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Research Article

METABOLIC SYNDROME AND RISK OF CARDIOVASCULAR DISEASE WITH THYROID DISORDER

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ABSTRACT

Objectives: Metabolic syndrome (MetS) is the most widely used term for the aggregation of metabolic abnormalities, which leads to an increase in the risk of developing cardiovascular pathology. The prevalence of MetS is increasing all over the world with distinct evidence of high prevalence in India and other South Asian countries. Thyroid dysfunction, prominently subclinical hypothyroidism, has been observed more frequently in patients of MetS than in the general population.

Methods: This cross-sectional, observational study was conducted among MetS patients in the general population and near and dear of patients (350) at the Pacific Institute of Medical Sciences, Udaipur. For the determination of gastric peptidases (ghrelin and obestatin), insulin was done by enzyme-linked immunosorbent assay. Thyroid hormones are determined by chemiluminescence.

Results: The key findings in this analysis are the significant negative correlation between insulin and ghrelin. This inverse relationship was observed in individuals without cardiovascular disease (CVD), suggesting that even in the absence of overt CVD, insulin may play a role in regulating ghrelin levels. This finding is particularly noteworthy given ghrelin's role in appetite regulation and energy balance.

Conclusion: The findings emphasize the need for a holistic approach to health assessment and management, considering individual factors such as age, sex, and the presence of underlying health conditions along with thyroid disorders.

Keywords: Insulin, Ghrelin, Obestatin, Thyroid, Metabolic syndrome.

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INTRODUCTION

The metabolic abnormalities that condense into metabolic syndrome (MetS) include insulin resistance, glucose intolerance, central obesity, dyslipidemia, and an increased blood pressure, all of which are well-documented risk factors for cardiovascular mortality [1]. There has been a striking increase in the incidence of MetS in the past two decades. This increase can be amounted to the global epidemic of diabetes and obesity. The number of people suffering from diabetes mellitus was recorded as 592 million patients worldwide and is expected to rise to 592 million by the year 2035. The implications of diabetes are not limited to metabolic and cardiovascular morbidity but also have a significant impact on the financial and mental well-being of the patients [2]. In India, a total of 25.2 million people are recorded to be suffering from diabetes, making India the second runner in the world with the most cases to diabetes. Projections of prevalence assume that the cases will rise up to 35.7 million people in the coming 20 years. Furthermore, it is also a major concern that about 57% of people still remain undiagnosed [3].

One of the estimations shows that around 20–25% of the world's population is suffering from MetS [4]. These people are 2 times more at risk to face fatal consequences and 3 times more at risk to suffer from a heart attack or stroke. The risk of developing MetS increases with age, about 19.5% of cases of MetS were found to be aged between 20 and 39 years as opposed to 48.6% of people aged 60 years or older [5].

The treatment course for positive patient outcomes of MetS is the early diagnosis by the physicians. There are many diagnosing criteria, which are being revised frequently, that help in the management of MetS.

MetS constitutes a cluster of risk factors characterized by hypertension, atherogenic dyslipidemia, hyperglycemia, prothrombotic, and proinflammatory conditions [6]. This cluster of metabolic abnormalities is associated with an increased risk for atherosclerotic cardiovascular disease (CVD) and type 2 diabetes mellitus [7]. The prevalence of MetS is increasing all over the world with distinct evidence of high prevalence in India and other South Asian countries [8]. Various studies have shown that 30% of Indian population suffers from MetS and it was also found that this disease is more prevalent in Indian females (36%) as compared to Indian men (22%) [9]. Thyroid dysfunction, prominently subclinical hypothyroidism has been observed more frequently in patients of MetS than in the general population [8].

Both MetS and hypothyroidism are considered to be independent risk factors for the development CVDs. The presence of both conditions may be compounded to an increase toward the risk for CVD and there is also a considerable overlap that occurs in the pathogenic mechanisms of atherosclerotic CVD by MetS and hypothyroidism.

This study aims to analyze the association of MetS with thyroid dysfunction for assessing the impact of these diseases on the development of CVDs.

