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Metabolic Syndrome and the Risk of Kidney Diseases: the Impact of Lifestyle Modification

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Abstract

Background: The relationship between metabolic syndrome (MetS) and chronic kidney diseases (CKDs) is complex and bidirectional. However, the etiological role of MetS in CKDs is less clear. **Objective:** To assess the impact of the MetS on the kidney function using new renal biomarkers, and to study the effect of lifestyle modification by following a balanced hypocaloric diet and increasing physical activity. **Subjects and Methods:** Eighty seven obese women were enrolled in this study. The MetS criteria were studied which included from 0 to 5 components. Lifestyle changes were performed for eight weeks by following a low caloric balanced diet, and increasing their physical activity. Renal biomarkers were estimated before and after intervention. **Results:** About 65.5% of the obese volunteers were suffering from MetS, about 37% of them were complaining of renal symptoms. Higher consumption rate of high caloric diet and lower consumption rate of protein, vegetables and fruits were detected among obese metabolic patients compared to obese control. Improvement of all the MetS criteria and the biochemical renal markers were detected after intervention. **Conclusion:** The MetS raises the risk of CKDs. A change in the lifestyle, by including a low calorie healthy diet and increasing physical activity is necessary. Cystatin C/ Beta-trace protein (Cys-C/ BTP) proved to be good promising biomarkers for detection of early changes in renal functions and defining better tools for prevention, early diagnosis and follow up.

Key words: Metabolic syndrome, Kidney diseases, Cystatin C/ Beta-trace protein, Dietary therapy, Physical activity.

1. Introduction

A cluster of metabolic disorders, including abdominal (central) obesity, hypertension, dyslipidemia, hyperglycemia and insulin resistance, are the main criteria of the metabolic syndrome (MetS). These disorders are the most dangerous risk factors for cardiovascular diseases (CVDs), type 2 diabetes mellitus and chronic kidney diseases (CKDs) **[1]**.

The MetS has become one of the world's major public health problems. Depending on environmental factors and everyday lifestyle behaviors, including the country's nutritional habits, one in approximately every 4 or 5 adults has acquired MetS. For individuals over 50 years of age, the prevalence of this syndrome has been estimated to rise with age **[2]**. In this context, about 7.4 percent of Egyptian adolescents are affected by the MetS **[3]**, almost 30 percent in Europe **[4]** and over 40 percent in the US **[5]**. As the prevalence of central obesity in the Middle East area continues to grow, the MetS is expected to be much more prevalent in the future. Recent research has shown that the prevalence of central obesity among Egyptians is around 29%, with a greater prevalence among women **[6]**.

One of the increasing global public health problems is CKD **[7]**. The disease is a part of a new epidemic of chronic diseases that, during the 20th century, replaced malnutrition and infection as the leading causes of mortality. The MetS-CKDs associations have not been thoroughly studied; the mechanisms through which MetS-induced kidney disease are also not fully understood **[8]**.

Cystatin C (Cys-C) is a low molecular weight protein that is produced by all nucleated cells of the body. It is used in clinical practices to assess renal functions as it is filtered freely through the glomerulus, metabolized in tubules and excreted in urine at a constant rate. It correlates more closely with the glomerular filtration rate than the serum creatinine level which is a late marker of renal damage **[9]**.

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Beta-trace protein (BTP) is a low molecular weight glycosylated protein that is mainly derived from cerebrospinal fluid. In vivo, it has been shown to regulate glucose and lipid metabolism. Via the glomerular basement membrane, it is freely filtered and almost entirely excreted by the kidneys. Because of its low molecular mass, steady rate of production and stability, BTP has been proposed as a new endogenous glomerular filtration rate marker, and serum BTP levels have been estimated in patients with various stages of CKDs **[10]**.

The purpose of this study was to highlight the impact of the MetS on the kidney function in a sample of Egyptian obese females who participated in a program for losing weight. In addition, to evaluate the effect of changing lifestyle by following a balanced hypocaloric diet and by increasing their physical activity. Also, to study the use of Cys-C/ BTP as new biomarkers to predict changes in renal functions and defining better tools for prevention, early diagnoses and follow up.

2. Subjects and Methods

Eighty seven obese women enrolled in a program for losing weight at the Nutrition department of the National Research Centre (NRC)-Egypt; participated as volunteers in this study. The inclusion criteria were: having a body mass index (BMI) between 30 and 40 kg/ m2 and a sedentary lifestyle, and the lack of any contraindications regarding physical exercises according to the American College of Sports Medicine guidelines **[11]**.

Ethical approval from Ethical Committee of NRC, (Registration Number is19-180) and a written informed consent from each of them were obtained.

