Original Research Article

The role of bio-chemic and metabolic risk factors of different gender in the development of severity of Metabolic Syndrome

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Received: 25-10-2021 / Revised: 16-11-2021 / Accepted: 28-12-2021

Abstract

Background: Obesity and IR reported as risk factors, and "an alarm to the CAD" in adults, even before the beginning of T2 DM. **Objectives**: To compare specific biochemical parameters, like fasting blood glucose, glycated hemoglobin, free insulin, insulin resistance, triglycerides, and high-density lipoprotein cholesterol in metabolic syndrome and severe metabolic syndrome of male and female. **Materials & methods:** The study conducted among 450 participants. Samples were analyzed for FBS using by a fully automated analyzer, HbA1c assessed by HPLC. Free Insulin was assessed by using an ELISA. HOMA-IR was a calculated value. Triglycerides was assessed by glycerol phosphate oxidase-peroxidase method, and HDL-Ch estimated by a colorimetric method. The data was analyzed by ANOVA with Student-Newman-Keul's multiple comparisons method. **Results:** A high significant difference (P =<0.001) was observed FBS, HbA1c, HOMA-IR, TG in males and females with control group vs MS and SMS groups, and when compared control with MS and SMS groups of HDL in males. The FI was not significant value when compared groups control vs MS in males and females, and HDL in females. Further, a highly significant value (P =<0.001) found compared with group MS vs SMS in the male and female, except (P =0.267) HDL in males. **Conclusion:** The diabetic parameters and lipid variables were highly significant in MS and SMS in both the gender. And all these parameters showed significance in intergroup analyses of MS and SMS in male and female groups, but insignificant HDL in males.

Keywords: Gender, Diabetic Mellitus, Dyslipidemia, Metabolic Syndrome & Severe MS.

Introduction

Metabolic syndrome (MS) is expressed as the grouping of diseases having three or more groups of interrelated factors like central adiposity or higher waist circumference, high values of triglycerides, elevated blood pressure (BP), impaired fasting glucose and lipid profile[1]. Obesity and insulin resistance are reported as risk factors, and "an alarm to the CAD" in adults, even before the beginning of T2 DM[2]. The global interest in MS is due to its impending relationship with T2 DM and cardiovascular complications. Insulin sensitivity, glucose tolerance, BP, distribution of body fat mass, and serum lipids were network of mutual functions and factors for CAD[3]. Kohnert demonstrated that HbA1c has a high significance with the hyperglycemia and fasting glucose[4]. So HbA1c was not depended on postprandial glucose (PPG), standardized meal test (MMT), duration of hyperglycemia, and standard deviation or mean amplitude of glycemic excursions (MAGE).

Cook [5] reported that prevalence of MS in adolescents aged between 12 to 19 years of average age was 4.2%, and in that, 6.1% were males and 2.1% females. In the aged between 20 to 29 years, an estimated incidence of MS was 7% were male and 6 % female.

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The prevalence was highest in the West and Middle specifically the Midwest, and Northeast was lowest by region of the Mexico. The impact of various risk factors on MS was differed among gender in several countries. A survey in Germany revealed, 40% of the adult population was diagnosed with impaired glucose tolerance (IGT) and T2 DM. Globally, individuals with IGT, IFG were observed common in men, whereas IGT was more in women. Lipid build up pattern was different in women and men[6]. Studies showed occurrence of MS was high in women, particularly in young women, during the last decade.

Environmental, genetic and metabolic aspects signify that the multidimensional interface of etiology was identified in MS individuals[7,8]. MS was a major risk factor for T2 DM and further, leads to MI, CVA, prothrombotic and proinflammatory condition[9-11]. A significant association with MS and adiposity, hyperinsulinemia, HOMA-IR, hypertriglyceridemia, and low HDL cholesterol, and elevated high sensitivity C-reactive protein (hs-CRP) levels was revealed in 2002[12,13].