METHODS

This cross-sectional, observational study was conducted among MetS patients in the general population and near and dear of patients at the Pacific Institute of Medical Sciences, Udaipur, after obtaining ethical clearance. Three hundred and fifty MetS and thyroid disorder patients aged 18–65 years were selected during the study period. The sample

size was calculated by taking the prevalence of thyroid dysfunction as 28.2% (approximate) in this region [10]. MetS was diagnosed based on modified Asian National Cholesterol Education Program Adult Treatment Panel III panel criteria [11]. The study population comprised total 350 patients divided into six groups.

1. MetS patients with CVD
2. MetS patient without CVD
3. Thyroid disorder patients with CVD
4. Thyroid disorder patients without CVD
5. Patients with MetS and thyroid disorders with CVD
6. Patient with MetS and thyroid disorders without CVD.

Inclusion criteria

Patients between 18 and 65 years of age who are suffering from MetS and thyroid disorders with and without CVD.

Exclusion criteria

Patient receiving medication may alter thyroid functions, patient <18 and >65 years were excluded from this study, pregnant women excluded from this study, patient using corticosteroid, patients suffering from active liver disease, patients suffering from kidney disease, patients who are suffering from diabetes mellitus, diagnosed cancer patients were excluded from this study. Patients having any other systemic illness diagnosed hypertensive patients were excluded from this study.

Study design

Collection and sample analysis

After taking informed consent form, each patient's height, weight, waist circumference, and blood pressure were taken from each subject. For the determination of gastric peptidases (ghrelin and obestatin), interleukin-6 and insulin will be done by enzyme-linked immunosorbent assay. Thyroid hormones are determined by chemilumenscence. 5 mL fasting sample will be collected by vein puncture in vacutainer and centrifuged at 3000 rpm for 15 min for serum separation.

Statistically analysis

The data were collected and entered in Microsoft Excel sheet in the form of master chart and were analyzed using standard statistical software (SPSS version 20) and other supporting online software.

RESULTS

These are the results of 350 subjects.

DISCUSSION

Diabetes, thyroid dysfunction, and CVD together form the deadly quartet, more commonly known as MetS. It is estimated that approximately 25% of the world's population suffers from MetS. This study aims to assess the risk of developing CVD in patients with MetS and thyroid dysfunction. Biochemical parameters such as ghrelin and obestatin are used to measure hormonal variation related to hunger and satiety.

Patients are divided into two groups: Those with MetS with and without CVD (Group 1) and patients with MetS with and without thyroid disorders. Biochemical parameters are analyzed across age groups: 18–34 years, 35–51 years, and 52–65 years in both males and females separately.

In Group 1, Table 1 shows male patients suffering from MetS and CVD. Metabolic markers (ghrelin, obestatin, insulin, blood sugar, and homeostatic model assessment of insulin resistance [HOMA-IR]) are analyzed in the age group of 18–35 years. The value of ghrelin was found to be 574.87±127.91 in the 18–35-year age group and 602.83±131.11 in the 52–65-year age group. The p-value across the three age groups was found to be 0.130. From the analysis of the p-value, it can be concluded that ghrelin plays no statistically significant role, but it can be clearly observed that there is a correlation between age and ghrelin levels, that is, the levels rise with age. The highest peak of this marker is observed in the age group of 52–65 years in males [12].

Further, in Table 1, an analysis of obestatin levels in patients with MetS along with CVD revealed no significant variations across all three age groups, as indicated by the p=0.84. Insulin levels were observed to be consistent across the three age groups with a value of 14.38±1.65 μIU/mL in the 18–34-year age group, 14.39±2.31 μIU/mL in the 35–51-year age group, and 14.34±1.39 μIU/mL in the 52–65-year age group. The p-value showed no significant difference on analysis with a value of 0.99. A similar trend is observed in the random blood sugar (RBS) analysis in patients of all three age groups, with a value of 120.37±9.17 mg/dL in the 18–34-year age group, 119.78±10.95 mg/dL in the 35–51-year age group, and 121.46±10.49 mg/dL in the 52–65-year age group. The p=0.81 indicates no statistically significant difference [1].

