International Clinical and Medical Case Reports Journal
Research Article (ISSN: 2832-5788)

Prevalence and Association of Primary Hypothyroidism with Metabolic Syndrome: A 1- Year Cross-Sectional Study

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Citation: *Ganavi Y P, Naveen S Angadi. Prevalence and Association of Primary Hypothyroidism with Metabolic Syndrome: A 1- Year Cross-Sectional Study Int Clinc Med Case Rep Jour.2023;2(17):1-9.*

Received Date: 07 November, 2023**; Accepted Date:** 14 November, 2023**; Published Date:** 16 November, 2023

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ABSTRACT

Background: Hypothyroidism and metabolic syndrome are associated with an abnormal lipid profile and impaired cardiac and endocrine functions. The coexistence of these two conditions may have a higher clinical impact on cardiovascular morbidity and mortality.

Aim: To study the prevalence and association of primary hypothyroidism in patients with metabolic syndrome.

Materials and Methods: This cross-sectional study was conducted from January 2013 to December 2013 in 117 patients with metabolic syndrome. Patients fulfilling the inclusion criteria were enrolled through simple random sampling and divided into euthyroid and hypothyroid groups based on thyroid profile. Patients were investigated for thyroid and lipid profiles, blood pressure, and glycemic levels. Data were analyzed using SPSS 20 and compared using the Chi-square test, and the p-value of p</=0.05 was considered statistically significant.

Results: Out of 117 patients, 29 (24.79%) showed hypothyroidism, of which 21 (72.41%) were women. Overt hypothyroidism was observed in 11 (37.93%) patients and subclinical hypothyroidism was observed in 18 (62.07%) patients. Systolic and diastolic blood pressure was higher in hypothyroid patients compared to euthyroid patients. Fasting blood glucose levels >/=100 mg/dL and cholesterol levels>/=200 mg/dL were higher in the hypothyroid group. A significant association was observed between hypothyroidism and gender (p = 0.005).

Conclusion: An abnormal increase in lipid and glycemic levels and blood pressure was observed in hypothyroid patients with metabolic syndrome. No significant association was found between hypothyroidism and components of metabolic syndrome.

Keywords: Hypothyroidism; Metabolic syndrome; Dyslipidemia; Hypertension and Dysglycemia

INTRODUCTION

Metabolic syndrome (MetS) includes a set of cardiovascular risk factors, including diabetes and prediabetes, abdominal obesity and cholesterol levels, and high blood pressure. Co-occurrence of these cardiometabolic abnormalities increases the risk of morbidity and mortality. Genetic and ethnic variability imparts a significant role in underlying causes of metabolic syndrome, even though insulin resistance and central obesity have a predominant role. Aging, physical inactivity, proinflammatory conditions, and changes in hormone levels also contribute to MetS. In the Indian urban population, the reported prevalence of MetS is more than 30% [1,2].

Hypothyroidism is associated with atherogenic cardiovascular diseases. Deficiency in thyroid function leads to increased peripheral arteriolar resistance, cardiac load, diastolic blood pressure, and myocardial contractility. An abnormal lipid profile and an increase in epicardial adipose tissue are observed in hypothyroidism. Inflammatory modifications and impaired endothelial function can lead to atherosclerosis and coronary artery diseases [3,4].

As hypothyroidism and MetS take part in abnormal lipid profiles and cardio endocrine functions, their coexistence may have a higher clinical impact. Therefore, the present study focuses on the prevalence of primary hypothyroidism in patients having MetS. This will help to estimate the overlap of hypothyroidism, MetS, and associated complications. Moreover, it also establishes the importance of thyroid function tests in detecting hypothyroid patients from MetS. This enables proper planning and adequate management strategies, which may significantly reduce cardiovascular morbidity and mortality.

MATERIALS & METHODS

This 1-year cross-sectional study was conducted at the Department of Medicine, Tertiary care hospital, Belgaum, from January 2013 to December 2013. Patients were recruited based on the three or more components of National Cholesterol Education Program-Adult Treatment Panel III criteria for metabolic syndrome: Abdominal obesity (waist circumference >102 cm in men, >88 cm in women), triglycerides levels ≥ 150 mg/dL, high-density lipoprotein (HDL) cholesterol level < 40 mg/dL in men, < 50 mg/dL in women, fasting blood glucose (FBS) level ≥ 110 mg/dL, systolic blood pressure ≥130 mmHg and diastolic blood pressure ≥85 mmHg. Patients were enrolled through a simple random sampling method.

