Original Article

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Website: www.jfcmonline.com

DOI: 10.4103/jfcm.jfcm_57_22

Evaluation of microalbuminuria in obesity phenotypes

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Abstract:

BACKGROUND: Obesity is a universal health issue of the present time. Nearly 2 billion people were estimated to be either overweight or obese in 2020, with nearly 3.4 million deaths worldwide. Proteinuria is now widely known to be a significant predictor of renal pathologies including end-stage renal disease. This study aimed to assess the relationship between the presence of microalbuminuria (MA) in obese individuals.

MATERIALS AND METHODS: This cross-sectional study was conducted among patients attending the outpatient department of Jawaharlal Nehru Medical College and Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha. From the subjects meeting the study criteria, selected 150 individuals with BMI $\geq$ 25 that formed the obese group. Obese individuals were further subdivided as metabolic healthy obese (MHO) and metabolic abnormal obese (MAO) based on metablic syndrome criteria. From the non-obese patients (BMI $\leq$25), one age and gender matched control was selected for each obese subject. All subjects were tested for MA by dipstick method. Data was analyzed using SPSS and Chi-square test was performed to test for statistical significance.

RESULTS: The study reflected the association of MA in the groups studied. The metabolic abnormal obese group was noted as having the highest percentage of positive cases (53.7%) of MA, followed by the MHO group (31.3%). A significant association of prevalence of MA was seen in MHO and MAO obese individuals ($P < 0.001$). MA was present in the urine samples of 26 (31.3%) obese subjects in the MHO group, 36 (53.7%) in the MAO group, and 8 (5.3%) in the control population.

CONCLUSION: Both MHO and MAO subgroups of obese individuals showed higher proportion of MA indicating adverse renal function. Therefore, primary prophylactic measures such as health education and lifestyle modification should be promoted for the obese to reduce their body weight and thereby possibly reduce the risk of future obesity-related renal complications.

Keywords:

Metabolic abnormal obese, metabolic healthy obese, metabolic syndrome, microalbuminuria, obesity

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Received: 05-02-2022
Revised: 13-04-2022
Accepted: 25-04-2022
Published: 13-05-2022

Introduction

Obesity is an unabating, relapsing, denounced, neurochemical condition that used to be more common in developed countries but is now increasing slowly in many developing countries, as socioeconomic development increases, changing the dynamics of dietary deficit in those societies into dietary surplus.[1] Many factors such as social, behavioral, environmental as well as genetic may be responsible for the occurrence of obesity.

Obesity is a universal health issue of the present day. Nearly 2 billion people were estimated to be either overweight or obese in 2020, resulting in nearly 3.4 million deaths. In India alone, approximately more than 135 million people are affected by obesity, and its incidence has seen a rapid rise in the last two decades. This rise in obesity in the Indian population is closely related to rising economic and social standards,

How to cite this article: Alagh AR, Shukla S, Acharya S, Vagha S, Dhingra L. Evaluation of microalbuminuria in obesity phenotypes. J Fam Community Med 2022;29:162-7.

further validating social factors as important in the increase in obesity. Recognizing these factors can help plan the necessary modifications for its population-based treatment strategy. Obesity can be measured by various methods including the body mass index (BMI), waist circumference (WC), waist–hip ratio (WHR), and skinfold thickness.[2,3]

One of the major consequences of obesity is syndrome X, also known as metabolic syndrome (MetS) defined by the International Diabetes Federation. They defined the MetS at their National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) as a syndrome showing at least three of the five mentioned criteria: (a) central obesity, (b) hypertriglyceridemia, (c) decreased high-density lipoprotein (HDL) levels, (d) hypertension, and (e) hyperglycemia.

As per these criteria, WC of more than 102 cm for males and more than 88 cm for females is considered central obesity. Serum triglyceride level higher than 150 mg/dl is considered hypertriglyceridemia. Serum HDL levels of <40 mg/dl for male and <50 mg/dl for female are considered significant. Sustained blood pressure of more than 130/85 mmHg is considered hypertension. Fasting blood glucose levels of more than 100 mg/dl or a patient who has been diagnosed with Type 2 diabetes mellitus (T2DM) are considered significant in fulfilling the criteria for hyperglycemia.

