancet. 1981;5:1278
14. N Akhter, S Hassan. Sub-clinical hypothyroidism and hyperprolactinemia in infertile women: Bangladesh perspective after universal salt iodination. Internet J EndocrinoL. 2008;5(1): 1-6.
15. Arojoki M, Jokimaa V, Juuti A. Hypothyroidism among infertile women in Finland. GynecolEndocrinol. 2000;14:127– 31.
16. Grassi G, Balsamo A, Ansaldi C. Thyroid autoimmunity and infertility. Gynecol Endocrinol. 2001;15: 389–96.
17. Raber W, Nowotny P, Vytiska-Binstorfer E, Vierhapper H. Thyroxine treatment modified in infertile women according to thyroxine-releasing hormone testing: 5 year follow-up of 283 women referred after exclusion of absolute causes of infertility. Hum Reprod. 2003 Apr;18(4):707-14
18. A Jesmin , A Shahanaz, K H Mohammad .Thyroid Status of Hypothyroid Infertile Women: A Study in a Tertiary Care Hospital of Bangladesh Saudi J Med Pharm Sci, Nov, 2020; 6(11):704-707
19. B. Shamima, B Rokeya, SA Qazi. Hypothyroidism and hyperprolactinemia in women with primary and secondary infertility. IMC J Med Sci 2020; 14(1): 009.