Research Article

Correlation of Hypothyroidism with Age and Comorbidities Among Women: A Cross-Sectional Study

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Abstract

Background: Hypothyroidism, an endocrine disorder caused by thyroid dysfunction found to be more prevalent globally in females than in males. Young females are more prone to subclinical hypothyroidism (SCH). The study aimed to estimate the different types of hypothyroidism based on the clinical profile of thyroid hormone and to detect various comorbidities in correlation with age in women. In female patients with hypothyroidism, there is a significant association between age groups and the type of hypothyroidism (subclinical, clinical, overt), with younger age groups showing a higher prevalence of SCH. Additionally, comorbidities, such as polycystic ovarian disorder (PCOD), are more prevalent in hypothyroidism patients, particularly in those with SCH.

Materials and Methods: A prospective cross-sectional study executed in a tertiary care hospital for one year with an inclusion of female hypothyroid patients above 18 years of age. An informed written consent form was received from each patient with clarification of the protocol.

Results: A total of 44.6% women were in the 18–28 years of age group (young females) and 42.8% of women with SCH. PCOD (38.2%) was a predominant comorbid condition among hypothyroidism women. In the age group of 18–28 years, there were significantly more patients 114 (81.4%) with SCH ($p < 0.01$) than those with clinical 22 (18.4%) and overt hypothyroidism 10 (14.7%). The hypothyroidism of women with PCOD 95 (67.8%) was significantly ($p < 0.01$) more in subclinical than clinical 28 (23.5%) and overt hypothyroidism 2 (2.9%).

Conclusion: Thyroid dysfunction is uncertain in females, bulges to complications of maternal and fetal outcomes, and is associated with other comorbidities, leading to an increase in the mortality rate. Hypothyroidism is a growing burden for other comorbidities. Pharmaceutical care by healthcare professionals is to be adopted with prompt diagnostic and screening techniques.

Keywords

Hypothyroidism, correlation, PCOD, thyroid dysfunction, diagnosis, treatment

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Introduction

Thyroid hormones (THs) are essential for growth, differentiation, and metabolism.[1] The self-regulatory system known as the hypothalamic-pituitary-thyroid axis controls TH production. It involves thyrotropin-releasing hormone (TRH) from the hypothalamus, thyroid-stimulating hormone (TSH) from the anterior pituitary gland, and the thyroid hormones thyroxine (T4) and triiodothyronine (T3). This system maintains feedback mechanisms and ensures homeostasis. Hypothyroidism, caused by an underactive thyroid gland, typically presents with symptoms such as bradycardia, cold intolerance, constipation, fatigue, and weight gain.[2] Hypothyroidism appears to be correlated with insulin resistance and other metabolic factors.[3]

A gender-based chronic inflammation of the thyroid, such as hypothyroidism or Hashimoto's thyroiditis (HT), is

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perceived with serum biomarkers and autoimmune biomarkers.[4] Hypothyroidism is more prevalent in Indian females with 1 in 10 adults, whereas thyroid dysfunction is joint in one in every eight young women with abnormal mild elevation of TSH.[5] In the determination of TH and TSH concentration, genetics is an essential factor.[6]

Based on the clinical level of TSH, hypothyroidism is classified as subclinical, clinical, and overt. Moreover, the occurrence of subclinical hypothyroidism (SCH) counts to be higher than overt hypothyroidism.[7] Around 6%–8% of women are exposed to SCH and 2%–3% of women are affected by clinical hypothyroidism (CH) in childbearing age. Annually, the risk of progression from subclinical to CH accounts for approximately 4%.[8] Comorbidity is defined as "any marked auxiliary subsistence that has existed or may occur during the disease evolution of a patient which is the marker of the disease under study." Another definition indicates that additional medical treatment to the patient's condition is a principle, or is the basis of, or is otherwise related to, another medical treatment for additional disease in the same individual patient.[9]

