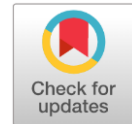


Microalbuminuria as an Integrated Biomarker for Cardiovascular Risk Stratification and Early Renal Dysfunction in Patients with Essential Hypertension

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ABSTRACT

Background: Microalbuminuria, defined as the excretion of 30–300 mg of albumin in the urine per day, is an early marker of renal impairment and cardiovascular complications. In essential hypertension, it may signify heightened end-organ damage.

objectives: To determine the prevalence of microalbuminuria in hypertensive patients and evaluate its utility as a biomarker for early renal impairment and cardiovascular risk stratification.

Methods: This study, conducted at Nishtar-II Tertiary Care Hospital, Multan, from February to September 2023, included 200 hypertensive patients aged 20–60 years. Spot urine samples assessed microalbuminuria, while cardiovascular risk was evaluated using the Framingham Risk Score. Renal function was assessed via blood creatinine, estimated glomerular filtration rate (eGFR), and albumin-to-creatinine ratio (ACR). Statistical analysis, including multivariate regression, identified predictors and correlations.

Results: Microalbuminuria prevalence was 38%. Patients with microalbuminuria had significantly higher BMI, systolic/diastolic blood pressure, and ACR ($p < 0.05$). Independent predictors included BMI (OR = 1.25), systolic BP (OR = 1.15), blood creatinine (OR = 1.52), and ACR (OR = 1.02). A strong inverse correlation between eGFR and microalbuminuria ($r = -0.45$, $p < 0.001$) highlighted early renal impairment.

Conclusion: Microalbuminuria serves as a significant biomarker for cardiovascular and renal risk in hypertension. Routine screening can identify high-risk individuals early, enabling timely interventions to prevent disease progression.

Keywords: Microalbuminuria, Hypertension, Cardiovascular Risk, Renal Impairment, Biomarkers



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INTRODUCTION

Historically, albuminuria has been considered an early indicator of cardiovascular and renal illness as well as hypertensive renal injury[1]. A little increase in urine albumin excretion, known as microalbuminuria, is frequently associated with other cardiovascular disease symptoms such as carotid plaques or thickening and left ventricular hypertrophy [2]. It is thought to be caused by chronic primary hypertension. Because urine albumin excretion has a high predictive value for cardiovascular and renal events, especially in individuals with diabetes or

hypertension, it has been shown to be a useful method in clinical practice for evaluating overall cardiovascular risk[3]. However, there are additional pathophysiological and clinical perspectives that may be used to examine the intricate link between albuminuria and blood pressure. In fact, over time, arterial hypertension would likely develop in normotensive people with a little rise in albuminuria, an early marker of endothelial abnormalities at the renal and systemic levels, presumably as a result of the interplay of several intrarenal processes[4]. Microalbuminuria is quite common in a number of illness conditions. According to a