Furthermore, an analysis of HOMA-IR follows the trends of RBS and insulin levels by showing no statistically significant variation. In the 18–34-year age group, the levels were recorded as 4.28±0.68, in the 35–51-year age group, a value of 4.26±0.79 was recorded, and in the 52–65-year age group, a value of 4.3±0.57 was recorded. The p=0.97 obtained across the three age groups does not show any significant variation [13].

In Table 1, it is clear that there is consistency in the levels of all metabolic markers across the three age groups in males. This consistency is reflected in p>0.5 for all the metabolic markers. These observations lead to the conclusion that the age of male patients does not have a significant impact on the metabolic markers included in this study.

In Table 2, an analysis of metabolic levels in female patients of MetS along with CVDs across three age groups is done. The levels of ghrelin in the age group of 18–34 years were found to be 678.37±162.22, in the age group of 35–51 years, the levels of ghrelin world recorded as 637.47±161.06, and in the age group of 52–65 years, the levels of this metabolic marker were observed as 626.4±122.87. Although a statistical analysis, a p=0.78 indicates no significant difference statistically, through this table, it is easy to observe that ghrelin levels are be in the youngest group that is 18–34 years and slightly decrease with age.

Another metabolic marker, obestatin, also shows no statistically significant variations among the three age groups with a p=0.67 but the levels show slight variations with the highest level of 13.82±3.02 in the age group 35–51 years followed by 13.48±2.25 in the age group 18–34 and 14.06±1.56 into the age group 52–65 years. These observations indicate that the levels of obestatin are relatively consistent in the female population of this study [14].

Table 1: Metabolic syndrome

Age group	Metabolic markers in MetS with CVD in males				
	Ghrelin	Obestatin	Insulin	RBS	HOMA-IR
18–34	574.87±117.50	2.81±0.58	14.38±1.65	120.37±9.17	4.28±0.68
35–51	538.48±127.91	2.92±0.49	14.39±2.31	119.78±10.95	4.26±0.79
52–65	602.83±131.11	2.89±0.46	14.34±1.39	121.46±10.49	4.3±0.57
p-value	0.1301	0.8429	0.9943	0.8121	0.9750

CVD: Cardiovascular disease, MetS: Metabolic syndrome, RBS: Random blood sugar, HOMA-IR: Homeostatic model assessment of insulin resistance

When comparing the levels of insulin across the three age groups, it was observed that levels of insulin increase slightly with age. The levels of insulin were recorded as follows, in the air group of 18–34 years 13.48±2.25, in the age group of 35–51 years 13.82±3.02, and in 52–65 years 14.06±1.56, although it can be noted that the levels of insulin rise with age, there is no statistically significant variation according to the p=0.92 [15].

The levels of RBS when analyzed across the females and age groups were observed that the levels of blood sugar are the highest at the age of 18–34 years, that is, 126.12±8.62, then slightly decrease by the age of 35–51 years and are recorded at 121.15±10.73 and then increase again in the oldest age group and were found to be 123±9.32. Although the trend of RBS seems clear in the initial observations, on statistical analysis, no significant variation was found, and the p-value was found to be 0.502 [15]. After the analysis of all these metabolic markers, an analysis of their overall metabolic health is evaluated using HOMA-IR. The analysis revealed that the HOMA-IR levels are relatively stable across all three age groups with a value of 4.22±0.79 in females of 18–34 years, 4.17±1.16 in the 35–51 years, and 4.28±0.66 in 52–65 years. On statistical analysis, a p=0.97 shows that there is no significant difference in the value of HOMA-IR and age [13]. In summary, Table 2 shows that age of female patients included in this study who are suffering from MetS and CVD does not have any significant impact on the metabolic markers. The consistent p > 0.5 backs up the above observation. Table 3 presents the metabolic profiles of females diagnosed with MetS without CVD, divided into three age groups: 18–34, 35–51, and 52–65 years. The metabolic parameters evaluated include ghrelin, obestatin, insulin, RBS, and HOMA-IR. In the 18–34 age group, the mean levels of ghrelin, obestatin, insulin, RBS, and HOMA-IR are 563.7 pg/mL, 2.87 ng/mL, 13.59 μIU/mL, 123.7 mg/dL, and 4.16, respectively. For the 35–51 age group, these values are 675.53 pg/mL, 2.85 ng/mL, 13.22 μIU/mL, 124.53 mg/dL, and 4.07. In the 52–65 age group, the mean values are 584.5 pg/mL, 2.63 ng/mL, 15.82 μIU/mL, 119.75 mg/dL, and 4.7. The p-values for ghrelin, obestatin, insulin, RBS, and HOMA-IR are 0.1276, 0.5337, 0.2220, 0.6758, and 0.0761, respectively [13].