Obesity has been associated as a risk factor for many conditions that increase the morbidity of patients. Conditions including diabetes mellitus, hypertension, gallstone disease, coronary heart diseases, and certain types of cancer have also been noted to have obesity as a significant positive risk factor. There is also an increased number of deaths from renal conditions in obese individuals compared to the normal population.[3]

Proteinuria is seen to be a significant forecaster of end-stage renal disease (ESRD). This was an observation made during screening programs conducted in large populations. At the same time, a higher risk of cardiovascular disease-related mortality was also noted in the participants of these screening programs.

Microalbuminuria (MA) is the excretion of albumin in the urine in the range of 30–300 mg/dl. MA predicts the possibility of future nephropathy in the studied individual. It is also associated with renal dysfunction in nondiabetics.[4,5] Principally, centrally located abdominal obesity (a constituent of MetS) and damage to other end organs may be due to underlying hyperinsulinemia. This ultimately leads to resistance of tissues peripherally for the action of leptin about sensitizing the tissues for the action of insulin. The other effect is the increase in infiltration of macrophages in lipid-rich adipose tissues along with corresponding pro-inflammatory cytokine release from these cells.[5] All of these ultimately result in integral functional loss of the renal endothelial wall leading to MA. Consequently, our study focused on the evaluation of MA in obese individuals. The objectives of the study were as folows:

1. To identify obese individuals according to the World Health Organization (WHO) Asia pacific guidelines[6] along with age- and gender-matched controls
2. To classify obese as metabolic healthy obese (MHO) and metabolic abnormal obese (MAO)
3. To compare MA in MHO, MAO, and obese groups.

Materials and Methods

This cross-sectional study was conducted from September 21, 2019 to September 20, 2021, and included 150 obese individuals with BMI ≥25 and 150 age and gender matched controls (MBI <25). The sample size was calculated using Krejcie and Morgan Formula. Ethical approval was obtained from the Institutional Review Board vide Letter No. DMIMS (DU)/IEC/August-2019/825 dated 04/09/2019, and informed written consent was taken from all individuals.

All adults aged more than 18 years who visited the outpatient department of Jawaharlal Nehru Medical College and Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha (patients, staff, students, etc.) were included in the study. Pediatric population, pregnant females, patients with chronic debilitating diseases such as human immunodeficiency virus infection, diabetic nephropathy, and patients with preexisting renal diseases were excluded from the study.

A proper clinical history was taken, and an appropriate physical examination was done bearing in mind the inclusion and exclusion criteria. All participants were asked about their demographic characteristics, previous medical diseases, and any medications used on a regular basis. We identified obese individuals by body mass index (BMI) as per the WHO guidelines for Asian-Pacific region, which considers BMI ≥25 kg/m^2 as an action line for obesity. Subjects with BMI in the range of 18–24.99 kg/m^2 that did not fulfill any criteria for MetS were considered for the control group after properly matching age and gender with obese cases.[6]

In the present study, the term metabolic abnormal obese (MAO) was used to denote the participants with BMI of ≥25 kg/m^2 as well as at least three or more criteria of MetS as proposed by NCEP ATP III criteria for Asians. The term MHO was used to denote those participants with BMI ≥25 kg/m^2 and <3 criteria

of MetS as proposed by NCEP ATP III criteria for Asians.[7,8]

In the study, the control group included individuals with a BMI <25 kg/m^2 with <3 MetS variables. The evaluation of the MA by the semi-quantitative method using a Micral kit was done in the laboratory on all the study participants.

Fresh urine samples were collected in glass bulbs and tested within 1 h at room temperature. This urine examination was done with the help of Micral (Cobas)-Test strips for urine, made by Roche Diagnostics for the evaluation of MA in the given sample [Figure 1]. It is a dip- and-read semi-quantitative albumin test that gives results in approximately 1 min.

