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ALTERATIONS IN ANTHROPOMETRIC INDICES, LIPID PROFOLE AND OXIDATIVE STRESS IN PATIENTS WITH METABOLIC SYNDROME

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ABSTRACT Metabolic syndrome (MetS) is one of the major public health issues of this century which describes a constellation of physical conditions and metabolic abnormalities, commonly occurring together, that increases an individual's risk for development of type 2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD). The present study was undertaken to assess the anthropometric indices, glucose level, lipid profile and the levels of pro-oxidant and anti-oxidant markers in MetS patients. BMI and WC were increased in MetS patients and WC was higher in women as compared to men. Serum TC, TG, LDL & VLDL levels were significantly higher and HDL levels were significantly lower in MetS patients compared to their age and sex-matched Controls. Blood levels of MDA, GSH and ascorbic acid were significantly higher in patients with MetS. BMI, WC, FPG, TC, TG, LDL & VLDL levels had significant positive, and HDL levels had significant negative correlations with the markers of OS.

KEYWORDS : Metabolic syndrome, Anthropometric indices, Lipid profile, Malon di-aldehyde, Glutathione, Ascorbic acid

Abbreviations:- BMI-Body mass index, CVD-Cardiovascular diseases, FBG-Fasting blood glucose, GSH-Glutathione (reduced form), MDA-Malon-dialdehyde, MetS-Metabolic syndrome, OS-Oxidative stress, HDL-HDL cholesterol, LDL-LDL cholesterol, OS-Oxidative stress, TC-Total cholesterol, T2DM-Type 2 diabetes mellitus, TG-Triglyceride, WC-Waist circumference

Introduction

Metabolic syndrome (MetS) is a widely prevalent and multi-factorial disorder that presents in a distinct, albeit heterogeneous phenotype. It is a cluster of disorders that occur together, increasing the risk of cardiovascular diseases (CVD) and type 2 diabetes mellitus (T2DM) [1, 2]. The disorders include elevated blood pressure, insulin resistance, and excess body fat around the waist and/or dyslipidemia [2, 3]. The prevalence of MetS depends on age, ethnic background, and gender. It rises linearly from 20 to 50 years and plateaus thereafter [4, 5]. With the increasing urbanization in developing countries like India, the incidence of MetS is expected to increase several-fold in the coming years [5, 6]. The current worldwide obesity epidemic also contributes to increased prevalence of MetS. The clinical relevance of MetS is related to visceral obesity and its role in the development of cardiovascular disease (CVD) [6, 7]. The two potential etio-pathogenetic factors of MetS are central obesity and insulin resistance. Other important factors also influence the development of MetS including genetic profile, physical inactivity, ageing and hormonal deregulation [7, 8].

MetS is a complex web of metabolic factors that are associated with a 2-fold risk of cardiovascular disease (CVD) and a 5-fold risk of diabetes [9]. Individuals with MetS have a 30%–40% probability of developing DM and/or CVD within 20 years, depending on the number of components present. Cardiovascular mortality is markedly increased in subjects with the MetS [10]. In the US, the unadjusted and age-adjusted prevalence of the MetS have been estimated to be 21.8% and 23.7%, respectively. The Third Report of the US National Cholesterol Education Program Adult Treatment Panel III (US NCEP ATP-III) has recommended appropriate measures to identify individuals with the MetS [11]. In 2005, the International Diabetes Federation (IDF) provided new modified criteria for the diagnosis of MetS, based on the following four features: waist circumference (WC), blood pressure (BP), fasting blood glucose (FBG) and serum triglyceride (TG) and high density lipoprotein cholesterol (HDL) levels [12].

The prevalence of MetS increases with increasing glucose intolerance and with the increasing worldwide prevalence of T2DM, the expected increase in the frequency of occurrence of the MetS will expectedly be in geometric proportions. The prevalence of the MetS in the general population is estimated to be between 17-25% and in people with DM, reported prevalence rates range from 59% to 61% [13]. Useful anthropometric markers in MetS are body mass index (BMI) and waist circumference (WC). Obesity is closely associated with the components of MetS including hyperglycemia, dyslipidemia and hypertension [13, 14]. Though (BMI) is the most common measure of obesity, it does not reflect body shape. WC is a more accurate measure of the distribution of body fat [18, 19]. The prognostic importance of high WC has been recognized within the diagnostic criteria to identify individuals with features of the MetS [14, 15].