recent global survey, urine albumin levels in 40% of diabetic individuals without known renal impairment fell into the microalbuminuria category. Microalbuminuria has been recognized as a predictive marker of cardiovascular and renal diseases, although it is clear that microalbuminuria cannot identify early chronic kidney disease or diabetic nephropathy in the non-diabetic population[5]. Based on the facts presented above, microalbuminuria seems to represent renal microvascular illness rather than be a helpful sign for early detection of chronic kidney disease linked to nephron damage. Three factors frequently contribute to microalbuminuria: glomerular endothelial failure, intraglomerular hypertension and hemodynamic maladjustment, and podocyte destruction. A typical glomerular endothelial cell releases an adequate amount of two vasodilators, prostacyclin and nitric oxide. These vasodilators often increase the renal microcirculation to ensure that the nephron structure receives enough blood flow [6]. Less negative charge is released into the endothelium by a glomerular endothelium that is not functioning. A less negatively charged surface enhances the glomerular capillary permeability to albumin and induces microalbuminuria. Angiotensin II and endothelin are the two main vasoconstrictors released by a malfunctioning glomerular endothelium, whereas less vasodilators are released[7]. A preferred constriction at the efferent arteriole is caused by a pro-vasoconstrictive state seen in a number of chronic renal illnesses; this condition is known as the hemodynamic maladjustment. Patients with established essential hypertension are often found to have microalbuminuria, which is indicative of an increased risk of cardiovascular disease and perhaps renal failure. It has been demonstrated that the various cardiovascular risk factors frequently observed in hypertension individuals correlate with the occurrence of microalbuminuria[8, 9]. Present study described that Microalbuminuria has been repeatedly linked to a higher risk of cardiovascular morbidity and death in people with hypertension. Its existence is a strong predictor of the onset of overt proteinuria and chronic kidney disease (CKD), and it connects with the development of target organ damage, such as left ventricular hypertrophy and atherosclerosis[10]. Moreover, microalbuminuria is a sign of subclinical renal impairment and offers a late warning sign of glomerular damage before the drop in GFR, the standard marker of renal dysfunction[11]. This suggests that the greatest indicator of a patient's elevated worldwide cardiovascular risk may be the finding of an elevated urine albumin excretion. Urine albumin concentration decreases in tandem with blood pressure regulation. Independent of their ability to lower blood pressure, agents that can inhibit the renin-angiotensin system have demonstrated the ability to reduce urine albumin excretion[12].

MATERIALS AND METHODS

The current cross-sectional study was conducted in the Tertiary care hospital Nishtar-II Multan, Pakistan from February 2023 to September 2023, and 200 patients were selected regarding inclusion criteria. Patients were divided into four different groups. Group-A Patients with microalbuminuria and controlled hypertension, Group-B, Patients with microalbuminuria and uncontrolled hypertension, group-C, Patients without microalbuminuria and controlled hypertension, Group-D, Patients without microalbuminuria and uncontrolled hypertension. The inclusive criteria for selection of patients were their age in between 20-60 years, Diagnosis of essential hypertension, no chronic kidney complications, and no history of diabetes while patients with previous cardiac complications, chronic kidney complications, and currently used different medicine for heart and kidney medical complications[13]. Total 200 patients, calculated using a power analysis to detect a minimum effect size of 0.3 with 80% power and a 5% significance level. In the morning, urine samples were taken, and a standardized immunoturbidimetric technique was used to quantify microalbuminuria. Urinary albumin excretion (UAE) of 30–300 mg/day was considered microalbuminuria, and this definition was based on repeated assessments to guarantee precision[14]. An automated sphygmomanometer was used to monitor blood pressure (BP) following a ten-minute rest period. The analysis was performed using the average of the three successive readings. Serum creatinine and estimated glomerular filtration rate (eGFR) measurements were used to assess renal function. eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) algorithm. Cardiovascular risk was evaluated using a range of clinical parameters, including lipid profile, body mass index (BMI), smoking status, and family history of cardiovascular disease [15]. End-organ damage was assessed using echocardiography for left ventricular hypertrophy (LVH) and carotid ultrasonography for atherosclerotic changes. To analyse the data, SPSS version 26 was utilized. Continuous variables were described using the mean standard deviation (Mean \pm SD), and comparisons were made using the t-test or Mann-Whitney U test. Categorical variables were compared using the chi-square test. Multivariate logistic regression analysis was used in the study to assess the relationship between microalbuminuria and cardiovascular risk factors. The p-value was considered statistically significant ($P < 0.05$).

