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# Microalbuminuria in metabolically healthy and unhealthy obese individuals: an early indicator of microvascular endothelial dysfunction

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## Abstract

To estimate spot urine microalbumin levels in metabolically healthy and metabolically unhealthy obese individuals in relation to metabolic syndrome risk factors of NCEP ATP III criteria. Total 50 (16 female; 34 male) obese subjects aged between age ranges between 29 to 62 years old were analyzed for metabolic syndrome parameters and spot urine microalbumin levels. 14 subjects who are having high urine micro albumin levels and urine samples which give positive (+) for dip stick were excluded from this study. Among the 36 obese subjects 25 subjects are having at least one other metabolic syndrome risk factor along with increased waist circumference considered as metabolically unhealthy (MUHO) and 11 subjects were considered as metabolically healthy (MHO). High (55.87±16.78) micro albumin levels noted in obese group. Very high levels of urine microalbumin noted among metabolically unhealthy obese (107.52±56.54). It was 13.98±5.34 among the metabolically healthy obese group. The mean urine microalbumin level among MHO individuals was towards the upper reference level but within the allowed reference level (< 25 mg/L) The correlation of urine microalbumin with number of metabolic syndrome risk factors was statistically significant (r=0.7020; p=0.0001). Among the risk factors blood pressure [systolic r=0.4149; p=0.0392 and diastolic r=0.6486**;** p=0.0005] and Fasting blood glucose (r=0.6938; p=0.0001) were highly correlated where as waist circumference was not correlated with urine micro albumin levels. Elevated spot urine microalbumin levels among the metabolically healthy obese individuals may predict the micro-vascular endothelial dysfunction.

**Keywords:** Microalbuminuria, glucose tolerance, metabolic syndrome

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## Introduction

Microalbuminuria is an early indicator for the expansion of extracellular matrix in glomerular and tubulointerstitial compartments of kidney. It was already established marker for cardiovascular and renal risk in type – 2 diabetes mellitus. The incidence of diabetes is rising in the current trend of life style. The high intake of saturated fat and lack of sufficient physical activity leads to deposition of fat in adipose tissue. Abdominal obesity or visceral adiposity is the major underlying cause for the early onset of diabetes mellitus. The related consequences like dyslipidemia (high triglycerides and low high density lipoproteins), hypertension, and irregular glucose tolerance – array of metabolic syndrome risk factors are strongly correlated with microalbuminuria in different scientific studies. World Health Organization (WHO) defined microalbuminuria as an indicator of metabolic syndrome [1].

The previous studies have shown that abdominal obesity defined by greater waist



circumference was associated with an increased risk for incident microalbuminuria. However obesity is not homogenous but heterogeneous-metabolically healthy obese (MHO) and metabolically unhealthy obese (MUHO). In MHO scenario, the metabolic and immunological dysfunctions such as insulin resistance, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C), hyperglycemia and hypertension are not present. Whereas increased inflammatory cytokines and adipokines in MHO individual will leads to accumulation of macrophages in adipose tissue there by dysfunction metabolic and immune systems, considered to be as MUHO otherwise used as metabolic syndrome (Mets) [2]. Accordingly we have undertaken a comparative study with an aim to estimate microalbumin levels in metabolically healthy and metabolically unhealthy obese individuals in relation to metabolic syndrome risk factors of NCEP ATP III criteria.

## Methods and materials

The present study was conducted at Department of Clinical Biochemistry, Santhiram Medical College and General Hospital (SRMC&GH) Nandyal. In this study we selected 36 adult obese individuals who are having increased waist circumference (measured at the level of umbilicus [males >90cm, females >80cm]) from outpatient department. None of the subjects have a history of infection or other ailments at the time of the study. Control group consists of 14 age and sex matched non healthy individuals with no history of diabetes, confirmed by fasting blood glucose estimate served as controls. Informed consent was taken from all the subjects before conducting the clinical and biochemical evaluation. The study was approved by institutional ethical committee.

The NCEP ATP III criterion (The National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults) was used to classify obese subjects [3]. The components of criteria include increased waist circumference [> 90 cm / > 80 in men /women], blood pressure [≥ 130 / ≥ 85 mmHg systolic /diastolic] or history of hypertension treatment, serum triglycerides [≥150 mg/dl], fasting serum glucose [≥100 mg/dl] or history of diabetes treatment and decreased serum HDL-cholesterol [< 40/< 50 mg/dl in men / women]. Microalbumin was estimated in random midstream urine by multistandard turbidometric immunoassay method. The quantity of microalbumin in urine between 0-25 mg/L considered as normal and >25 mg/L considered as abnormal.

