FREQUENCY OF METABOLIC SYNDROME IN TYPE 2 DIABETES MELLITUS, SUDANESE POPULATION – WAD MEDANI-GEZIRA STATE-SUDAN- FEBRUARY 2015

Dr. Yasir A.H. Hakim1*, Dr. A. A. Abbas1, Dr. Yasir Mohamed Abdelrahim2

*1Department of Basic Medical Science, College of Medicine, Dar Al Uloom University, Riyadh, KSA.
1Department of Basic Medical Science, College of Medicine, Dar Al Uloom University, Riyadh, KSA.
2University of Gezira, Faculty of Science.

*Corresponding Author: Dr. Yasir A.H. Hakim
Department of Basic Medical Science, College of Medicine, Dar Al Uloom University, Riyadh, KSA.

ABSTRACT
Background: Metabolic syndrome is a disorder of energy utilization and storage, diagnosed by a co-occurrence of three out of five of the following medical conditions: abdominal (central) obesity, elevated blood pressure, elevated fasting plasma glucose, high serum triglycerides, and low high-density cholesterol levels. This study was to review the prevalence of the metabolic syndrome in Sudanese type 2 diabetes mellitus. Materials and Methods: The study included 80 Sudanese patients; half of them with type 2 diabetes mellitus (cases) and the rest are non-diabetics (control group). Cases and controls blood pressure, abdominal circumference and body mass index were reported. Venous blood samples were taken from all after at least 10 hours fasting for determination of serum level of cholesterol, triglycerides, high density lipoprotein and low density lipoprotein. Glucose level and HbA1c were also measured. Cases and controls were compared in all measures above looking for the differences. The metabolic syndrome was diagnosed according to criteria of national cholesterol education program. Result: In cases fasting blood glucose, waist circumference, high density lipoprotein, low density lipoprotein, triglyceride, total cholesterol, blood pressure were found to be 87.5% (35 cases), 130% (52 cases), 64.5% (28 cases), 77.5% (31 cases), 50% (20 cases), 32.5% (17 cases), 62.5% (25 cases) respectively. In control group, fasting blood glucose, waist circumference, high density lipoprotein, low density lipoprotein, triglyceride, total cholesterol, blood pressure were found to be 100% (40 cases), 150% (59 cases), 100% (40 cases), 100% (40 cases), 100% (40 cases), 100% (40 cases), 95% (cases), 100% (40 cases) respectively. Conclusion: In this study, the frequency of the metabolic syndrome was found significantly high in type 2 diabetic patients based in cases compared to non-diabetic control group. The study showed that, the metabolic syndrome was high in type 2 diabetic patients particularly in females (60%) which represent in (22 cases) plus 7 cases with no metabolic syndrome compared to males. In males, the metabolic syndrome occurred in 4 patients and with no metabolic syndrome in 7 patients out of 40% compared to normal control group. The serum level of HDL in female patients was 23(37.5%) which was less than 50 mg/dl, which was poor. The HDL level was lower in females 23(57%) than males 12 (30%) that’s indicated increased level of lipid profile and this can lead to cardiovascular and coronary artery disease as result of thermogenic dyslipidemia.

KEYWORDS: Metabolic syndrome; Diabetes mellitus; Prevalence; Sudanese.

INTRODUCTION
Metabolic syndrome is a disorder of energy utilization and storage, diagnosed by a co-occurrence of three out of five of the following medical conditions: abdominal (central) obesity, elevated blood pressure, elevated fasting plasma glucose, high serum triglycerides, and low high-density cholesterol (HDL) levels. Metabolic syndrome increases the risk of developing cardiovascular disease, particularly heart failure, and diabetes. Some studies have shown the prevalence in the USA to be an estimated 34% of the adult population and the prevalence increases with age. Metabolic syndrome is also known as metabolic syndrome X, cardiometabolic syndrome, syndrome X, insulin resistance syndrome, Reaven’s syndrome (named for Gerald Reaven), and CHAOS (in Australia). Metabolic syndrome and prediabetes appear to be the same disorder, just diagnosed by a different set of biomarkers. The principal symptom of metabolic syndrome is central obesity (also known as visceral,
male-pattern or apple-shaped adiposity), overweight with adipose tissue accumulation mainly around the waist and trunk.[4] Other signs of metabolic syndrome include:

High blood pressure, decreased fasting serum HDL cholesterol, elevated fasting serum triglyceride level (VLDL triglyceride), impaired fasting glucose, insulin resistance, or prediabetes. Associated conditions include: hyperuricemia, fatty liver (especially in concurrent obesity) progressing to NAFLD, polycystic ovarian syndrome (in women), erectile dysfunction (in men), and acanthosis nigricans.

