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Case Series: Multiple Risk Factors Related Metabolic Syndrome

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Case Report

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Abstract: Indians have a high prevalence of Metabolic Syndrome (MetS) which carries multiple risk factors. Since a scarce information is available about the magnitude of Metabolic Syndrome amongst the geriatric population in India. Present case was taken up to ascertain the risk factors and management MetS. In this cases hypertension, T2DM, insulin resistance, obesity, dyslipidemia, IHD, low sedentary life style activities, and non-adherence to the medications are the major contributing risk factors for MetS and it was managed by the effective therapeutic regimens, supportive therapy and counselled the patient about disease condition, medications usage, and life style modifications to overcome or control the MetS.

Keywords: Metabolic syndrome, insulin resistance, non-adherence, hypertension, type-2 Diabetes mellitus.

INTRODUCTION

Metabolic syndrome (MetS) represents a cluster of related metabolic abnormalities, including hypertension, abnormal glucose tolerance, type 2 diabetes, dyslipidemia (increasedplasma triacylglycerol, decreased high density lipoproteins, and smaller, denser low density lipoproteins), coronary artery disease (CAD), and obesity, are all linked to insulin resistance and have been collectively termed also as syndrome X [1,2]. Abnormalities of fibrinolysis and hyperuricemia also appear to be members of the cluster of maladies comprising syndrome X [2]. Recent research studies show that the deficiency of vitamin D causes MetS, diabetes mellitus, heart failure, stroke, cancer, polycystic ovary syndrome, gout, and asthma and coronaryartery disorders [3]. MetSaffects all age groups. Not only age but stress is also one of the sources for metabolic syndromes and sedentary lifestyle also leads to metabolic syndrome [4].

The pathogenesis of MetS and its components is not well understood, central obesity and insulin resistance are recognized as causative factors. Several different organizations have outlined diagnostic criteria for MetS, which designates values for obesity (waist circumference or BMI), triglyceride levels, HDL (High Density Lipoprotein) levels, hypertension, hyperglycemia, and sometimes urine albumin or albumin: creatinine ratio (Table1) [5]. A panel of MetS biomarkers could provide a relatively easy, minimally-invasive means of identifying those who are at risk for developing MetS and subsequent complications. Furthermore, many of these biomarkers are interrelated in how they play a role in MetS, so correlations between biomarkers would be helpful to assess patients. Accumulation of adipocytes leads to the dysregulated production of adipokines, which contributes to the development of Met [6]. The mechanism by which adipose accumulation elucidates dysregulation is not entirely clear at this time, but some suggest that it is at least partly due to systemic oxidative stress brought on by obesity [7]. Obesity produces oxidative stress is mitochondrial and peroxisomal oxidation of fatty acids, which can generate reactive oxygen species (ROS) in oxidation reactions. Malondialdehyde (MDA), a lipid peroxidation end product, is increased in conditions marked by obesity and insulin resistance. It is able to enhance expression of pro-inflammatory cytokines, resulting in systemic stres [8]. Leptin's role as a biomarker for MetS has been researched in different populations. Regardless of which demographic studied, elevated leptin levels are associated with MetS. This is not surprising given that elevated leptin is associated with obesity, insulin resistance, myocardial infarction, and congestive heart failure [9]. MetSis associated with lower levels of ghrelin, and progressively lower ghrelin levels are associated with increasing MetS severity. Ghrelin levels decrease with increasing number of MetS

derangements [10-13]. Leptin: adiponectin ratio (LAR), Plasminogen Activator Inhibitor-1 (PAI-1), uric acid, Interleukin-6 (IL-6), Tumor Necrosis Factor-Alpha (TNF-α), and Oxidized LDL (OxLDL) have all been shown to be elevated in MetS, across different populations andgenerally are correlated with the number of components of MetS present. On the other hand, adiponectin, ghrelin, Interleukin-10 (IL-10), and PON-1 have all been shown to be decreased in MetS. Some ratios, such as HMW- adiponectin: adiponectin and LAR are better predictors than any alone. To date, there is no established panel to test for MetS, but this review has compiled a panel of the best candidates. [14].

