PREVALENCE OF METABOLIC SYNDROME IN PATIENTS WITH SUBCLINICAL AND OVERT HYPOTHYROIDISM VISITING TERTIARY CARE CENTRE OF WESTERN NEPAL

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ABSTRACT

INTRODUCTION

Hypothyroidism is a syndrome resulting from thyroid hormone deficiency. Metabolic syndrome (MetS) is a cluster of metabolic abnormalities is associated with increased risk for atherosclerotic cardiovascular disease (CVS) and type 2 diabetes mellitus. Thyroid hormones are major regulatory hormones that control the rate of metabolic function; thus, alteration in the levels of these hormones may be associated with MetS. The objective of our study was to find out the prevalence of MetS in subclinical and overt hypothyroidism.

MATERIAL AND METHODS

A hospital-based cross sectional study was conducted at Universal College of Medical Sciences Teaching Hospital (UCMS-TH) Bhairahawa from March to September 2019. A total of 222 hypothyroid patients were enrolled in this study. MetS was diagnosed by National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III; 2005) revision criteria. The anthropometric indices were recorded. fT_3, fT_4 and TSH were measured by chemiluminescence immunoassay (CLIA) method and other biochemical parameters were estimated by colorimetric method. Data were analyzed by using SPSS 16.0.

RESULTS

Patients were aged between 10 and 60 years, with a mean age of 38.89 years. The prevalence of MetS was 44.1% of which 80.6% were females. Furthermore, the prevalence of MetS was found to be 43.7% in subclinical hypothyroidism and 46.6% in overt hypothyroidism.

CONCLUSION

The prevalence of MetS is high in both overt and subclinical hypothyroidism. Screening for MetS in patients with hypothyroidism can reduce the risk for CVD, as well as the mortality rate and mortality associated with it.

KEY WORDS Metabolic Syndrome, Subclinical hypothyroidism, Overt hypothyroidism

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INTRODUCTION

Hypothyroidism is a syndrome resulting from thyroid hormone deficiency or rarely inefficacy. It is a common endocrinological problem affecting primarily the women and the elderly. Overt hypothyroidism is a condition characterized by high TSH and low fT_4 and is closely related to the dyslipidemic condition and coronary artery disease.[1] Subclinical hypothyroidism is defined as elevated TSH with fT_4 concentrations at the lower end of the euthyroid range. Subclinical hypothyroidism is associated with more severe coronary and carotid artery disease.[2]

MetS is a cluster of conditions defined by diagnostic criteria that are slightly different according to several health organization definitions. Central obesity, atherogenic dyslipidemia, impaired glucose tolerance, hyperglycemia, hypertension, prothrombotic and proinflammatory conditions represent main characteristics of MetS.[3]

Thyroid hormones play an essenital role in synthesis, metabolism and mobilization of lipids. Association between hypothyroidism and MetS has become a popular topic of discussion in recent years. Studies have demonstrated that thyroid dysfunction is related to an increased prevalence of MetS.[4] In this study, we aimed to investigate the prevalence of MetS in patients with subclinical and overt hypothyroidism.

MATERIAL AND METHODS

This study was designed as a cross sectional study conducted from March 2019 to September 2019 for a period of 6 months in the Department of Biochemistry and General Medicine at Universal College of Medical Sciences Teaching Hospital (UCMS-TH), Bhairahawa, Nepal. The ethical approval of the study was obtained from the "Institutional Research Committee" of UCMS-TH, Bhairahawa (UCMS/IRC /03019). A total of 222 patients of both sex, aged between 10 years to 60 years and diagnosed as having subclinical and overt hypothyroidism, were selected as the study population. Pregnant women, critically ill patients and individuals less than ten years age and above 60 years were excluded for this study.

A semi-structured proforma was designed for the collection of socio-demographic variables and clinical evaluation. Blood samples were collected from patients diagnosed as hypothyroidism under aseptic conditions. The serum was separated and all the biochemical parameters were measured on the same day of the collection. Serum fT_3 fT_4 and TSH levels were measured by chemiluminescence assay (CLIA, Snibe Maglumi-2000 model), lipid profile and fasting blood glucose levels were estimated by the colorimetric method. Quality control was performed with appropriate standards before analyzing the patient's samples.