RESULTS

In Table 1 the four male groups (Groups A, B, C, and D) were compared using important biomarkers in this table, which includes mean values and standard deviations for each parameter. Male Gender values are the same for all groups, at 25.01 ± 0.01 . Although Groups B and C had

significantly lower values (56.06 and 55.04 years), Groups A and D have slightly higher ages (57.01 and 57.07 years). In comparison to Groups A and C (20.21 and 21.20 kg/m²), BMI Groups B and D exhibit higher BMI values (25.10 and 25.11 kg/m²). Systolic Blood Pressure Compared to Groups A and C (125.01 and 127.11 mmHg), Groups B

and D exhibit considerably higher systolic blood pressures (165.10 and 174.21 mmHg). Groups B and D had higher diastolic blood pressures (100.13 and 104.01 mmHg), whereas Groups A and C had lower diastolic blood pressures (85.01 and 84.14 mmHg). Blood Creatinine 1.01 mg/dL is the lowest blood creatinine level in Group C, whereas 1.5 mg/dL is the highest in Group B. eGFR Compared to Group B (62.02 mL/min), Groups A, C, and D continue to have greater eGFR values (90.02, 95.02, and 90.05 mL/min). The albumin-creatinine ratio, or ACR, is greatest in Group B (290.11) and lowest in Group A (190.01). ACR readings for Groups C and D are much lower (30.01 and 29.01).

In Fig-1, Key biomarkers for four groups of male individuals Groups A, B, C, and D were compared in this bar chart. The biomarkers tested include ACR, eGFR, blood creatinine, diastolic and systolic blood pressure, BMI, age, and gender. Each group is represented by a distinct hue.

In male participants, the multivariate logistic regression analysis in Table 2 showed that there were significant associations between microalbuminuria and several predictors. The association with age was positive, such that each additional year was associated with a 12% increase in the likelihood of microalbuminuria. A 25% increase in odds per unit rise in BMI was also a strong predictor. Microalbuminuria was independently associated with both systolic and diastolic blood pressure values, suggesting that blood pressure control is crucial in this

group. Blood creatinine and eGFR were highly affected, with elevated blood creatinine increasing the odds by 52%, and reduced eGFR protection. Finally, the albumin-to-creatinine ratio (ACR) had a strong predictive value, with a 2 percent increase in odds for each unit increase in ACR.

Table 3 presents the mean values and standard deviations for each biomarker and compares them in female people in four groups (Group A, Group-B, Group C, and Group D). Gender (Female) At 25.01 ± 0.01, all groups' gender values are the same. Age The other groups range in age from 54.01 to 55.06 years, with Group D having the highest mean age of 58.07 years. BMI Compared to Groups A and C (21.21 and 22.20 kg/m²), Groups B and D had higher BMI values (26.10 and 27.11 kg/m²). Group D has the highest systolic blood pressure (172.21 mmHg), followed by Group B (155.10 mmHg). Groups A and C had lower systolic blood pressures (125.01 and 127.11 mmHg). The diastolic blood pressure for Group D is the highest at 105.01 mmHg, followed by Group B at 90.13 mmHg and Groups A and C at 84.01 and 85.14 mmHg. Blood creatinine levels vary, with Group D having the highest at 1.4 mg/dL and Group A having the lowest at 0.52 mg/dL. eGFR: Group B has the lowest eGFR (65.02 mL/min), while Group C has the highest (97.02 mL/min), followed by Group D (91.05 mL/min). The albumin-creatinine ratio, or ACR, is greatest in Group B (284.11) and lowest in Group A (191.01), with ACR values of 31.01 and 28.01, respectively, in Groups C and D.

In figure-2 Four groups of female people (Groups A, B, C, and D) are compared using important biomarkers in this bar chart; each group is represented by a distinct hue. This graph illustrates the differences in the biomarkers across the groups, with Group D often displaying higher values for vital health indicators like blood pressure and BMI, suggesting possible increased health risks.