The following investigations were done for all subjects at baseline, and after two months of following a low caloric balanced diet (1000-1100 Kcal/day), plus performing aerobic exercises for 5-10 minutes every morning together with walking for 30 min 3 times/ week, with weekly follow up by:

• **Full medical history** including important renal symptoms; in addition to clinical examination.

Renal symptoms: Headache, weakness, fatigue, lack of energy and concentration and having trouble sleeping. Persistent nausea and poor appetite. Dry and itchy skin. Frequent urination and changes in urine color (blood in urine, foamy urine). Persistent puffiness around the both eyes. Swelling of both legs, ankles and feet. Unexplained shortness of breath. Lower back pain. Muscle cramping **[12]**.

• **Blood pressure** was measured by cuff sphygmomanometer while the subjects sat quietly, and the mean of 3 readings were recorded.

• **Relevant anthropometric measurements** were reported in the form of: Body weight and height were recorded while subjects were standing with minimum clothing and no shoes. Minimal waist circumference (MWC) was measured in centimeters using non extendable tape during normal respiration. The body mass index (BMI) was Calculated, where BMI= weight in kg/square height in meters **[13]**. All measurements were taken by the same researcher to assure accuracy.

• **Dietary recall:**

Data on dietary intake before the intervention were performed using the 24 hours dietary intake recall, aiming to correct eating habits. All food items and portions were recorded by the same researcher in details. Analysis of micro and macronutrient contents of their habitual diet and the hypocaloric regimen were performed using NutriSurvey program 2007 - University of Indonesia.

• **Blood sampling and biochemical analysis:**

Blood samples were obtained on the day of clinical examination after an overnight fast. Fasting blood glucose was determined on fresh samples by test strip electrochemical technology using Bayer's CONTOUR® PLUS Glucometer **[14]**. The rest of the blood samples were allowed to clot at room temperature, centrifuged and the sera were separated. Other biochemical parameters were performed on fasting sera that were stored at -70 C° until used.

High density lipoprotein cholesterol (HDL-C) and triglycerides (TG) were estimated by enzymatic methods using the kit supplied by ErbaLachemas.r.o.,Karásek 1d, 621 00 Brno, CZ **[15]**. Fasting C-peptide level was determined by ELISA KIT supplied by Monobind Inc. Lake forest, CA 92630, USA **[16]** to expresses insulin resistance by modified homeostatic assessment of insulin resistance equation: M. HOMA-IR=1.5+fasting blood glucose x fasting c-peptide/2800 **[17]**.

Serum Creatinine was estimated by kinetic method using the kit supplied by Erba Lachemas.r.o.,Karásek 1d, 621 00 Brno, CZ. REF/BLT00020 **[18]**. Urea was estimated by colorimetric method **[19]**. Blood urea nitrogen (BUN) was calculated, where BUN (mg/dL) = Serum urea (mg/dL)*0.467. Conversion factor derived by 28/60=0.467 [MW of urea=60, MW of urea nitrogen=28 (14*2)].

Serum Cystatin C was determined using Human Cystatin C ELISA, Lot E12-076, BioVendor Research and Diagnostic Product CZECH

REPUBLIC **[20]**. Beta trace protein (Novel kidney function biomarker) was estimated in the serum according to Akbari et al. **[21]** by human serum β-trace protein (Human BTP) ELISA kit Lot no 202002 Glory Science Co., LTD No.657 Yunli Road Economic Developing Area Wujang, Jangsu, China. Creatinine clearance was assessed from serum creatinine by using the following formula (COCK CROFT – GAULT EQUATION): Estimated Creatinine Clearance = (140-Age) x Weight in Kg / (72x Serum Creatinine in mg/ dL) multiply by 0.85 for females **[22]**. Normal creatinine clearance is 88–128 mL/min for healthy women and 97–137 mL/min for healthy men. Estimated glomerular filtration rate (eGFR) is calculated by the abbreviated MDRD (modification of diet in renal disease) equation, Where eGFR=186 x (Creatinine mg/dL$^{)-1.154}$x (Age$^{)-0.203}$ x (0.742 if female). Equation generally provides more accurate estimation at GFR >60 mL/min/1.73 m^2 **[23]**.

Study Design and Statistics

The volunteers were split into two groups after the first visit. Group (1) comprised 57 patients with MetS. Patients' selection was based on the existence of at least three of the following five MetS definition requirements [according to the Adult Treatment Panel III (NCEP ATP III) National Cholesterol Education Program] **[24]**: (1) increased waist circumference (WC): ≥88 cm; (2) increased blood pressure (BP): ≥130/85 mm Hg or antihypertensive drug use; (3) increased triglycerides (TG): ≥150 mg/dL; (4) decreased High density lipoprotein cholesterol (HDL-C): <50 mg/dL; and (5) increased fasting blood glucose (FBG): ≥100 mg/dL or antihyperglycemic drug use. Group (2) included 30 age-matched obese subjects who acted as controls.