SCH is defined as mild thyroid failure with slight elevation in the TSH concentration to the normal range (0.4 to 4.0 mIU/L) and with serum-free thyroxine (fT4) with its benchmark value (0.9 to 2.3 ng/dL). CH or overt hypothyroidism is defined as a serum TSH concentration wide-ranging above the normal range with serum fT4 concentration and below the range of normal. Overt hypothyroidism is an elevated TSH concentration present at the same time as a low serum fT4 concentration affecting up to 1%–2% in the reproductive age.[10] Inadequate thyroid levels can lead to various complications, including defects in the fetus during birth, infertility in women, menstrual disturbances, and neurological deficits in offspring.[11] Additionally, autoimmune hypothyroid patients often exhibit a significant imbalance in the ratio of Th1–Th2 types of cells, with an exaggerated secretion of interferon gamma (IFN-γ). The discrepancy in interleukin-17 (IL-17) levels among pregnant women is identified as a prognostic risk factor for the progression of SCH. These factors underscore the critical importance of thyroid function in reproductive health and fetal development[12,13]

In most women of reproductive age, the more prevalent endocrine problems are polycystic ovary syndrome, which coexists with metabolic abnormalities. Women censor their problem of irregular menstruation and its causative reasons until they are marked out for infertility. According to the researchers, about 5%–10% of the Indian young women population are affected by polycystic ovary syndrome (PCOS), and in the Western population, 4%–8% of young women are afflicted.[14,15]

Overweight hypothyroid women have an augmented risk for health problems such as metabolic syndrome, atherosclerosis, hyperglycemia (diabetes mellitus), hyperlipidemia, and uterine and cervical cancer. Factors that ascertain the inability of the monotherapy of levothyroxine in the patients have to achieve the desired therapeutic results of the treatment.[16] Rheumatoid arthritis in hypothyroid women compromise a tributary risk factor for congestive heart failure.[17,18] Owing to the coexistence of many other disorders with hypothyroidism, which is evident from all international and national literature, clinical manifestations of the disease are to be managed with appropriate rational hormonal therapy, which can accelerate to average quality of life.[19]

Materials and Methods

It is a prospective observational study, and it was conducted from October 2021 to September 2022 in a tertiary care hospital in South India.

Inclusion Criteria

Female patients aged above 18–60 years.

Exclusion Criteria

Women of age below 18 years, and those who were on medications that are capable of interceding the TH, patients with hyperthyroidism, and those with congenital abnormalities were excluded from the study. The protocol for the study was reviewed and approved by our Institutional Human Research Ethical Committee of Karpagam Faculty of Medical Sciences and Research (IHEC/222/10/2021). An informed written consent was retrieved from all patients with clarification of the study protocol.

Study Procedure

A prospective cross-sectional study was conducted at a tertiary care hospital over one year to investigate hypothyroidism in females aged 18 years and above. The study aimed to assess the prevalence of different types of hypothyroidism based on clinical profiles of THs and to identify associated comorbidities in correlation with age. Female patients diagnosed with hypothyroidism were included in the study. The institutional ethics committee approved the study protocol. Participants were required to be above 18 years of age. Informed written consent was obtained from each participant after providing detailed explanations of the study protocol.

Data collection involved obtaining demographic information, clinical history, and laboratory results from the participants. Clinical profiles of TH levels were analyzed to categorize participants into SCH, CH, and overt hypothyroidism groups as per the American Thyroid Association guidelines.

Statistical Analysis

Statistical analysis was performed to examine the distribution of hypothyroidism types across different age groups. The prevalence of comorbid conditions, particularly polycystic ovarian disorder (PCOD), was determined and compared among hypothyroidism subtypes and age groups. Statistical significance was assessed using appropriate tests, with a p value of less than 0.05 considered statistically significant.

Results

A total of 327 hypothyroidism women were included in this study. Patients' clinical and demographic details are shown in Table 1. In the age-wise distribution, a total of 44.6% were in the 18–28 years of age group (young females) and 42.8% of women with SCH. PCOD (38.2%) was a predominant comorbid condition among hypothyroidism women, followed by arthritis (29.7%), dyslipidemia (20.5%), and hypertension (16.2%). In the duration of hypothyroidism, >2 years (60.6%) was more than ≤ 2 years (39.4%).

Table 1. Evaluation of Age, Clinical Profile, Types, and Comorbidities in Female Hypothyroid Patients.