The analysis reveals that there are no significant differences in the metabolic parameters across the different age groups for females with MetS without CVD, as all p-values exceed the significance threshold of 0.05. However, the slight variations in means suggest some age-related trends, such as higher mean ghrelin levels in the 35–51 age group compared to the other age groups and higher insulin levels in the 52–65 age group. Although these differences are not statistically significant, they may indicate subtle metabolic changes associated with aging in females with MetS without CVD. This highlights the need for ongoing monitoring and individualized management strategies for metabolic health in this population [15]. Table 4 presents the metabolic profile of females with MetS but without CVD, categorized by age groups. The variables analyzed include ghrelin levels, obestatin levels, insulin levels, RBS, and HOMA-IR. In the age group of 18–34 years, the mean ghrelin level is 563.7±125.80 pg/mL, obestatin level is 2.87±0.40 ng/mL, insulin level is 13.59±1.79 mU/mL, RBS is 123.7±9.76 mg/dL, and HOMA-IR is 4.16±0.62. For the 35–51 age groups, the corresponding values are ghrelin: 675.53±125.16 pg/mL, obestatin: 2.85±0.32 ng/mL, insulin: 13.22±1.89 mU/mL, RBS: 124.53±9.46 mg/dL, and HOMA-IR: 4.07±0.76. In the 52–65 age groups, the means are ghrelin: 584.5±163.22 pg/mL, obestatin: 2.63±0.48 ng/mL, insulin: 15.82±3.86 mU/mL, RBS: 119.75±7.97 mg/dL, and HOMA-IR: 4.7±1.33. The p-values indicate the statistical significance of the differences observed among the age groups for each variable, with none of the p-values being below the conventional threshold of 0.05, except for HOMA-IR (p=0.0761), suggesting a borderline significance. This table suggests potential age-related variations in metabolic parameters among females with MetS but without CVD, with HOMA-IR showing a tendency toward significance across age groups [15]. Table 5 illustrates the thyroid profile among males with MetS and CVD, categorized by age groups. The parameters analyzed include triiodothyronine (T3) levels, thyroxine (T4) levels, and thyroid-stimulating hormone (TSH) levels. In the 18–34 age groups, the mean T3 level is 2.05±0.53 nmoL/L, T4 level is 0.87±0.12 ng/dL, and TSH level is 3.41±0.60 μIU/mL. For the 35–51 age groups, the respective values are T3: 2.38±0.70 nmoL/L, T4: 1.21±0.58 ng/dL, and TSH: 3.76±2.07 μIU/mL. In the 52–65 age

Table 2: Metabolic markers in metabolic syndrome with CVD in males

Age group	Metabolic markers in MetS with CVD in females				
	Ghrelin	Obestatin	Insulin	RBS	HOMA-IR
18–34	678.37±162.22	2.78±0.35	13.48±2.25	126.12±8.62	4.22±0.79
35–51	637.47±161.06	2.89±0.49	13.82±3.02	121.15±10.73	4.17±1.16
52–65	626.4±122.87	2.72±0.26	14.06±1.56	123±9.32	4.28±0.66
p-value	0.7881	0.6733	0.9252	0.5021	0.9750

CVD: Cardiovascular disease, MetS: Metabolic syndrome, RBS: Random blood sugar, HOMA-IR: Homeostatic model assessment of insulin resistance