The principle of this test is "immunological detection of human albumin" with the help of a conjugate soluble antibody with gold. A color change suggests a positive test indicating MA. The presence of albumin in the urine in the concentration of <20 mg/L is indicative of its physiological nature, which can be detected by comparing the reaction color of the test sample with the color block corresponding to the 20 mg/L levels. Hence, a sample color lighter than the standard color was considered the physiological presence of albumin in the urine.

The Statistical Package for the Social Sciences (SPSS), version 27 (IBM Corp., Armonk, NY, USA), and GraphPad prism (version 7) were used for statistical analysis. Chi-square test was performed to test for statistical significance; $P \leq 0.05$ was considered significant.

Results

The baseline particulars of the study participants are given in Table 1. In our study, MA was present in the urine samples

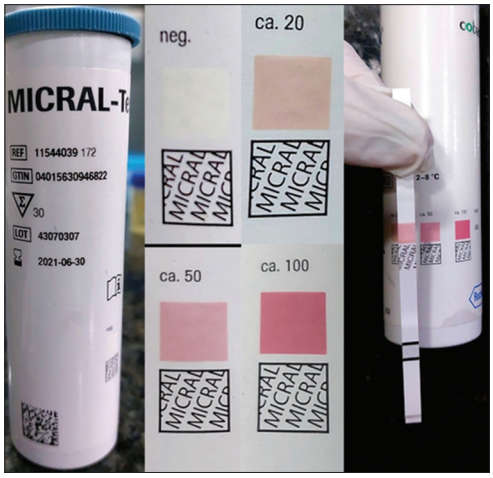

Figure 1: Microalbuminuria detection by dipstick

Table 1: Baseline characteristics of study participants

Variables	Obese (cases)		Control (*n*=150) Mean±SD	*P*-value
	MHO (*n*=83) Mean±SD	MAO (*n*=67) Mean±SD		
Age (years)	39.80±13.24	43.50±10.85	41.49±12.85	0.49
Gender, *N* (%)				
Male	48 (57.8)	37 (55.2)	85 (5677)	0.95
Female	35 (42.2)	30 (44.8)	65 (43.3)	
BMI (kg/m^2)	29.70±2.45	28.94±3.09	21.98±1.80	< 0.0001
WC	87.28±9.71	96.86±11.53	78.30±8.49	< 0.0001
SBP	115.22±9.23	135.04±12.86	115.57±9.90	< 0.0001
DBP	76.11±7.68	88.26±8.75	75.56±7.45	< 0.0001
FBS	91.74±15.45	145.44±47.97	91.80±13.77	< 0.0001
Serum TG	166.06±67.52	166.79±78.57	130.14±55.46	< 0.0001
HDL	40.89±9.82	39.28±10.78	42.44±12.67	0.164
Microalbuminuria, *N* (%)	26 (31.3)	36 (53.7)	8 (5.3)	< 0.0001

BMI=Body mass index, WC=Waist circumference, SBP=Systolic blood pressure, DBP Diastolic blood pressure, FBS=Fasting blood sugar, TG=Triglycerides, HDL=High-density lipoprotein, NS=Not significant, S=Significant, MHO=Metabolic healthy obese, MAO=Metabolic abnormal obese

Table 2: Comparison of microalbuminuria among cases (metabolic healthy obese and metabolic abnormal obese) and controls

Urine microalbuminuria	Obese (cases)		Control *N* (%)	χ^2, *P*-value (overall)
	MHO *N* (%)	MAO *N* (%)		
Present	26 (31.3)	36 (53.7)	8 (5.3)	64.74, < 0.0001
Absent	57 (68.7)	31 (46.3)	142 (94.7)	
Total	83 (100)	67 (100)	150 (100)	

S=Significant, MHO=Metabolic healthy obese, MAO=Metabolic abnormal obese

of 26 (31.3%) obese subjects in the MHO group, 36 (53.7%) in the MAO group, and 8 (5.3%) in the control population. Results revealed a significant positive correlation between metabolic abnormal obesity and and the presence of MA [Table 2]. Table 3 shows that 41.3% of all obese individuals had MA compared to only 5.3% of non-obese control group and it was statistically significant ($P = 0.0001$).