Dyslipidemia was a major risk factor in macrovascular diseases like CAD, MI, and CVA. Elevated triglycerides (TG) and reduced HDL commonly observed in CKD due to decreased lipoprotein activity[14,15]. Reduced HDL cholesterol was a greater risk for CAD and MI[16]. Epidemic of MS increased in different regions of the world, specifically in South Asia, especially in India[17-19]. Among older age group, gender, obesity, hypercholesterolemia, inadequate fruit intake, and socioeconomic status contributed to MS in the urban Eastern India[5]. A Study reported that fasting blood glucose, triglycerides, HDL, insulin resistance (HOMA-IR), glycated hemoglobin (HbA1c), and free insulin (FI) showed significant difference with MS and SMS groups[20]. Innes et al, in 2005, reported that MS was associated with insulin resistance (IR), cardiovascular disease, and yoga controls MS[21].

In the present study apart from analyzing the significance of biochemical variables of metabolic risk factors such as FBS, HbA1c, FI and HOMA-IR, TG, and HDL with MS, and severity of MS, it is extended to find the influence of gender in the severity of MS.

Materials and methods

Participants

A total number of 450 participants (211 men and 239 women) aged ≥35 years attending Katuri Medical College and Hospital are included in this study. The study conducted among 450 participants by dividing them into three groups (150 participants in each group), according to the number of components of MS risk factors. Group I: Individuals with two or less than two components of metabolic syndrome (Control group); Group II: Individuals with any three elements of metabolic syndrome (MS group); Group III: Individuals with more than three risk factors of metabolic syndrome (SMS group). All the participated individuals in the study gave informed consent. The study protocol is approved by the IHEC of SIMATS (005/06/2014/IEC/SU; Dated 24th June 2014).

The inclusion and exclusion criteria

Insulin resistance, hypertension, type 2 diabetes mellitus, increased BMI (≥ 23), increased waist circumference (of ≥36 inches: 90cm in males and ≥32 inches: 80 cm in females), of age ≥35 years were included. Exclusion criteria were if any recent infections, fatty liver disease, and polycystic ovarian syndrome in women.

Methodology

As per the guidelines given by international organizations in 2009, MS was defined as a combined statement of International Diabetes Federation with the grouping of three or more of the following five criteria [22]: 1) Waist circumference in South Asians >90 cm in men and >80 cm in women, 2) Serum triglycerides levels >150 mg/dL, 3) Serum HDL cholesterol levels < 40 mg/dL in men and < 50 mg/dL in women, under treatment is an alternate indicator, 4) Systolic blood pressure >130 mmHg or diastolic blood pressure >85 mmHg) under treatment is an alternate indicator, and 5) Fasting serum glucose levels >100 mg/dL under treatment. The same standard was also stated in the modified NECP ATP III definition [23].

Biochemical analysis

Five mL of venous blood obtained from the individuals in fasting condition and centrifuged at 2000×g for 10 min. Samples were analyzed for fasting blood glucose using by ERBA EM-360, a fully automated analyzer, HbA1c assessed by high-performance liquid chromatography (HPLC). Free Insulin was assessed by using an enzyme-linked immunosorbent assay (ELISA) (Diametra, Spello, Italy). Insulin resistance was calculated HOMA- IR (μmol/L) = FI mIU/L x FPG (mmol/L)/ 22.5. Triglycerides were assessed by glycerol phosphate oxidase-peroxidase method, and HDL cholesterol estimated by a colorimetric method.

Statistical analysis

Data was entered in Excel sheet and imported for statistical analysis and graph plotting was carried out, using SigmaPlot 13.0 (Systat Software, USA). The data was analyzed by one-way analysis of variance (ANOVA) with Student-Newman-Keul's multiple comparisons method. Statistical significance was considered if the P-value is less than 0.05.