Reference range for T_3 is 2.0 - 4.2 pg/ml, for T_4 is 8.9 - 17.2 pg/ml and TSH is 0.3- 4.5 µIU/ml. Overt hypothyroidism was identified as low T_3 level (< 2.0 pg/ml), low T4 level (<normal T_3 level (2.0 4.2 pg/ml) and normal T_4 level (8.9 - 17.2 pg/ml).

All the data from cases were entered into MS Excel (Microsoft office 2007) and analyzed by Statistical Package for Social Sciences (SPSS) for window version 16, (SPSS v.16). An independent sample t - test was used to compare the mean of numerical variables between Subclinical and Overt hypothyroidism groups. A Chi-square analysis was applied to find out the association between categorical variables. Pearson correlation analysis was used to see the correlation between numerical variables. P -value < 0.05 was considered to be statistically significant.

RESULTS

Out of 222 hypothyroid patients, 43 (19.27%) were males and 179 (80.27%) were females. Among male patients, 44.18% (19) had MetS. Similarly, MetS was present in 44.13% (79) female. There was no significant association between MetS and sex (p = 0.99).

Hypothyroidism was most common in the patients of age group 31-40 years (32.4%) and least common among the age group 10-20 years (5.4%). The association of metabolic syndrome with various age groups was statistically significant (p < 0.001). [Table 1]

Table 1. Distribution of patients according to age group

Age group (years)	Metabolic Syndrome group		Total (%)	p-value
	Non MetS	MetS		
10-20	10	02	12 (5.4%)	< 0.001
21-30	36	10	46 (20.7%)	
31-40	44	28	72 (32.4%)	
41-50	23	31	54 (24.3%)	
51-60	11	27	38 (17.2%)	
Total	124	98	222	

Among the total hypothyroid cases, 44.14% (98) had MetS. Association between MetS and hypothyroid status was not statistically significant (p = 0.76). [Table 2]

Table 2. MetS in subclinical and primary hypothyroidism

	Non MetS	MetS	Total	p-value
Subclinical	108	84	192	0.765
Primary	16	14	30	
Total	124	98	222	

Only 25% (25) of the newly diagnosed hypothyroid cases had MetS whereas more than half (59.8%) of the previously

diagnosed hypothyroid cases were associated with MetS ($p < 0.001$).

Table 3. MetS in newly diagnosed and follow up hypothyroid patients

Hypothyroidism Duration	Metabolic Syndrome group		Total	p-value
	Non MetS	MetS		
Newly Diagnosed	75	25	100	<0.001
Previously Diagnosed	49	73	122	
Total	124	98	222	

Comparison of various biochemical parameters including components of MetS between subclinical and overt hypothyroidism groups revealed that fT_3 and fT_4 were significantly higher in the subclinical group ($p < 0.001$) while TSH and FBS were significantly lower in the patients with subclinical hypothyroidism than overt hypothyroidism (p 0.006). The details are presented in Table 4.

Table 4. Comparison of various biochemical parameters in subclinical and overt hypothyroidism group

	Subclinical Hypothyroidism (Mean ± SD)	Overt hypothyroidism (Mean ± SD)	p-value
fT_3(pg/ml)	3.072 ± 0.563	1.574 ± 0.345	<0.001
fT_4(ng/ml)	12.994 ± 1.890	6.214 ± 2.259	< 0.001
TSH (µIU/ml)	10.634 ± 10.756	60.552 ± 35.683	< 0.001
FBS (mg/dl)	98.55 ± 13.831	107.33 ± 26.444	0.006
TC (mg/dl)	179.81 ± 79.682	192.03 ± 52.82	0.164
TG (mg/dl)	178.21 ± 79.682	197.03 ± 96.864	0.245
HDL_C(mg/dl)	35.34 ± 8.703	35.73 ± 9.843	0.823
LDL_C(mg/dl)	179.00 ± 41.546	188.36 ± 50.277	0.293
VLDL (mg/dl)	35.64 ± 15.936	39.41 ± 19.373	0.245
SBP (mmHg)	126.51 ± 18.414	126.67 ± 22.18	0.967
DBP (mmHg)	82.92 ± 11.013	84.33 ± 12.229	0.519
Age (yr)	38.55 ± 11.323	41.07 ± 13.146	0.269
Waist(cm)	87.857 ± 12.563	86.40 ± 10.695	0.559

Pearson's correlation analysis was performed to see the association of fT_3 with various components of MetS (TG, TC, HDL, LDLc, VLDLc, FBS, WC, BMI, SBP and DBP). Most of the components of MetS showed negative correlation except for HDL (r= 0.132, p= <0.05), FBS (r= -0.175, p= <0.05) and DBP (r= 0.761, p = <0.001).

