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Relationship between Urinary Albumin Creatinine Ratio and Severity of Coronary Artery Disease in Non-Diabetic Patients

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Abstract

Background: Coronary artery disease (CAD) is leading cause of mortality worldwide. CAD accounts for 20% of all deaths in the South Asia region. The burden of CAD is emerging as a public health concern in developing countries like Bangladesh. There are some new biomarkers for detection of CAD. The aim of this study was to find out the relationship between ACR and severity of coronary artery disease in non-diabetic. **Material & Methods:** This cross-sectional analytical study was conducted in the department of cardiology, National Heart Foundation Hospital and Research Institute from April, 2018 to March, 2019. Purposive sampling was done to select a total 101 study subjects. Data were collected in a predesigned data collection form through clinical history, examination, laboratory findings and coronary angiogram report. Study population was divided into two groups: Group–A: Non-diabetic patients with ACR > 30mg/g Group–B: Non-diabetic patients with ACR ≤ 30mg/g. **Results:** Participants had a mean age of 52.5 ± 9.9 years with 75.24% men. Group A patients had higher ACR level (49.98±15.83 vs 13.36±7.08; p<0.01) than group B patients. Relation between urinary ACR and severity of CAD remained significant. **Conclusions:** In this study, there found a significant relationship in ACR and severity of coronary artery disease in non-diabetic patients.

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INTRODUCTION

Acute coronary syndrome is a common presentation of ischemic heart disease (IHD).[1] The World Health Organization (WHO) has estimated that 3.8 million men and 3.4 million women die from cardiovascular disease (CVD) each year, and since 1990, more people have died from CVD than any other cause.[2] Coronary artery disease (CAD) is leading cause of mortality worldwide and by the year 2020, will be first in the leading causes of disability.[3] Cardiovascular diseases account for more than 17 million deaths globally each year. It contributes 30% of all deaths. Among them 80% occur in low and middle-economic countries. This figure is expected to grow to 23.6 million by year 2030. Coronary artery disease alone caused 7 million deaths worldwide in 2010 and it is an increase of 35% since 1990.[4] In the last three decades, the prevalence of CAD has increased from 1.1% to about 7.5% in the urban population and from 2.1% to 3.7% in the rural population.[5] CAD tends to occur at a younger age in Indians, with more extensive angiographic involvement contributed genetic, metabolic, conventional and nonconventional risk factors.[6,7,8] Bangladesh is experiencing steep and sustained increases in the incidence of CAD during recent decades.[9] The exact prevalence of CAD in Bangladesh is not known. WHO WORLD HEALTH RANKINGS report' 2014 shows mortality rate of CAD in Bangladesh is 6.96%, the 4th leading cause of death and top most of all non-Communicable diseases of the country. CAD is a multifactorial disorder with several different risk factors. Advancing age, male sex, hypertension, diabetes mellitus, cigarette smoking and dyslipidemia are the major and independent well known risk factors for CAD.[10] Besides these many individual new biomarkers have been related to cardiovascular risk, like levels of CRP (C-reactive protein), B-type natriuretic peptide (BNP), fibrinogen, D-dimer, homocysteine and microalbuminuria. The term microalbuminuria (MAU) is defined as urinary albumin levels of more than or equal to 30-300mg/24 hours in 24 hours urine collection. Although a 24h urine collection is the gold standard for the detection of MAU, several studies have found that a urinary albumin-creatinine ratio (ACR) is equally sensitive, specific and can be easily utilized on a daily basis.[11] ACR of ≥30-300mg/gm creatinine in random spot urine sample is significant. The measurement of ACR in random spot urine has become a widely accepted clinical tool for assessing urinary albumin excretion.[12] It is observed that patient with microalbuminuria had a greater atherosclerosis burden in the form of multi vessels coronary artery disease than in patient without it.[13] Study in diabetic patients.[14] In non-diabetic patients showed the co-relation between angiographic severity and microalbuminuria was significant revealed in a study.[13] The aim of this study was to find out the relationship between ACR and severity of coronary artery disease in non-diabetic.