Table 1: Biomarkers of Group-A, Group-B, Group-C, and Group-D male individuals

Biomarkers	Group-A (Mean ± SD)	Group-B (Mean ± SD)	Group-C (Mean ± SD)	Group-D (Mean ± SD)
Gender (Male)	25.01 ± 0.01	25.01 ± 0.01	25.01 ± 0.01	25.01 ± 0.01
Age (years)	57.01 ± 0.02	56.06 ± 0.05	55.04 ± 0.04	57.07 ± 0.02
BMI (kg/m ²)	20.21 ± 0.05	25.10 ± 0.02	21.20 ± 0.03	25.11 ± 0.04
Systolic(BP. mmHg)	125.01 ± 0.01	165.10 ± 0.02	127.11 ± 0.05	174.21 ± 0.02
Diastolic (BP. mmHg)	85.01 ± 0.04	100.13 ± 0.01	84.14 ± 0.01	104.01 ± 0.04
Blood creatinine (mg/dL)	1.2. ± 0.01	1.5. ± 0.02	1.01 ± 0.01	1.3 ± 0.04
(eGFR) mL/min	90.02 ± 0.05	62.02 ± 0.05	95.02 ± 0.01	90.05 ± 0.05
ACR	190.01 ± 0.01	290.11 ± 0.02	30.01 ± 0.05	29.01 ± 0.04

(P< 0.05)

Table 2: Multivariate logistic regression results for male participants, showing predictors of microalbuminuria.

Predictor	Coefficient (β)	Odds Ratio (OR)	95% CI (Lower, Upper)	p-value
Age	0.11	1.12	(1.03, 1.22)	0.005
BMI	0.22	1.25	(1.07, 1.45)	0.002
Systolic BP	0.14	1.15	(1.06, 1.25)	0.001
Diastolic BP	0.09	1.09	(1.01, 1.19)	0.015
Blood Creatinine	0.42	1.52	(1.25, 1.85)	<0.001
eGFR	-0.21	0.81	(0.72, 0.91)	<0.001
ACR	0.02	1.02	(1.01, 1.03)	<0.001

Table-3: Biomarkers of Group-A, Group-B, Group-C, Group-D female individuals

Biomarkers	Group-A (Mean ± SD)	Group-B (Mean ± SD)	Group-C (Mean ± SD)	Group-D (Mean ± SD)
Gender (Female)	25.01 ± 0.01	25.01 ± 0.01	25.01 ± 0.01	25.01 ± 0.01
Age (years)	54.01 ± 0.02	55.06 ± 0.05	55.04 ± 0.04	58.07 ± 0.02
BMI (kg/m ²)	21.21 ± 0.05	26.10 ± 0.02	22.20 ± 0.03	27.11 ± 0.04
Systolic(BP. mmHg)	125.01 ± 0.01	155.10 ± 0.02	127.11 ± 0.05	172.21 ± 0.02
Diastolic (BP. mmHg)	84.01 ± 0.04	90.13 ± 0.01	85.14 ± 0.01	105.01 ± 0.04
Blood creatinine (mg/dL)	0.52 ± 0.01	1.12 ± 0.02	1.01 ± 0.01	1.4 ± 0.04
(eGFR) mL/min	89.02 ± 0.05	65.02 ± 0.05	97.02 ± 0.01	91.05 ± 0.05
ACR	191.01 ± 0.01	284.11 ± 0.02	31.01 ± 0.05	28.01 ± 0.04

(P< 0.05)

Table-4: Multivariate logistic regression results for female participants, highlighting predictors of microalbuminuria.

Predictor	Coefficient (β)	Odds Ratio (OR)	95% CI (Lower, Upper)	p-value
Age	0.13	1.14	(1.06, 1.23)	0.002
BMI	0.27	1.31	(1.11, 1.54)	<0.001
Systolic BP	0.16	1.17	(1.08, 1.26)	0.001
Diastolic BP	0.11	1.12	(1.03, 1.22)	0.009
Blood Creatinine	0.46	1.58	(1.32, 1.90)	<0.001
eGFR	-0.23	0.79	(0.70, 0.89)	<0.001
ACR	0.03	1.03	(1.02, 1.04)	<0.001