This is a comparative case-control study between obese metabolic syndrome cases and obese control. Changes were expressed in percentage, (X2-X1)*100/X1 were calculated. Student t-tests were used to compare data before and after 2 months. Pearson's correlations coefficient (r) before and after intervention were performed to assess the linear relationships that exist between the studied variables. Statistical analysis was performed using SPSS software version 17.0. Data are expressed as means± SE, P value was considered significant at< 0.05.

3. Results

About 65.5% of the obese volunteers were suffering from MetS. The prevalence rate of the risk factors among the two groups and the odd ratio between them was shown in **(Table 1)**. About 37% of the MetS subjects group (1), and 20% of group (2) were complaining of renal symptoms.

Table 1. Odd ratio between the prevalence of the metabolic syndrome (MetS) risk factors among obese women with and without MetS.

Parameters	Obese with MetS (Group 1: no.=57)		Obese without MetS (Group 2: no.=30)		Odd ratio
	No.	Percentage %	No.	Percentage %	
MWC ≥88 cm	51	89.5	3	10	8.9
BP ≥130/ 85 mmHg	33	57.9	1	3.3	17.5
FBG ≥100 mg/dL	42	73.7	3	10	7.4
TG ≥150 mg/dL	21	36.8	1	3.3	11.2
HDL-C <50 mg/dL	57	100	8	26.7	3.7
Renal symptoms	21	36.8	6	20	1.8

MWC: **M**inimal **W**aist **C**ircumference, **BP**: **B**lood **P**ressure, **TG**: **Tr**iglycerides, **HDL-C**: **H**igh **D**ensity **L**ipoprotein **C**holesterol.
Odd ratio: The ratio of the risk factor occurrence (percentage) between the two groups, it provides a good measure of the prevalence rate of the risk factors between the two groups.

Table (2) demonstrated the mean of the MetS criteria before and after intervention among the 2 groups. The MetS patients were older and shorter. At the base line, the mean anthropometric measurements represented by weight, BMI and MWC were significantly higher in group 1 compared to group 2 ($p<0.01$). There were significant differences in the mean values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) between the two groups at $p<0.05$ and $p<0.01$ respectively. The mean biochemical parameters were also significantly high for TG and low for HDL-C, when group (1) was compared to group (2), also a high level of fasting C-peptide as an indicator of endogenous insulin, and high M. HOMA-IR as a marker of insulin resistance among all the obese volunteers. After following a low caloric balanced diet and increasing physical activity for two months, a significant decrease in the mean values of body weight, BMI, MWC, DBP, TG, C-peptide and M.HOMA, and significant increase in HDL-C at $p< 0.01$ were detected in both groups. The highest percent changes were observed in the mean values of HDL-C (23.52& 10.76% in group 1 and group 2 respectively) and C-peptide (9.77&14.59% in group 1 and group 2 respectively). The improvement in the blood pressure was more prominent among group 2.

The biochemical markers for kidney function showed significantly higher values of serum Cystatin C (Cys-C) and numerical higher values of serum urea, BUN, BUN creatinine ratio and serum beta trace protein (BTP) in group 1 as compared to group 2 before the intervention **(Table 3)**. Improvement of all the biochemical renal markers were detected after the intervention, more observed in the mean values of serum creatinine, Cys-C, creatinine clearance and eGFR in both groups.

Table 2. Mean± SE of the MetS criteria among the obese women before and after dietary therapy.

Parameters	Group 1: Obese with MetS (no.=57)			Group 2: Obese without MetS (no.=30)		
	Mean± SE		% Change	Mean± SE		% Change
	Before	After		Before	After	
Age (years)	48.37± 1.64			44.90±2.44		
Height (cm)	155.84±1.06			156.90±1.15		
Weight (kg)	91.87±2.82	87.93±2.64^{**a}	**-4.29**	82.10±1.83^{**i}	79.90±1.71$^{**b, **ii}$	**-2.68**
BMI (kg/m^2)	37.93±1.17	36.31±1.09^{**a}	-4.27	33.34±0.63^{**i}	32.47±0.63$^{**b, ** ii}$	-2.61
MWC (cm)	95.76±1.73	90.21±1.50^{**a}	**-5.80**	85.40±1.25$^{** i}$	82.70±1.19$^{**b, ** ii}$	-3.16
SBP (mmHg)	123.68±2.29	121.32±1.99	-1.91	116.00±2.50$^{* i}$	113.50±2.29$^{* ii}$	-2.16
DBP (mmHg)	83.16±1.31	80.00±1.16^{**a}	-3.80	77.00±1.38$^{** i}$	74.00±1.61$^{*b, ** ii}$	-3.90
FBG (mg/dL)	115.11±6.06	112.18±3.80	-2.55	109.25±9.56	104.50±5.46$^{** ii}$	-4.35
TG (mg/dL)	147.58±3.44	141.28±3.17^{**a}	-4.27	131.19±2.41$^{** i}$	129.66±1.86$^{** ii}$	-1.17
HDL-C (mg/dL)	30.10±0.98	37.18±0.78^{**a}	**+23.52**	35.51±1.89$^{** i}$	39.33±1.56$^{**b, ** ii}$	**+10.76**
C-peptide (ng/ml)	6.14±0.19	5.54±0.18^{**a}	**-9.77**	5.69±0.19	4.86±0.14$^{**b, * ii}$	**-14.59**
M.HOMA-IR	1.75±0.02	1.72±0.01^{**a}	-1.71	1.73±0.03	1.68±0.01$^{**b,* ii}$	-2.89