OBJECTIVE

The objective of this cross-sectional comparative study was to determine the relationship of urinary albumin creatinine ratio and severity of coronary artery disease in non-diabetic patients.

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MATERIAL AND METHODS

This cross-sectional comparative study was carried out in the Department of Cardiology, National Heart Foundation Hospital and Research Institute, from April 2018 to March 2019 (one year) at the Department of Cardiology, NHFH & RI. After ethical approval study population was selected based on the inclusion and exclusion criteria and the study was conducted. The study included non-diabetic patients who were admitted for CAG (Coronary angiogram) with the clinical diagnosis of IHD (ischemic heart disease) in the department of cardiology, National Heart Foundation Hospital and Research Institute. Purposive sampling technique was used to collect the study patients. Ater that a total 101patients was selected as the study subject and were divided in two groups. (1)Group A: Non-diabetic IHD patients with ACR ≥ 30mg/g; (2)Group B: Non-diabetic IHD patients with ACR <30mg/g. In that case, we collected a morning random urine sample before coronary artery catheterization. Urinary albumin concentration was measured by turbidimetric immunological technique, using Dimension EXL with LM Integrated Chemistry System. Urine ACR was calculated and reported as mg/g creatinine. Patients with albumin levels less than 30 mg/g of creatinine were defined as having normoalbuminuria, those with albumin levels 30 - 300 mg/g as having ACR significant. All collected data had been entered into SPSS data file after thorough checking. Obtained data had been expressed in frequency, percentage, mean and standard deviation as applicable. Comparison between groups had been done by Student's T-test for continuous variables. Categorical data had been compared by chi-square test. The whole analysis had been done with the help of computer-based SPSS (Statistical programed for social science) programme version 16.0. P-value of <0.05 had been considered as significant.

Inclusion criteria:

Both male & female non-diabetic patients who were admitted for CAG with the clinical diagnosis of IHD in the department of cardiology, National Heart Foundation Hospital and Research Institute.

Exclusion criteria:

- Patients with Diabetes Mellitus
- Patients with s. creatinine level over 1.4 mg/dl
- Recent urinary tract infection in the last 3 months
- Presence of active infection
- Patients with malignant disease
- Patients with congestive heart failure and LV systolic dysfunction
- Past history of PTCA or CABG
- Patient who didn't give consent.

RESULTS

In [Figure 1] Pie diagram showed that 33.66% of total sample had ACR >30 mg/g and rest 66.34% had ACR ≤ 30mg/g. The [Table 1] showed age distribution among the study participants. Majority of patients were in the age range of >60 years in group A & 51-60years in group B. The mean age of Group-A was 61.41±11.04 years and Group-B was 55.94±8.26 years. Mean age difference was statistically significant (p<0.05) between groups. The [Figure 2], Bar diagram showed sex

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distribution among the study population. Study showed male patients were predominant in both groups. The [Table 2] showed distribution of BMI of study participants between two groups became statistically significant (p<0.05). The [Table 3] showed distribution of risk factors between two groups were almost similar and statistically not significant (p>0.05) except hypertension and smoking in which it was more in group A and became statistically significant (p<0.05). The [Table 4] showed distribution of association diagnosis of the study patients between two groups not became statistically significant (p>0.05). The [Table 5] showed distribution of comparison of biochemical variables between two groups. Among them urinary ACR became statistically significant (p<0.05). The [Table 6] showed distribution of comparison of lipid profile between two groups not became statistically significant (p>0.05). The table-VIII showed distribution of relation of ACR with involvement of number of vessels between two groups became statistically significant (p<0.05).