Results

As per the first objective of the present study, the parameters of three groups were compared. The result of diabetes mellitus parameters, fasting blood sugar (FBS; mg/dL), glycated hemoglobin (HbA1c; %), free Insulin (FI; mU/L), Insulin resistance (HOMA-IR; μmol/L), and lipid variables, triglycerides (TG; mg/dL) and high-density lipoprotein (HDL; mg/dL) levels in the different MS groups in males and females were shown in Table 1. Statistical analysis of mean FBS levels were significantly higher (P<0.001) in MS (133.9 ± 6.7) and severe MS groups (152.1 ± 6.9) than that of the control group (82.8 ± 1.2 mg/dL) in male. Same as in the case of female also, the mean FBS levels were significantly higher (P<0.001) in MS group (110.7 ± 5.6) and SMS groups (165.0 ± 6.6) than that of the control group (79.5 ± 1.8) in a female. Further, Figure. 1 showed that the value of FBS found significant in the intergroup analysis done between I and II; I and III, also II and III, in both genders.

Table. 1: Comparison of FBS, HbA1c, FI), HOMA-IR, TG, and HDL in male and female participants in Control, MS and SMS.

Variable	Gender	Control Group I	MS Group II	SMS Group III	Statistical information
FBS (mg/dL)	Male	82.8 ± 1.2	133.9 ± 6.7	152.1 ± 6.9	(P<0.001)
	Female	79.5 ± 1.8	110.7 ± 5.6	165.0 ± 6.6	(P<0.001)
HbA1c (%)	Male	5.9 ± 0.1	6.2 ± 0.1	6.8 ± 0.1	(P<0.001)
	Female	5.9 ± 0.1	6.7 ± 0.1	7.9 ± 0.2	(P<0.001)
F I (mU/L)	Male	8.9 ± 0.6	9.5 ± 0.6	12.7 ± 1.0	(P<0.001)
	Female	9.0 ± 0.4	9.7 ± 0.7	13.4 ± 0.7	(P<0.001)
HOMA-IR (μmol/L)	Male	2.1 ± 0.2	3.7 ± 0.3	4.8 ± 0.5	(P<0.001)
	Female	1.7 ± 0.1	2.9 ± 0.3	5.8 ± 0.4	(P<0.001)
TG (mg/dL)	Male	128.0 ± 5.1	213.2 ± 7.8	307.1 ± 12.0	(P<0.001)
	Female	133.0 ± 5.1	158.0 ± 5.6	240.9 ± 9.6	(P<0.001)
HDL (mg/dL)	Male	44.6 ± 0.4	42.4 ± 0.2	41.9 ± 0.2	(P<0.001)
	Female	45.8 ± 0.6	45.0 ± 0.2	43.7 ± 0.2	(P<0.001)

Values expressed as mean ± SE. (Male control n= 72, MS n= 75 and SMS n= 64; Female control n= 78, MS= 75 and SMS = 86 respectively)

Similarly, HbA1c values were significantly higher (P<0.001) in MS (6.2 ± 0.1) and SMS groups (6.8 ± 0.1) than that of the control group (5.9 ± 0.1) in males. Mean HbA1c values were also significantly high (P<0.001) in MS (6.7 ± 0.1) and SMS groups (7.9 ± 0.2) than that of the control group (5.9 ± 0.1) in females. The statistical analysis of these values showed a significantly (P<0.001) higher values in both MS groups than that of the control group in both genders. Added, in Figure.1 the intergroup analysis of genders showed that the value of HbA1c was highly significant in I and II (P<0.001) in male and I vs. III in female, but in the case of I vs. III it was significant (P = 0.005) only in the male. It was highly significant among groups II and III in males and females.