The exact mechanisms of the complex pathways of metabolic syndrome are under investigation. The pathophysiology is very complex and has been only partially elucidated. Most patients are older, obese, sedentary, and have a degree of insulin resistance. Stress can also be a contributing factor. The most important factors are genetics,[5][6][7][8] aging, diet (particularly sugar-sweetened beverage consumption),[9] sedentary behavior[10] or low physical activity,[11][12] disrupted chronobiology/sleep,[13] mood disorders/psychotropic medication use,[14][15] and excessive alcohol use.[16] There is debate regarding whether obesity or insulin resistance is the cause of the metabolic syndrome or if they are consequences of a more far-reaching metabolic derangement.

Diabetes mellitus type 2: The metabolic syndrome quintuples the risk of type 2 diabetes mellitus. Type 2 diabetes is considered a complication of metabolic syndrome. In people with impaired glucose tolerance or impaired fasting glucose, presence of metabolic syndrome doubles the risk of developing type 2 diabetes.[17] It is likely that prediabetes and metabolic syndrome denote the same disorder, defining it by the different sets of biological markers. The presence of metabolic syndrome is associated with a higher prevalence of CVD than found in patients with type 2 diabetes or IGT without the syndrome.[25] Hypoadiponectinemia has been shown to increase insulin resistance,[18] and is considered to be a risk factor for developing metabolic syndrome.[19]

Pathophysiology: It is common for there to be a development of visceral fat, after which the adipocytes (fat cells) of the visceral fat increase plasma levels of TNFα and alter levels of a number of other substances (e.g., adiponectin, resistin, and PAI-1). TNFα has been shown not only to cause the production of inflammatory cytokines, but also possibly to trigger cell signaling by interaction with a TNFα receptor that may lead to insulin resistance.[20] An experiment with rats fed a diet with 33% sucrose has been proposed as a model for the development of metabolic syndrome. The sucrose first elevated blood levels of triglycerides, which induced visceral fat and ultimately resulted in insulin resistance.[21]

The progression from visceral fat to increased TNFα to insulin resistance has some parallels to human development of metabolic syndrome. The increase in adipose tissue also increases the number of immune cells present within, which play a role in inflammation. Chronic inflammation contributes to an increased risk of hypertension, atherosclerosis and diabetes.[22]

**Diagnosis:** A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity published a guideline to harmonize the definition of the metabolic syndrome.[23] This definition recognizes that the risk associated with a particular waist measurement will differ in different populations. Whether it is better at this time to set the level at which risk starts to increase or at which there is already substantially increased risk will be up to local decision-making groups. However, for international comparisons and to facilitate the etiology, it is critical that a commonly agreed-upon set of criteria be used worldwide, with agreed-upon cut points for different ethnic groups and sexes. There are many people in the world of mixed ethnicity, and in those cases, pragmatic decisions will have to be made. The previous definitions of the metabolic syndrome by the International Diabetes Federation[24] and the revised National Cholesterol Education Program are very similar and they identify individuals with a given set of symptoms as having metabolic syndrome. There are two differences, however: the IDF definition states that if body mass index (BMI) is greater than 30 kg/m², central obesity can be assumed, and waist circumference does not need to be measured. However, this potentially excludes any subject without increased waist circumference if BMI is less than 30. Conversely, the NCEP definition indicates that metabolic syndrome can be diagnosed based on other criteria. Also, the IDF uses geography-specific cut points for waist circumference, while NCEP uses only one set of cut points for waist circumference regardless of geography. These two definitions are much more similar than the original NCEP and WHO definitions. IDF: The International Diabetes Federation[24] consensus worldwide definition of the metabolic syndrome (2006) is: Central obesity (defined as waist circumference≥ with ethnicity-specific values) AND any two of the following.