Table-1: Diagnostic Criteria for Metabolic Syndrome

	IDF (Obesity + ≥2)	AHA (≥3)	NCEP ATP III (≥3)	WHO (Insulin resistance/Dia-betes + ≥2)	EGIR (hyperinsuline-mia + ≥2)
Obesity	BMI >30kg/m^2 or specific gender and ethnicity waist circumference cutoffs	Waist circumference for males > 40 in females >35 in	Waist circumference for males >40in, females >35in	Waist/hip ratio >0.9 in males and >0.85 in females or BMI >30kg/m^2	Waist circumference for males ≥ 94cm, females ≥80cm
Elevated Triglycerides	TG≥150mg/dL or treatment of this lipid abnormality	Fasting TG≥150 mg/dL or treatment of this lipid abnormality	TG≥150mg/dL or treatment of this lipid abnormality	TG≥150mg/dL	TG≥177mg/dL
Decreased HDL	HDL <40mg/dL in males and <50mg/dL in females or specific treatment for this lipid abnormality	HDL<40mg/dL in males and <50mg/dL in females or treatment for this lipid abnormality	HDL<40mg/dL in males and <50mg/dL in females or treatment for this lipid abnormality	HDL<35mg/dL in males and <39mg/dL in females	HDL< 39 mg/dL
Hypertension	SBP ≥130 or DBP ≥85 mm Hg or treatment of previously diagnosed hypertension	BP>130/85 mmHg or taking medication for hypertension	SBP ≥130 or DBP ≥85 mm Hg or taking medication for hypertension	≥140/90mm Hg	≥140/90mm Hg or taking medication for hypertension
Hyperglycemia	Fasting plasma glucose >100mg/dL or previously diagnosed type 2 diabetes	Fasting glucose >100mg/dL or taking medicine for high glucose	Fasting glucose >100mg/dL or taking medicine for high glucose	Insulin resistance required	Insulin resistance required(plasma insulin >75th percentile)
Other				Urine albumin ≥ 20µg/min or Albumin: creatinine ratio ≥ 30mg/g	

IDF- International Diabetes Federation, AHA- American Heart Association, NCEP ATP III- National Cholesterol Education Program-Adult Treatment Panel III, WHO- World Health Organization, EGIR- European Group for the Study of Insulin Resistance, BMI- Body Mass Index, SBP - Systolic Blood pressure, DBP- Diastolic Blood Pressure, BP - Blood Pressure, TG- Triglycerides, HDL-High Density Lipoprotein

CASE REPORTS

Case-1

A 62years old male patient presented with the chief complaints of fever since 8 days, body pains since 4days. Past medical history of Hypertension, type-2 Diabetes mellitus since 20years, Ischemic heart disease (IHD) since 9years and it was treated 5 years back with coronary artery stent to increase the blood flow to ischemic heart muscle. He was on treatment with Aspirin 75mg, Human insulin 20/15U, Glimipride 1mg + Metformin 500 mg BD and Metformin 500mg. On physical examination he was well built with the vitals of afebrile, blood pressure (BP) -150/90mmHg, pulse rate-85b/min and respiratory rate-20/min. Social history is Alcoholic and mixed diet.

On day-1, patient was advised for glycosylated hemoglobin (HbA_1C) levels are 9.7% indicates that the patient is suffering with uncontrolled type-2 Diabetes mellitus. Random blood sugar (RBS) found to be normal (table-2) and blood urea-55mg/dl (slightly

elevated). On day-2, Blood urea(27mg/dl) and liver function tests found to be normal.

Table-2: Day wise alteration of serum glucose levels

Days	FBS (mg/dl)	RBS(mg/dl)	
Day-1	--	--	142-7pm
Day-2	238-7am↑	244-1pm ↑	297-7pm ↑
Day-3	268-7am↑	250-1pm ↑	339-7pm ↑
Day-4	224-7am↑	230-1pm ↑	320-7pm ↑
Day-5	267-7am↑	136-1pm ↑	352-7pm ↑
Day-6	199-7am↑	122-1pm ↑	170-7pm ↑
Day-7	236-7am↑	198-1pm ↑	214-7pm ↑
Day-7	150-7am↑	214-1pm↑	228-7pm↑

On day-1 & day-2 serum electrolytes were found to be abnormal and on day-3 maintained to normal levels (table-3). Complete urine examinationshowed Urine sugar and Yeast cells positive, TSH- 2.9 µIU/ml, T_4-136.36nmol/L (increased), T_3-1.15mol/L, Prostate specific antigen 0.44ng/ml and Ultra scan of abdomen was normal.

Table-3: Day wise alteration of serum electrolyte levels

Serum electrolyte levels	Day-1	Day-3	Day-7
Sodium-121	121mEq/L↓	132 mEq/L↓	134 mEq/L
Potassium	6.1mEq/L↑	6.3 mEq/L↑	3.6 mEq/L
Chloride	89 mEq/L↓	102 mEq/L	102 mEq/L

On admission patient was treated with Cefaperazone+Salbactum 1.5g IV BD, Amikacin 250mg IV, Pantoprazole 40mg IV, Paracetamol 650mg, Human Insulin 15U SC 6th hourly, Alprazolam 0.25mg, Metformin+Sitagliptin 500/50mg, IV fluids Normal saline 1pint and Ringer lactate 1pint. Self-medications take by patient was Telmisartan+Chlorthalidone 40mg/12.5mg OD, Amlodipine+Sildinafil 5mg/5mg OD, Metformin 500mg OD, Aspirin 150mg OD, Clopidogrel 75mg OD.

