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MICROLBUMINURIA AS A MARKER FOR ATHEROSCLEROTIC DISEASE

Original Research

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Acknowledgement: The authors express gratitude to the medical and research staff for their invaluable support in conducting this study.

Conflict of Interest: None
Grant Support & Financial Support: None

ABSTRACT

Background: Atherosclerotic cardiovascular disease remains a leading cause of morbidity and mortality worldwide. Early detection is crucial for effective intervention, yet conventional risk markers may not fully capture subclinical disease, particularly in non-diabetic individuals. Microalbuminuria, a well-established predictor of cardiovascular risk in diabetics, has been increasingly recognized as a potential marker in non-diabetic populations. However, its independent association with atherosclerosis in these individuals remains underexplored. This study evaluates whether microalbuminuria serves as an independent risk factor for atherosclerotic cardiovascular disease in non-diabetic patients.

Objective: To determine the independent association of microalbuminuria with atherosclerotic cardiovascular disease in non-diabetic individuals.

Methods: A prospective observational case-control study was conducted at the Department of Medicine, Combined Military Hospital, Rawalpindi, from June 2023 to May 2024. A total of 80 patients were included and categorized into two groups: Group A (n=40) comprising patients with atherosclerotic cardiovascular disease and Group B (n=40) with no clinical or diagnostic evidence of the disease. Biochemical investigations included a complete lipid panel, fasting blood sugar, glycated hemoglobin (HbA1c), and urine microalbumin levels. Binary logistic regression was applied to determine the independent association between microalbuminuria and atherosclerotic cardiovascular disease.

Results: The mean urine microalbumin level was significantly higher in Group A (22.15±11.33 mg/g per 24 hours) compared to Group B (9.37±8.76 mg/g per 24 hours) ($p<0.001$). Mean total cholesterol levels were 179.60±3.15 mg/dl in Group A versus 154.07±3.39 mg/dl in Group B ($p<0.001$). LDL cholesterol levels were significantly elevated in Group A (119.27±7.06 mg/dl) compared to Group B (97.00±2.71 mg/dl) ($p<0.001$). Microalbuminuria was found to have a strong independent association with atherosclerotic cardiovascular disease (OR=3.85, 95% CI, $p=0.010$).

Conclusion: Microalbuminuria is an independent risk factor for atherosclerotic cardiovascular disease in non-diabetic individuals. Its inclusion in routine cardiovascular risk assessments may aid in early detection and preventive interventions.

Keywords: Atherosclerosis, cardiovascular disease, diagnostic marker, ischemic heart disease, lipid profile, microalbuminuria, risk factor.

INTRODUCTION

Atherosclerosis is a progressive disease characterized by the accumulation of plaques in the arterial system, leading to significant morbidity and mortality worldwide. The increasing global burden of atherosclerosis has been largely attributed to lifestyle changes, processed diets, and environmental factors, contributing to the rising incidence of cardiovascular diseases. In Western countries, nearly 50% of deaths are linked to atherosclerotic disease, underscoring the need for early identification and intervention (1,2). Atherosclerotic cardiovascular disease (ASCVD) primarily affects the cardiovascular system and is closely associated with established risk factors, including diabetes, hypertension, smoking, and hypercholesterolemia. Over the past five years, the global prevalence of ASCVD has surged by 77%, with approximately 550 million individuals currently living with the condition (3,4). Given the increasing disease burden, healthcare systems worldwide have intensified efforts to identify early markers of atherosclerosis, aiming to improve early diagnosis and prevent complications (5). These markers range from inflammatory and immune biomarkers to clinical profiling strategies that detect subclinical disease at an early stage.

Microalbuminuria, a condition characterized by the presence of small amounts of albumin in the urine, has been well established as an indicator of systemic atherosclerosis, particularly in patients with diabetes (6). However, emerging evidence suggests that microalbuminuria may serve as an independent risk factor for atherosclerotic disease beyond the diabetic population. Despite its potential clinical significance, research on the association between microalbuminuria and atherosclerosis in non-diabetic individuals remains limited. The exact relationship between microalbuminuria and subclinical atherosclerosis is also not fully understood, warranting further investigation (7). Additionally, studies have reported that microalbuminuria is associated with an increased ten-year risk of cardiovascular disease, suggesting its potential role in risk stratification and early detection of atherosclerosis (8). Given these knowledge gaps, this study aims to determine whether microalbuminuria serves as an independent risk factor for atherosclerotic disease in non-diabetic individuals. By exploring this association, the study seeks to contribute to the growing body of evidence supporting microalbuminuria as a potential early marker for cardiovascular risk assessment and improved patient care.