Patients with liver and renal disorders, congestive cardiac failure, hypothyroidism, and under treatment for any thyroid-related disorders or statins were excluded from the study. Pregnant women and women on oral contraceptives were also excluded from the study. Ethical approval was obtained from the Institutional Ethics Committee. Patients were briefed about the nature of the study, and written informed consent was obtained before conducting the study.

STATEMENT OF HUMAN RIGHTS

This study has complied with all relevant international and national regulations and institutional policies and has been carried out after obtaining the ethics committee approval from JNMC Institutional Ethics Committee for Human Subjects Research with the Ref: MDC/DOME/894

DATA COLLECTION

Demographic details, including family and personal history of diabetes, hypertension, and dyslipidemia, were collected. Blood pressure was recorded to the nearest 2mmHg by a mercury sphygmomanometer with the arm supported at heart level after sitting quietly for 5 min. Systolic and diastolic blood pressure was obtained with an average of ≥2 measurements obtained on ≥2 occasions. Fasting blood sugar (FBS) by Hexokinase, HbA1c by High-Performance Liquid Chromatography (HPLC), triglycerides, total cholesterol, HDL, and low-density lipoprotein (LDL) were measured by colorimetric method.

The thyroid profile was assessed by withdrawing venous blood under aseptic precautions, and estimation of thyroid-stimulating hormone (TSH) and fT4 (free thyroxine) was done using a fully automated electrochemiluminescence immunoassay analyzer (Roche Cobas E 601from Roche Hitachi). Patients were divided into hypothyroid and euthyroid groups based on thyroid profile. Patients with TSH levels>/= 4.25 µIU/mL and fT4 levels of 0.7 to 1.24 ng/dL or < 0.7 ng/dL were considered hypothyroid groups. Overt hypothyroidism was defined as TSH >/= 4.25 µIU/mL and fT4</=0.7 ng/dL. Subclinical hypothyroidism was defined as TSH >/=4.25 µIU/mL and fT4 between 0.7 to 1.24 ng/dL. Patients with TSH level 0.34-4.25 µIU/mL, fT4 level 0.7-1.24 ng/dL, and free triiodothyronine level 2.4-4.2 pg/mL were considered under the euthyroid group.

Waist circumference was measured using a standard measuring tape which was stretch resistant in centimeters (cm) in the horizontal plane of the superior border of the iliac crest to the nearest 0.1 cm at the end of a normal expiration asper the NCEP ATP III guidelines and as a waist circumference of >102 cm in men and >88 cm in women were considered abnormal. Body height was recorded to the nearest 0.5 cm and body weight to the nearest 0.1 kg. Body mass index (BMI) in the <18.5 kg/m2 range was considered underweight, and 18.5-24.9 kg/m2 was evaluated as normal. Range of 25.0-29.9 kg/m2 and >30 kg/m2 were considered overweight and obese, respectively, as per the WHO definition. SPSS 20 was used to analyze the data. Data were compared using the Chi-square test. Continuous data were expressed as mean ± standard deviation (SD) and compared using an independent t-test. The association of hypothyroidism with various parameters was analyzed by the Chi-square test and Fisher's exact test. $p<0.05$ was considered statistically significant.

RESULTS

Out of 117 patients with MetS, 49.57% were men, and 50.43% were women. Most patients were 51-60 years (28.21%), followed by 41-50 years (27.35%). Table *1* represents the patients' demographic, laboratory, and clinical characteristics.

According to NCEP-ATP III criteria of metabolic syndrome, 71.79% of patients had a minimum of three components of metabolic syndrome. In the total study population, 63.25% had a history of diabetes mellitus in which, a majority (40.54%) had diabetes for ≤3 Years. Also, 76.07% of patients had a history of hypertension, of which 43.82% had hypertension for ≤3 Years. Results also showed that 65.81% of the patients had a history of dyslipidemia. The mean BMI of patients was 27.20 ± 4.22 Kg/m2. 37.61% of patients were overweight, and 22.22% were obese; however, normal waist circumference was observed in most (61.54%) of the patients. The mean waist circumference was 90.78 ± 9.74 cm.