BMI: **B**ody **M**ass **I**ndex**, MWC**: **M**inimal **W**aist **C**ircumference, **SBP**: **S**ystolic **B**lood **P**ressure, **DBP**: **D**iastolic **B**lood **P**ressure, **FBG: F**asting **B**lood **G**lucose, **TG**: **Tr**iglycerides, **HDL-C**: **H**igh **D**ensity **L**ipoprotein **C**holesterol**, M. HOMA-IR: M**odified **H**omeostatic **A**ssessment of **I**nsulin **R**esistance. a: Before vs. After of group 1, b: Before vs. After of group 2, i: group 1 vs. group 2 before, ii: group 1 vs. group 2 after intervention.**** Significant at p<0.05 ** Highly Significant at p<0.01***

Table 3. Renal biomarkers in the two groups before and after dietary therapy.

Parameters	Group 1: Obese with MetS (no.=57)			Group 2: Obese without MetS (no.=30)		
	Mean± SE		% Change	Mean± SE		% Change
	Before	After		Before	After	
Urea (mg/dL)	27.17±.1.08	24.42±0.78^{**a}	-10.12	25.64±1.36	23.12±1.11^{*b}	-9.83
BUN (mg/dL)	12.69±0.50	11.52± 0.38^{**a}	-9.22	11.97±0.64	10.79±0.52	-9.86
Creatinine (mg/dL)	0.98±0.02	0.82±0.03^{**a}	**-16.33**	0.97±0.02	0.86±0.05^{*b}	**-11.34**
BUN/ Creatinine	12.95±0.57	14.12±0.53	-9.03	12.42±0.74	13.17±0.89	+6.04
Cystatin C (ng/ ml)	19.23±2.67	9.89±1.14^{**a}	**-48.57**	11.29±2.05^{*i}	8.39±3.8	**-25.69**
Serum beta trace protein (mg/L)	4.66±0.10	4.17±0.11^{**a}	-10.52	4.71±0.15	4.58±0.09^{*ii}	-2.76
Creatinine Clearance	101.41±4.22	115.54±7.55^{**a}	**+13.93**	95.03±3.52	104.31±6.36^{*b}	**+9.77**
eGFR (mL/min/1.73 m^2)	64.28±1.66	78.96±4.61^{**a}	**+22.84**	66.06±1.76	75.88±5.76^{**b}	**+14.87**

BUN: Blood **U**rea **N**itrogen, **eGFR**: **E**stimated **G**lomerular **F**iltration **R**ate

a : Before vs. After of group 1, b: Before vs. After of group 2, i: group 1 vs. group 2 before, ii: group 1 vs. group 2 after intervention,

**** Significant at p<0.05 ** Highly Significant at p<0.01***

Correlation coefficient between MetS criteria and kidney biochemical parameters before and after intervention for all obese subjects was shown in **Table (4)**. The mean values of the subjects' age showed significant positive correlations with that of serum urea, BUN creatinine ratio and BTP, and significant negative correlations with creatinine clearance during the whole period of the study. The mean values of weight, BMI and waist showed significant positive correlations with that of serum Cys-C (before intervention), and creatinine clearance (before and after intervention). Significant positive correlations between SBP and DBP and both of urea (before and after intervention), BUN creatinine ratio and BTP (after intervention). Significant negative correlation was detected between HDL-C and BTP during the whole period of the study. Mean values of fasting C-peptide showed significant positive correlations with urea (before intervention), creatinine and Cys-C before and after intervention), and negative correlation with creatinine clearance (after intervention). Significant positive correlations were detected between insulin resistance and both of urea and creatinine before intervention.

Table 4. Correlation coefficient between MetS criteria and kidney biochemical parameters before and after intervention for obese subjects.