- Raised triglycerides: > 150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality
- Reduced HDL cholesterol: < 40 mg/dL (1.03 mmol/L) in males, < 50 mg/dL (1.29 mmol/L) in females, or specific treatment for this lipid abnormality
- Raised blood pressure (BP): systolic BP > 130 or diastolic BP >85 mm Hg, or treatment of previously diagnosed hypertension
Raised fasting plasma glucose (FPG): >100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes. If FPG is >5.6 mmol/L or 100 mg/dL, an oral glucose tolerance test is strongly recommended, but is not necessary to define presence of the syndrome. If BMI is >30 kg/m², central obesity can be assumed and waist circumference does not need to be measured.

WHO: The World Health Organization 1999 criteria require the presence of any one of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

- Blood pressure: ≥ 140/90 mmHg
- Dyslipidemia: triglycerides (TG): ≥ 1.695 mmol/L and high-density lipoprotein cholesterol (HDL-C) ≤ 0.9 mmol/L (male), ≤ 1.0 mmol/L (female)
- Central obesity: waist:hip ratio > 0.90 (male); > 0.85 (female), or body mass index > 30 kg/m²
- Microalbuminuria: urinary albumin excretion ratio ≥ 20 µg/min or albumin:creatinine ratio ≥ 30 mg/g

EGIR: The European Group for the Study of Insulin Resistance (1999) requires insulin resistance defined as the top 25% of the fasting insulin values among nondiabetic individuals AND two or more of the following:

- Central obesity: waist circumference ≥ 94 cm or 37 inches (male), ≥ 80 cm or 31.5 inches (female)
- Dyslipidemia: TG ≥ 2.0 mmol/L and/or HDL-C < 1.0 mmol/L or treated for dyslipidemia
- Hypertension: blood pressure ≥ 140/90 mmHg or antihypertensive medication
- Fasting plasma glucose ≥ 6.1 mmol/L

NCEP: The US National Cholesterol Education Program Adult Treatment Panel III (2001) requires at least three of the following:

- Central obesity: waist circumference ≥ 102 cm or 40 inches (male), ≥ 88 cm or 35 inches (female)
- Dyslipidemia: TG ≥ 1.7 mmol/L (150 mg/dl)
- Dyslipidemia: HDL-C < 40 mg/dL (male), < 50 mg/dL (female)
- Blood pressure ≥ 130/85 mmHg (or treated for hypertension)
- Fasting plasma glucose ≥ 6.1 mmol/L (110 mg/dL)

American Heart Association: There is confusion as to whether, in 2004, the AHA/NHLBI intended to create another set of guidelines or simply update the NCEP ATP III definition. According to Scott Grundy, University of Texas Southwestern Medical School, Dallas, Texas, the intent was just to update the NCEP ATP III definition and not create a new definition.

- Elevated waist circumference:
  - Men — greater than 40 inches (102 cm)
  - Women — greater than 35 inches (88 cm)
- Elevated triglycerides: Equal to or greater than 150 mg/dL (1.7 mmol/L)
- Reduced HDL (“good”) cholesterol:
  - Men — Less than 40 mg/dL (1.03 mmol/L)
  - Women — Less than 50 mg/dL (1.29 mmol/L)
- Elevated blood pressure: Equal to or greater than 130/85 mm Hg or use of medication for hypertension
- Elevated fasting glucose: Equal to or greater than 100 mg/dL (5.6 mmol/L) or use of medication for hyperglycemia

MANAGEMENT
The first line treatment is change of lifestyle (e.g., Dietary Guidelines for Americans and physical activity). However, if in three to six months of efforts at remediying risk factors prove insufficient, and then drug treatment is frequently required. Generally, the individual disorders that compose the metabolic syndrome are treated separately. Diuretics and ACE inhibitors may be used to treat hypertension. Cholesterol drugs may be used to lower LDL cholesterol and triglyceride levels, if they are elevated, and to raise HDL levels if they are low. Use of drugs that decrease insulin resistance, e.g., metformin and thiazolidinediones, is controversial; this treatment is not approved by the U.S. Food and Drug Administration. Weight loss medications may result in weight loss. As obesity is often recognized as the culprit behind many of the additional symptoms, with weight loss and lifestyle changes in diet, physical activity, the need for other medications may diminish.

