

## ORIGINAL ARTICLE

**Association of Hypothyroidism with Metabolic Syndrome**Fakhra Noureen<sup>1</sup>, Muhammad Nadeem Akbar Khan<sup>2</sup>, Abid Saeed Khan<sup>3</sup>, Shazia Qayyum<sup>4</sup>, Aqsa Liaquat<sup>5</sup>**ABSTRACT****Objective:** To determine the association between hypothyroidism and metabolic syndrome**Study Design:** Observational cross sectional study**Place and Duration of Study:** Data was collected from Medical unit and Department of Pathology, Pakistan Railways Hospital, Islamic International Medical College, Rawalpindi and Capital Hospital Islamabad from April 2017 to April 2018.**Materials and Methods:** One hundred and fifty adult subjects participated in this study. Hundred hypothyroid subjects were recruited as cases on the basis of laboratory findings of raised serum thyroid stimulating hormone (TSH) levels and low serum free thyroxine (FT4) level. Newly diagnosed/ untreated cases of Hypothyroidism and adults of either sex were included. After an overnight fasting, participants were tested for various components of metabolic syndrome. Fifty euthyroid subjects were taken as controls. Data was analyzed by SPSS-21.**Results:** Among 150 total recruited subjects, 25% hypothyroid cases and 10% euthyroid controls were diagnosed with metabolic syndrome. These results were statistically significant with p value 0.030. Mean serum triglycerides 183 ±26 and 153±26 mg/dl and mean fasting blood glucose 100 ±30 and 96 ±18 mg/dl respectively among hypothyroid and euthyroid patients were significant with p-value 0.001. Whereas, waist circumference, high density lipoprotein cholesterol and blood pressure measurement of hypothyroid and euthyroid individuals were not significant.**Conclusion:** Hypothyroidism is associated with various components of metabolic syndrome.**Key Words:** *Free Thyroxine, Fasting Blood Glucose, Hypothyroid, Metabolic Syndrome, Serum Triglycerides, Thyroid Stimulating Hormone***Introduction**

Thyroid dysfunction and metabolic syndrome are major encountered endocrine abnormalities in clinical practice.<sup>1</sup> High blood glucose level, raised serum triglyceride level, increased waist circumference, elevated blood pressure measurements and low high density lipoprotein cholesterol are common in these two entities.<sup>2</sup> Thyroid hormones regulate wide range of functions

in body such as basal metabolic rate, protein synthesis, cardiac and gastrointestinal function, maturation of the central nervous system and maintain body mass index.<sup>3</sup> Hypothyroidism has prevalence of 3.8%–4.6% in Asian population as per data of different studies.<sup>4</sup> Definition of Metabolic syndrome given by American Heart association and the National Heart, Lung and Blood Institute (AHA/NHLBI) declared that clinical diagnosis of metabolic syndrome can be established if any three of the following factors are present, elevated triglyceride level (TG), elevated waist circumference, decreased HDL-cholesterol (HDL-C) level, elevated fasting plasma glucose and elevated blood pressure.<sup>5</sup> The estimated prevalence of metabolic syndrome in general population is between 17 and 25%.<sup>3</sup> Decreasing thyroid function is associated with occurrence of obesity and hence can potentially contribute to the development of MS.<sup>6</sup> As thyroid hormones decrease, components of metabolic syndrome get more prominent.<sup>7</sup> Study conducted in western population and India showed that thyroid

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hormones significantly affect each component of metabolic syndrome.<sup>8,9</sup> Extensive literature review revealed that studies have been done regarding this topic in developed countries, however, reported clinical data is scarce in Pakistan. This knowledge gap was addressed by designing a study with an objective to find the relationship between hypothyroidism and metabolic syndrome.

### Materials and Methods

It was an observational, cross-sectional study conducted at department of chemical pathology, Islamic International Medical College in collaboration with medical unit of Pakistan Railways Hospital, Rawalpindi and Medical unit of Capital Hospital Islamabad. The study extended over a period of 12 months from April 2017 to April 2018.

A total of 150 subjects were enrolled by non-probability convenient sampling after approval from Ethical Review Committee. Written informed consents were obtained from participants. With the help of medical specialist of Pakistan Railways and Capital hospital, serum TSH was done of clinically diagnosed patients who visited Medical OPD. Subjects who had raised serum TSH levels > 4.5  $\mu$ U/ml were further tested for serum fT4. Similarly hundred newly diagnosed patients of hypothyroidism on the basis of raised serum TSH and low serum Ft4 were taken as cases. Fifty age and gender matched controls with normal serum TSH level (0.4–4.5  $\mu$ U/ml) were enrolled.