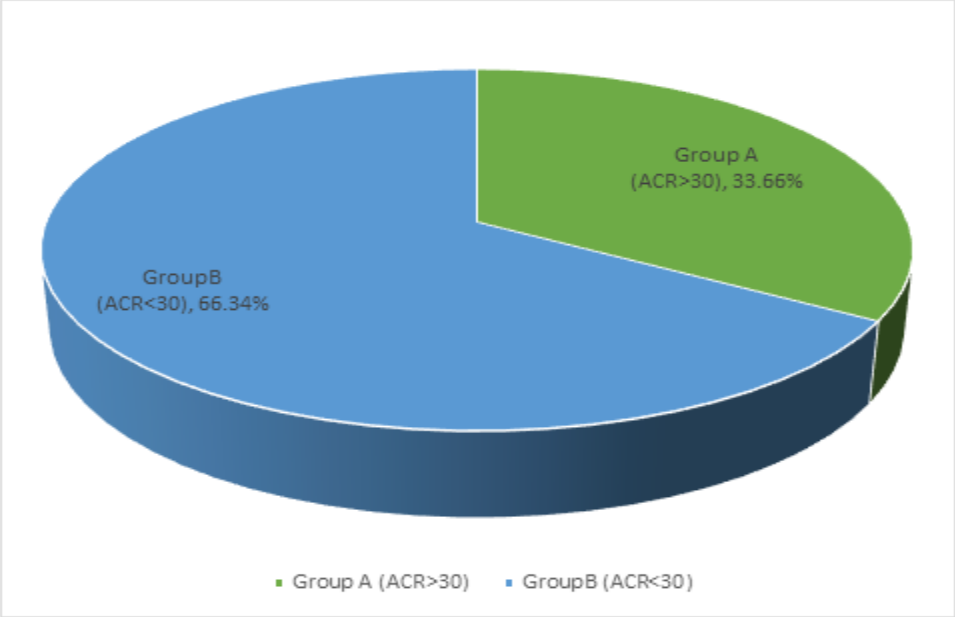

Figure 1: Pie diagram showing two groups where one group presents urinary ACR >30 mg/g and another group presents urinary ACR ≤ 30mg/g

Table 1: Comparison of age between two groups (n=101).

Age (in years)	Group A ACR (≥ 30) (n=34)	Group B ACR (< 30) (n=67)	p value
<40	2(5.9)	0(0.0)	0.006[s]
41-50	4(11.8)	19(28.4)	
51-60	12(35.3)	34(50.7)	
>60	16(47.1)	14(20.9)	
Total	34(100.0)	67(100.0)	
Mean±SD	61.4±11.0	55.9±8.2	

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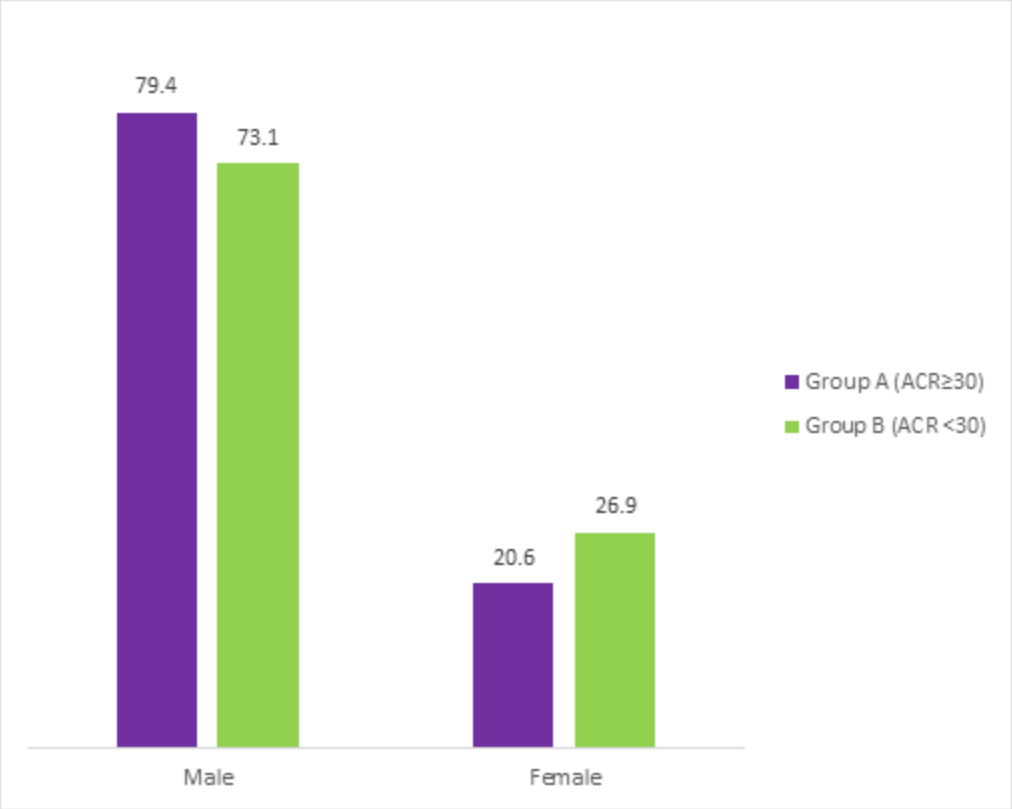