OBJECTIVE

General Objective
To detect the prevalence of metabolic syndrome among Sudanese diabetic patients type 2 in Gezira State – Sudan.

Specific objectives
1. To compare the effects of metabolic syndrome between male and female gender.
2. To identify the risk factor for metabolic syndrome.

MATERIALS AND METHODS
This cross-sectional study involved 40 type 2 diabetes mellitus patients and 40 patients as control group of both sexes were conducted at the Diabetes Centre in Sudan. The study involved the use of a questionnaire to obtain some information of personal data undertaking anthropometric measurements, as well as collecting blood samples for the measurement of some biochemical parameters; fasting blood glucose, high density lipoprotein, low density lipoprotein, triglyceride, total cholesterol. MetS was defined according to the National Cholesterol Education Program/Adult Treatment Panel III criteria.

Subjects
This study was conducted between February and April 2013. Eighty (80) participants of 40 diabetic patients &
40 control group at the Diabetic Centre -Medani-Gezira State-Sudan. (37 males and 43 females) were involved. The study participants were of ages between 20 and 100 years. Participants fasted overnight before blood sampling. Excluded from the study were type 1 diabetics and pregnant women.

Blood sample collection and processing.
About 5 ml venous blood samples were collected after an overnight fast; 4 ml was dispensed into vacutainer® plain tubes and 1 ml into fluoride-oxalate tubes. After centrifugation at 500 g for 15 min, the serum and plasma were stored at −80°C until assayed. Parameters that were determined included; fasting blood glucose (FBG), high-density lipoprotein, low-density lipoprotein, triglyceride, total cholesterol. The protocol for the determination of the parameters was as indicated in the manufacturer's instructions (Fortress Diagnostics Limited, Unit 2C Antrim Technology Park, Antrim BT41 1QS, United Kingdom).

Anthropometric variables
Using a questionnaire and patients medical records, information on demographic and clinical characteristics, such as age, sex, duration, body mass index, type of treatment & age of onset of diabetes, family history of diabetes were extracted. Blood pressure was measured using a sphygmomanometer. Blood pressure was recorded in the sitting position in the right arm. Two readings were taken 5 min apart, and the mean of the two was taken as blood pressure. Height was measured to the nearest 0.1 cm without shoes, using a stadiometer and weight to the nearest 0.1 kg in light clothing, using a bathroom scale (Zhongshan Camry Electronic Co. Ltd, Guangdong, China). Body mass index (BMI) was calculated by dividing weight (kg) by height squared (m2). Waist circumference was measured to the nearest 0.1 cm, using a Gulick II spring-loaded measuring tape midway between the inferior angle of the ribs and the supraclavicular crest.

Statistical analysis
The results are expressed as means ± standard error of mean (SEM), using GraphPad Prism 5.01 for windows (GraphPad Software, San Diego California USA, www.graphpad.com). Student's t-test was used to ascertain the significance of the difference between two means of continuous variables and ANOVA for difference in mean values of grouped data. A level of P < 0.05 was considered as statistically significant. Using STATA (version 16.0, Inc., Chicago, IL) statistical software, multiple logistic regression was performed to estimate the relationship between MetS and some risk factors, in order to find the most significant observed predictor of MetS by estimating the odds ratio (OR) of the predictors (i.e. the measure of association between a predictor and an outcome, which in this case is MetS). The coefficients or ORs, give an estimate of the magnitude of each predictor. Without adjusting for these predictors, the ORs were calculated at 95% confidence interval. Next, the adjusted ORs were calculated, using the variables that showed statistical significance, with P < 0.05.

RESULTS
The metabolic syndrome was diagnosed according to criteria of national cholesterol education program (NCEP). In this study, there was strong association between diabetes mellitus and metabolic syndrome which was occurred clearly in table (1,2,3,4) with correlation between Independent variable to dependent variable of all patients parameters with highly positively significant, that’s expressed the body mass index, fasting blood glucose, blood pressure, HDL duration of DM, type of treatment and abdominal circumference. In this study, the metabolic syndrome appeared well in most patients based in an increased waist circumference in 16 cases which represent in (40%) compared to those patients with the normal waist circumference in 23 cases which represent (60%) in male group. In females, the waist circumference increased in 36 case (90%) compared to 5 cases (10%) with normal waist circumference. E elevated serum triglyceride for more than 150 mg/dl in 26 cases(52%) , poor high density lipoprotein in males 12(30%) for less than 40 mg/dl which was low, and in females 23 cases(57.5%) which were low for less than 50 mg/dl. Elevated blood pressure 25(62.5%)of patients for more than 140/90. The majority of patients with metabolic syndrome occurred in patients on oral hypoglycemic agents 34 cases (85%) compared to the patients on insulin therapy which represent in 6 cases(15%), particularly in those patients with the duration of diabetes mellitus from 5 to 10 years with poor glycemic control.