Willing participants reported the next morning after an overnight 10-12 hours fast. 5ml blood was taken for analysis. The blood samples were centrifuged at 15000 rpm x g for about 15 minutes and serum was separated. Serum TSH and fT4 test was performed using the Vitros Eci Immunodiagnostic Systems. HDL-C was measured by enzymatic precipitation method on semi-automated chemistry analyzer micro-lab 300. Enzymatic end-point method (GPO-PAP) was used to determine the triglycerides level and Glucose concentrations were determined on fasting serum samples, using glucose oxidase method on semi-automated micro lab 300. Using the pubic crest and the umbilicus as land marks abdominal obesity was determined by measurement of the waist circumference in centimeters. Blood pressure was measured with the help of Mercury Sphygmomanometer. The average of two readings

taken fifteen minutes apart was considered.

Data was entered and analyzed using Statistical Package for Social Sciences (SPSS) version 21. Simple descriptive statistics (frequencies, percentages) was computed for each categorical variable such as age and gender. Whereas mean and standard deviation was calculated for numerical (continuous) variables which included serum TSH, serum fT4, blood glucose fasting, serum HDL-C, serum triglycerides, waist circumference and blood pressure measurements. Independent sample t test was applied to compare the means of various components of metabolic syndrome. Chi square test was applied to determine the relationship between hypothyroid and different components of metabolic syndrome. *p* value of < 0.05 was considered statistically significant.

### Results

Mean age (years) of total recruited subjects was 41.64 $\pm$ 3 among them 33.3% were males and 66.7% were female. Mean age (years) of hypothyroid subjects was 42.48 $\pm$ 11.56 having 26% male and 74% females. Among 50 euthyroid subjects age in years was 39.36 $\pm$ 12.01 with 48% male and 52% female. Hypothyroid subjects who had metabolic syndrome were 25 in number with mean age of 46.50 $\pm$ 8.97, and male to female ratio were 16.7% and 83.3% respectively. Descriptive statistics of serum TSH in hypothyroid and euthyroid subjects was 32  $\pm$ 28 and 3.2  $\pm$ 0.6, which was statistically significant i.e (p 0.001). Whereas mean serum fT4 levels was 0.4  $\pm$ 0.2 in hypothyroid subjects and 1.5  $\pm$ 0.4 in euthyroid subjects and was statistically significant i.e (p 0.001). Mean serum TSH levels and fT4 levels were 35  $\pm$ 28, 19  $\pm$ 25 and 0.61  $\pm$ 0.5, 0.8  $\pm$ 0.5 in subjects having metabolic syndrome and subjects who did not present with metabolic syndrome respectively and was statistically significant (p-value 0.005) as shown in Table I.

Different variables of metabolic syndrome were compared among hypothyroid and euthyroid patients. Mean serum triglycerides mg/dl among hypothyroid and euthyroid patients were 183  $\pm$  26 and 153  $\pm$  26 respectively, the difference in two groups was significant (p value 0.001). Mean fasting blood glucose mg/dl levels were 100  $\pm$ 30 and 96  $\pm$ 18 in hypothyroid and euthyroid subjects and was statistically significant with p value 0.001. Independent sample t-test was used to compare

waist circumference, HDL and blood pressure measurements among hypothyroid and euthyroid subjects which was statistically not significant, as shown in Table II.

Chi-square test was applied to determine the association of hypothyroidism with metabolic syndrome as shown in Table III. Among 100 hypothyroid and 50 euthyroid subjects 25 (25%) and 05 (10%) individuals presented with metabolic syndrome respectively. The results were statistically significant with p value 0.030.