Sl. No.	Parameters	Number of Patients (*n*) (%)
1	Age (in years)	
	18–28	146 (44.6)
	29–38	52 (16)
	39–48	46 (14.1)
	49–58	47 (14.3)
	>58	36 (11)
2	Types of hypothyroidism	
	Subclinical	140 (42.8)
	Clinical	119 (36.4)
	Overt	68 (20.8)
3	Comorbidities	
	Anemia	11 (3.4)
	Arthritis	97 (29.7)
	Asthma	05 (1.5)
	Diabetes	43 (13.1)
	Dyslipidemia	67 (20.5)
	Hypertension	53 (16.2)
	Myocardial infarction	25 (7.6)
	PCOD	125 (38.2)
	No comorbidities	15 (4.6)
4	Duration of hypothyroidism	
	<2 years	129 (39.4)
	>2 years	198 (60.6)
5	Clinical variables.	(mean ± SD)
	Sub clinical hypothyroidism	
	TSH (mean ± SD)	4.56 ± 0.424
	T3 (mean ± SD)	144.28 ± 35.24
	T4 (mean ± SD)	10.6 ± 0.577
	Clinical hypothyroidism	
	TSH (mean ± SD)	7.43 ± 1.20
	T3 (mean ± SD)	60.32 ± 9.84
	T4 (mean ± SD)	3.18 ± 0.826
	Overt hypothyroidism	
	TSH (mean ± SD)	12.4 ± 1.65
	T3 (mean ± SD)	34.82 ± 5.04
	T4 (mean ± SD)	2.14 ± 0.547

The correlation of age with hypothyroidism has been shown in Table 2. In the age group of 18–28 years, there were statistically more patients 114 (81.4%) with SCH ($p < 0.01$) than those with clinical 22 (18.4%) and overt hypothyroidism 10 (14.7%). There was no significant difference ($p > 0.05$) in the number of patients among subclinical, clinical, and overt hypothyroidism in the 29–38 years of age group. In the 39–48 years of age group, there were significantly more patients with CH (28, 23.5%) than subclinical (04, 2.8%), and overt hypothyroidism (14, 20.6%). In the 49–58 years of age group, the number of patients was significantly more ($p < 0.01$) in CH 31 (26%) than subclinical 02 (1.4%) and overt hypothyroidism 14 (20.6%). In the >58 years of age group, the number of patients was significantly more ($p < 0.01$) in overt hypothyroidism (18, 26.5%) than subclinical (3, 2.1%) and CH (15, 12.6%). SCH was common in young females (18–28 years), CH was common in the females of 29–38, 39–48, and 49–58 years of age groups (middle-aged women), and overt hypothyroidism was common in women > 58 years of age (older women).

Table 3 shows the correlation of comorbid conditions with hypothyroidism. There were 125 hypothyroidism patients with PCOD, 97 patients with rheumatoid arthritis, 5 patients with asthma, 43 patients with diabetes, 67 patients with hypertension, 25 patients with myocardial infarction, and 11 patients with no comorbid conditions.

The hypothyroidism of women with PCOD (95, 67.8%) was significantly ($p < 0.01$) more in subclinical than in clinical (28, 23.5%) and overt (2, 2.9%). Arthritis was statistically ($p < 0.01$) more in overt 2(29, 42.6%) than in

Table 2. Evaluation of Correlation of Age with the Level of Dysfunction of Thyroid Hormone in the Study Population.

	Types of Hypothyroidism			
Age groups	**Subclinical (*n* = 140)**	**Clinical (*n* = 119)**	**Overt (*n* = 68)**	***p* Value**
18–28	114 (81.4%)	22 (18.4%)	10 (14.7%)	0.0001
29–38	17 (12.1%)	23 (19.3%)	12 (17.6%)	0.0724
39–48	04 (2.8%)	28 (23.5%)	14 (20.6%)	0.0001
49–58	02 (1.4%)	31 (26%)	14 (20.6%)	0.0001
>58	03 (2.1%)	15 (12.6%)	18 (26.5%)	0.0003

Table 3. Assessment of Comorbidities in Various Types of Hypothyroidism in Female Patients.