All the subjects were assessed for waist circumference, systolic and diastolic blood pressure.5 ml of blood sample and midstream urine samples were collected using standard protocol, biochemical parameters such as serum triglycerides, serum HDL-cholesterol, and fasting serum glucose were estimated using serum sample and microalbuminuria was estimated using urine sample.

**Statistical analysis:** Statistical analysis was done by student‘t’ test using online Graph pad Calculator software and results were expressed as mean ± SD. Pearson’s bivariate correlation analysis was used to correlate risk factors with microalbumin levels. P value <0.05 were considered as statistically significant.

## Results

In the current study, total 50 (16 female; 34 male) obese subjects were analyzed for metabolic syndrome parameters and spot urine microalbumin levels. Their age ranges between 29 to 62 years old. 14 subjects who are having high urine micro albumin levels towards upper reference level and urine samples which gives positive (+) for dip stick were excluded from this study. Among the 36 obese subjects 25 subjects are having at least one other metabolic syndrome risk factor along with increased waist circumference considered as MUHO and 11 subjects were considered as MHO.

The risk parameters for metabolic syndrome were significantly elevated in obese group compared to control group (Table 1). A significant difference was noted among Group I, Group II and Group III in respect to spot urine microalbumin levels. No significant differences was noted between control and MHO group in respect to metabolic syndrome risk factors and were significantly elevated in MUHO group compared to MHO group. Waist circumference is the common metabolic syndrome risk factor in MHO and MUHO groups (Table 2). Elevated blood pressure (systolic and diastolic) and fasting blood glucose levels were significantly correlated with spot urine microalbumin levels among the obese individuals (Table 3 and graph 1)



| Parameter studied | | Controls (n=14) | Obese (n=36) | Significant groups at 5% Level (Control Vs Other Groups) |
|---|---|---|---|---|
| Waist circumference | | 91.29±12.58 | 106.14±7.01 | P=0.0001 |
| Blood pressure | Systolic | 120.07±5.78 | 125.21±9.23 | P=0.0264 |
| | Diastolic | 75.23±4.6 | 79.02±6.20 | P=0.0185 |
| Triglycerides (TGL) | | 134.89±11.58 | 170.17±33.53 | P=0.0001 |
| High density lipoprotein | | 48.15±8.24 | 37.26±9.81 | P=0.0001 |
| Fasting Blood sugar | | 88.4±8.12 | 107.60±23.15 | P=0.0007 |
| Microalbumin | | 11.76±2.11 | 55.87±16.78 | P=0.0001 |

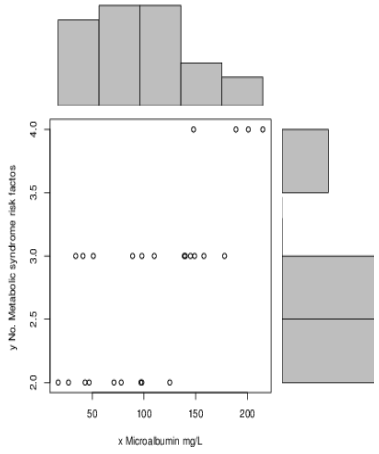
**Table 1: Comparison of studied parameters**

| PARAMETER | | Group I CONTROLS (N=14) | Group II MUHO (N=25) | Group III MHO (N=11) | Significant at 5% Level (Control Vs Other Groups) | Significant at 5% Level (MUHO Vs. MHO) |
|---|---|---|---|---|---|---|
| Waist circumference | | 91.29±12.58 | 106.4±6.77 | 105.75±7.35 | S(Group II & III) | NS |
| Blood pressure | Systolic | 120.07±5.78 | 127.76±10.23 | 121.25±5.37 | S(Group II) | S |
| | Diastolic | 75.23±4.6 | 80.56±6.60 | 76.62±4.56 | S(Group II) | S |
| Triglycerides (TGL) | | 134.89±11.58 | 193.52±18.43 | 133.68±12.94 | S(Group II) | S |
| High density lipoprotein | | 48.15±8.24 | 32.12±3.05 | 45.31±11.22 | S(Group II) | S |
| Fasting Blood sugar | | 88.4±8.12 | 118.84±23.09 | 90.06±6.00 | S(Group II) | S |
| Microalbumin | | 11.76±2.11 | 107.52±56.54 | 13.98±5.34 | S(Group II & III) | S |

