ORIGINAL ARTICLE

The Association of Total Antioxidant Capacity with Metabolic Syndrome

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ABSTRACT

Objective: To determine the association between Total antioxidant capacity (TAC) with metabolic syndrome

Study Design: A cross sectional study design.

Place and Duration of Study: The study was conducted at department of Chemical Pathology, Islamic International Medical College Pakistan Railways Hospital, Rawalpindi. One year (2nd Sep 2018 to 2nd September 2019).

Materials and Methods: A total of 88 subjects, 44 with metabolic syndrome and 44 controls were recruited through non probability convenient sampling. Group I comprised of 44 metabolic syndrome individuals from both genders. Patients having FPG ≥ 100mg/dl were investigated for TG and HDL-C and their waist circumference and BP was measured. According to AHA/NHLBI guidelines, the individuals were labeled with MS on fulfilling three or more than three criteria i.e Fasting Plasma Glucose ≥ 100mg/dl, Serum Triglycerides ≥ 150mg/dl, HDL-C ≤ 40mg/dl in men and ≤ 50 in women, Blood Pressure ≥ 130/85 and waist circumference ≥ 40" in men or ≥ 35" in women.[8] Group 2 comprised of 44 healthy individuals.

In addition to the above mentioned lab tests, Total Antioxidant capacity (TAC) was measured for both the groups. Statistical Package for Social Sciences (SPSS) version 23.0 was used for entering and analyzing all data. Descriptive statistics were described for nominal data; mean and standard deviation were described for quantitative variables which included serum TAC, FBG, serum HDL-C, serum triglycerides, waist circumference and BP measurement.

Results: The mean age of metabolic disease group was 48.14 ± 10.48 years, and that of control group was 23.04 ± 5.82 years. TAC recorded levels were found to be considerably higher in the control group (18.13 ± 12.90 mmol/L) as compared to the Metabolic Syndrome group (4.56 ±.7.43). Serum HDL-C (37.09 ± 6.37 mg/dl) vs (43.09 ± 46.15 mg/dl) levels were lower in MS individuals. Whereas, Triglycerides (240.03 ± 93.19) vs (107.41 ± 56.50), FPG (139.43 ±57.56) vs (69.66 ± 30.46), BP (133.86 mm Hg + 13.59) vs (120.00 ± 0.00) were found to be higher in MS patients as compared to control group.

Conclusion: TAC gets depleted in MS individuals more as compared to healthy individuals. Estimation of TAC at an early stage can be useful for early detection of Metabolic Syndrome and further to prevent its complications such as DM, CVD and other metabolic disorders.

Key Words: *Cardiovascular Disease, Diabetes Mellitus, High Density Lipoprotein Cholesterol, Metabolic Syndrome, Total Antioxidant Capacity.*

Introduction

A group of disorders including hypertension, insulin resistance, dyslipidemias and abdominal obesity collectively contribute to the condition termed as Metabolic Syndrome (MS).[1] The incidence of MS is on the rise globally.[2] The individuals who are labeled to have metabolic syndrome are more prone to adverse cardiovascular incidents and death due to CVD.[3] Classical cardiovascular risk factors include low HDL-C, hypertriglyceridemia, hypertension and dysfunctions in glucose metabolism.[4] In addition, metabolic syndrome also causes a significant impact on health care cost and resource utilization.[5] A stringent clinical criteria, described by the American Heart Association and the National Heart, Lung and

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Blood Institute (AHA/NHLBI, 2009)used to define MS is described below. If any three of the following are met, the patient would be classified as having Metabolic Syndrome;

1. Serum triglyceride rising above 150 mg/dl (or the patient is on drug therapy for hypertriglyceridemia).
2. Circumferential waist of patients rises above around 102 cm in affected males and around 88 cm in affected females.
3. High Density Lipoprotein Cholesterol (HDL-C) levels ≤ 40 mg/dl for males (or the patient is on drug therapy for improving HDL-C level); or ≤ 50 mg/dl for females (or the patient is on drug therapy for improving HDL-C level).
4. Glucose levels rise above 100 mg/dl in the fasting state (or the patient is on drug therapy for hyperglycemia).
5. Blood pressure readings are higher than 130/85 mm Hg (or the patient is on drug therapy for hypertension).[6]