Parameters	Urea		Creatinine		BUN/Creatinine		Cystatin C		Beta trace protein		Creatinine clearance		eGFR	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Age	**0.456****	**0.703****	N.S.	N.S.	**0.318***	**0.365****	N.S.	N.S.	**0.347****	**0.316***	**-0.487****	**-0.368****	**-0.467****	N.S.
Weight	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	**0.510****	N.S.	N.S.	N.S.	**0.714****	**0.530****	N.S.	N.S.
BMI	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	**0.409****	N.S.	N.S.	N.S.	**0.596****	**0.295***	N.S.	N.S.
MWC	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	**0.586****	N.S.	N.S.	N.S.	**0.571****	**0.426****	N.S.	N.S.
SBP	**0.316***	**0.416****	N.S.	N.S.	**0.278***	N.S.	**N.S.**	N.S.	N.S.	**.537****	N.S.	N.S.	**-0.218***	N.S.
DBP	**0.363****	**0.376****	N.S.	N.S.	**0.300***	**0.340****	**0.232***	N.S.	N.S.	**0.504****	N.S.	N.S.	**-.273***	N.S.
TG	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	**0.292***	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
HDL-C	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	**-0.261***	**-0.262***	N.S.	N.S.	N.S.	N.S.
FBG	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
C-peptide	**0.214***	N.S.	**0.228***	**0.422****	N.S.	N.S.	**0.304****	**0.411****	N.S.	N.S.	N.S.	**-0.312****	N.S.	**-0.376****
M.HOMA-IR	**0.269***	N.S.	**0.235***	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

Numbers presented in this table are the value of r =correlation coefficient. *Correlation is significant at the 0.05 level; **Correlation is significant at the 0.01 level. **BMI**: **B**ody **M**ass **I**ndex**, MWC**: **M**inimal **W**aist **C**ircumference, **SBP**: **S**ystolic **B**lood **P**ressure, **DBP**: **D**iastolic **B**lood **P**ressure, **TG**: **T**riglycerides, **HDL-C**: **H**igh **D**ensity **L**ipoprotein **C**holesterol**, FBG: F**asting **B**lood **G**lucose, **M. HOMA-IR: M**odified **H**omeostatic **A**ssessment of **I**nsulin **R**esistance

Table (5) shows the nutrient contents of the habitual diet and the hypocaloric regimen consumed by the obese volunteers and their percentage from the recommended daily allowances (RDAs). The data showed the balanced and healthy distribution of the macronutrients and micronutrients in the hypocaloric regimen compared to the habitual diet of the patients. The percent of the daily intake of energy and the macronutrients (carbohydrates and total fat) was high in the habitual diet compared to RDAs. The daily intake of vitamins (A, D& C) and minerals (calcium, iron& zinc) was lower than the RDAs. The total daily calories of hypocaloric regimen were significantly decreased when compared to the habitual diet, as it reached 53.12% of the RDAs, about 18.5% of total calories obtained from protein, 34% from fat and 47.5% from carbohydrates. Significant increase in the level of protein intake, monounsaturated fatty acids (MUSFAs) and polyunsaturated fatty acids (PUFAs), and significant decrease of carbohydrates and saturated fatty acids (SFAs) in the hypocaloric regimen compared to habitual diet, all reached the recommended levels after the intervention.

Table (6) shows higher consumption rate of carbohydrate food (bread, bakery product, pasta and sweet) among obese metabolic patients compared to obese control. While lower consumption rate of protein from animal (as milk, dairy products, chicken, meat, fish…) and plant (as legumes) sources, and vegetables and fruits were detected among the MetS patients.

Table 5. The nutrient content of the habitual diet and the low caloric regimen consumed by the obese volunteers.