Figure 2 shows MA in the study groups. The metabolic abnormal obese group revealed the highest percentage of MA positive cases (53.7%), followed by MHO (31.3%), whereas the control group showed the least number of cases with MA (5.3%).

No significant correlation was observed between MetS parameters and MA among MHO (Table 4). A significant positive correlation between elevated triglyceride levels and MA was observed among MAO subjects [Table 5].

Discussion

Obesity is rising at an alarming rate throughout the world. The ever-growing rapid rise in the prevalence of obesity in India is much higher than the world average. This is giving rise to an increase in obesity-related complications, a serious socioeconomic problem. Obesity-related conditions that cause mortality are some of the most easily preventable. Obesity affects every aspect of human life from health to relationships, from economic to social. Obesity is also the risk factor for many noncommunicable diseases such as T2DM and hypertension, leading to nephrolithiasis, malignancies, chronic kidney disease (CKD), and ESRD. The burden of obesity-related glomerulopathy is dramatically rising in our society leading to an increase in morbidity and mortality. Therefore, renal function needs to be assessed in obese individuals to know its prevalence and its effects on clinically asymptomatic individuals to provide a better understanding of the obesity-related renal disease.

Table 3: Comparison of microalbuminuria among overall cases and controls

Urine microalbuminuria	Obese (cases) *N* (%)	Control *N* (%)	χ^2, *P*-value (overall)
Present	62 (41.3)	8 (5.3)	54.33, <0.00001
Absent	88 (58.7)	142 (94.7)	
Total	150 (100)	150 (100)	

S=Significant

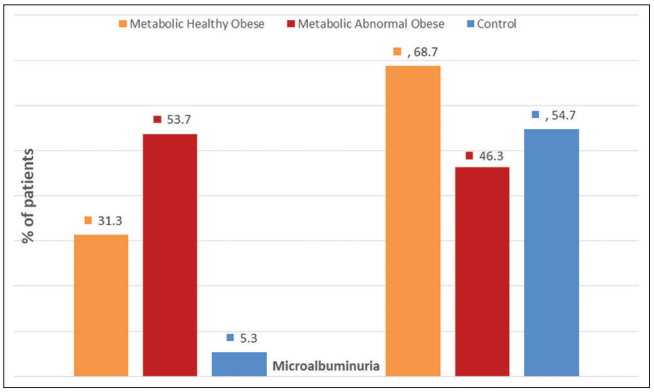

Figure 2: Comparison of microalbuminuria among cases (metabolic healthy obese and MAO) and controls

Table 4: Correlation of metabolic syndrome parameters and microalbuminuria in metabolic healthy obese

Variables	Unstandardized coefficients		Standardized coefficients (β)	*t*	*P-value*
	B	SE			
Microalbuminuria	3.231	0.850			
WC	−0.003	0.005	−0.059	0.517	0.607
FBS	−0.005	0.004	−0.162	1.374	0.173
SBP	−0.002	0.007	−0.030	0.222	0.825
DBP	−0.008	0.008	−0.132	1.010	0.316
TG	−0.001	0.001	−0.136	1.194	0.236
HDL	0.002	0.005	0.050	0.428	0.670

SE=Standard error, WC=Waist circumference, SBP=Systolic blood pressure, DBP Diastolic blood pressure, FBS=Fasting blood sugar, TG=Triglycerides, HDL=High-density lipoprotein, NS=Not significant

Table 5: Correlation of metabolic syndrome parameters and microalbuminuria in metabolic abnormal obese

Variables	Unstandardized coefficients		Standardized coefficients (β)	*t*	*P-value*
	B	SE			
Microalbuminuria	1.956	1.044			
WC	−0.005	0.005	−0.108	0.886	0.379
FBS	0.000	0.001	0.027	0.215	0.830
SBP	0.001	0.005	0.030	0.214	0.832
DBP	−0.004	0.008	−0.073	0.534	0.595
TG	0.002	0.001	0.291	2.049	0.045
HDL	−0.006	0.006	−0.124	0.887	0.379

WC=Waist circumference, SBP=Systolic blood pressure, DBP Diastolic blood pressure, FBS=Fasting blood sugar, TG=Triglycerides, HDL=High-density lipoprotein, NS=Not significant, S=Significant, SE=Standard error

The correlation between the presence of MA was statistically significant in the control group and obese group (MHO and MAO) using the Chi-square test.