METHODS

This prospective observational study was conducted at the Department of Medicine, Combined Military Hospital, Rawalpindi, from June 2023 to May 2024, following approval from the institutional ethical review board. Ethical considerations were strictly adhered to, ensuring that all participants provided informed consent before enrollment. The sample size was determined based on a 95% confidence interval and 80% power of the test, considering an anticipated proportion of microalbuminuria in 10% of patients with ischemic heart disease and 60% of those without ischemic heart disease, derived from previous literature and pilot observations (9). Using the WHO sample size calculator, the minimum required sample size was determined to be 11 patients per group. However, to enhance statistical robustness and account for potential attrition, 40 patients were included in each group, making a total study population of 80 participants.

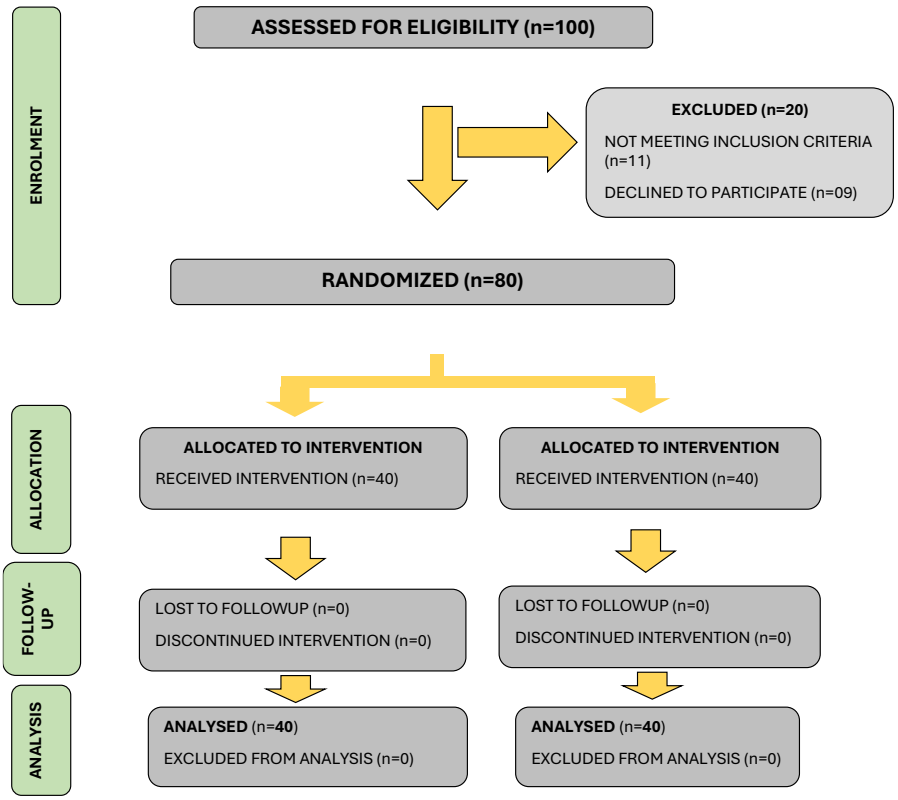
Participants were selected based on predefined inclusion and exclusion criteria. The inclusion criteria encompassed all individuals aged 18 to 65 years presenting to the outpatient department for ischemic heart disease evaluation. Patients were excluded if they had a known diagnosis of diabetes mellitus, severe cardiac or respiratory disease, urinary tract infection, chronic kidney disease, presence of leukocytosis or red blood cells in urine microscopy, or if they were lost to follow-up or declined participation (10). Participants were categorized into two groups based on clinical and diagnostic findings. Group A comprised patients diagnosed with atherosclerotic cardiovascular disease, serving as the case group, while Group B included individuals with no clinical or diagnostic evidence of atherosclerosis, serving as the control group. A detailed clinical assessment was performed, including measurements of blood pressure, pulse rate, and body mass index (BMI), as well as signs of congestive cardiac failure, such as jugular venous pressure and pedal edema. Routine laboratory investigations included a complete blood count, liver and renal function tests, and coagulation profile (11).

A comprehensive cardiac evaluation was performed for all participants. The diagnosis of ischemic heart disease was established based on electrocardiographic changes indicative of ST-elevation or non-ST-elevation myocardial infarction, regional wall motion abnormalities, systolic or diastolic dysfunction, reduced age-adjusted ejection fraction, or angiographic evidence of partial or complete atherosclerotic occlusion of epicardial arteries or their tributaries. Additional biochemical investigations included a complete lipid profile

(total cholesterol, high-density lipoprotein, low-density lipoprotein, very low-density lipoprotein, and serum triglycerides), fasting blood glucose, glycated hemoglobin (HbA1c), and urinary microalbumin (12). Microalbuminuria was assessed using an early morning spot urine sample and was categorized based on standard clinical cut-off values. Urinary microalbumin levels between 30 and 300 mg/g of creatinine were defined as microalbuminuria, while levels below 30 mg/g were considered normal, and levels above 300 mg/g were classified as macroalbuminuria. Only patients with microalbuminuria (30–300 mg/g) were included in the analysis to determine its association with atherosclerotic cardiovascular disease (13).