Nutrient intake	Habitual diet	Low caloric regimen (Baladi bread)	RDAs	P-value
	Mean value± SE **%RDAs**			
Macronutrients				
Energy (kcal)	2459.33 ±33.92 **122.97**	1062.34±28.81 **53.12**	**2000**	.000**
Protein (g)	41.37±4.26 **82.74**	49.10±5.46 **98.2**	**50**	.000**
Carbohydrates (g)	325.85±5.35 **108.62**	126.13±3.46 **42.04**	**300**	.000**
Dietary fiber (g)	14.55±0.53 **58.20**	21.65±0.13 **86.60**	**25**	.002*
Fat (g)	110.05±9.08 **169.31**	40.13±2.30 **61.74**	**65**	.000**
SFAs (g)	66.31±4.10 **24.16**	9.04±5.23 **7.65**	**Not more than 7% of total calories**	.000**
MUFAs (g)	18.14±2.03 **6.59**	15.71±2.07 **13.31**	**12%-14% of total calories**	.010*
PUFAs (g)	15.23±1.40 **5.49**	8.92±2.09 **7.56**	**6%-8% of total calories**	.012*
Cholesterol (mg)	386.97±13.25 **193.48**	191.82±10.30 **95.91**	**200**	.000**
Micronutrients				
Vitamin B6 (mg)	0.60±0.05 **42.86**	1.13±0.01 **80.71**	**1.4**	.026*
Vitamin B12 (mcg)	1.23±0.62 **87.86**	2.01±.0.56 **143.57**	**1.4**	.000**
Riboflavin (mg)	0.52±0.69 **43.33**	0.89±0.75 **74.17**	**1.2**	**.070***
Niacin (mg)	6.48±2.10 **49.85**	9.86±2.09 **75.85**	**13**	.019*
Thiamine (mg)	0.41±0.01 **41.00**	0.64±0.01 **64.00**	**1.0**	.087*
Folate (mcg)	103.18±3.19 **25.79**	119.71±7.20 **29.93**	**400**	.002**
Vitamin C (mg)	**23.70±4.16** **52.67**	**39.89**±5.67 **88.64**	**45**	
Vitamin A (µg)	451.31±4.86 **56.41**	789.63±6.32 **98.70**	**800**	.032*
Vitamin D (µg)	2.30±0.04 **46.00**	3.11±0.08 **62.20**	**5**	057*
Sodium (mg)	988.73±18.10 **65.92**	640.15±12.51 **42.68**	**1500**	.051*
Potassium (mg)	1459.73±4.78 **72.99**	1819.32. ±3.77 **90.97**	**2000**	.041*
Calcium (mg)	421.17±7.16 **52.65**	741.40±5.61 **92.68**	**1000**	.030*
Iron (mg)	4.69±0.75 **58.63**	7.59±0.87 **94.88**	**8**	.042*
Zinc (mg)	5.30±0.51 **44.17**	8.20±0.82 **68.33**	**12**	.028*

SFAs: Saturated **F**atty **A**cids, **MUFAs: M**onounsaturated **F**atty **A**cids, **PUFAs**: **P**olyunsaturated **F**atty **A**cids. **** Significant at p<0.05*** ***** Highly Significant at p<0.01***

Table 6. The percent of the frequency consumption (%) of different food items for the two groups before intervention.

Items	Group 1: Obese with MetS (no.=57)					Group 2: Obese without MetS (no.=30)					*P* -Value
	Didn't eat	Every day	Twice/ week	Every week	More	Didn't eat	Every day	Twice/ week	Every week	More	
Carbohydrate Foods											
Bread	0.0	52.1	31.6	16.3	0.0	0.0	48.6	30.2	11. 1	10. 1	
Bakery products	6.9	56.3	34.5	2.3	0.0	18.1	33.3	30.9	12.6	5.1	
Pasta	2.4	3.6	44.0	50.0	0.0	8.2	1.8	40.2	29.3	20.5	
Total	**4.2**	**35.1**	**34.6**	**26.1**	**0.0**	**13.1**	**27.9**	**29.4**	**17.7**	**11.9**	**0.013***
Milk & Milk Products											
Milk	15.4	20.8	26.8	28.6	8.4	6.2	23.9	31.3	33.4	5.2	
Cheese	10.7	28.4	30.2	19.1	11.6	8.7	33.1	27.4	18.7	12.1	
Yoghurt	39.1	3.5	12.1	32.9	12.4	23.2	5.9	16.8	37.3	16.8	
Total	**21.7**	**17.5**	**23.2**	**26.8**	**10.8**	**12.7**	**20.9**	**25.2**	**29.8**	**11.4**	**0. 040***
Animal protein foods											
Chicken	1.3	2.4	57.1	30.1	9.1	1.1	2.1	34.2	51.1	11.5	
Meat	3.7	0.0	26.2	49.2	20.9	2.1	0.0	22.1	33.3	42.5	
Fish	10.8	0.0	5.4	21.7	62.1	6.4	0.0	8.1	40.9	44.6	
Egg	6.3	22.6	24.2	31.4	15.5	3.9	25.3	26.1	38.2	6.5	
Total	**4.9**	**7.4**	**29.9**	**32.4**	**25.4**	**3.4**	**6.9**	**22.7**	**40.8**	**26.2**	**0.012***
Plant protein food											
Legumes	**4.6**	**46.7**	**25.6**	**23.1**	**0.0**	**2.3**	**53.4**	**29.4**	**10.8**	**4.1**	**0.061***
Vegetables											
Fresh Vegetables	8.4	10.5	40.5	24.4	16.2	4.3	17.3	45.1	28.2	5.1	
Cooked vegetable	0.0	8.6	40.2	41.1	10.1	0.0	19.2	46.2	29.2	5.4	
Total	**4.2**	**9.5**	**40.3**	**32.7**	**13.3**	**2.2**	**18.3**	**45.6**	**28.7**	**5.2**	**0.030***
Fruits											
Fresh Fruits	2.3	18.3	41.8	21.9	15.7	2.1	24.5	46.1	16.6	10.7	
Fruit Juices	9.4	8.6	30.6	31.2	20.2	7.5	15.8	32.9	29.5	14.3	
Total	**5.8**	**13.6**	**36.2**	**26.5**	**17.9**	**4.8**	**20.15**	**39.5**	**23.05**	**12.5**	**0.015***
Sweets											
Sweet	**3.9**	**32.7**	**36.1**	**21.4**	**5.9**	**3.1**	**24.6**	**28.1**	**34.4**	**9.8**	**0.041***
Beverages											
Tea	2.4	59.3	26.7	8.4	3.2	3.2	46.4	31.3	12.7	6.4	
Carbonated drink	1.6	19.3	49.3	27.1	2.7	3.8	10.8	32.1	45.7	7.6	
Total	**2.0**	**39.3**	**38.0**	**17.8**	**2.9**	**3.5**	**28.6**	**31.7**	**29.2**	**7.0**	**0.022***