Figure 2: Bar diagram showing the sex distribution of the study subjects

Table 2: Distribution of the study patients by BMI between two groups (N=101)

BMI (kg/m^2)	Group A ACR (≥ 30) (n=34)	Group B ACR (< 30) (n=67)	p value
Normal (18.5-23.0)	3(8.8%)	21(31.3%)	<0.001
Overweight (23.0-27.5)	3(8.8%)	31(46.3%)	
Obese (>27.5)	28(82.4%)	15(22.4%)	
Mean±SD	29.99±4.17	24.76±2.74	

Table 3: Association of risk factors of the study patients between two groups (N=101)

Risk factors	Group A ACR (≥ 30) (n=34)	Group B ACR (< 30) (n=67)	p value
Smoking	22(64.7%)	28(41.8%)	0.030
Hypertension	31(91.2%)	31(46.3%)	<0.001
Dyslipidemia	23(67.6%)	40(59.7%)	0.436
Family history of CAD	7(20.6)	9(13.4)	0.352

Table 4: Diagnosis of the study patients between two groups (N=101)

Diagnosis	Group A ACR (≥ 30) (n=34)	Group B ACR (< 30) (n=67)	p value
STEMI	9(26.5%)	24(35.8%)	0.430^{ns}
NSTEMI	5(14.7%)	7(10.4%)	

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UA	3(8.8%)	11(16.4%)	
CSA	17(50.0%)	25(37.3%)	

Table 5: Comparison of biochemical variables between two groups (N=101)

Biochemical variables	Group A ACR (≥ 30) (n=34) Mean±SD	Group B ACR (< 30) (n=67) Mean±SD	p value
RBS	6.74±0.72	6.54±0.66	0.184
HbA1c	5.44±0.43	5.36±0.37	0.343
Urinary ACR	49.98±15.83	13.36±7.08	<0.001
Serum creatinine	1.20±0.17	1.26±0.98	0.732

Table 6: Comparison of lipid profile between two groups (N=101)

Lipid profile	Group A ACR (≥ 30) (n=34) Mean±SD	Group B ACR (< 30) (n=67) Mean±SD	P value
TC	154.38±39.81	149.39±33.59	0.509
LDL	126.53±37.66	122.87±27.34	0.578
HDL	32.56±4.38	34.75±5.66	0.051
Triglyceride	157.74±44.72	150.57±41.17	0.424

Table 7: Relation of ACR with involvement of number of vessels (N=101)

Number of vessels	Group A ACR (≥ 30) (n=34)	Group B ACR (< 30) (n=67)	P value
SVD (Single vessel disease)	2(5.9%)	23(34.3%)	<0.001
DVD (Double Vessel Disease)	9(26.5%)	16(23.9%)	
TVD (Triple vessel disease)	23(67.6%)	5(7.5%)	
Normal/non critical	0(0.0%)	23(34.30%)	