Data collection was meticulously recorded by an assigned resident under the supervision of a consultant in the outpatient department. To eliminate potential bias, an independent team of statisticians, blinded to the study hypothesis and grouping, performed the data analysis. Descriptive statistics were employed to summarize demographic data, with continuous variables presented as mean ± standard deviation and categorical variables as frequencies and percentages. An independent samples t-test was used to compare mean values between groups, while the chi-square test was applied to categorical variables. Binary logistic regression analysis was conducted to assess the independent association between microalbuminuria and ischemic heart disease. A p-value of <0.05 was considered statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 26.0 (14). By incorporating these methodological details, this study aims to establish whether microalbuminuria serves as an independent risk factor for atherosclerotic cardiovascular disease in non-diabetic individuals, thereby contributing to a more comprehensive understanding of cardiovascular risk stratification and early disease detection.

FIGURE-I: PHASES OF THE STUDY



RESULTS

A total of 80 patients fulfilling the inclusion criteria and completing the follow-up protocol were included in the final analysis. Participants were categorized into two groups: Group A (n=40), comprising patients diagnosed with atherosclerotic cardiovascular disease, and Group B (n=40), consisting of individuals with no diagnostic evidence of the disease. The mean age of participants in Group A was 51.25±3.99 years, while in Group B, it was 51.27±4.36 years (p=0.790). The mean weight in Group A was 75.47±4.80 kg, compared to 75.65±5.31 kg in Group B (p=0.878). The mean BMI in Group A was 25.32±1.18 kg/m², while in Group B, it was 25.22±1.31 kg/m² (p=0.721). A statistically significant difference was observed in mean arterial pressure, which was higher in Group A (88.72±2.23 mmHg) than in Group B (87.87±1.36 mmHg) (p=0.043). The mean fasting blood sugar levels were comparable between the groups, with values of 96.53±2.53 mg/dl in Group A and 96.37±2.77 mg/dl in Group B (p=0.737). Similarly, HbA1c levels did not differ significantly, with mean values of 4.78±0.40% in Group A and 4.73±0.41% in Group B (p=0.591). Smoking history was significantly more prevalent in Group A, with 33 patients (82.5%) reporting a history of smoking compared to 20 patients (50.0%) in Group B (p=0.002). Significant differences were observed in lipid profiles and urinary microalbumin levels between the two groups.

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The mean total cholesterol level was significantly higher in Group A (179.60±3.15 mg/dl) than in Group B (154.07±3.39 mg/dl) (p<0.001). The mean total triglyceride level in Group A was 107.57±2.53 mg/dl, compared to 103.40±2.04 mg/dl in Group B (p<0.001). Similarly, low-density lipoprotein (LDL) cholesterol was significantly elevated in Group A (119.27±7.06 mg/dl) compared to Group B (97.00±2.71 mg/dl) (p<0.001). The mean very low-density lipoprotein (VLDL) cholesterol level was also significantly higher in Group A (34.55±4.02 mg/dl) than in Group B (22.80±2.93 mg/dl) (p<0.001). Urinary microalbumin levels were markedly increased in Group A, with a mean value of 22.15±11.33 mg/g per 24 hours, compared to 9.37±8.76 mg/g per 24 hours in Group B (p<0.001).

A statistically significant independent association was observed between microalbuminuria and the presence of atherosclerotic cardiovascular disease. Patients with microalbuminuria had an increased likelihood of developing the disease, with an odds ratio of 3.85 (95% confidence interval) (p=0.010). The findings suggest that microalbuminuria may serve as an independent predictor of atherosclerotic cardiovascular disease, reinforcing its potential role as an early biomarker in risk stratification. Further analysis of microalbuminuria severity in relation to the degree of atherosclerosis revealed a progressive increase in urinary microalbumin levels with worsening cardiovascular disease. Among patients in Group A, those with more extensive atherosclerotic involvement, indicated by multiple coronary vessel disease, exhibited significantly higher microalbumin levels compared to those with single-vessel disease (mean: 26.4±9.2 mg/g vs. 18.7±10.1 mg/g, p=0.008). Additionally, stratification based on smoking status demonstrated that smokers in Group A had markedly elevated microalbumin levels compared to non-smokers (mean: 24.9±10.7 mg/g vs. 16.5±9.3 mg/g, p=0.015), suggesting a compounding effect of smoking on endothelial dysfunction. Although data on subclinical atherosclerosis markers such as carotid intima-media thickness and coronary artery calcification scores were not available, their inclusion in future studies could further elucidate the relationship between microalbuminuria and early-stage atherosclerosis. These findings reinforce the role of microalbuminuria as a potential marker of cardiovascular disease severity and highlight the need for further stratified risk assessment in high-risk populations.