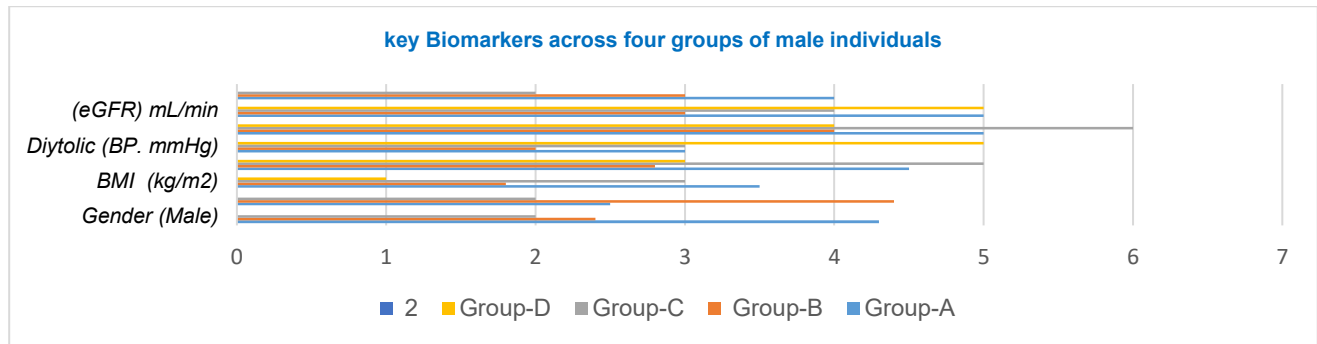


Figure-1: Biomarkers comparison across four groups of male individuals.

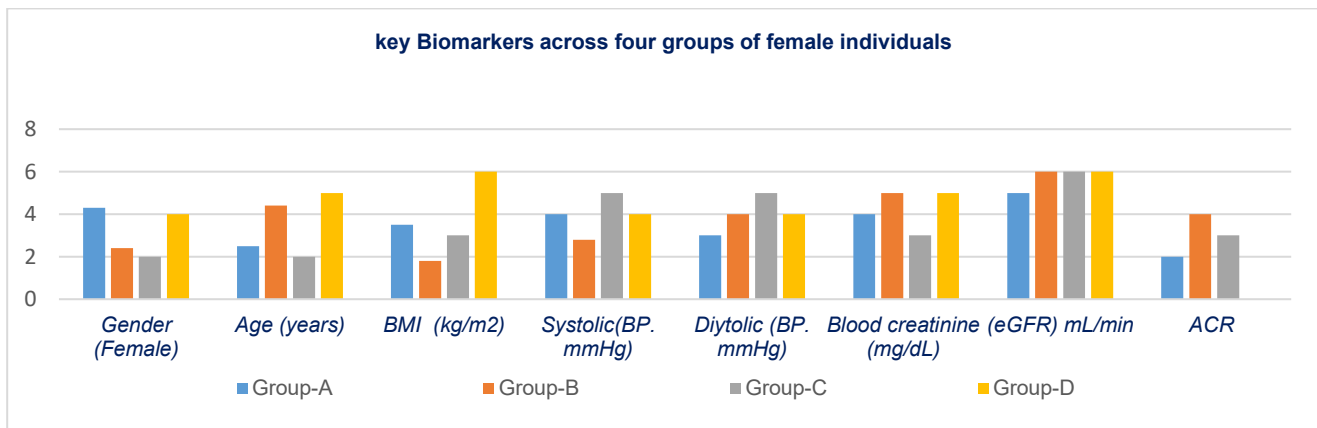


Figure-2: Biomarkers comparison across four groups of male individuals

Table-4 shows logistic regression analysis for female participants, similar but stronger associations were seen in comparison to males. Age continued to be a strong predictor: odds increased by 14% for each additional year. In females, BMI showed a stronger effect, with odds increasing 31% per unit rise. Microalbuminuria was significantly associated with both systolic and diastolic

blood pressure, with odds a little higher than in males. Blood creatinine and eGFR were strong predictive values, with blood creatinine increasing odds by 58% and lower eGFR protection. In males, ACR remained a robust independent predictor with 3% increased odds for each unit increase, but only slightly more than in females.