Table 3: Metabolic markers in metabolic syndrome with CVD in females

Age group	Metabolic markers in MetS without CVD in males				
	Ghrelin	Obestatin	Insulin	RBS	HOMA-IR
18–34	581.14±116.08	3.08±0.53	14.41±1.76	124.14±4.37	4.41±0.57
35–51	630.91±137.41	2.87±0.42	13.78±2.06	122.2±8.91	4.16±0.71
52–65	587.21±137.25	2.86±0.53	14.26±1.47	122±10.49	4.28±0.49
p-value	0.4359	0.5279	0.6984	0.8572	0.5793

CVD: Cardiovascular disease, MetS: Metabolic syndrome, RBS: Random blood sugar, HOMA-IR: Homeostatic model assessment of insulin resistance

Table 4: Metabolic markers in metabolic syndrome without CVD in males

Age group	Metabolic profile in MetS without CVD in females				
	Ghrelin	Obestatin	Insulin	RBS	HOMA-IR
18–34	563.7±125.80	2.87±0.40	13.59±1.79	123.7±9.76	4.16±0.62
35–51	675.53±125.16	2.85±0.32	13.22±1.89	124.53±9.46	4.07±0.76
52–65	584.5±163.22	2.63±0.48	15.82±3.86	119.75±7.97	4.7±1.33
p-value	0.1276	0.5337	0.2220	0.6758	0.0761

CVD: Cardiovascular disease, MetS: Metabolic syndrome, RBS: Random blood sugar, HOMA-IR: Homeostatic model assessment of insulin resistance