Results showed that 28.21% of patients had >200 mg/dL of total cholesterol. The mean total cholesterol level was 172.7 ± 53.3 mg/dL. A total of 48.72% of patients had abnormal LDL cholesterol levels, and the mean LDL level was 107.2 ±48.8 mg/dL. Abnormally low HDL levels were observed in 86.32% of patients, and the mean HDL level was 34.71 ± 10.16 mg/dL. Triglyceride levels were abnormally high in 52.14% of patients, and the mean triglyceride level was 144.7 ± 65.09 mg/dL.

A total of 24.79% of patients had hypothyroidism with abnormally high TSH levels, of which 72.41% were women. In the hypothyroid group, the distribution of overt hypothyroidism and subclinical hypothyroidism was observed as 37.93% and 62.07%, respectively.

The comparison between euthyroid and hypothyroid groups in various clinical parameters is shown in Table 2. Systolic and diastolic blood pressure were slightly higher in the hypothyroid group. The majority of patients (65.52 %) had blood pressure >130/85 mmHg in the hypothyroid group. Lipid profiles were abnormally higher in the hypothyroid group but were not statistically significant ($p \geq 0.29$). Also, 31.03% of patients in the hypothyroid group showed total cholesterol levels >200 mg/dL compared to the euthyroid group (27.27%). The mean FBS level was more (124.80±28.95 mg/dL) in the euthyroid group compared to the hypothyroid group (119.59±26.55 mg/dL). However, there was a high prevalence of patients with FBS levels >100 mg/dL in the hypothyroid group (82.76%).

The association of hypothyroidism with various parameters is shown in Table 3. A significant association was observed between hypothyroidism and gender ($p = 0.005$). The association of hypothyroidism with metabolic syndrome components, age, waist circumference, hypertension, diabetes mellitus, lipid profile, and BMI were statistically insignificant.

Table 1: Demographic, laboratory, and clinical characteristics of the patients

Characteristics	Frequency, n (%)
Men	58 (49.57)
Women	59 (50.43)
History of diabetes	74 (63.25)
History of hypertension	89 (76.07)
History of dyslipidemia	77 (65.81)
Alcohol consumption	33 (28.21)
Smoking	34 (29.06)
Abnormal waist circumference	45 (38.46)
Body Mass Index	
18.5–22.99	20 (17.09)
23.00–24.99	27 (23.08)
25.00–29.99	44 (37.61)
30 or more	26 (22.22)
Components of metabolic syndrome	
Three	84 (71.79)
Four	32 (27.35)
Five	1 (0.85)
Lipid profile	
Total cholesterol > 200 mg/dL	33 (28.21)
Low density lipoprotein > 100 mg/dL	57 (48.72)
High density lipoprotein (men: ≤ 40 mg/dL; women: ≤50 mg/dL)	101 (86.32)
Triglycerides > 150 mg/dL	61 (52.14)
Blood sugar level	
Fasting blood sugar>100 mg/dL	94 (80.34)

Table 2: Comparison between euthyroid and hypothyroid group in various clinical parameters

Parameters	Euthyroid (n = 88)	Hypothyroid (n = 29)	P-value
Age	53.10±13.68	49.66±12.78	0.2216
Blood pressure (mmHg)			
Systolic	136.10±17.25	139.17±18.42	0.57
Diastolic	85.93±9.76	87.17±8.97	0.53
Blood pressure >130/85 Prevalence (%)	57.95	65.52	0.47
Lipid profile (mg/dL)			
Total cholesterol	169.70±53.84	181.66±51.51	0.30
Triglycerides	141.25±67.10	155.07±58.41	0.29
Low density lipoprotein	104.95±49.22	114.10±48.10	0.38
Low density lipoprotein	34.18±10.56	36.31±8.77	0.29
Total Cholesterol > 200 Prevalence (%)	27.27	31.03	0.69
Thyroid profile			
Serum thyroid stimulating hormone (µIU/mL)	1.94±1.04	17.77±37.33	0.03
Free thyroxine (pg/mL)	1.25±0.26	0.88±0.32	<0.0001
Diabetic profile			
Fasting blood sugar (mg/dL)	124.80±28.95	119.59±26.55	0.37
Glycated Haemoglobin(HbA1c) (%)	8.91±1.67	8.18±1.42	0.07
Fasting blood sugar >100 mg/dL Prevalence (%)	79.55	82.76	0.70
Glycated Haemoglobin(HbA1c)> 6.5 Prevalence (%)	100	100	1.00