Moreover, the contribution of oxidative stress phenomenon in the pathology of the metabolic disorders is considerably significant in relation to MS.[7] Oxidative stress, can be understood as a disturbance in balance between free radicals genesis and the physiological capacity to counter the destructive process brought about by antioxidants. Oxidative stress has an integral contribution towards the progression of MS, Diabetes mellitus (DM) and cardiovascular diseases (CVD).[8] To manage the oxidative stress, many antioxidant defense systems operate through enzymatic or non-enzymatic systems. Non-enzymatic antioxidant comprises of glutathione, beta-carotene, vitamin A, C and E, Whereas enzymatic pathways include intracellular antioxidant enzymes catalase (CAT), glutathione reductase (GR), glutathione (GPx), and superoxide dismutase (SOD).[9] Total antioxidant capacity (TAC) is used as an instrument for diagnostic purposes and for treating CVD and DM.[10] Moreover, the levels of TAC are used as biological marker to monitor oxidative stress in humans.[11] Rationale behind the study, measurement of TAC can play a significant role in assessing oxidative stress and taking timely action to prevent MS complications such as DM, CVD and other metabolic disorders.[11] This study was aimed to determine the association between Total antioxidant capacities (TAC) with Metabolic syndrome

Materials and Methods

A cross-sectional study was conducted at the Department of Chemical Pathology at the Pakistan Railways Hospital Rawalpindi over the period of one year (2nd Sep 2018 to 2ndSep2019). Study started after the approval from the Ethical Review Committee, Riphah International University, Islamabad. An overall of 88 subjects, 44 cases and 44 controls were included in this study. Adults from both genders having MS were included. Patients with acute infections, chronic diseases like RA, SLE, pregnant and lactating women were excluded. Patients already on antioxidant and lipid lowering drugs were also excluded. Two groups of subjects were recruited for the study.

Group 1 This group comprised of 44 metabolic syndrome individuals from both genders. Patients having FPG ≥ 100mg/dl were investigated for TG and HDL-C and their waist circumference and BP was measured. According to AHA/NHLBI guidelines, the individuals were labeled with MS on fulfilling three or more than three criteria i.e. Fasting Plasma Glucose≥ 100mg/dl, Serum Triglycerides≥ 150mg/dl, HDL-C ≤ 40mg/dl in males and ≤ 50 in females, Blood Pressure ≥ 130/85 and waist circumference ≥ 102cm in males or ≥ 88cm in females.

Group 2 A total of 44 healthy individuals of both genders was recruited from faculty and lab staff of PRH as controls.

Patient was seated comfortably and 5ml of venous blood was taken in plain sample vacutainer. The collected blood sample was centrifuged at 1000xg for 15 min to extract serum and then this serum was stored at -70C.

All of the data was then entered and analyzed using, Statistical Package for Social Sciences (SPSS) version 23.0.Descriptive statistics (frequencies and percentages) weredescribed for nominal data, such as age and gender. Mean and standard deviation values were described for quantitative variables including the serum Total Anti-Oxidant Capacity, Fasting blood glucose, serum HDL-C, serum triglycerides, waist circumference and blood pressure measurements. Kolmogrov-Smirnov test was then applied to test the normality of the

distribution of the data. Since all variables were found to be irregularly distributed, the non-parametric Mann Whitney U test was applied to compare the various variables between the two groups, one with the metabolic diseases and the other control group of normal individuals. *P* value <0.05 was found to be statistically significant.

Results

A total of 88 subjects were encompassed according to the inclusion criteria of the study. Descriptive statistics of age (in years) were calculated as mean and standard deviation. Mean age of all the recruited subjects was 38.59 ± 15.19 years. The recorded mean age of Metabolic Syndrome group was 48.14 ± 10.48 years, and the mean age of control group was 23.04 ± 5.82 years.

Majority of subjects 36.3% were between 41-50 years, 31.3% participants were between 51-60 years. About 8.5% participants were between 33-40 years and 11.1%participants were between 61-70 years.Only2.27% participants were between 21-30 years in (Table I).

Table I: Descriptive Statistics of Age (N = 88)

	Mean	Standard Deviation
Metabolic Syndrome Group(n = 44)	48.14	10.48
Control Group (n = 44)	23.04	5.82
Total (n = 88)	38.59	15.19

A significant difference was found between values of different risk factors of MS (obesity, hypertension; and high Fasting plasma glucose, Triglycerides and HDL-C levels). The results showed that the values for MS patients were found to be considerably raised than those recorded for the control group.

The affiliation between the Total Antioxidant Capacity with HDL-C showed a positive correlation whereas TAC showed negative correlation with abdominal obesity, blood pressure, triglycerides and fasting blood glucose. (Table II).

TAC values were found significantly high in the control group (18.13 ± 12.90 mmol/L) as compared to the MS group 4.56 ± 7.43mmol/L in (Table III)

A valid instrument to quantify MS is by measuring TAC levels (Table III). The comparison was done between the MS and control groups. TAC levels were found to be severely depleted in the MS patients, in comparison to the control group.