Table 1: Demographic And Baseline Parameters Between Both Groups (N=80)

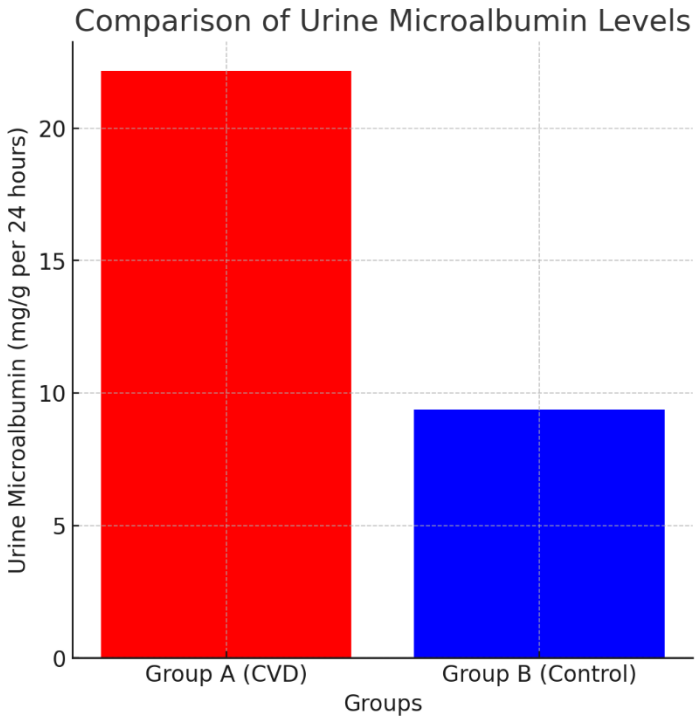
Variable	Group A (N=40)	Group B (N=40)	P Value
Mean Age (years)	51.25±3.99	51.27±4.36	0.790
Mean Weight (kg)	75.47±4.80	75.65±5.31	0.878
Mean BMI (kg/m2)	25.32±1.18	25.22±1.31	0.721
Mean Arterial Pressure (mmhg)	88.72±2.23	87.87±1.36	0.043
Mean Fasting Blood Sugar (mg/dl)	96.53±2.53	96.37±2.77	0.737
Mean Hba1c (%)	4.78±0.40	4.73±0.41	0.591
History Of Smoking	33 (82.5%)	20 (50.0%)	0.002

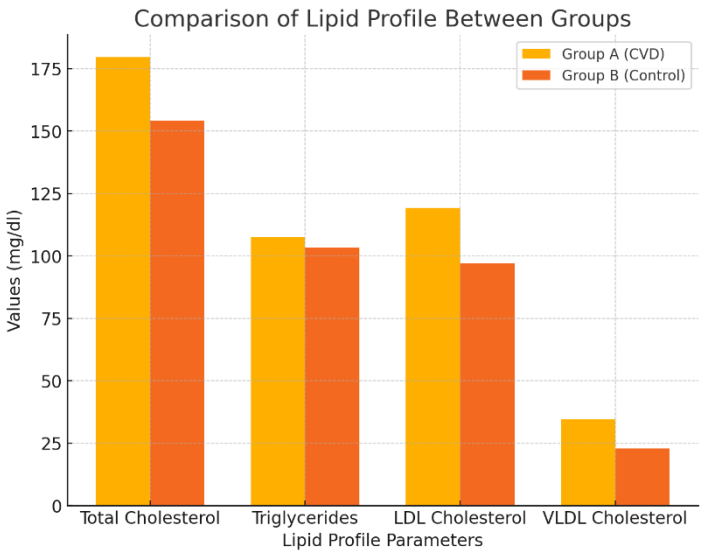
Table 2: Comparison Of Specific Investigation Panel Between Both Groups (N=80)