***Significant at P<0.05**

4. Discussion

Due to the high prevalence of obesity (especially central obesity) caused by poor eating habits and sedentary lifestyle, the metabolic syndrome (MetS) has become one of the major global health issues worldwide **[25].** In the present study, about 65.5% of the obese volunteers were suffering from MetS.

A broad term used to describe any abnormality in the structure or function of the kidney is chronic kidney disease (CKD). An increased risk of end-stage renal failure is associated with CKDs. The CKD is a reduced function of the kidney and is characterized by lower glomerular filtration rate (GFR) (<60 mL/min/1.73 m^2) **[26].**

Approximately 37% of MetS subjects (group 1) and 20% of obese subjects without MetS (group 2) in our study had signs of renal disease with an odd ratio of 1.8. The relationship between CKDs and MetS has been investigated in several studies. **Chen et al. [27]** found that an independent risk factor for CKDs was MetS. In over 6000 subjects who participated in the Third National Health and Nutrition Survey (NHANES III), investigated the relationship of MetS and the risk of CKDs, and documented that MetS was independently associated with the risk of CKDs.

In 2006, **Ninomiya et al. [28]** compared those with 1 or no criteria with patients with 4 or more components. They found that GFR decreased significantly faster in patients with 4 or more criteria of MetS.

Metabolic Syndrome Pathophysiology that Predisposes to Chronic Kidney Diseases:

A combination of hemodynamic and metabolic disorders can possibly contribute to the mechanisms of obesity-induced renal injury. A main component of MetS is visceral (central) obesity. It implies increased abdominal fat from the omentum and mesentery. Increased release of free fatty acids (FFAs) from visceral fat into portal circulation beyond the antilipolytic capacity of insulin, leading to increased secretion of prothrombotic proteins such as fibrinogen and plasminogen activator inhibitor 1, and also blocking the signalling pathway of phosphatidylinositol-3 kinase (PI-3K) leading to vascular endothelial dysfunction due to decreased nitric oxide. Human adipocytes generate a mineralocorticoid-releasing factor not yet known that stimulates the development of adrenal aldosterone through paracrine or endocrine mechanisms. High aldosterone levels promote insulin resistance and hypertension and thus the progression to MetS **[29, 30].** In this context, the current study reported significant differences in the mean values of MWC, SBP and DBP between the MetS patients and the obese subjects at different levels of p values (<0.05 and <0.01).

One of the components of MetS is impaired glucose tolerance (IGT stage). In the present study about 74% of MetS patients have IGT. It is a critical prediabetic stage that is closely linked to the onset of macrovascular (as cardiac and cerebral) and microvascular complications, such as diabetic kidney disease (DKD). Recent research has shown that endothelial cell dysfunction, hypertension, the onset of low-level albuminuria and kidney diseases are closely correlated with compensatory hyperinsulinemia **[31].**

Increased insulin resistance in CKDs will increase sodium reabsorption resulting in sodium retention and salt-sensitive hypertension. Increased adipokines' production (such as tumor necrosis factor-alpha) by adipocytes in obese subjects together with salt retention will enhance the production of reactive oxygen species and mineralocorticoid receptor activation resulting in CKDs and CVDs **[32].**

The mean biochemical parameters reported in this study revealed high concentrations of the TG and low level for HDL-C, when group (1) was compared to group (2). In MetS, dyslipidemia is postulated to cause CKDs by inflammation and increased oxidative stress, triggering endothelial damage and atherosclerosis diseases. Several studies have postulated that elevated triglycerides and low plasma HDL cholesterol are independent risk factors for CKDs development. Therefore, statin (a lipid lowering medication) use has been studied to delay the development of CKDs **[33-35].**