**Table 2: Comparison of studied groups**

| Microalbumin levels vs. | Correlation (r-value) | p-value |
|---|---|---|
| Waist circumference | 0.07253 | 0.7304 |
| Systolic BP | 0.4149 | 0.0392 |
| Diastolic BP | 0.6486 | 0.0005 |
| Triglycerides | 0.1550 | 0.4594 |
| High density lipoprotein | 0.067 | 0.7503 |
| Fasting Blood Glucose | 0.6938 | 0.0001 |
| No. Metabolic syndrome risk factors | 0.7020 | 0.0001 |

**Table 3: Correlation of metabolic syndrome parameters with microalbumin**




**Graph 1: Correlation of number of risk factors with microalbuminuria**





## Discussion

Obesity induced reversible micro vascular endothelium dysfunction may progressive to a fully established irreversible microvascular diseases. The major causes for medical emergency among obese individuals are cerebral ischemia, brain injury [4], atherosclerotic vascular disease (AVD), myocardial infarction (MI) [5], chronic kidney diseases (CKD) and coronary heart diseases (CHD) [6, 7] which arise from a single cause that is micro and macro vascular diseases. Detection of micro vascular changes in obesity at an early stage helps us to save the relative number of patients from obesity related mortality. Microalbuminuria is a marker of endothelial dysfunction and vascular damage. The Third National Health and Nutrition Examination Survey (NHANES III) demonstrated the association between metabolic syndrome and microalbuminuria [8]**.** The present study has also noted high (55.87±16.78) micro albumin levels in obese subjects compared to normal non obese subjects (11.76±2.11) [**Table 1]**. The study has also noted a clear cut variation between metabolically healthy obese to unhealthy obese and non obese normal healthy control to metabolically healthy obese in relation to microalbumin. A very high level of (107.52±56.54) urine microalbumin was noted among metabolically unhealthy obese group compared to metabolically healthy obese (13.98±5.34) group. Also, the mean urine microalbumin level among MHO individuals was towards the upper reference level but within the allowed reference level (< 25 mg/L) which high when compared to normal non obese healthy control [**Table 2 ]**. These findings creates an impression that waist circumference alone may not greatly affect the vascular endothelium function.

The study has also noted significant correlation of urine microalbumin with number of metabolic syndrome risk factors (r=0.7020; p=0.0001). Among the risk factors blood pressure [systolic r=0.4149; p=0.0392 and diastolic r=0.6486**;** p=0.0005] and Fasting blood glucose (r=0.6938; p=0.0001) were highly correlated where as waist circumference was not correlated with urine micro albumin levels [**Table 3 and Graph 1**]. The results of current study are in the line with results of Chang SS et al [9] and contradictory with Lin CC et al [10] and Chen BD et al [11] who found significant correlation with all the metabolic syndrome risk factors. The results may vary with the protocol implemented to conduct the study.

The mechanism for microalbuminuria among obese with increased diastolic blood pressure and high fasting glucose is not yet understood. It was hypothesized that before type 2 diabetes mellitus (DM) or systolic hypertension (SBP) is developed in obese individuals, the metabolic syndrome is probably a vascular disease in the periphery, which may cause high diastolic blood pressure and hyperglycemia. This can be explained as decreased perfusion to expanded abdominal visceral adipose tissue of an obese individual will lead to altered adipokine secretion, Increased in inflammatory components, development of peripheral insulin resistance and elevated free fatty acids which causes higher levels of Triglycerides and decreased high density lipoprotein collectively called as metabolic syndrome.

World Health Organization (WHO) has estimated that 370 million people will suffer from obesity associated comorbidities by the end of 2030.The present study suggesting that, obese individuals with urine microalbumin levels towards the upper normal reference limit are in high risk for the progression of endothelial dysfunction from micro to macro vascular and to develop established metabolic syndrome related comorbidities. In our view, the screening of obese individuals for urine microalbumin levels even with normal physical and metabolic function helps us to detect the stage of metabolic transition of an obese from healthy to unhealthy. The initiation of ACE inhibitors, decrease in weight may help to delay or prevent the establishment of metabolic syndrome and related comorbidities. Thereby we can decrease the group of obese individuals with risk of metabolic comorbidities related mortality.

In the present study we have not considered lipid lowering drug medication among the subjects. The urine microalbumin levels were estimated in spot urine microalbumin levels not in 24 hours urine.

## Conclusion

Screening for urine microalbumin levels among metabolically healthy obese individuals may beneficial to predict the microvascular endothelial dysfunction. And it helps to detect and prevent the clinical manifest atherosclerotic vascular, cardiovascular and renal complication at an early stage.



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