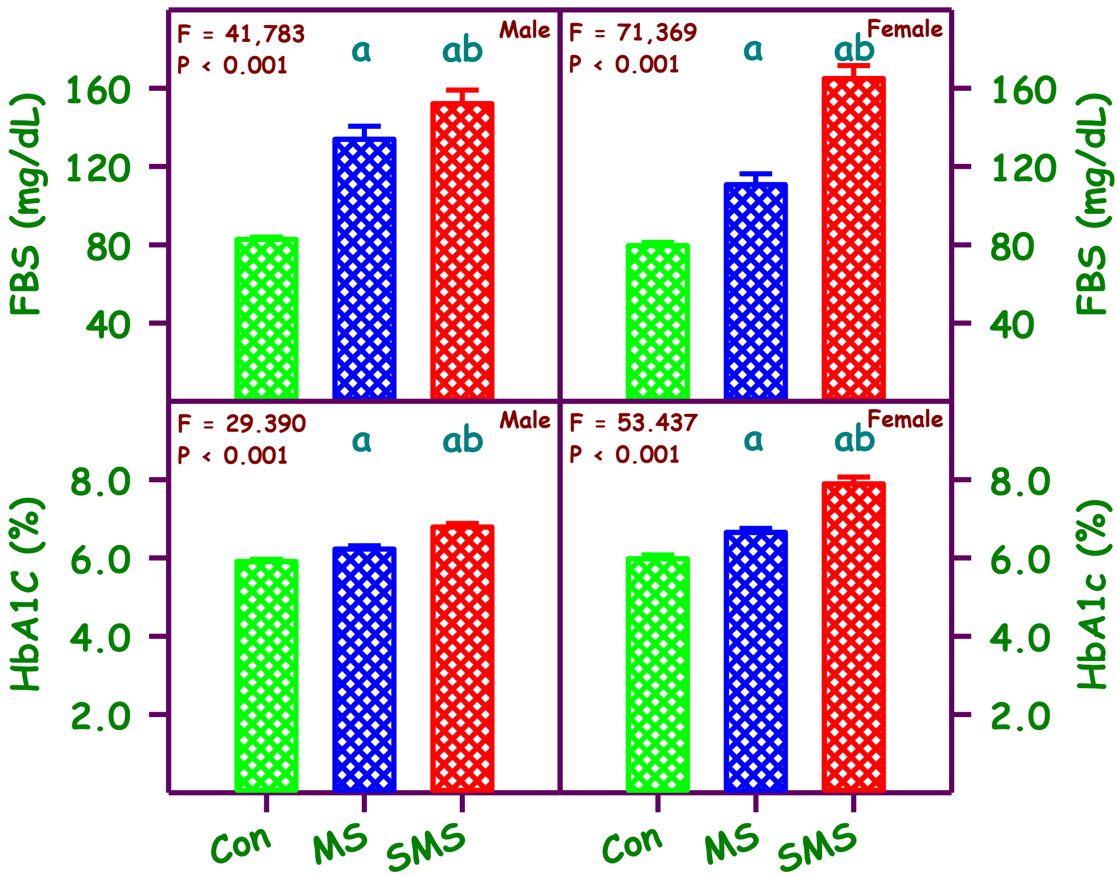

Figure. 1: The levels of FBS, HbA1C in control, MS and SMS of males and females. Values are mean ± SE. n – male – Con = 72; MS = 75; SMS = 64, and n –female – Con = 78; MS = 75; SMS = 86. The 'F' and 'P' values are by one-way ANOVA with Student Newman Keul's multiple comparison test.
[a] Significantly different from control group, [b] Significantly different from MS group

The result of T2 DM parameters, FI and HOMA- IR levels in the different MS groups were given in Table 1. Statistical analysis of mean FI levels were significantly higher (P<0.001) in MS group (9.5 ± 0.6) and SMS groups (12.7 ± 1.0) than that of the control group (8.9 ± 0.6 mU/L) in male. In the same way, the mean FI levels were significantly higher (P<0.001) in MS group (9.7 ± 0.7) and SMS groups (13.4 ± 0.7) than that of the control group (9.0 ± 0.4) in female. In addition, in Figure. 2, the value of FI observed highly significant (P<0.001) when the intergroup comparison of groups I vs. III. But in groups I and II of both genders, the intergroup comparison of FI was not significant (P = 0.559) in males and (P = 0.470) females. Among groups II and III, it was highly significant in both males and females (P<0.001).