The study showed that, the metabolic syndrome was high in type 2 diabetic patients particularly in females(60%) which represent in (22 cases) plus 7 cases with no metabolic syndrome compared to males. In males the metabolic syndrome occurred in 4 patients and with no metabolic syndrome in 7 patients out of 40% compared to normal control group.

Overall of this study, Pearson correlation analyses showed that there was association between type 2 diabetic patients and metabolic syndrome (fig 4, 5, 6, 7).
Fig 1: Pearson correlation analyses showed that there was association between type 2 diabetic patients and metabolic syndrome with positively significant.

<table>
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<td></td>
<td>Blood pressure</td>
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<td>.256*</td>
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<td></td>
<td>Abdominal circumference</td>
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<td></td>
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<td></td>
<td>low density lipoprotein</td>
<td>.876</td>
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<td>high density lipoprotein</td>
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<td></td>
<td>fasting blood glucose</td>
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<td>.513**</td>
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<tr>
<td></td>
<td>HbA1C</td>
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*Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).

Fig 2: Pearson correlation analyses showed that there was association between type 2 diabetic patients and metabolic syndrome with positively significant.

<table>
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<td>Type of treatment</td>
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<td>high density lipoprotein</td>
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<td>HbA1C</td>
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*Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).

Fig 3: Pearson correlation analyses showed that there was association between type 2 diabetic patients and metabolic syndrome with positively significant.

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<td></td>
<td>Type of treatment</td>
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<td>Blood pressure</td>
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<tr>
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<td>HbA1C</td>
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*Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).
Fig 4: Pearson correlation analyses showed that there was association between type 2 diabetic patients and metabolic syndrome with positively significant.

<table>
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<td>.217</td>
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Correlation is significant at the 0.01 level (2-tailed).
Correlation is significant at the 0.05 level (2-tailed).

**DISCUSSION**

This study included 80 patients, 40 patients with type 2 diabetes mellitus and 40 patients as control group of both sex (males & females). The study consisted 43 females (27 ill female patients compared to 17 well female patients as control group, and 37 males (13 ill male patients compared to 24 well male patients) as control group (F:43 & M:37). The patients were stratified to age group and sex (on the of 20 years interval). The proportions of patients, females to males were 107.5: 92.5% within the age group of 40 to 60 (77.5%). The least percentage of patients 19 (47.5%) were an age group 60 to 80 years. 3 (5.5%) patients within the age group of 80-100 years, and 15 patients (37.5%) within the age group of 20-40. The patients were stratified to marital status; all of the patients were married. A large percentage of patients were married 68(170%) and 12(30%) were singles. The patients were stratified also according to educational status, the majority of them were of basic education 25(62.5), while illiterates were 23 (57.5%), secondary were 15 (37.5%) and the rest percentage were universities education 17 (42.5%). One of the major parameters studied was the body mass index BMI which used as indicator for body weight. In this study about 34 (85%) of the patients were overweight, 16 (40%) were obese, while normal weight were 30 (70%). In USA, American overweight estimated were 60.5%, 23.9 were obese and 3% were extremely obese, thus extracted from behavioral risk factor surveillance system in 2005 (Olga M. Petrucelli, MD, 2008). The patients stratified according to abdominal circumference value among male patients were abnormal weight (abdominal obesity) 16 (40%) more than 102 cm, while had 23 (60%) patients were normal weight less than 102 cm. The patients stratified according to abdominal circumference value, females patients were 36(90%) had abdominal obesity more than 88 cm. While 5 patients (10%) were normal weight. The distribution of patients according to duration of diabetes mellitus in all patients, 16 (40%) had diabetes for 5-10 years, 13 (32.5%) having diabetes from 10 to 15 years, and 2 (5%) had diabetes 15 to 20, and 7 (17.5%) having diabetes for less than 5 years, and 2(5%) had diabetes for more than 20 years. The most prevalent treatment was diet and oral hypoglycemic agents (tablets), which was used by 34 (85%) of patients, and 6(15%) on insulin therapy with dietary control. According to the blood pressure (mm/Hg), showed that the majority of patients were hypertensive accounted as 25 (62.5%) for more than 140/90, and 15 (37.5%) with in the normal reference.