Comorbidities	**Subclinical (*n* = 140)**	**Clinical (*n* = 119)**	**Overt (*n* = 68)**	***p* Value**
PCOD	95 (67.8%)	28 (23.5%)	2 (2.9%)	0.0001
Arthritis	43 (30.7%)	25 (21%)	29 (42.6%)	0.0195
Dyslipidemia	16 (11.4%)	26 (21.8%)	25 (36.7%)	0.1303
Hypertension	10 (7.1%)	17 (14.2%)	26 (38.2%)	0.0458
Anemia	8 (5.7%)	2 (1.6 %)	1 (1.4%)	0.0028
Myocardial infarction	2 (1.4%)	10 (8.4%)	13 (19.1%)	0.0029
Diabetes	1 (0.7%)	19 (15.9%)	23 (33.8%)	0.0001
Asthma	1 (0.7%)	2 (1.8%)	2 (2.9%)	0.7408
No comorbidities	13 (9.3%)	1 (0.8 %)	1 (1.4%)	0.0001

clinical (25, 21%) and SCH (43, 30.7%). Hypertension was significantly more ($p < 0.01$) in overt 26(38.2%) than in subclinical (10, 7.1%) and CH (17, 14.2%). Anemia was significantly more ($p < 0.01$) in subclinical (8, 5.7%) than in overt (1, 1.4%) and CH (17, 14.2%). Myocardial infarction and diabetes were significantly ($p < 0.01$) more 13 (19.1%), 23 (33.8%) in overt than in clinical (10, 8.4%), (19, 15.9%) and SCH (2, 1.4%), (1, 0.7%). Patients with arthritis, dyslipidemia, hypertension, myocardial infarction, and diabetes had more overt hypothyroidism than those with subclinical and CH. However, patients with PCOD had more SCH than those with clinical and overt hypothyroidism.

Discussion

The biochemical connection between thyroid disease and irregularities in the ovarian cycle and ovulation is still mostly unknown. Women with hypothyroidism have lower rates of androstenedione and estrone metabolic clearance, which is accompanied by an increase in peripheral aromatization.[20] Women who have hypothyroidism also often have reproductive disorders such as infertility, low birth weight, and congenital anomalies in preterm infants, anovulation, ovarian cysts, irregular menstruation, and estrogen levels, delayed puberty, and irregular menstruation.[21]

Patients of age 36–45 years accounted for the greatest number of cases, with a distinct female predominance. It was discovered that the illness was prevalent in other age groups as well. In all cases, 40.5% were found to be in the 16–35 years of age group, indicating that hypothyroidism can be seen in younger people.[22] While women are more likely to have chronic autoimmune thyroiditis and to have greater amounts of estrogen than males, they also have a higher prevalence of SCH. The thyroid-pituitary axis is altered during pregnancy caused by an increase in metabolic needs.[23]

In addition to these negative cardiac end goals, SCH may also be linked to lower bone mineral density, fractures, neuropsychiatric symptoms, atrial fibrillation, cardiac dysfunction, and mortality from systemic and circulatory diseases.[24] According to numerous research, high BMI and high blood pressure are linked to SCH, as are heart illness, elevated low-density lipoprotein cholesterol, depression, and cognitive dysfunction in female participants.[25] In our study, SCH was significantly more common in women with PCOS than in previous studies, and it was widespread with SCH. Deficits in THs can result in decreased glucose synthesis and utilization since they can also function as antagonists in the liver and as agonists of insulin in muscle. The resulting hypothyroidism leads to insulin resistance, which has been identified as the primary cause in the pathophysiology of PCOS.[26]

The complex relationship between these two disorders appears to be mediated by obesity, enhanced insulin resistance, elevated leptin, and signs of disturbed autoimmunity, all of which are present in both disease states.[27] The thyroid is a key player in the etiology, growth, and progression of PCOS and diseases associated with PCOS in reproduction. The thyroid's

function in PCOS is multifaceted and intricate.[28] The possible mechanism of the link between thyroid disease and PCOS is a genetic predisposition to the onset of both disorders; however, a shared genetic profile has not yet been identified.[29]