Table 3: Association of hypothyroidism with various clinical parameters

Parameters	Hypothyroidism		P-value
	Present, n (%)	Absent, n (%)	
Metabolic syndrome components			
Three	20 (23.81)	64 (76.19)	0.316
Four	8 (25)	24 (75)	
Five	1 (100)	0 (0)	
Gender			
Men	8 (13.56)	51 (86.44)	0.005*
Women	21 (36.21)	37 (63.79)	
Age group			
≤30	3 (50)	3 (50)	0.216
31–40	3 (17.65)	14 (82.35)	
41–50	11 (34.38)	21 (65.63)	
51–60	5 (15.15)	28 (84.85)	
>60	7 (24.14)	22 (75.86)	
Waist circumference			
Normal	18 (25)	54 (75)	0.946
Abnormal	11 (24.44)	34 (75.56)	
Hypertension			
Present	26 (25.74)	75 (74.26)	0.401
Absent	3 (18.75)	13 (81.25)	
Diabetes mellitus			
Present	20 (25.97)	57 (74.03)	0.680
Absent	9 (22.50)	31 (77.50)	
High-density lipoprotein level			
Normal	3 (18.75)	13 (81.25)	0.401
Abnormal	26 (25.74)	75 (74.26)	
Triglyceride level			
Normal	15 (26.79)	41 (73.21)	0.631
Abnormal	14 (22.95)	47 (77.05)	
Body mass index (Kg/m^2)			
18.5–22.99	3 (15)	17 (85)	0.292
23.00–24.99	9 (33.33)	18 (66.67)	
25.00–29.99	13 (29.55)	31 (70.45)	
≥30	4 (15.38)	22 (84.62)	

*-statistically significant

DISCUSSION

The study included 117 patients with MetS to analyze the prevalence of hypothyroidism. Of (24.79%) of hypothyroid patients, 29 were diagnosed with subclinical hypothyroidism, with a high majority of women. An epidemiological study conducted in eight cities of India by Unnikrishnan et al. and a prevalence study conducted in the south Indian population by Velayutham et al. also found a similar prevalence of hypothyroidism in women [5,6]. Similar observations were made by various studies conducted worldwide [7-9]. Therefore, it may be beneficial to screen women with MetS for hypothyroidism. The majority of the patients were in the age-group of 41-60 years. Similar kind of prevalence was observed in various studies and few showed an association with advanced age and MetS [1,10-13]. According to NCEP ATP III criteria, most of the patients (71.79%) had three components of metabolic syndrome. Hypothyroidism was the most prevalent irrespective of metabolic syndrome components. A significant percentage of study population had the history of hypertension, diabetes,

and hyperlipidemia. High incidence of family history of diabetes and hypertension was observed in results. A study conducted by Das et al. observed a significant effect of diabetes in patients with MetS. This association may help in the early diagnosis and prevention of metabolic syndrome in Asian Indians [14]. Also, Yadav et al. observed a significant increase in dyslipidemia and hypertension in type II diabetes patients with MetS [15].

Abnormally low HDL levels were observed in 86.32% of patients, which was similar to the results observed in other studies [16-19]. Recent transitions in nutrition and lifestyle along with physical inactivity may be a core contributing factor for the increased prevalence of metabolic abnormalities. This emphasises the importance of lifestyle modifications in the management of metabolic syndrome. In this study, a statistically significant association of hypothyroidism with metabolic syndrome components, age, waist circumference, hypertension, diabetes mellitus, lipid profile and BMI could not be established; however, other studies have well correlated these parameters with hypothyroidism [20-24].