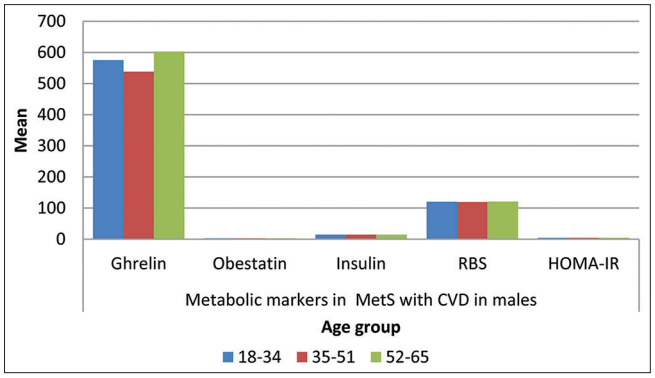

Fig. 1: Metabolic markers in MetS with CVD in males

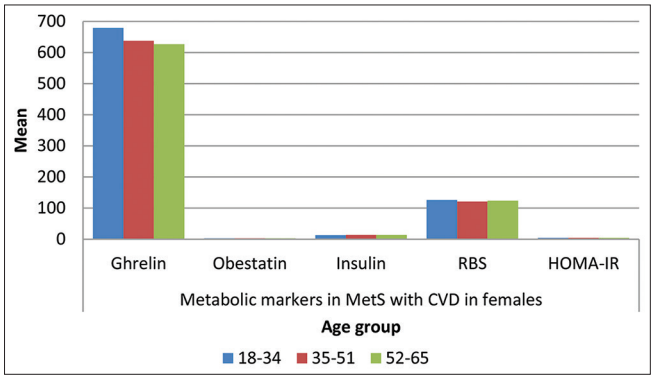

Fig. 2: Metabolic markers in MetS with CVD in females

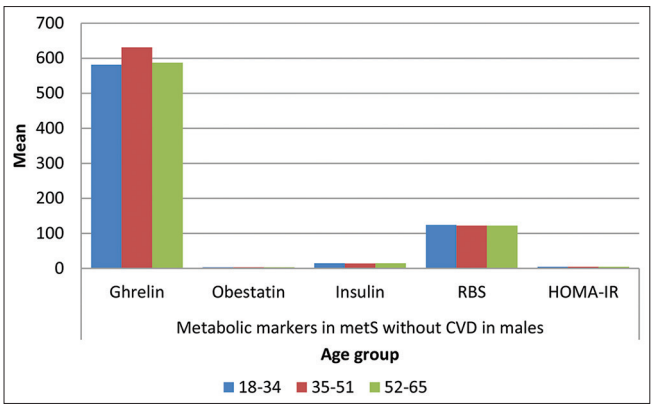

Fig. 3: Metabolic markers in MetS without CVD in males

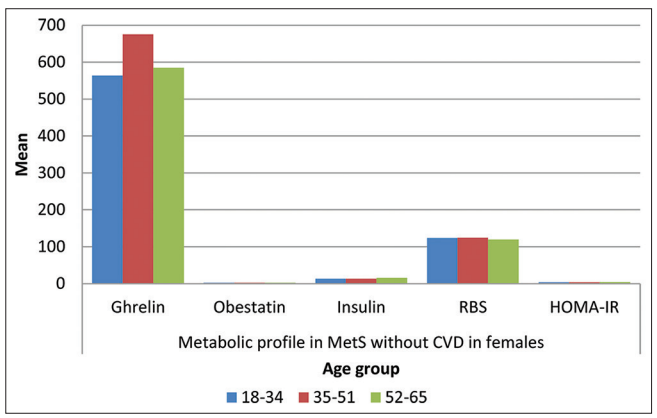

Fig. 4: Metabolic profile in MetS without CVD in females

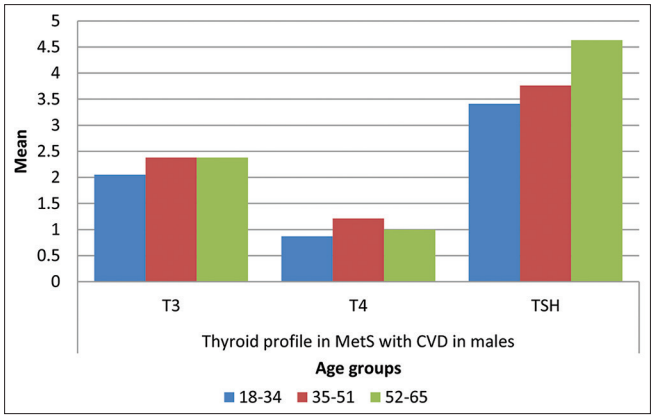

Fig. 5: Thyroid profile in MetS with CVD in males

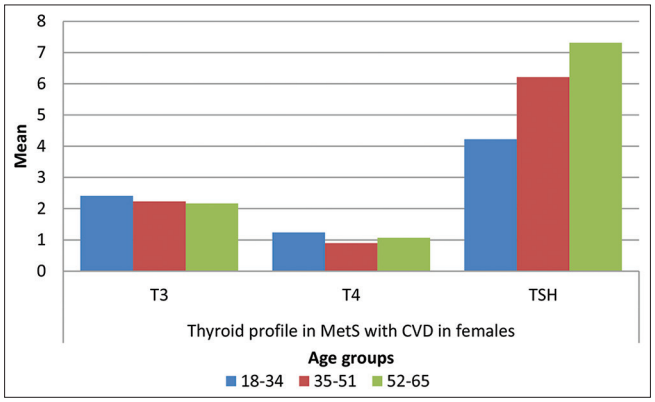

Fig. 6: Thyroid profile in MetS with CVD in females

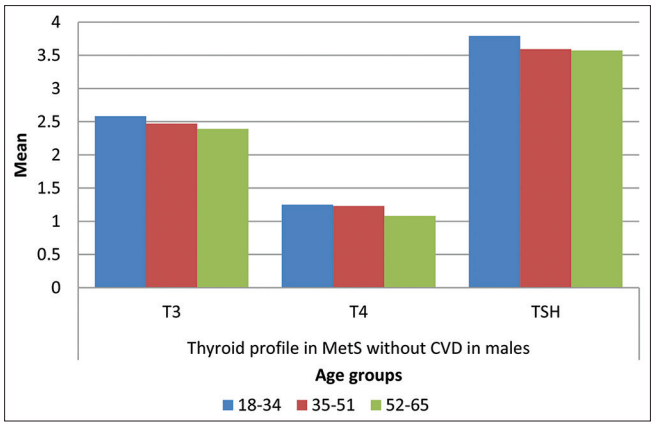

Fig. 7: Thyroid profile in MetS without CVD in males.