One of the defining features of MetS is atherogenic dyslipidemia, manifested by lipoprotein disturbances like elevated TG, diminished HDL and increased low-density lipoprotein cholesterol (LDL) levels [16, 17]. Other features of MetS dyslipidemia include elevated very low density lipoproteins (VLDL), and reduced HDL-2, which are the large buoyant anti-atherogenic subspecies of total HDL [17, 18]. In some individuals, apo lipoproteins B (apo B) levels may be elevated, reflecting an increase in VLDL and LDL. All of these abnormalities have been implicated as being independently atherogenic [19, 20].

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Oxidative stress (OS) results due to disturbed equilibrium between pro-oxidants and anti-oxidants and plays a role in pathophysiology of T2DM and CVD. Some factors of MetS, such as hyperglycemia and a pro-inflammatory state may lead to increased production of reactive oxygen species (ROS) [21, 22]. Antioxidants delay or inhibit cellular damage mainly through their free radical scavenging properties [22, 23]. Malondialdehyde (MDA) is a lipid peroxidation bye product that is used as markers in lipid per oxidation assay [23, 24]. Glutathione (GSH) is the most abundant intracellular thiol-based anti-oxidant, prevalent in millimolar concentrations in all living aerobic cells, and plays an important role in the cellular defense cascade against

oxidative injury [22-24]. Ascorbic acid is a powerful water-soluble antioxidant, and it protects LDL-C from oxidation, reduces harmful oxidants in the stomach and promotes iron absorption [25].

Even though MetS is reported to be one of the major atherogenic and thrombotic risk factor, studies investigating the link between atherogenic factors and OS in MetS patients from Kerala population are almost scanty [26-28]. Hence, the present study was undertaken to investigate the variations of anthropometric indices and pro-oxidant and anti-oxidant markers in subjects with MetS compared to their age & sex-matched controls, and to evaluate the correlations, if any of the anthropometric indices with the pro-oxidant state in subjects with MetS.

Materials

This study was conducted at Pushpagiri Institute of Medical Sciences, Thiruvalla for a period of two months. Men and women between the age 30-65 years, selected from among the staff and their siblings of Pushpagiri Medical College Hospital formed the study subjects (n=52). Subjects in the MetS group were selected using the 2009 IDF criteria, and apparently healthy, age and sex matched subjects without MetS were selected as the Control group. According to the revised IDF criteria for Asian populations, in addition to the other criteria in the original IDF definition, WC ≥ 90 cm in men and 80 cm in women are considered as diagnostic of MetS. As per the above criteria, 22 subjects were included in the MetS group and 30 subjects were included in the Control group. After obtaining Institutional Ethics Committee (IEC) approval, detailed clinical and anthropometric characteristics of all subjects were recorded using clinical Proforma.

Methods

After obtaining written informed consent from all the volunteering subjects, 8.0 ml of fasting venous blood was collected from each one, and the serum glucose, TG, HDL, LDL and VLDL were analyzed by using Enzymatic End-Point method in Bio Lis 24i Premium Fully Automated Biochemistry Analyzer, marketed in India by M/s. Agappe Diagnostics Ltd. Erythrocyte MDA, GSH and vitamin C were analyzed by using Kinetic method in the UV-VIS 118 Spectrophotometer of M/s. Shimadzu Inc., Japan. The results from the above investigations were compared between MetS and Control groups using One Way Anova statistics in Sigmastat 3.5 version software of M/s. Sigma-Aldrich Co., St. Louis, USA. This study was designed at a confidence limit of 95%, and hence, p values <0.05 were considered statistically significant [29].

Results:-The results of the present study are summarized in Table 1-3 & Figures 1-2. There were 53.8% men (n=28) and 46.2% women (n=24) in the MetS group, while men and women constituted 55.5% (n=20) and 44.5% (n=16) respectively, in the Control group. Based on BMI, 36% of subjects in the MetS group were normal weight (<25 kg/m^2), 46% were overweight (25-30 kg/m^2) and the remaining 18% were obese (>30 kg/m^2). The corresponding figures for the Control group were 56%, 41% and 3% respectively. Of the total men in the MetS group, 58% had WC >90 cm and 42% had WC <90 cm, but all women in the MetS group had WC >80 cm. On the contrary, all men in the Control group had WC <90cm while 90% women had WC >80 cm and the remaining 10% had <80 cm. FBG of 41% of subjects in the MetS group was ≥100mg/dl and in the remaining 59%, it was <100mg/dl. In the Control group subjects, 19% had FBG ≥100 mg/dl and 81% had <100mg/dl. In MetS group, 82% of the subjects were hypertensive (BP>130/85 mmHg) and 18% were normotensive (BP <130/85 mmHg) and the corresponding figures in the Control group were 16% and 84% respectively. In the present study, FBG showed a significant increase in subjects with MetS as compared to controls. Moreover, serum TC, TG, LDL and VLDL levels were significantly higher, while HDL levels were significantly lower in the MetS group, than that of the age and sex-matched Control group. Erythrocyte MDA was found to be higher whereas GSH and vitamin C were found to be lower in the MetS group than in the Control group. All these differences were statistically significant (p< 0.05).