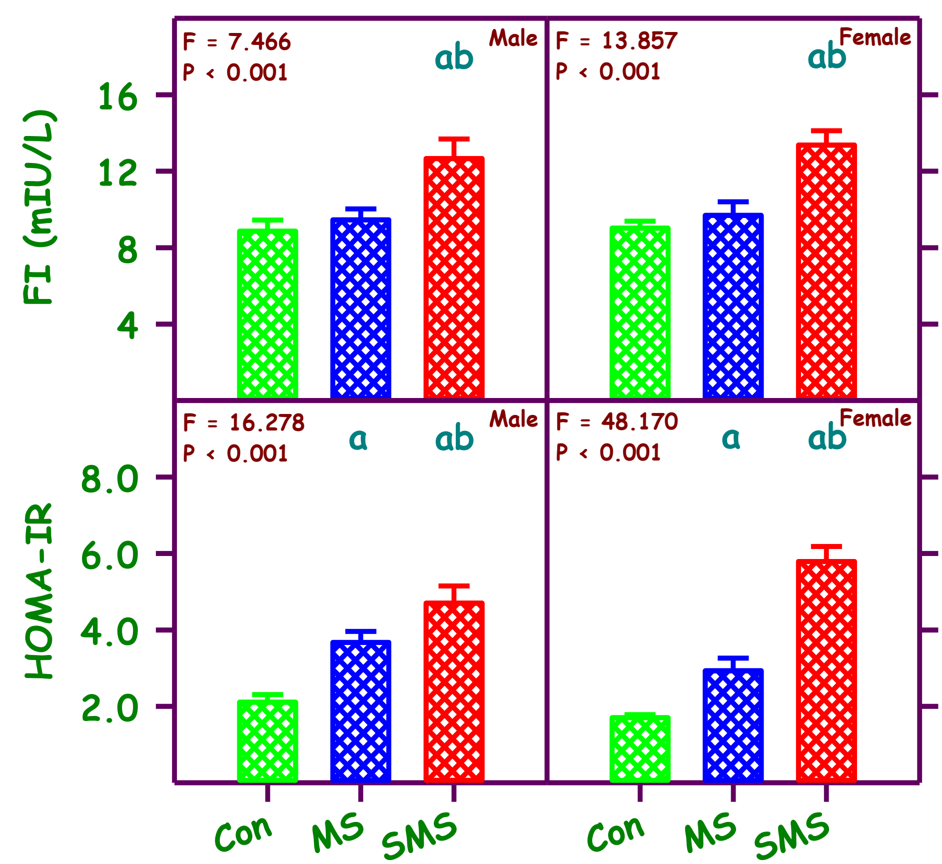

Figure. 2: The levels of FI and HOMA-IR in Control, MS and SMS of males and females. Values are mean ± SE; n – male – Con = 72; MS = 75; SMS = 64 and n – female – Con = 78; MS = 75; SMS = 86. The 'F' and 'P' values are by one-way ANOVA with Student Newman Keul's multiple comparison test.
[a] Significantly different from control group, [b] Significantly different from MS group

The HOMA- IR values were significantly higher (P<0.001) in MS group (3.7 ± 0.3) and SMS groups (4.8 ± 0.5) than that of the control group (2.1 ± 0.2) in males. Same as in the females mean HOMA- IR values were significantly high (P<0.001) between MS (3.7 ± 0.3) and SMS groups (4.8 ± 0.5) compared to that of the control group (2.1 ± 0.2). Further, in Figure. 2 observed that the values of HOMA- IR were with a significant difference in both genders in all the groups (I vs. II; I vs. III and II vs. III), included the intergroup analysis.

The result of biochemical as well as dyslipidemia parameters, TG in different MS groups were also given in Table 1. Statistical analysis showed that the mean TG levels were significantly higher (P<0.001) in MS group (213.2 ± 7.8) and SMS groups (307.1 ± 12.0) than that of the control group (128.0 ± 5.1 mg/dL) in male. In the same way, the mean TG levels were significantly high (P<0.001) in MS group (158.0 ± 5.6) and SMS groups (240.9 ± 9.6) than the control group (133.0 ± 5.1) in the female. In addition, as in Figure .3 observed that the value of MS risk parameter TG was found significant in an intergroup comparison between all the three groups (I vs. II; I vs. III and II vs. III) in male and female participants.