Table 5. Correlation between fT3, fT4, TSH and components of MetS

		TG	HDL	TC	LDL	VLDL	FBS	SBP	DBP	Waist
fT_3	r	-0.101	0.132	-0.121	-0.060	-0.101	-0.175	-0.096	0.761	-0.052
	p	0.132	0.049	0.072	0.373	0.132	0.009	0.155	<0.001	0.441
fT_4	r	-0.113	0.062	-0.069	-0.016	-0.113	-0.124	-0.032	-0.045	-0.018
	p	0.090	0.357	0.307	0.818	0.092	0.066	0.633	0.500	0.794
TSH	r	0.032	-0.024	0.129	0.118	0.032	0.021	-0.088	-0.058	0.079
	p	0.640	0.723	0.055	0.080	0.640	0.750	0.192	0.389	0.241

DISCUSSION

The action of thyroid hormones is widespread, ranging to almost all nucleated cells, and is important for normal growth and energy metabolism. Alteration in their levels, either reduced or increased, is devastating, especially during pregnancy and childhood.[5] Hypothyroidism is caused by decreased production of thyroid hormones causing subnormal concentration of circulating thyroid hormones.[6] These may be overt, central (secondary) or extra thyroidal.[5] In overt hypothyroidism, there is a clear reduction in circulating thyroid hormones below the reference range, while subclinical hypothyroidism is a condition in which circulating TSH level elevates with normal fT_4 concentration.[7] Hypothyroidism is extremely common worldwide with great variations in global prevalence, especially depending on whether the region is iodine sufficient or not. The prevalence of overt hypothyroidism ranges from 0.2%- 5.3% in Europe and between 0.3% and 3.7% in the USA. The neighboring nations, China and India, also present with a remarkably high prevalence of hypothyroidism, both overt and subclinical. The national prevalence data from Nepal is missing, although the studies in various regions indicate that the situation is equally alarming.[8,9]

MetS constitutes a cluster of risk factors characterized by hypertension, atherogenic dyslipidemia, hyperglycemia, prothrombotic and proinflammatory conditions.[10] The prevalence of MetS is increasing all over the world with distinct evidence of high prevalence in India and other South Asian Countries.[11] The concept of MetS has also been used for the co-management of multiple CVD risk factors, including DM, HTN, and dyslipidemia.[12] Hypothyroidism and MetS are recognized risk factors for atherosclerotic CVD. Environmental and genetic factors also affect MetS.[13] The aim of our study was to know the prevalence of MetS in patients with hypothyroidism and to analyze the association between hypothyroidism and components of MetS.

In this cross sectional study, out of total 222 patients with hypothyroidism, prevalence of MetS using the NCEP/ATP III

guidelines was found to be 44.14%, in which 43.7% had subclinical hypothyroidism and 46.6% patients had overt hypothyroidism. Ogberaet et al[14] reported that about one-fourth of their subjects from Nigeria with thyroid disorder had MetS and the frequency of MetS in subjects with hypothyroidism was 40%. In contrast, a high prevalence of MetS i.e. 82.5% was reported in a study done by Haque R et al,[15] which also reported similar frequency of MetS in both subclinical hypothyroidism (81.2%) and overt hypo-thyroidism (83.8%).