groups, the means are T3: 2.38±0.67 nmoL/L, T4: 1.00±0.38 ng/dL, and TSH: 4.63±2.51 µIU/mL. The p-values indicate the statistical significance of differences observed among the age groups for each parameter, with none of the p-values falling below the conventional threshold of 0.05, suggesting no significant age-related variations in the thyroid profile among males with MetS and CVD. However, T4 levels show a trend toward significance (p=0.0849), indicating a possible association with age in this population [16].

Table 6 displays the thyroid profile of females diagnosed with both MetS and CVD, categorized by age groups. The parameters analyzed include T3 levels, T4 levels, and TSH levels. In the 18–34 age group, the mean T3 level is 2.41±0.74 nmoL/L, the T4 level is

Table 5: Metabolic markers in metabolic syndrome without CVD in females

Age groups	Thyroid profile in MetS with CVD in males		
	T3	T4	TSH
18–34	2.05±0.53	0.87±0.12	3.41±0.60
35–51	2.38±0.70	1.21±0.58	3.76±2.07
52–65	2.38±0.67	1.00±0.38	4.63±2.51
p-value	0.4280	0.0849	0.1821

CVD: Cardiovascular disease, MetS: Metabolic syndrome, T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid-stimulating hormone

Table 6: Thyroid profile in Met with CVD in males

Age groups	Thyroid profile in MetS with CVD in females		
	T3	T4	TSH
18–34	2.41±0.74	1.24±0.35	4.22±2.20
35–51	2.23±0.93	0.90±0.52	6.21±3.03
52–65	2.17±1.07	1.07±0.70	7.31±3.70
p-value	0.8664	0.2847	0.1571

CVD: Cardiovascular disease, MetS: Metabolic syndrome, T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid-stimulating hormone

1.24±0.35 ng/dL, and the TSH level is 4.22±2.20 µIU/mL. For the 35–51 age groups, the respective values are T3: 2.23±0.93 nmol/L, T4: 0.90±0.52 ng/dL, and TSH: 6.21±3.03 µIU/mL. In the 52–65 age groups, the means are T3: 2.17±1.07 nmoL/L, T4: 1.07±0.70 ng/dL, and TSH: 7.31±3.70 µIU/mL. The p-values suggest no statistically significant differences among the age groups for T3, T4, and TSH levels, with all p-values above the conventional threshold of 0.05. This implies that there are no significant age-related variations in the thyroid profile among females with MetS and CVD in this study population. However, there is a trend toward significance for TSH levels (p=0.1571), indicating a potential association with age that might warrant further investigation [16].

Tables 7 and 8 present the thyroid profile of males with MetS but without CVD, categorized by age groups. The parameters analyzed include T3 levels, T4 levels, and TSH levels. In the 18–34 age groups, the mean T3 level is 2.58±0.44 nmol/L, T4 level is 1.25±0.30 ng/dL, and TSH level is 3.79±2.50 µIU/mL. For the 35–51 age groups, the respective values are T3: 2.47±0.75 nmoL/L, T4: 1.23±0.44 ng/dL, and TSH: 3.59±1.61 µIU/mL. In the 52–65 age groups, the means are T3: 2.39±0.66 nmoL/L, T4: 1.08±0.38 ng/dL, and TSH: 3.57±2.25 µIU/mL. The p-values indicate no statistically significant differences among the age groups for T3, T4, and TSH levels, with all p-values above the conventional threshold of 0.05. This suggests that there are no significant age-related variations in the thyroid profile among males with MetS but without CVD in this study population. These findings imply that age does not significantly influence the thyroid profile in this subgroup of males with MetS [17].