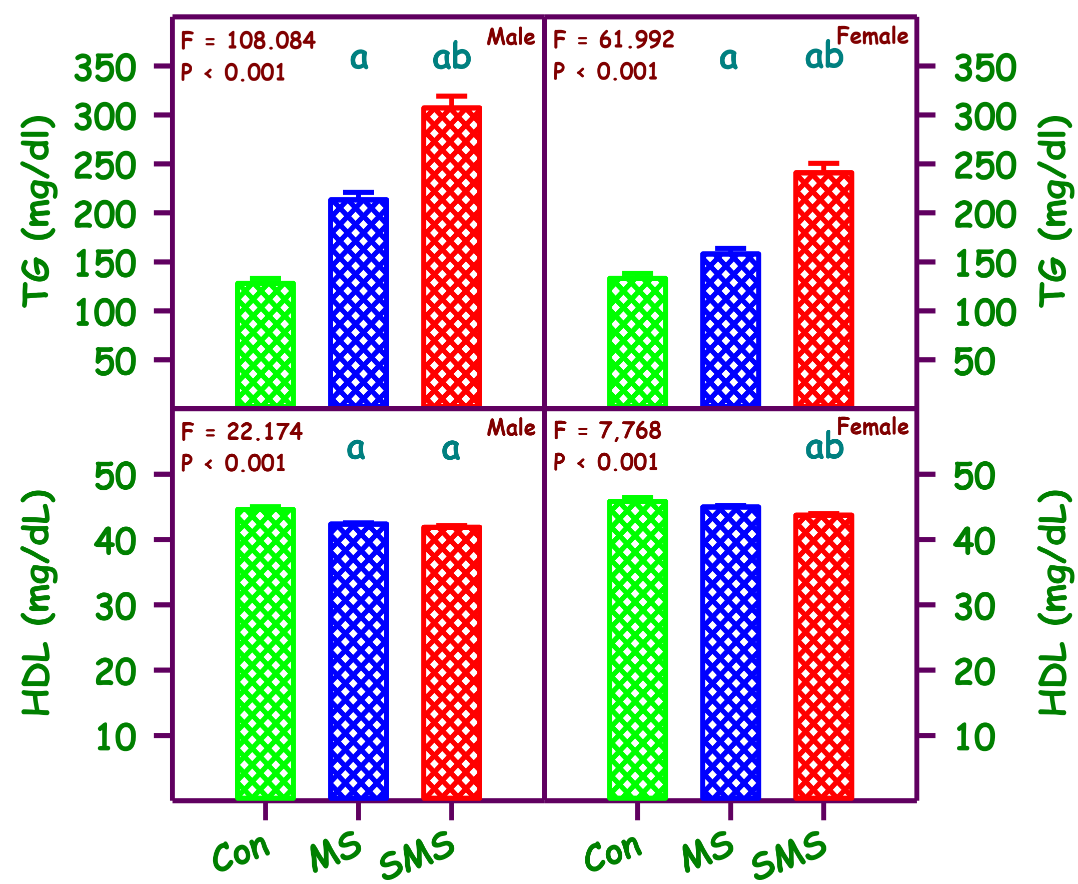

Figure. 3: The levels of TG, HDL in control, MS and, SMS of males and females. Values are mean ± SE. n – male – Con = 72; MS = 75; SMS = 64 and n – female – Con = 78; MS = 75; SMS = 86. The 'F' and 'P' values are by one-way ANOVA with Student Newman Keul's multiple comparison test.
[a] Significantly different from control group and [b] Significantly different from MS group

A similar analysis of HDL also showed (Table. 1) that HDL values were significantly high (P<0.001) in MS group (42.4 ± 0.2) and SMS groups (41.9 ± 0.2) than that of the control group (44.6 ± 0.4) in males. In the female group, mean HDL values with MS were higher (45.0 ± 0.2) than the SMS group (43.7 ± 0.2), which was significantly elevated (P<0.001) compared to the control group (45.8 ± 0.6). Further, in Figure. 3, a highly significant (P<0.001) difference observed in the comparison of HDL values in between I vs. II and I vs. III groups in the males, and the groups I and III in females. It was not significant within I and II groups (P = 0.118) in the female. And was a significant difference among groups II and III in the female, but not significant in groups II vs. III (P = 0.267) in male.

