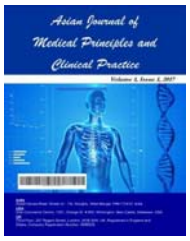

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# Microalbuminuria as a Marker of Cardiovascular Risks in Egyptian Hypertensive Patients

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***Authors' contributions***

*This work was carried out in collaboration between all authors. Author EME designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors GAR and OZ managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.*

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## ABSTRACT

Hypertension (HTN) is one of the modifiable atrial fibrillation (AF) risk factors, and management of HTN may reduce the incidence of AF. Microalbuminuria (MAU) increases cardiovascular risk in hypertension.

**Aim of the Study:** To determine the association of microalbuminuria in Egyptian hypertensive patients and its relationship with AF.

**Patients and Methods:** Five hundred hypertensive patients without a history of pre-existing kidney diseases participated in this study. A questionnaire was used for collecting information on demographics, lifestyle, and family history of cardiovascular and kidney disease, and spot morning urine samples were collected for albuminuria estimation.

**Results:** A total of 500 Egyptian hypertensive patients, aged 47 ± 7.3 years were enrolled in this study. Two hundred and ninety three were males and 207 were females. The mean duration of hypertension was 5.6 ± 2.7 years. Mean body mass index (BMI) was 27.1 ± 2.4 kg/m2. There were 354 (70.8%) patients whose BP well controlled (<140/<90 mmHg), while 146 (29.2%) patients were

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not controlled. 249 (49.8%) patients had MAU. Logistic regression analysis revealed that male gender, lower glomerular filtration rates, higher mean BP, higher heart rates and ejection fraction less than 50% had a significant effect on prevalence of MAU with an odds ratio > 1 and P value < 0.05. Two hundred patients had AF, 173 (86.5%) of them had MAU. There was a positive correlation between MAU and AF and left ventricular hypertrophy (LVH) with P value < 0.05.
**Conclusion and Recommendation:** Screening for albuminuria may be useful in early risk assessment of cardiovascular disease in Egyptian hypertensive patients, identification of a patient at risk of CV events provides an opportunity for early treatment, to slow the progression of disease.

*Keywords: Hypertension; AF; CV risks; microalbuminuria.*

## 1. INTRODUCTION

Hypertension is still the main risk factor for the development of atrial fibrillation (AF). Several pathophysiologic mechanisms (such as structural changes, neurohormonal activation, fibrosis, atherosclerosis, etc.) have been advocated to explain the onset of atrial fibrillation [1]. AF is often hidden [paroxysmal], and is associated with an about fivefold risk of stroke. This risk can be reduced by the use of appropriate therapy for hypertensive patients with increased cardiovascular risk [2].

Hypertension and microalbuminuria (MAU) commonly coexist. The mechanism is controversial but is thought to be a renal manifestation of generalized vascular endothelial dysfunction [3]. Microalbuminuria is a well-recognized marker of cardiovascular complications and increased cardiovascular risk in hypertension [4].

However, reliable data about the association of microalbuminuria in hypertensive patients and its relation with cardiovascular and renal morbidity are limited in Egypt. There is still a debate concerning whether screening for microalbuminuria is cost-effective in risk assessment and prevention of cardiovascular disease, so the aim of this study is to determine the association of microalbuminuria in Egyptian hypertensive patients and its relationship with AF.

## 2. PATIENTS AND METHODS

A cross-sectional study was performed from January to December 2016 at internal medicine outpatient clinic of El Fayoum University Hospital, on five hundred Egyptian hypertensive non diabetic patients. Subjects were excluded from the study if they had co-morbidities like cardiomyopathy, valvular heart diseases, diabetes mellitus (DM), pulmonary diseases, liver diseases, renal impairment, proteinuria, urinary tract infection (UTI), anaemia or thyrotoxicosis. All cases of secondary hypertension were excluded. All participants gave written informed consent. This study was approved by our ethical committee.

A structured questionnaire regarding the demographic data such as age, gender, height, body weight and family history of DM. BMI was calculated as weight (Kg) divided by height (m2). Blood pressure was measured with a suitable mercury sphygmomanometer. Readings were taken after the patients had been resting comfortably, back supported in the sitting or supine position, for at least 5 minutes and at least 30 minutes after smoking or coffee ingestion. Mean arterial pressure (MAP) was calculated as [systolic + (2 x diastolic) pressure]/3. High blood pressure was defined as systolic blood pressure (SBP) ≥140 mmhg and/ or diastolic blood pressure (DBP) of ≥90 mmhg or use of anti-hypertensive medications. Heart rate, cardiac examination, electrocardiogram (ECG) and echocardiography (ECHO) were done. Lipid profile, liver profile, fasting and 2 hours post prandial blood glucose, HA1C and renal function tests (glomerular filtration rate, serum creatinine) were done. Estimated glomerular filtration rate (GFR) was by the Modification of Diet in Renal Diseases (MDRD):

GFR=186 x serum CR-1.154*age*1.212(if patient is black)*0.742(if female). Morning mid-stream urine sample, negative for proteinuria by Albustix, was used to calculate microalbumin: creatinine ratio in mg/g. Microalbumin was carried out using ELISA assay. If the ratio was <30 mg/g the patient was considered normo-albuminuric, ratios between 30-300 mg/g were indicative of microalbuminuria and above 300 mg/g revealed macro-albuminuria [3].

### 2.1 Statistical Analysis

All the collected data were expressed as mean ± SD and analyzed by using SPSS version 20 using the following tests: Student T, Chi square, Perason correlation coefficient and logistic regression. P>0.05 was considered non-significant, P< 0.05 was considered significant P< 0.01 was considered highly significant.