On day-2 patient complained of loss of appetite, lower limbs pain and hyponatremia. FBS & RBS are found to be elevated. Blood pressure was 140/100mmHg and physician advised same medications. On day-3, patient continued to preset with hyponatremia, FBS & RBS are found to be elevated. Blood pressure was 140/100mmHg and physician advised same medications. On day-4, patient's BP was 140/90mmHg and FBS & RBS are found to be elevated. Physician added Saroglitazar 4mg and other medications were continued. On day-5, patient's BP was 160/90mmHg, developed heat exhalation, hyperkalemia, hyponatremia and acute kidney infection. Medications added are Empagliflozin 25mg OD, Furosemide+Spironolactone 20mg/50mg OD. On day-6, patient developed pain in the calf region. His BP was 160/90mmHg and all the medications were continued the same.

On discharge patient's final diagnosis was Diabetic Glomerular Necrosis and discharge medications include Paracetamol 650mg, Injection Human Insulin 15U 6th hourly, Alprazolam 0.25mg, Metformin+Sitagliptin, IV fluids Normal saline 1pint and Ringer lactate 1pint. Patient was on self-medications likeTelmisartan+Chlorthalidone 40mg OD, Amlodipine+Sildinafil 5mg/5mg, Metformin 500mg OD, Aspirin 150mg OD, Clopidogrel 175mg OD, Saroglitazar 5mg OD, Empagliflozin 25mg OD, Furosemide+Spironolactone OD.

Case-2

A 68 years old male patient presented with the chief complaints of fever since 5 days, body pains since 7 days. Past medical history of Hypertension, type-2 Diabetes mellitus since 18 years, Ischemic heart disease (IHD) since 5 years. He was on treatment with Aspirin 75mg, Human insulin 20/15U, Glimipride 1mg + Metformin 500 mg BD. On physical examination he was well built with the vitals of afebrile, blood pressure (BP) -140/90mmHg, pulse rate-80b/min and respiratory rate-21/min. Social history is Alcoholic since 15 years and mixed diet.

On day-1, patient was advised for glycosylated hemoglobin (HbA_1C) levels are 10 % indicates that the patient is suffering with uncontrolled type-2 Diabetes

mellitus. Random blood sugar (RBS) found to be normal (table-4) and blood urea- 50mg/dl (slightly elevated). On day-2, Blood urea (30mg/dl) and liver function tests found to be normal.

Table-4: Day wise alteration of serum glucose levels

Days	FBS (mg/dl)	RBS(mg/dl)	
Day-1	--	--	130-7pm
Day-2	240-7am↑	244-1pm ↑	287-7pm ↑
Day-3	258-7am↑	250-1pm ↑	339-7pm ↑
Day-4	224-7am↑	220-1pm ↑	310-7pm ↑
Day-5	257-7am↑	146-1pm ↑	342-7pm ↑
Day-6	200-7am↑	122-1pm ↑	180-7pm ↑
Day-7	236-7am↑	188-1pm ↑	214-7pm ↑
Day-7	160-7am↑	224-1pm↑	228-7pm↑

On day-1 &day-2 serum electrolytes were found to be abnormal and on day-3 maintained to normal levels (table-5). Complete urine examination showed Urine sugar and Yeast cells positive, TSH- 2.9 µIU/ml, T_4-136.36nmol/L (increased), T_3-1.15mol/L, Prostate specific antigen0.44ng/ml and Ultra scan of abdomen was normal.

Table-5: Day wise alteration of serum electrolyte levels

Serum electrolyte levels	Day-1	Day-3	Day-7
Sodium-121	123 mEq/L↓	130 mEq/L↓	134 mEq/L
Potassium	6.6 mEq/L↑	6.2 mEq/L↑	3.7 mEq/L
Chloride	89 mEq/L↓	102 mEq/L	102 mEq/L

On admission patient was treated with Cefaperazone+Salbactum 1.5g IV BD, Pantoprazole 40mg IV, Paracetamol 650mg, Human Insulin 15U SC 6th hourly, Alprazolam 0.25mg, Metformin+Sitagliptin 500/50mg, IV fluids Normal saline 1pint and Ringer lactate 1pint. Self-medications take by patient was Telmisartan+Chlorthalidone4 0mg/12.5mgOD, Amlodipine+Sildinafil5mg/5mgOD, Metformin 500mg OD, Aspirin 150mgOD, Clopidogrel 75mgOD.
On day-2 patient complained of loss of appetite, lower limbs pain and hyponatremia. FBS & RBS are found to be elevated. Blood pressure was 140/100mmHg and physician advised same medications.