Kramer *et al*.,[9] analyzed the data from Hypertension Detection and Follow-Up Program in 5897 hypertensive adults. This study showed that obese individuals had higher proteinuria and were also at a higher risk for CKD among the overweight (odds ratio of 1.22 with 95% confidence interval ranging 1.05–1.43), and obese individuals (odds ratio 1.38 with 95% confidence interval ranging from 1.17 to 1.63). These findings were statistically significant for the establishment of a direct positive association.

Panwar *et al*.,[10] study that analyzed 21,840 participants for such renal parameters as estimated glomerular filtration rate (eGFR) and MA revealed that obese individuals with MetS were more likely to have MA than those without MetS.

A cohort study conducted by Hashimoto *et al*.,[8] in the Japanese population showed that the incidence of MA was 0.5% (11 of 2122) for the control group, 1.0% (three of 302) for the MHO group, and 5.6% (15 of 267) for the MAO group. The study concluded a significant association of proteinuria in the MAO group than in the MHO group, i.e., the presence of proteins in the urine in the metabolic abnormal obese group (odds ratio of 2.80 with a 95% confidence interval ranging from 1.45 to 5.35). On logistic regression analyses, $P = 0.02$ was noted, suggestive of a significant finding.

Ah *et al*.,[5] conducted a study on 200 elderly Egyptians. An independent *t*-test along with paired *t*-test was used for the analyses, statistically. The study concluded that obesity was strongly associated with MA ($P < 0.05$).

In a multinational, observational study of 20,828 participants by Thoenes *et al*.,[11] a significantly high prevalence of MA was noted in obese individuals. In the univariate analysis, a higher BMI was found to correlate with a higher risk of MA (odds ratio of 1.36 with a 95% confidence interval ranging from 1.26 to 1.47) in obese individuals compared to the control group.

In their study, Foster *et al*.,[12] analyzed 2676 participants in the second and seventh cycles of the Framingham Heart Study. The study observed a significant association of MA with all measures of adiposity in men, whereas in women, only SAT was found to be associated with the risk of MA ($P > 0.3$). Obese individuals did not show a significant association with MA after standardization for related risk factors such as diabetes mellitus and hypertension (odds ratio of 1.09 with a 95% confidence interval ranging from 0.69 to 1.73). However, *P* value for this finding was 0.7, suggesting the probability of it being insignificant.

Fotheringham *et al*.,[13] analyzed data on 3611 participants in the Chronic Renal Insufficiency Cohort Study and examined albumin-to-creatinine ratio (ACR) in the obese and found that ACR was normal or similar to that seen in normal individuals.

Muthuvel *et al*.,[14] conducted a study on 138 diabetic participants in which the presence of MA was analyzed according to BMI. The study concluded that MA was not significant with the BMI and WHR ($P = 0.138$).

In the present study, MA was present in 53.7% MAO group and 31.3% in the MHO group, suggestive of renal function derangement in the obese individuals compared to the control group. The study was in tandem with the studies done by Kramer *et al*.,[9] Panwar *et al*.,[10] Ah *et al*.,[5] and Thoenes *et al*.,[11] but not in accord with the studies by Foster *et al*.,[12] Fotheringham *et al*.,[13] and Muthuvel *et al*.[14]

Our study had some limitations. (a) Obesity measurement needs to be assessed by various parameters, the most important being BMI. However, BMI does not take body fat percentage and muscle mass into consideration. Other measurements of obesity like WHR should also be given its due importance. (b) The study needs to be followed up over a period for a much better and more accurate assessment of the effect of obesity on renal function.

Conclusion

The study concluded that there was an adverse impact of metabolic abnormal obese and MHO on renal function, i.e., the presence of MA in obese individuals. Therefore, even in clinically asymptomatic obese individuals, weight loss strategies such as regular exercise and other lifestyle modifications should be promoted to reduce the risk of obesity-related renal complications.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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