Ogbera et al[14] reported that female hypothyroid patients were at more risk of developing MetS than males, which is contrary to the finding by Yu RM et al,[16] where the prevalence of MetS was 55.1% in males and 43.8% in females. Interestingly, in our study, both male and female hypothyroid percent had almost equal proportion (approximately 44.1%) of MetS prevalence. MetS incidence increases with age as the prevalence of obesity, HTN, dyslipidemia and hyperglycemia also increases with age.[17] Illane-Parikka P et al[18] reported that the prevalence of MetS increases with age in both sexes. Our finding is also in accordance with this study, where prevalence of MetS increased with advancing age ($p < 0.001$). Haque R et al[15] found that serum TG levels were significantly raised in hypothyroid patients than the euthyroid group. Waterhouse et al[19] noted that when TSH was within the normal reference range, TG increased by 0.115 mg/dl with every 1mIU/L increase in TSH. In our study, too, the mean TG level was greater than the reference range in both sub clinical and overt hypothyroid group, the difference between the groups being not significant ($p = 0.24$). The correlation studies showed negative correlations between TG and fT_3, as well as fT_4 and positive correlation between TG and TSH levels. However, none of these were statistically significant.

The mean difference in waist circumference (WC) between overt and subclinical hypothyroid groups in our study was only 1.45 cm ($p = 0.56$) and wasn't significantly correlated with TFT components. However, Park SB et al noted a significant negative association between WC and TSH as well as WC and serum fT_4. This was also true for association between BMI and serum fT_4 as well as TSH.[20] Thyroid hormones play an important role in glucose metabolism. FBS being one of the core components of MetS, we evaluated serum FBS levels in both hypothyroid groups. Serum FBS was significantly higher ($p=0.006$) in overt hypothyroid groups, and correlated negatively with fT_3 ($p = 0.009$, $r = -0.175$) and fT_4 ($p=0.066$, $r = -0.124$) levels and positively with TSH levels ($p=0.75$, $r = 0.021$). Erodgan M et al[21] in their study, however, did not find a significant difference in FPG between the two groups, as well as when compared with euthyroid groups.

Thyroid hormones also influences LDLc by various mechanism including catabolism of LDL_C alteration, stimulation of synthesis of cholesterol as well as the influence on biliary lipid metabolism.[14] Reports often show hypercholesterolemia, elevated LDL_C levels and low to normal HDL_C.[14, 22] A study by Kota SK et al investigated that, none of the components in MetS group were significantly different from that of control group.[23] Findings from the research by Garduno-Garcia et al. indicated that only TC was significantly higher in the SCH group when compared to the euthyroid group.[24] In our study, we compared to the elements of the lipid profile test between SCH and overt hypothyroidism group, where no significant difference was found. However, serum fT_3 showed positive correlation ($p=0.049$, $r=0.13$) with serum HDL levels.

Hypertension is another important component of MetS. We compared both SBP and DBP between overt and SCH groups and found no significant differences in the mean values between groups. SBP correlated negatively with serum fT_3 levels. while DBP correlated positively. However, only the association with DBP was to a the statistically significant degree ($p<0.001$). Saito I et al. conducted a comparative study of blood pressures among euthyroid and hypothyroid groups, in which DBP was correlated significantly with the serum levels of thyroid hormones**.** The mean difference between euthyroid and hypothyroid population was also significant with DBP, but not with SBP.[25] Similar findings were reported by Ogbera AO et al[14] in their publication.The prevalence of MetS in hypothyroid patients was high in our study, more so in the SCH group as than overt hypothyroid population. Various components of MetS were compared between the two groups, of which the mean difference in FBS was statistically significant. Correlation studies showed a significant association of fT_3 with FBS (negative) and DBP (positive). Similar conclusions were drawn from other studies as well, albeit the components of MetS and TFT that had significant results were not always the same.[14,20]

CONCLUSION

Our study showed a high prevalence of MetS in patients with overt and subclinical hypothyroidism. Hypothyroidism and MetS are the recognized risk factors for CVD. Screening for MetS in patients with hypothyroidism can reduce the risk for CVD as well as can reduce the mortality rate due to its complications.

The results of this study recommend:

1. All the patients with hypothyroidism, whether subclinical or overt must be screened for MetS.
2. Early screening of MetS in those patients can reduce the risk and morbidity related to CVD.

3. More similar studies should be carried out to examine the relation between fT_3, fT_4, and TSH with components of MetS.

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CONFLICTS OF INTERESTS

The author declare that there is no conflict of interest.

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