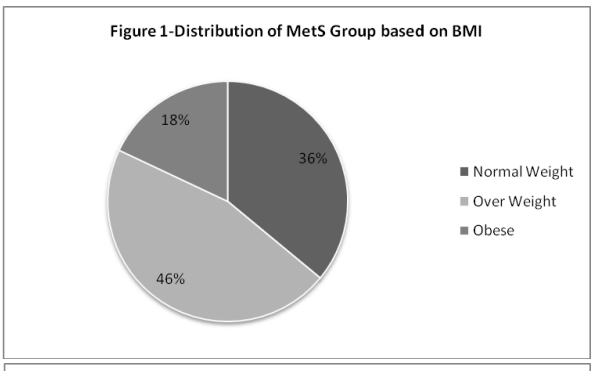
Discussion:- MetS is one of the major public health issues of this century which describes a constellation of physical conditions and metabolic abnormalities, commonly occurring together, that increases an individual's risk for development of T2DM and CVD [1-3, 10-12]. It is an undisputed fact that MetS and other cardiometabolic risk factors had a positive correlation with central obesity, and the overall abdominal adiposity is a strong and independent risk factor for T2DM and MetS [13-15]. Abdominal obesity is reported to be associated with metabolic abnormalities and increased risk of CVD [16-20]. Several authors reported that all cardiometabolic risk factors had a positive correlation with increasing waist, and the overall abdominal adiposity is a strong and independent risk factor for T2DM and MetS [13, 14]. BMI and WC are widely accepted as the anthropometric indices of obesity [13, 14]. In the present study majority of the subjects with MetS had elevated measurements of WC and BMI which is in agreement with the previous studies [13-15]. Studies unequivocally showed that serum TG, LDL and VLDL are elevated while HDL is decreased in persons with MetS [16-18]. Obesity, an invariable component of MetS, itself has been reported to reduce HDL levels and obese patients with MetS almost always have low HDL levels [16-19]. The observation in the present study of elevations in TG, LDL and VLDL and decrease in HDL levels in patients with MetS is consistent with previous reports [16-20].

OS is involved in the pathophysiology of diabetes and cardiovascular complications of MetS [21, 22]. Four of the five criteria of MetS defined in NCEP-ATP III, namely, hypertriglyceridemia, hypertension, hyper-glycemia and abdominal obesity are independently associated with elevated systemic OS [21-24]. Moreover, several studies showed that there is a significant decline in the levels of vitamin C and GSH in T2DM patients as compared to controls [21-25]. In the present study, MDA levels were found to be elevated while vitamin C and GSH levels were decreased in MetS patients as compared to the age and sex-matched controls, which is concordant with reports previous studies [21-25].

Conclusions:- Anthropometric measurements including BMI and WC were increased in MetS patients as compared to controls. FBG, TC, LDL, VLDL & TG were significantly higher in MetS patients than that of age & sex matched controls. HDL was significantly lower than the control group.The oxidative stress as assessed by erythrocyte MDA was significantly higher, whereas GSH and ascorbic acid were lower in MetS patients than that of age & sex matched controls.

Ethical approval: "All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

Informed consent: "Informed consent was obtained from all individual participants included in the study."



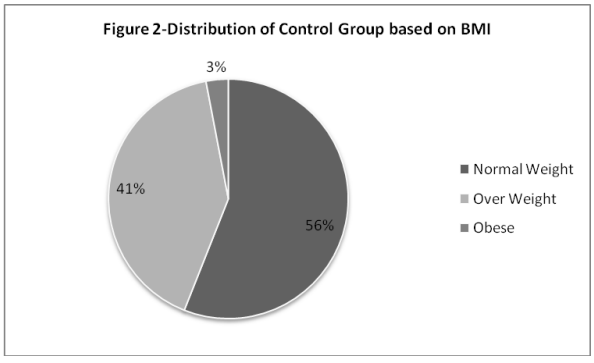


Table 1-Gender and Age-wise distribution of the Control and MetS group subjects

Control group (n= 36)				MetS group (n=52)			
Men (n= 20)		Women (n=16)		Men (n= 28)		Women (n=24)	
31-45 yrs.	46-60 yrs.	31-45 nyrs.	46-60 yrs.	31-45 yrs.	46-60yrs.	31-45 yrs.	46-60 yrs.
n= 11 (55%)	n= 9 (45%)	n= 6 (37.5%)	n= 10 (62.5%)	n= 15 (53.6%)	n= 13 (46.4%)	n= 11 (45.8%)	n= 13 (54.2%)