Comparison between euthyroid and hypothyroid group in various clinical parameters such as systolic and diastolic blood pressure, lipid profile, and blood sugar levels did not show statistical significance (P=<0.57, <0.38, 0.37 and 0.07 respectively). Systolic and diastolic blood pressure was increased in hypothyroid group. This may be due to increase in peripheral vascular resistance and decrease in cardiac output linked to hypothyroidism. Enhanced norepinephrine release in hypothyroid patients also contributes to increase in blood pressure. Chaker et al. estimated that patients with low thyroid function have 1.4 times higher risk of developing type 2 diabetes [25]. A high prevalence of patients in hypothyroid group with FBS>100 mg/dL and HbA1c> 6.5 % indicates that hypothyroidism may potentiate the risk for diabetes.

Even though thyroid hormones affect thermogenesis and body energy expenditure and may potentially lead to obesity and associated increased waist circumference, the study could not establish a significant difference in obesity and waist circumference between hypothyroid and euthyroid group. Results showed increased levels of total cholesterol, triglycerides, and LDL in hypothyroid patients compared to euthyroid. Reduced function of hydroxy methylglutaryl coenzyme A reductase, decreased catabolism of LDL, and decreased clearance of triglycerides-rich lipoproteins are linked to hypothyroidism [22]. The cardio thyroid disease prevalence study conducted by Canaris et al. concluded that high TSH levels linked to changes in lipid levels and can affect cardiovascular health [23].

The present study has certain limitations, as it was cross-sectional in design. A causal relationship between low-normal thyroid function and MetS cannot be ascertained. Also, the sample size was relatively small, which restricted from subgroup analysis. Further studies with large sample size and specific cluster of MetS components such as systemic inflammatory markers and insulin resistance would further focus the epidemiology of hypothyroid patients with MetS. A cut-off of 88 and 102 cm for abdominal obesity was taken as a component of metabolic syndrome definition. For Asians, a lower

cut-off 80 and 90 cm, respectively have been proposed. This is a limitation of the paper because the study population was possibly underrepresented by the use of higher cut-offs which apply for the Western population. The selection bias of tertiary care centre which is more likely to enroll patients with severe metabolic syndrome is another limitation.

CLINICAL PEARLS

The prevalence rates vary greatly depending upon the definition of MetS, ethnicity, age, population, etc. Recently, a rapid increase in its prevalence has been noted in India due to socioeconomic transitions to increasing affluence, urbanization, mechanization, and urban migration. About one-third of the urban population in large Indian cities has MetS with the overall prevalence varying between 11% and 56%. Several studies have shown a correlation between thyroid function and the indices of MetS. Our study assessed the prevalence of hypothyroidism in South Indian patients with MetS.

CONCLUSIONS

We observed a high prevalence of primary hypothyroidism in patients with MetS. An abnormal increase in lipid levels, glycaemic levels, and blood pressure was observed in hypothyroid patients with MetS. The association of hypothyroidism and MetS might result in a compounded cardiovascular risk, which needs to be addressed by prompt evaluation and management in order to reduce the cardiovascular risk in these patients.

LIMITATIONS

The present study has certain limitations, as it was cross-sectional in design.

REFERENCES

1. Gupta R, Deedwania PC, Gupta A, Rastogi S, Panwar RB, Kothari K. Prevalence of metabolic syndrome in an Indian urban population. Int J Cardiol. 2004;97(2): 257-261.
2. De Flines J, Scheen AJ. Management of metabolic syndrome and associated cardiovascular risk factors. Acta. gastro-enterologica. Belgica. 2010;73(2):261-266.
3. Klein I, Danzi S. Thyroid disease and the heart. Circulation. 2007;116(15):1725-1735.
4. Cerit ET, Akturk M. Atherosclerotic and metabolic effects of hypothyroidism due to chronic thyroiditis. Medical. Science and Discovery. 2016;3(5):213-218.
5. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. Indian J Endocrinol Metab. 2013;17(4): 647-652.
6. Velayutham K, Selvan SS, Unnikrishnan AG. Prevalence of thyroid dysfunction among young females in a South Indian population. Indian J Endocrinol Metab. 2015;19(6):781-784.
7. Bjoro T, Holmen J, Kruger O, et al. Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population. The Health Study of Nord-Trondelag (HUNT). Eur J Endocrinol. 2000;143(5):639-647.