Table 9 illustrates the thyroid profile of females diagnosed with MetS but without CVD, categorized by age groups. The parameters examined include T3 levels, T4 levels, and TSH levels. In the 18–34 age groups, the mean T3 level is 1.98±0.84 nmoL/L, T4 level is 0.99±0.35 ng/dL, and TSH level is 3.80±2.74 µIU/mL. For the 35–51 age groups, the respective values are T3: 2.12±0.76 nmoL/L, T4: 0.92±0.36 ng/dL, and TSH: 4.32±2.88 µIU/mL. In the 52–65 age groups, the means are T3: 2.45±0.78 nmoL/L, T4: 1.16±0.33 ng/dL, and TSH: 3.58±0.48 µIU/mL. The p-values suggest no statistically significant differences among the age groups for T3, T4, and TSH levels, with all p-values exceeding the conventional threshold of 0.05. This indicates that there are no significant age-related variations in the thyroid profile among females with MetS but without CVD in this study population. These findings suggest that age does not significantly impact the thyroid profile in this subgroup of females with MetS [17,18].

Table 7: Thyroid profile in Mets with CVD in females

Age groups	Thyroid profile in MetS without CVD in males		
	T3	T4	TSH
18–34	2.58±0.44	1.25±0.30	3.79±2.50
35–51	2.47±0.75	1.23±0.44	3.59±1.61
52–65	2.39±0.66	1.08±0.38	3.57±2.25
p-value	0.8167	0.4025	0.9645

CVD: Cardiovascular disease, MetS: Metabolic syndrome, T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid-stimulating hormone

Table 8: Thyroid profile in Mets without CVD in males

Age groups	Thyroid profile in MetS without CVD in females		
	T3	T4	TSH
18–34	1.98±0.84	0.99±0.35	3.80±2.74
35–51	2.12±0.76	0.92±0.36	4.32±2.88
52–65	2.45±0.78	1.16±0.33	3.58±0.48
p-value	0.6118	0.5002	0.8416

CVD: Cardiovascular disease, MetS: Metabolic syndrome, TSH: Thyroid-stimulating hormone

Table 9: Thyroid profile in MetS without CVD in females

Age groups	Antioxidant in Mets with CVD in males	
	MDA	Vitamin-c
18–34	1.11±0.22	2.99±0.64
35–51	1.12±0.24	3.18±0.52
52–65	1.18±0.19	2.92±0.67
p-value	0.4894	0.2034

CVD: Cardiovascular disease, MetS: Metabolic syndrome, MDA: Malondialdehyde

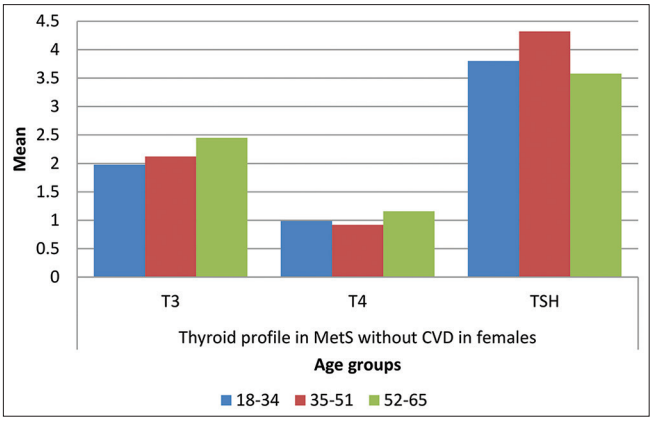

Fig. 8: - Thyroid profile in MetS without CVD in females

CONCLUSION

The key findings in this analysis are the significant negative correlation between insulin and ghrelin. These findings suggest specific interactions where higher insulin levels may suppress ghrelin levels. Other relationships among the biomarkers are weak and not statistically significant, indicating minimal interdependencies in individuals with thyroid disorders without CVD. This study provides valuable insights into the complex interplay of metabolic and CVD-related biomarkers. The findings emphasize the need for a holistic approach to health assessment and management, considering individual factors such as age, sex, and the presence of underlying health conditions. Further research in this area has the potential to inform the development of targeted interventions and personalized strategies for preventing and managing metabolic and CVD.

CONFLICTS OF INTEREST

None.

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