Table 2-Incidence of the major symptoms in MetS subjects

MetS group (n= 52)		IGT	BP	Obesity	2 or more
Men (n= 28)	31-45 yrs. (n= 15)	n= 4 (26.7%)	n= 5 (33.3%)	n= 2 (13.3%)	n= 4 (26.7%)
	46-60 yrs. (n= 13)	n= 4 (30.8%)	n= 4 (30.8%)	n= 2 (15.4%)	n= 3 (23.0%)
Women (n= 24)	31-45 yrs. (n= 11)	n= 4 (36.4%)	n= 2 (18.2%)	n= 2 (18.2%)	n= 3 (27.2%)
	46-60 yrs. (n= 13)	n= 5 (38.6%)	n= 3 (23.0%)	n= 2 (15.4%)	n= 3 (23.0%)

Table-3:- One Way Anova Statistics of the anthropometric, diabetogenic, atherogenic & pro-oxidant markers of MetS patients and their age & sex-matched Control subjects. All values are Mean SD.

Parameter (Units)	Groups of the Study Population						
	Gender	31-45 Years			46-60 Years		
		Control	MetS	p-value	Control	MetS	p-value
BMI (kg/m^2)	Men	21.52 2.71	25.62 3.16	<0.001	22.15 1.67	27.83 4.05	<0.001
	Women	20.46 2.62	24.78 2.97	<0.001	21.74 1.82	26.61 3.94	<0.001
WC (cm)	Men	83.77 3.26	96.73 4.21	<0.001	85.98 3.84	99.73 6.88	<0.001
	Women	75.68 2.23	85.56 3.43	<0.001	77.27 2.45	90.85 6.23	<0.001
FBG (mg/dl)	Men	85.22 ± 6.34	96.26 10.87	<0.001	89.75 ± 8.76	108.73 21.92	<0.001
	Women	84.46 ± 6.15	94.74 10.23	<0.001	88.63 ± 8.14	104.02 20.77	<0.001
TC (mg/dl)	Men	167.38 12.85	208.76 16.34	<0.001	172.45 14.52	212.74 18.43	<0.001
	Women	165.38 11.76	201.96 15.84	<0.001	171.71 14.13	210.84 17.67	<0.001
TG (mg/dl)	Men	91.85 10.51	136.47 15.73	<0.001	101.75 13.96	148.63 17.84	<0.001
	Women	90.77 10.22	138.95 15.84	<0.001	100.93 13.67	151.65 16.26	<0.001
HDL-C (mg/dl)	Men	48.95 7.86	35.24 4.51	<0.001	47.75 6.663	33.72 3.98	<0.001
	Women	56.71 5.14	47.66 5.63	<0.001	55.64 5.02	46.37 5.28	<0.001
LDL-C (mg/dl)	Men	106.58 28.79	158.75 42.33	<0.001	113.64 30.55	159.98 22.30	<0.001
	Women	103.91 27.54	156.62 41.17	<0.001	110.98 30.06	145.88 22.31	<0.001
VLDL-C (mg/dl)	Men	17.23 4.87	23.75 10.36	<0.001	18.87 5.21	27.27 12.85	<0.001
	Women	16.98 4.23	22.08 10.11	<0.001	18.14 5.02	25.96 12.04	<0.001
MDA (µmol/ml)	Men	0.81 0.47	1.74 0.51	<0.001	0.98 0.53	2.18 0.62	<0.001
	Women	0.72 0.36	1.68 0.43	<0.001	0.92 0.46	1.97 0.59	<0.001
Ascorbic acid (mg/dl)	Men	0.49 0.07	0.37 0.11	<0.001	0.45 0.07	0.35 0.13	<0.001
	Women	0.48 0.05	0.40 0.09	<0.001	0.45 0.06	0.37 0.08	<0.001
GSH (mg/dl)	Men	10.74 4.13	9.26 3.27	<0.001	9.66 3.83	8.58 3.14	<0.001
	Women	11.18 4.22	9.73 3.12	<0.001	10.09 3.78	9.11 3.24	<0.001

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