DISCUSSION

In Bangladesh, IHD is the major presenting form of CAD and accounts for 45% of all cause cardiac hospitalization.[15] CAD is a multifactorial disorder with several different risk factors. Advancing age, male sex, hypertension, diabetes mellitus, cigarette smoking and dyslipidemia are the major and independent well-known risk factors for CAD10. Many individual new biomarkers have been related to cardiovascular risk, including levels of CRP (C-reactive protein); B-type natriuretic peptide (BNP); fibrinogen; D-dimer and homocysteine.[16,17,18,19,20] Among these new biomarkers, microalbuminuria (MUA), which is gaining recognition as a marker of an atherogenesis, owing to its association with several atherosclerotic risk factors and early systemic vascular (endothelial) damage.[21] Few studies have reported the correlation of angiographic severity of CAD with MA. The current study showed that patients with microalbuminuria have a greater atherosclerotic burden and a more severe coronary artery disease in the form of total number of vessels affected and total number of lesions per patient than those without microalbuminuria.

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In present study the study participants had predominance of age group of 51 to 60 years. Mean age was 52.5 ± 9.9 years. Rahman, et al.[22] showed nearly similar pattern of distribution in IHD was 57.47±11.59 years. But mean age was more in studies done abroad. The mean age difference between two groups were significant in this study (Mean ± SD 61.41±11.04, 55.94±8.26 in group A and group B respectively).

In this study, male patients were predominant in both groups. Nearly similar pattern of distribution was reported by Akanda, et al., in their study in Bangladesh.[23]

There was similar type of risk factors like hypertension, smoking, dyslipidemia, and family history of CAD in both groups except hypertension and smoking. In this study, these were more in group A and became statistically significant ($p<0.05$) between two groups. As a risk factor, smoking was significantly higher in both groups. In this study 72% of total study participants were smoker. Similarly, in Ullah, et al,[24] in patients with NSTEMI the prevalence of the smoker was 72%. Cigarette smoking causes a nicotine- induced stimulation of the sympathetic nervous system (i.e. adrenaline and nor adrenaline release) that acutely increases arterial pressure and heart rate.

Hypertension is a well-known risk factor for coronary artery disease. In this study, hypertension, was present 91.2% vs. 46.3% in group A and group B respectively, which was statistically significant ($p<0.001$). A recent study Ahmed, et al.[25] was found 36.13% hypertensive.

In this study, in case of obesity BMI was 29.99±4.17 kg/m^2 in group A and 24.76±2.74 kg/m^2 in group B and it was statistically significant difference (p value 0.001). Some studies have found no increased risk of cardiovascular disease in overweight and obese individuals without metabolic syndrome, leading to suggestions that overweight and obesity in these individuals are benign conditions.[26,27]

It was found that only triple vessel; neither single nor double vessel involvement was significantly associated with ACR. This observation was not in agreement with Hoseini and Rasouli.[28] They found that patients with microalbuminuria compared with the controls had increased prevalence of one ($p< 0.001$), two ($p< 0.001$), and three vessel disease ($p< 0.001$).[28] But this observation was similar to Lohani Md Tajul Islam, et al,[29] a similar study done in Bangladesh. They showed triple vessel disease and stenotic score were more common in ACR positive patients than normal ACR patients which were statistically significant.

Gosling, et al,[30] considered MAU as an emerging cardiovascular risk factor in the non-diabetic patients. The present study agrees with these observations as it shows a significant MAU in non-diabetic CAD patients. In a study of Kumar Jha, et al31 shows that the prevalence of double vessel CAD and triple vessel CAD was significantly higher in MAU positive group and the study showed that patients with MAU have a greater atherosclerotic burden and a more severe CAD in the form of total number of vessels affected per patient than those without MAU.

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Limitations of the Study

The study was conducted in a single tertiary care hospital which may not represent the general population; Non randomized purposive sampling was done; Majority of study population was male and short term and long-term mortality and morbidity were not seen which may not reflect the whole community.

CONCLUSIONS

This study demonstrated that ACR is a predictor of cardiovascular mortality and morbidity in non-diabetic patients. It has been postulated that ACR is a marker of generalized endothelial dysfunction. For that reason, individuals with IHD should have their urinary ACR measurement, because this piece of information contributes to the classification of the individual as a high-risk or high-susceptibility individual. It is concluded that ACR can be considered as a simple, inexpensive and practical risk marker for CAD in non-diabetic patients.

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