The distribution of HbA1C among patients as measure of glycemic control showed that the most patients 32 (80%) were poor in glycemic control more than 7%, while 48(120%) patients were fair glycemic control less than 7%. Blood lipids play a vital role as important risk factor for diabetic patients. As result of impaired action of insulin, there is an increase in triglyceride hydrolysis release of non-esterified fatty acids which are associated with alteration of blood lipid concentration and metabolism resulting in dyslipidemia. According to serum level of triglycerides, most patients 35 (87.5%) showed a level of triglycerides was less than 150 mg/dl, in 29 (70%) of patients in between 150-199 mg/dl and 17 (42.5%) of patients more than 200 mg/dl were strongly high. The level of cholesterol in serum patients 40 (100%), the total cholesterol was less than 200 mg/dl of normal value. 31 (77.5%) of patients, the cholesterol level was 200-239 mg/dl was slightly increased. In 9(22.5%) of patients was high more than 240 mg/dl. The serum high density lipoprotein among male patients was more than 60 mg/dl in 45 (112.5%) male patients, while the level of HDL in 12(30%) of male patients was less than 40 mg/dl. The serum level of HDL in female patients was 23 (57.5%) which was less than 50 mg/dl, which was poor. The HDL level was lower in females 23 (57%) than males 12 (30%). The fasting blood glucose among the majority of patients was increased more than 120 mg/dl in 37(92.5%), 28 (70%) in between 101-126 mg/dl was slightly increased and the rest of patients 15 (37.5%), the blood glucose level was in normal range between 70 to 100 mg/dl. The metabolic syndrome was diagnosed according to criteria of national cholesterol education program (NCEP). In this study, the metabolic syndrome...
appeared well in most patients based in abdominal obesity (40%) than the normal weight circumference in 23(60%) which was less than 120 cm in males, the abdominal obesity in females 36 (90%) compared to 5 (10%) with normal waist circumference less than 88 cm, elevated serum triglyceride more than 150 mg/dl in 26 (52%), poor high density lipoprotein in males 12(30%) less than 40 mg/dl, 23(57.5%) in females less than 50 mg/dl and elevated blood pressure 25(62.5%) of patients for more than 140/90 mm/Hg. The majority of patients with metabolic syndrome increased in patients on oral hypoglycemic agents 34(85%) than the patients on insulin therapy 6(15%), the duration of diabetes mellitus for 5 to 10 years and fair glycemic control 32(80%). The study showed that, the metabolic syndrome was high in type 2 diabetic patients particularly in females than males compared to the normal group based on diagnosis according to criteria of national cholesterol education program.

The study revealed that the metabolic syndrome was increased particularly in females, that’s accounted as 22 females with metabolic syndrome than 7 females with no metabolic syndrome out of 60% compared to males and control group. In males the metabolic syndrome occurred in 4 patients with no metabolic syndrome in 7 patients out of 40% compared to normal control. Finally, the frequency and occurrence of metabolic syndrome in Sudanese type 2 diabetic patients is highly serious increased problem and I recommended for screening of all type 2 diabetic patient to prevent complications and safe the life of patients.

CONCLUSION
1. The study revealed high frequency of the metabolic syndrome especially in women between 40 to 60 years.
2. Screening for metabolic syndrome is highly recommended.

REFERENCES
1. MedlinePlus: Metabolic Syndrome
3. In his case studies poster presented at the Chronic Fatigue Syndrome Conference in Sydney, Australia (February 12–13, 1998), Dr Allen E. Gale, Consultant Physician (Allergy), identifies the acronym CHAOS as an abbreviation for Coronary artery disease, Hypertension, Atherosclerosis, Obesity, and Stroke.