Discussion

The result of the present study showed that a significant difference among three groups of FBS in males and females and was similar the report of an earlier study[24,25]. FBS slightly acclimatized by intensive lifestyle (ILS) changes and appeared as an important factor in the development of T2 DM in men than women. Greater success with the ILS reduced incidence of T2 DM in men versus women, in part because of the higher baseline risk factors, especially FBS concentration, in men in the diabetes prevention program[26]. So, the lifestyle changes help to control the FBS in both men, and women, thus prevent development of SMS from MS individuals. And the FBS becomes under control and complications in treated cases of T2 DM also reduced by these ILS changes.

Present study revealed that, HbA1c levels were significantly differed among MS groups. Similar results were reported with a significant difference in FBS and HbA1c values in severe MS, when compared with that of MS and control group[24,25]. However, this association existed even in nondiabetics with increasing HbA1c levels. Evidence showed that fatty liver by alterations in hepatic insulin signaling pathway was independent risk factor for muscle and adipose tissue IR, caused due to insulin sensitivity[27].

In the present study, observations were made that the FI levels significantly differed in MS and SMS groups in both genders. Similar results were reported[20,24]. Insulin increases renal tubular reabsorption of sodium, and water increased in the kidney. Further, the blood volume increases which in-turn elevates BP[28]. IR accompanied by hyperinsulinemia that increases PAI-1 in turn increased platelet aggregation and endothelin-1[29,30]. Hence, the FI levels must be maintained with in normal limits in both treated and untreated cases that helps to control BP and endothelial alterations, that decreases CVD.

In this study, a significant difference was observed in HOMA- IR among the groups also in males and females. Table. 1 (Figure. 2) HOMA-IR showed high significance between all groups, in both genders ($P<0.001$). Various studies supported the results of this study, same as Moran[31] reported that the IR was raised with decreased HDL in MS in adolescence males. The physique was different in gender due to sex hormones, and female had a fortunate effect on insulin sensitivity, and higher adiposity when compared with male. As the study also reports that estrogen levels play a major role in the insulin sensitivity and insulin resistance[32]. The present study supports that IR is one of the principal factors for the development of MS. Further, the increase in IR level proportionately increases MS risk and severity of MS. Also, a significant effect was observed in IR with MS and severe MS in both male and female. Thus, this study indicates diabetic variables may be one of the causative factors of MS and SMS in both male and female. The HOMA-IR is reduced by increasing HDL in MS by controlling BMI and WC of male and female, by taking omega 3 fatty acids, and unsaturated fatty acids. Especially in menopausal women due to lack of estrogen on management aspect insulin resistance is controlled by advising certain foods.

Lipid profile was analyzed to assess dyslipidemia, which is one of the components of MS. In this study, the result of lipid parameter TG was observed a significant difference in male and female participants. The increase in the TG level was equivalent to the development of severe MS, it supports the study of Bhagyashree[20]. A similar observation narrated by Cook on his survey[5]. It was reported that an increase in TG and the decrease in HDL cholesterol with MS, parallel to the results of the present study. The TG cholesterol showed a significant rise among all the groups in both genders.

In the present study, the value of HDL showed a proportionate decrease in the severity of MS, and the TG levels recorded in MS and severe MS significantly increased than the control. On the other hand, the decreased HDL cholesterol obtained in severe MS remained lower than the control group but did not show any significant difference[33]. Dyslipidemia is also one of the parameter results in MS and SMS in both genders. To control triglycerides by maintaining the BMI according to the south Asian standards, and WC in both male and female by doing productive work, and regular habit of physical exercises. And maintain the intake of food calories must be lesser than the working calories in a day/week.

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Conflict of Interest: Nil
Source of support:Nil