## 3. RESULTS

A total of 500 hypertensive patients, aged 47 ± 7.3 years were enrolled in this study. Two hundred and ninety three were males and 207 were females. The mean duration of hypertension was 5.6 ± 2.7 years. Mean body mass index (BMI) was 27.1±2.4 kg/m2. Beta blockers (BBs) were prescribed in 50,9%, followed by calcium channel blockers (CCBs) 23.5%, Angiotensin converting enzyme inhibitors (ACEI) (21.1%) and thiazide type diuretic (4.5%). There were 354 (70.8%) patients whose BP well controlled (<140/<90 mmHg), while 146 (29.2%) patients were not controlled. 249 (49.8%) patients had MAU. Logistic regression analysis revealed that male gender, lower glomerular filtration rates, higher mean BP, higher heart rates and ejection fraction (EF) less than 50% had significant effect on prevalence of MAU with an odds ratio > 1 and P value < 0.05. Two hundred patients had AF (173 (86.5%) of them had MAU. There was a positive correlation between MAU and AF and LVH (diagnosed by ECG) in essential hypertension patients, there was no correlation between renal function and lipid profile, BBs, diuretics, as shown in Tables 1 and 2.

## 4. DISCUSSION

In this study, 249 (49.8%) patients had MAU, increase BMI, male gender, lower glomerular filtration rates, higher mean BP, higher heart rates and ejection fraction less than 50% had significant effect on prevalence of MAU with an odds ratio > 1 and P value < 0.05.

Prevalence of microalbuminuria in hypertensive patients is ranging in the different countries between 53% and 71%, with the highest rate in patients with uncontrolled hypertension [5]. This variation might be due to patient characteristics.

Microalbuminuria is independently associated with numerous modifiable CV risk factors and markers of CV diseases. These include: obesity; smoking; insulin resistance syndrome; left ventricular hypertrophy (LVH); left ventricular (LV) dysfunction and elevated C reactive protein levels [6-7].

**Table 1. Correlation between microalbuminuria and different parameters**

| Parameter | P value | Parameter | P value |
|---|---|---|---|
| Age | <0.05 | AF | <0.05 |
| Male | <0.05 | HR | <0.05 |
| Female | >0.05 | LVH | <0.05 |
| BMI | <0.05 | EF | <0.05 |
| Duration of HTN | <0.05 | GFR | <0.05 |
| Control on HTN | <0.05 | DIURETICS | >0.05 |
| ACEI | <0.05 | BB | >0.05 |
| CCB | <0.05 | lipid profile | >0.05 |

**Table 2. Multivariate logistic regression in all patients and odds ratio (OR) of different predictors for presence of microalbuminuria**

| Predictor | OR | 95 CI% | P value |
|---|---|---|---|
| Age (middle vs young) | 1.030 | 0.931–1.427 | 0.762 |
| Gender (male vs female) | 1.220 | 1.170-1.250 | **0.04** |
| BMI (>25 vs <25) | 1.066 | 1.021-1.322 | 0.235 |
| GFR (<30 vs > 80) | 1.598 | 1.498-1.683 | **0.023** |
| GFR (30-60 vs > 80) | 1.345 | 1.294-1.413 | **0.049** |
| GFR (60-80 vs > 80) | 1.531 | 1.481-1.601 | **0.034** |
| Duration of hypertension | 1.030 | 1.011-1.463 | 0.247 |
| Mean blood pressure | 1.395 | 1.298-1.410 | **0.037** |
| HR (>100 vs < 80) | 1.154 | 1.054-1.236 | **<0.001** |
| HR (80-100 vs < 80) | 1.396 | 1.376-1.412 | **0.028** |
| EF (>50% vs <50%) | 1.002 | 0.981-1.031 | **<0.001** |

Obesity, by several mechanisms (glomerular hyper-filtration, focal segmental glomerulosclerosis, insulin resistance and adiponectin) can lead to the development of albuminuria [8].

We found a positive correlation between MAU and AF and LVH in essential hypertension patients, there was no correlation between renal function and lipid profile, BBs, diuretics.

Many studies [9] have shown an association between microalbuminuria and risk of CV events. Microalbuminuria was shown to predict ischaemic heart disease [9].

Moreover Wachtell et al. [10] reported that microalbuminuria is associated with persistent electrocardiographic (ECG) LVH independent of established risk factors for cardiac hypertrophy , multivariate analysis showed that LVH was associated with a 1.6-fold higher prevalence of microalbuminuria and 2.6-fold higher prevalence of macroalbuminuria (both $p<0.001$). This relationship was independent of age, systolic and diastolic blood pressure (SBP and DBP), diabetes, gender, race, serum creatinine or smoking status, and, therefore, it has been postulated that cardiac damage and albuminuria occur in parallel [10].

The main determinant of albumin excretion rate in subjects with mild hypertension and no cardiovascular complications seems to be the hemodynamic load, whereas in subjects with more severe hypertension and associated target organ damage, the augmented urinary albumin leak is probably the consequence of glomerular damage. Further evidence for the link between microalbuminuria and CV disease comes from the fact that microalbuminuria is considered a reliable indicator of endothelial dysfunction, this being associated with transendothelial escape rate of albumin and plasma levels of von Willebrand factor [11]. Endothelial dysfunction is considered an early step of atherosclerosis and represents increased risk for CV events [12].

## 5. CONCLUSION AND RECOMMENDATION

Screening for albuminuria may be useful in early risk assessment of cardiovascular disease in Egyptian hypertensive patients. Early identification of a patient at risk of CV events provides an opportunity for early treatment, to slow the progression of disease.

## CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

## ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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