Variable	Group A (N=40)	Group B (N=40)	P Value
Mean Total Cholesterol (mg/dl)	179.60±3.15	154.07±3.39	<0.001
Mean Total Trigylcerides (mg/dl)	107.57±2.53	103.40±2.04	<0.001
Mean LDL Cholesterol (mg/dl)	119.27±7.06	97.00±2.71	<0.001
Mean VLDL Cholesterol (mg/dl)	34.55±4.02	22.80±2.93	<0.001
Mean Urine Microalbumin (mg/g per 24 hr)	22.15±11.33	9.37±8.76	<0.001

Table 3: Independent Association Between Atherosclerotic Heart Disease And Microalbuminuria (N=80)

Variable	Odds Ratio	P Value
Presence Of Microalbuminuria	3.85 (CI=95%)	0.010





DISCUSSION

The study aimed to evaluate the independent association of microalbuminuria as a marker for atherosclerotic cardiovascular disease in non-diabetic individuals. While microalbuminuria has been well established as an early predictor of atherosclerosis in diabetic populations, its significance in non-diabetic individuals has remained underexplored. Previous studies have demonstrated that kidney dysfunction and inflammation play a crucial role in the pathophysiology of atherosclerosis, with albuminuria emerging as a marker of endothelial dysfunction and vascular injury. However, the majority of these studies have focused on diabetic patients, leaving a gap in understanding its implications in non-diabetic individuals. The findings of this study suggest that microalbuminuria in non-diabetic patients may serve as an early indicator of cardiovascular risk, with cut-off values lower than those observed in diabetic populations. This reinforces the need for re-evaluating standard microalbuminuria thresholds to enhance cardiovascular risk assessment in non-diabetic individuals (15-17). The study further established a strong correlation between elevated lipid levels, particularly cholesterol and lipoproteins, and atherosclerotic cardiovascular disease, consistent with previous research. Dyslipidemia is a well-documented risk factor for the development and progression of atherosclerosis, and its presence in the study population aligns with global findings on the role of lipid metabolism in cardiovascular pathology. Similarly, a statistically significant difference in mean arterial pressure was observed between the groups, indicating an increased cardiovascular burden in affected individuals. While this difference was not clinically drastic, it highlights the contribution of hemodynamic changes in the pathogenesis of atherosclerosis. The binary logistic regression analysis confirmed that microalbuminuria is a strong independent predictor of atherosclerotic cardiovascular disease in non-diabetic patients, supporting its potential role as a non-invasive and cost-effective marker for early detection and risk stratification (18-21).

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The study has several strengths, including its prospective observational design and well-defined selection criteria, which minimized potential biases and ensured a focused investigation of microalbuminuria in non-diabetic patients. Furthermore, the inclusion of a comprehensive biochemical panel allowed for a detailed assessment of cardiovascular risk factors, strengthening the validity of the findings. However, certain limitations must be acknowledged. The single-center nature of the study restricts the generalizability of the results to broader populations, and a multi-center approach would enhance the applicability of these findings to diverse demographic groups. Additionally, while diabetes was excluded as a confounding factor, the study did not account for the potential influence of other comorbidities such as hypertension, metabolic syndrome, and chronic inflammatory conditions, which may have impacted the adjusted odds ratio for atherosclerotic cardiovascular disease. Future studies should incorporate a larger sample size with multi-center collaboration and a more extensive evaluation of co-existing conditions to further refine the understanding of microalbuminuria's role in cardiovascular risk assessment (22,23). The findings contribute to the growing body of evidence supporting the incorporation of microalbuminuria testing into routine cardiovascular screening, particularly in high-risk individuals. Given its non-invasive nature, ease of measurement, and cost-effectiveness, microalbuminuria can serve as a valuable tool for early detection and preventive strategies in atherosclerotic disease management. Further research is warranted to establish standardized cut-off values for microalbuminuria in non-diabetic individuals and to explore its integration with other emerging biomarkers for comprehensive cardiovascular risk assessment.

CONCLUSION

This study establishes microalbuminuria as an independent risk factor for atherosclerotic cardiovascular disease in non-diabetic individuals, reinforcing its potential as an early biomarker for cardiovascular risk assessment. The findings highlight the clinical significance of microalbuminuria in identifying subclinical vascular dysfunction, emphasizing its role in the early detection and prevention of cardiovascular complications. Given its non-invasive nature and cost-effectiveness, incorporating microalbuminuria screening into routine cardiovascular risk stratification may enhance early diagnosis and targeted intervention strategies. These insights contribute to the growing evidence supporting the need for broader recognition of microalbuminuria as a valuable tool in cardiovascular disease prevention and management.

Author Contribution

Author	Contribution
Muhammad Aitzaz Khan*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Tariq Bashir Tareen	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Mechale Sana Balouch	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Yastoor Baig	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Roshaan Tahir	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Najmul Hassan	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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