**Table I : Descriptive Statistics of Serum TSH and Serum fT4 Levels in Metabolic Syndrome (MS) Patients**

	MS present n= (30)	MS absent n= (120)	p value *
Serum TSH (0.4–4.5U/ml)	35 ±28	19 ±25	0.005 *
Serum fT4 (0.78–2.19ng/dl)	0.61 ±0.5	0.8 ±0.5	0.005 *

\*P<0.05 was taken as level of significant

**Table II: Descriptive Statistics of Metabolic Syndrome Variables in Hypothyroid and Euthyroid Subjects**

Metabolic syndrome Variables	Hypothyroid n= 100	Euthyroid n= 50	p value
Waist Circumference cms	91 ±12	86 ±9	0.07
HDL cholesterol mg/dl	40 ±7	44 ± 4	0.21
Serum Triglycerides mg/dl	183 ± 26	153 ± 26	0.001*
Blood Pressure systole mmHg	120 ± 12	118 ± 6	0.06
Blood Pressure diastole mmHg	79 ±8	78 ±7	0.16
Fasting Blood Glucose mg/dl	100 ±30	96 ±18	0.001*

\*P<0.05 was taken as level of significant

**Table III: Association of Hypothyroidism With Metabolic Syndrome**

	Metabolic Syndrome		p-value
	present	absent	
Hypothyroid n=100	25 25%	75 75%	0.030*
Euthyroid n=50	5 10%	45 90%	

\*P<0.05 was taken as level of significant

**Discussion**

The study showed that mean age of hypothyroid and euthyroid participants were 42.48± 11.5 and

39± 12, respectively as compared to the patients of metabolic syndrome in which mean age was 46.5 ±8.9. This shows that prevalence of metabolic syndrome increases with age as decline in immunocompetence with age is accompanied by the increase in the incidence of autoimmune diseases. Similar findings are present in study by Ervin RB.<sup>10</sup>

In total of 150 participants, 30 subjects were diagnosed with metabolic syndrome in which 37.5% were male whereas 62.5 % were female which shows that in females MS is common. Study by Gurav et al reports similar findings.<sup>11</sup> Another study by Louai Razzouk et al demonstrated increase prevalence of the metabolic syndrome in older age and higher among females. This can be explained by increased caloric intake, dyslipidemia, and sedentary lifestyle, hormonal changes in women and obesity in older age.<sup>12</sup>

Mean serum TSH and fT4 in metabolic syndrome patients was 35 ±28, 19 ±25 and 0.61 ±0.5, 0.8 ±0.5 respectively which was statistically significant. TSH is more sensitive indicator of thyroid function. Even small changes in Thyroid hormone levels may cause a marked shift in TSH level these findings have shown a similar relationship with thyroid hormones by Shehzad et al.<sup>13</sup>

In our study it was found that 25(83%) hypothyroid subjects were diagnosed with MS and had high serum TSH levels as compared to the euthyroid subjects where 5 subjects were diagnosed with MS, who had TSH levels within normal reference range. The study conducted in Nepal by Gyawali et al showed significant difference.<sup>14</sup>

Fasting blood glucose levels were found higher in hypothyroid patients as compare to euthyroid (control) group. This finding is in agreement to previous study by Maratou at al.<sup>15</sup>

Serum triglyceride levels were found to be elevated; on the other hand the HDL-C levels were lower in hypothyroid patients. TH affects HDL-C through cholesterol ester transfer protein and hepatic lipase activity. These findings are similar with results of previous studies by Sanyal et al and Pearce et al.<sup>16,17</sup> In our study, it has been observed that high serum TSH levels are directly related with various components of metabolic syndrome. Study by Renehr et al has found increased serum TSH levels to be correlated

with obesity. This may be due to involvement of leptin protein from adipose tissues which also fluctuates with body adiposity.<sup>18</sup>

Extensive literature review has revealed that scanty work has been done in our setup to determine association between hypothyroidism and metabolic syndrome. Our study results showed that MS is highly prevalent among hypothyroid patients. There were 25 (83.3%) hypothyroid and 05 (16.7%) euthyroid patients (control group) who were diagnosed with metabolic syndrome. These results are in agreement with the previous study by Gyawali P<sup>14</sup> and Roos et al.<sup>19</sup> Another study conducted by Tehrani F on large cohort of 5786 subjects also found that hypothyroidism is associated with metabolic syndrome.<sup>20</sup>

### Conclusions

Our study shows association of MS among hypothyroid patients in our setting in Rawalpindi and Islamabad, Pakistan. The coexistence of two diseases MS and thyroid dysfunction increases the chance of cardiovascular disease and diabetes. Therefore, diagnosed patients of hypothyroidism should be evaluated for all components of MS.

### Limitations

The study design was Cross-Sectional, so it did not help to determine cause and effect relationship between low-normal thyroid function and MS. Sample size was small i.e. 100 hypothyroid patients and 50 euthyroid participants, a large scale clinical trials should be carried out. Due to limited resources subjects were recruited from two centers, a multicenter study should be carried out involving all main hospitals of the city.

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