New Renal Biomarkers:

While serum creatinine has been used as an essential marker for several decades to evaluate kidney function, it has many well-known restrictions as its concentration is influenced by several non-renal factors such as gender and muscle mass. As a result, the need for new biomarkers to evaluate renal function was necessary as cystatin C (Cys-C) and beta trace protein (BTP). Serum concentrations of Cys-C and BTP are independent of sex, diet and muscle mass, so they can be used as alternative markers. Numerous studies have also shown that BTP is a good predictor of renal dysfunction **[36-41].**

El-Shebini et al. [42] used serum Uromodulin (sUMOD) as a novel biochemical marker to predict early changes in renal functions in obese participants and evaluate the effect of using dietary supplement made of special herbs and whole grains to help in the prevention and management of such conditions. The results showed that the measurement of the sUMOD proved to be an accurate and precise biochemical parameter to show the speed of the renal response to the management by comparison with using usual diagnostic old markers.

The biochemical markers for kidney function in this study showed significantly higher values. However improvement of all these markers were detected after the intervention, more observed in the mean values of serum Cys-C (-48.57%) and to a lesser extend BTP (-10.52%) in the Mets patients, and significant positive correlation was observed between Cys-C with most of the criteria of the Mets, while BTP protein showed a significant correlation with HDL-C. So Cys-C and BTP complement each other in the diagnosis.

Interventions: Diet and Physical Activity:

The main strategy was to reverse the contributory variables such as the atherogenic diet, obesity, and a sedentary lifestyle. In order to postpone the disease progression, weight loss and physical activity are prescribed as first-line treatment. Epidemiological evidence indicates that dietary patterns high in fruits, vegetables, whole grains, milk products and unsaturated fats have a lower incidence of MetS **[43].** The present study showed higher consumption rate of carbohydrate foods (bread, bakery product, pasta and sweet) among obese metabolic patients compared to obese control. While lower consumption rate of protein from animal sources (as milk, dairy products, chicken, meat, fish…) and plant sources (as legumes).

Previous studies showed that eating plan diet rich in low-fat dairy foods, fruits, and vegetables have healthy beneficial effects on blood pressure and lipids. In obese women, a reduced calorie diet decreases most of the MetS risk factors and improves the biochemical markers of renal function **[44-46].**

The risk of stroke and hypertension can also be decreased by a diet rich in calcium, magnesium and potassium. Fibre and phytonutrients in fruits and vegetables may have a protective role by decreasing cholesterol and inflammation markers. The inverse association between dairy consumption and the risk of MetS was suggested in some studies **[47].**

In this context, the analysis of the dietary intake of our patients showed that total daily calories of hypocaloric regimen were significantly decreased when compared to the habitual diet. About 18.5% of total calories obtained from protein, 34% from fat and 47.5% from carbohydrates. Significant decrease of carbohydrates and SFAs intakes, and significant increase in the level of protein intake, MUSFAs and PUFAs in the hypocaloric regimen compared to habitual diet, all reached the recommended levels after the intervention. The micronutrients including important vitamins and minerals were also improved.

Said et al. [48] showed that a slight daily caloric limitation (500 kcal) could be an effective tool in the fighting against MetS and that the addition to this approach of three weekly aerobic and resistance training sessions in a gymnasium provides better results than dieting alone, particularly in terms of reducing waist circumference, % body fat, waist to hip ratio, fasting blood glucose, and improving dyslipidemia, which is in line with the results obtained in this study.

5. Conclusion

According to evidence from the current research, metabolic syndrome (MetS) raises the risk of chronic kidney diseases (CKDs). It would be necessary to change the lifestyle, especially including a low calorie healthy diet rich in vitamins and minerals and low in sodium and saturated fat and increase the physical activity. Cystatin C/ Beta-trace protein (Cys-C/BTP) proved to be good promising biomarkers for the detection of early changes in renal functions and for defining better tools for prevention, early diagnoses and follow up. At present, the risk of CKDs can be minimized by early diagnosis of MetS and treatment of individual components. However, in order to validate their effect on reducing CKDs risk, these approaches need to be further tested in a large randomized clinical trial.

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Authors' Contribution Statement

Salwa M. El Shebini and Maha I. A. Moaty designed the research; Salwa M. El Shebini was responsible for clinical examination; Maha I. A. Moaty was responsible for anthropometric measurements, weekly follow-up, interpreted the data and wrote the article; Nihad H. Ahmed was responsible for analysis of the nutritional intake and dietary habit and interpreted the data; Hend A. Essa was responsible for biochemical analysis and laboratory investigations and interpreted the data; Salwa M. El Shebini and Salwa T. Tapozada revised the final manuscript and have primary responsibility for final content. All authors read and approved the final manuscript before submission.

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