On day-3, patient continued to preset with hyponatremia, FBS & RBS are found to be elevated. Blood pressure was 140/100mmHg and physician advised same medications. On day-4, patient's BP was 140/90mmHg and FBS& RBS are found to be elevated. Physician added Saroglitazar 4mg and other medications were continued. On day-5, patient's BP was 160/90mmHg, developed heat exhalation, hyperkalemia, hyponatremia and acute kidney infection. Medications added are Empagliflozin 25mg OD, Furosemide+Spironolactone 20mg/50mg OD. On day-6, patient developed pain in the calf region. His BP was 160/90mmHg and all the medications were continued the same.

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DISCUSSION

The MetS is a major and escalating public-health and clinical challenge worldwide in the wake of urbanization, surplus energy intake, increasing obesity, and sedentary life habits. MetS confers a 5-fold increase in the risk of type 2 diabetes mellitus (T2DM) and 2-fold the risk of developing cardiovascular disease (CVD) over the next 5 to 10 years. [15] Further, patients with the MetS are at 2 to 4-fold increased risk of stroke, a 3 to 4-fold increased risk of myocardial infarction (MI), and 2-fold the risk of dying from such an event compared with those without the syndrome [16] regardless of a previous history of cardiovascular events [17]. In this cases, patient with past history of IHD, obesity (BMI-32.19 kg.m^2, 33.15 kg.m^2, in case-1&2 almost hypertension since 20 years (150/90 mmHg initially, throughout the hospital stay blood pressure is not depleted/maintained to be normal and after discharge also it was elevated i.e. 160/90 mmHg), T2DM since 20 years-serum glucose levels are elevated, insulin resistance (showed minimal response to a given concentration of insulin i.e. per day patient requires 60Units of insulin and also showed minimal

effect with five oral hypoglycemicagents), serum cholesterol levels also elevated (triglycerides-190 mg/dl, LDL-170 mg/dl, HDL-30 mg/dl), and electrolyte imbalance.

Age is clearly a factor, with a prevalence of 43.5% of those aged 60-69 years compared with a prevalence of only 6.7% among those aged 29-29 years [18]. The geriatric individuals (i.e. those more than 60 years of age) accounts for 7.4% of the total population in India and is projected to rise to 12.4% by the year 2026 which may pose mounting pressures on burden on health care facilities as well as health expenditures as this segment of population faces multiple and enormous medical and psychological problems [19]. Monounsaturated fatty acids, such as olive oil and canola oil, do not impair insulin function; in contrast, saturated fatty acids reduce insulin activity even in healthy subjects [20]. Polyunsaturated fats, such as fish oil and flaxseed oil, also can play a role in the management of dyslipidemia associated with the MetS. Consumption of coldwater fish, such as salmon and tuna, which are rich in omega-3 fatty acids, will lower triglycerides and has been linked to decreased cardiovascular mortality [21]. Fish oil supplements (capsules) can decrease levels of triglycerides by up to 39% [22]. Increased soluble fiber intake also is recommended as a means to limit intestinal cholesterol absorption. Weight reduction and exercise are particularly important forms of lifestyle modification in this patient population, as both lessen insulin resistance [23, 24].

In this case, patient may have higher risk factor with age i.e. 62 years and patient was non adherence to the medications with low sedentary life style activities and alcoholic sine 20 years which are also a major risk factor. Saroglitazarisa novel dual peroxisome proliferator-activated receptor (PPAR) agonist with predominant PPAR-α and moderate –γagonism designed to optimize a lipid and glycemic benefitswith minimum effects of weight gain and edema. [25]Empagliflozin is a potent and selective sodium glucose cotransporter-2 (SGLT2) inhibitor [26] used in the treatment of T2DM. By reducing renal glucose reabsorption and so increasing urinary glucose excretion, inhibiting SGLT2 leads to a reduction in hyperglycemia in patients with T2DM. The mechanism of action of SGLT2 inhibitors is independent of β-cell function; therefore, SGLT2 inhibitors are associated with a low risk of hypoglycemia [27]. So both the medications are used in the treatment of dyslipidemia and T2DM which are the abnormal conditions of MetS. In both cases to avoid drug interactions and to decrease number of medications usage i.e. to improve the rational use of medications patient prescribed with the effective medication with two pharmacological actions like saroglitazar which is the better drug of choice in this MetS it is used in this three conditions like insulin resistance, dyslipidemia, and T2DM and also empagliflozin is the best drug of choice in insulin resistance which is not linked with beta cell function it effects on only SGLT2 which reduces the renal absorption of glucose thereby it increases the urinary glucose excretion.

CONCLUSION

However, in our cases hypertension, T2DM, insulin resistance, obesity, dyslipidemia, IHD, low sedentary life style activities, and non-adherence to the medications are the major contributing risk factors for MetS and it was managed by the effective therapeutic regimens, supportive therapy and counselled the patient about disease condition, medications usage, life style modifications to overcome or control the MetS.

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