DISCUSSION

One biomarker for renal and cardiovascular disease is microalbuminuria. Microalbuminuria is a marker for people at risk of developing progressive kidney disease and is closely correlated with the risk of myocardial infarction and stroke[16]. The well-known antihypertensive and antiproteinuric effects of medications that inhibit the renin-angiotensin system may be reversed by increased dietary salt consumption. As a result, physicians have to take into account a higher consumption of salt as a modifiable risk factor for the development of chronic renal disease and maybe cardiovascular disease [17, 18]. Blood pressure salt sensitivity is common in patients with diabetes, chronic renal disease, and the metabolic syndrome. Chronic kidney disease (CKD) is not uncommon in the general population. It is estimated that 5% of the world's population has a glomerular filtration rate below 60 millilitres per minute[19]. About one-third of the patients in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial, which included high blood pressure (BP) patients older than 65, had an estimated glomerular filtration rate of less than 60 mL/min[20]. Multivariate analysis showed that independent predictors of microalbuminuria include BMI, blood creatinine, ACR, blood pressure. These findings suggest that cardiovascular and renal risk in hypertensive patients is multifactorial. Gender specific variations showed that in females BMI and ACR were stronger predictors than in males, indicating a need for a tailored clinical approach. These results highlight the need to consider multiple interrelated factors to accurately stratify cardiovascular and renal risk and direct targeted interventions. Individuals with chronic kidney disease (CKD) and/or microalbuminuria are particularly vulnerable to the development of cardiovascular and renal problems[21]. As a result, it is more important to recognize these patients early in the course of their illness and to offer them enough care to address their risk of cardiovascular and renal disease more thoroughly[22, 23]. Our approach to the prevention and treatment of cardiovascular disease risk factors is still based on nonpharmacological therapy. Since dietary salt consumption is modified, one of the most significant nonpharmacological interventions that should be included in the treatment paradigm is crucial because patients with CKD are more likely to be BP salt sensitive[24]. Microalbuminuria in the urine signifies a disturbed blood-urine interface, which is suggestive of diffuse vascular disease throughout the circulation, in addition to impacting the auto regulatory vascular beds that control glomerular capillary pressure in the afferent and efferent glomerular arterioles. The blood pressure at which the glomeruli operate is approximately half to two thirds of the systemic blood pressure [25, 26]. The findings of this study showed that there are notable differences in the major biomarkers between male and female participants in each of the four groups (Group A, Group B,

Group C, and Group D). These results offer important new information on possible health hazards and physiological variations between the groups, especially in terms of renal and cardiovascular health[27]. Group D continuously showed higher blood pressure, systolic and diastolic blood pressure, and blood creatinine levels in both males and females[28, 29]. These results imply that Group D members may be more susceptible to renal impairment and cardiovascular illnesses. Concerning biomarker values were also shown by Group B, especially in relation to elevated ACR (Albumin-Creatinine Ratio) in both genders. The known indicator of early renal impairment, a high ACR is frequently linked to a higher risk of cardiovascular illnesses. In order to prevent long-term health consequences, persons in Group B may need greater monitoring and intervention. This is because elevated blood pressure and BMI in this group further exacerbate the risk factors.[30, 31].

CONCLUSION

Significant disparities between male and female patients across four groups in critical indicators, including as BMI, blood pressure, creatinine levels, eGFR, and ACR, are highlighted by this study. The results show that rising BMI, blood pressure, and ACR levels all recognized markers of health risks put those in Groups B and D at an increased risk for cardiovascular and renal problems. Groups A and C, on the other hand, had better biomarker profiles, indicating a decreased risk for these illnesses.

Ethical considerations: The study was carried out in accordance with the principles of the Helsinki Declaration. Ethical approval was obtained from the institutional review board (IRB) of Nishtar-II Multan (Ethical Certificate Ref#: 04/01/Medicine/N-II/2024). All participants were included in the study with informed consent. All measures were taken to ensure confidentiality and anonymity of the participants during the final research process and data were processed in accordance with institutional and international ethical guidelines.

Conflict of interest: The authors declared no conflict of interest.

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Authors contribution: All authors contributed equally.

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