In this study, 27.9% of hypothyroidism women had arthritis. Hypothyroidism risk was found to be significantly higher in individuals with RA, and hypothyroidism risk may also be higher in patients with concomitant cardiovascular illnesses.[30] Despite the exact causes of thyroid dysfunction in patients with RA are unknown, genetic, environmental, and other factors have a major role. Additionally, there is still overlap in the genes responsible for the pathogenesis of these two diseases.[31,32] Since RA treatment may make thyroid dysfunction worse, it is critical to evaluate thyroid function in patients with RA. When used in high doses, the RA medication glucocorticoids, which lower inflammation, can directly suppress TSH secretion without raising FT3 or FT4.[33] Study showed that 145 (44.1%) of hypothyroidism women affected with dyslipidemia or hypertension or myocardial infarction. In this clinical and overt hypothyroidism, patients were significantly related to hypertension and dyslipidemia compared to subclinical hyperthyroidism. Clinically, cardiac conditions such as dyslipidemia, atherosclerotic vascular disease, atrial and ventricular arrhythmias, and heart failure can be spurred on by overproduction or underproduction of TH, resulting in the risk of morbidity and death from cardiovascular diseases earlier than expected.[34]

In individuals with both overt and SCH, prior research has documented cardiovascular disorders, including left ventricular dysfunction and decreased vascular relaxation. Raised intima-media thickness, bradycardia, endothelial dysfunction, diastolic dysfunction, elevated vascular resistance, and pericardial effusion are among the conditions that can arise from insufficient serum TH.[35]

Reduced arterial compliance, elevated systemic vascular resistance, decreased cardiac output, and atherosclerosis are all possible outcomes of hypothyroidism.[36] THs regulate the mitochondrial activity of the heart. Thyroid axis dysfunction affects the bioenergetic state of the heart. Overt and SCH have been associated with an increased risk of progression of heart failure and an increased incidence of coronary events.[37] According to experimental research, anomalies in diastolic and systolic function, heart shape, gene expression, and histology are caused by impaired thyroid metabolism, causing aberrant post-ischemic remodeling.[38]

In this study, diabetes mellitus was more in overt, CH than SCH, and overall, 13% of patients with DM with hypothyroidism. Individuals with type 2 diabetes mellitus seemed to have a significantly greater prevalence of thyroid disorders. Diabetic patients with longstanding hyperlipidemia, obesity, and anemia are at higher risk of having underlying hypothyroidism.[39] In fact, thyroid dysfunction may have an impact on the development of diabetes mellitus while TH has the ability to regulate the carbohydrate metabolism.[40] Diabetes is associated with thyroid dysfunction, whereas thyroid abnormalities can aggravate type 2 diabetes. Thyroid disorders and type 2 diabetes have been linked to insulin resistance.[41]

While metabolic diseases, including diabetes, hypertension, dyslipidemia, and obesity, may act as confounders between the mediator and the outcome that is impacted by exposure, our results consistently show that the likelihood of bias resulting from a breach of this assumption is unlikely.[42,43] To overcome these limitations and reproduce and validate our findings, more research utilizing larger sample sizes, additional outcome events, and longitudinal measurements of TSH levels and age or comorbid conditions is needed.

Conclusion

In young women, SCH was found to be more prevalent and hypothyroidism materializes to other co-morbidities. There is a strong association between hypothyroidism with polycystic ovarian syndrome and rheumatoid arthritis. Screening of thyroid functions is to be adopted frequently in all women to avoid complicated states. Proper management and, follow-up rely on the challenges of pharmaceutical care by healthcare professionals.

Summary

A one-year prospective observational study was conducted in a tertiary care hospital in South India, aiming to investigate hypothyroidism in females aged 18 years and above. A total of 327 hypothyroid women were included.

The study found that SCH was more prevalent in young females (18–28 years), CH in middle-aged women (29–58 years), and overt hypothyroidism in older women (>58 years). PCOD was the predominant comorbidity among hypothyroid women, followed by arthritis, dyslipidemia, and hypertension.

The study highlights the complex relationship between hypothyroidism and comorbid conditions such as PCOD, arthritis, dyslipidemia, hypertension, myocardial infarction, and diabetes. Further research with larger sample sizes is needed to validate these findings and assess the longitudinal impact of thyroid dysfunction and comorbid conditions.

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Ethical Approval

The protocol for the study was reviewed and approved by our Institutional Human Research Ethical Committee of Karpagam Faculty of Medical Sciences and Research (IHEC/222/10/2021).

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Informed Consent

An informed written consent was retrieved from all patients with clarification of the study protocol.

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