Table II: Kolmogrov Smirnov Significance Values for Different Variables for Normality Tests

Variable	P Value
HDL-C	< 0.001
TGL	0.002
FPG	< 0.001
Systolic BP	< 0.001
Diastolic BP	< 0.001
Waist Circumference	0.011
Total Antioxidant Capacity	< 0.001

Table III: Mean, SD and *p* Values for Different Elements of MS (N = 88)

Metabolic Syndrome Indicators	Metabolic Syndrome Group	Control Group	P Value
HDL-C (mg/dl)	37.09 ± 6.37	43.09 ± 46.15	0.008
TGL (mg/dl)	240.03 ± 93.19	107.41 ± 56.50	< 0.001
FPG (mg/dl)	139.43 ± 57.56	69.66 ± 30.46	< 0.001
Systolic BP (mm Hg)	133.86 ± 13.59	120.00 ± 0.00	< 0.001
Diastolic BP (mm Hg)	87.27 ± 8.52	80.00 ± 0.00	< 0.001
Waist Circumference(cm)	37.84 ± 3.67	31.91 ± 3.12	< 0.001
TAC (mmol/L)	4.56 ± 7.43	18.13 ± 12.90	< 0.001

*$p \leq 0.05$ was taken as level of significant

Discussion

The present study has been carried out to determine the association between TAC with MS. Both Males and female between those 18-65 years of age were recruited. These results depict that incidence of MS increases with age. Ervin RB has also documented the increased incidence of MS in middle and old aged people.[12] However, Weiss et al found that MS is also common among children and young adults. Zhiyan Li et al has documented similar findings about the increased prevalence of MS among male population.[13] In our study it has been found that serum HDL-C levels were suggestively lower in MS group (37.09 ± 6.37 mg/dl) as compared to control group comprising of healthy adults(43.09 ± 46.15 mg/dl). In present study we have found that HDL-C has a positive correlation with Total (TAC). This positive correlation indicates the antioxidant activity. HDL-C exerts its anti atherogenic and anti-inflammatory properties, including anti oxidative activity by scavenging reactive oxygen species ROS.[14] In our study, the mean serum TG(>150 mg/dl) in MS patients and control subjects was 240.03 ± 93.19 and 107.41 ± 56.50 respectively. The raised levels of triglycerides in MS individuals indicate reverse correlation between triglycerides and TAC. Bitla et al, Abbasian et al and Zheng et al have also reported an inverse relation between triglycerides and TAC.[15] In

present study it has been found that the levels of FPG(≥ 100mg/dl) were much higher in MS individuals (139.43 ± 57.56 mg/dl) as compared to healthy adults (69.66 ± 30.46 mg/dl). Exposure to prolonged periods of hyperglycemia causes non-enzymatic glycation of extracellular proteins.[16] The study, by Maxwell et al and Ceriello et al have reported similar findings raised plasma glucose levels in MS subjects.[17] In present study, the mean and SD of systolic BP(mmHg) was 133.86 ± 13.59, and 120.00 ± 0.00 in MS patients and control groups respectively. The difference of systolic and diastolic BP was evidently raised in MS group as compared to control group due to increased ROS production, redox-signaling and decreased TAC in MS.[17] Sanchez-Rodriguez et al, in his study reported a negative correlation amongst BP and TAC similar to our study.[18] In this study the mean waist circumference (cm) was 37.84 ± 3.67, and 31.91 ± 3.12 in MS and control group respectively. Increased waist circumference in MS subjectis due to dysregulations of adipokines and development of MS which further reduces TAC. The waist circumference showed an inverse correlation with TAC. Research work conducted and documented by Chrysohoou et al and Hartwich et al reached to similar conclusions.[19]According to the results of this study TAC has a positive correlation with HDL-C; however it has an inverse correlation with TG, FPG, BP and waist circumference. TAC levels were found significantly increased in the control group (18.13 ±12.90 mmol/L) in comparison to the MS group (4.56±7.43mmol/L).A number of studies have been done to study the relationship between the components of MS & MDA i.e an oxidant bio-marker.[20]To conclude, this study, it can be stated that the oxidative stress in MS is worsened as a result of increased activity of the biochemical pathways which in turn influences increase in the rate of transport of ROS and thus enhancing the changes in antioxidant protection.[21] This study has certain limitations. The sample size was small and study was conducted at single center, hence, restricting us to generalize the findings of our study.

Conclusion

TAC gets depleted in Metabolic Syndrome individuals more as compared to healthy individuals. Estimation of TAC at an early stage can be useful for early detection of Metabolic Syndrome and further to prevent its complications such as DM, CVD and other metabolic disorders.

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