8. Leese G, Flynn R, Jung R, Macdonald T, Murphy M, Morris A. Increasing prevalence and incidence of thyroid disease in Tayside, Scotland: The Thyroid Epidemiology Audit and Research Study (TEARS). Clin Endocrinol. 2008;68(2):311-316.
9. Agarwal G, Sudhakar M, Singh M, Senthil N, Rajendran. The prevalence of thyroid dysfunction among south Indian women with metabolic syndrome. J Clin Diagn Res. 2011;5: 213-216.
10. Park E, Kim J. Gender- and age-specific prevalence of metabolic syndrome among Korean adults: analysis of the fifth Korean National Health and Nutrition Examination Survey. J Cardiovasc Nurs. 2015;30(3):256-266.
11. Kuk JL, Ardern CI. Age and sex differences in the clustering of metabolic syndrome factors: association with mortality risk. Diabetes. care. 2010;33(11): 2457-2461.
12. Moreira GC, Cipullo JP, Ciorlia LAS, Cesarino CB, Vilela-Martin JF. Prevalence of metabolic syndrome: association with risk factors and cardiovascular complications in an urban population. PLoS One. 2014;9(9):105056.
13. Sawant A, Mankeshwar R, Shah S, et al. Prevalence of metabolic syndrome in urban India. Cholesterol. 2011;20:11-12.
14. Das M, Pal S, Ghosh A. Family history of type 2 diabetes and prevalence of metabolic syndrome in adult Asian Indians. J Cardiovasc Dis Res. 2012;3:104-108.
15. Yadav D, Mishra M, Tiwari A, Bisen PS, Goswamy HM, Prasad G. Prevalence of dyslipidemia and hypertension in Indian type 2 diabetic patients with metabolic syndrome and its clinical significance. Osong. Public. Health Res Perspect 2014;5(3):169-175.
16. Mahalle N, Garg M, Naik SS, Kulkarni MV. Study of pattern of dyslipidemia and its correlation with cardiovascular risk factors in patients with proven coronary artery disease. Indian J Endocrinol Metab. 2014;18(1):48-49.
17. Mohan V, Deepa R, Rani SS, Premalatha G. Prevalence of coronary artery disease and its relationship to lipids in a selected population in South India: The Chennai Urban Population Study (CUPS No. 5 2001;38(3):682-687.
18. Guptha S, Gupta R, Deedwania P, et al. Cholesterol lipoproteins and prevalence of dyslipidemias in urban Asian Indians: a cross sectional study. Indian Heart J. 2014;66(3):280-288.
19. Joshi SR, Anjana RM, Deepa M, et al. Prevalence of dyslipidemia in urban and rural India: The ICMR-INDIAB study. PLoS One. 2014;9(5):96808.
20. Liu D, Jiang F, Shan Z, et al. A cross-sectional survey of relationship between serum TSH level and blood pressure. J Hum Hypertens. 2010;24(2):134-138.
21. Saito I, Ito K, Saruta T. Hypothyroidism as a cause of hypertension. Hypertension. 1983;5(1): 112-115.
22. Rizos C, Elisaf M, Liberopoulos E. Effects of thyroid dysfunction on lipid profile. Open. Cardiovasc. Med J. 2011;5:76-84.
23. Canaris GJ, Manowitz NR, Mayor G, Ridgway E. The colorado thyroid disease prevalence study. Arch Intern Med. 2000;160(4):526-534.

24. Shantha GP, Kumar AA, Jeyachandran V, et al. Association between primary hypothyroidism and metabolic syndrome and the role of C reactive protein: a cross-sectional study from South India. Thyroid research. 2009;2: 2-3.
25. Chaker L, Ligthart S, Korevaar TI, et al. Thyroid function and risk of type 2 diabetes: a population-based prospective cohort study. BMC Medicine. 2016;14:150-151.