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Original Article

Correlation between Microalbuminuria and Coronary Angiographic Severity in Non-diabetic Myocardial Infarction patients

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Key Words : *Coronary angiography, Gensini score, Microalbuminuria, Myocardial infarction, diabetes mellitus.*

Abstract

Background: *Microalbuminuria may have an association with myocardial infarction in absence of traditional risk factors like diabetes. The present study was intended to find the association between microalbuminuria and angiographic severity of coronary artery disease in non-diabetic myocardial infarction patients.*

Methods: *This cross sectional analytical study included 105 non-diabetic patients with myocardial infarction who underwent coronary angiography (CAG). The microalbuminuria was defined as urine albumin to creatinine ratio (ACR) of 30 -300 mg/g, while angiographic severity was measured by Gensini score with score e" 36 was taken as moderate to severe coronary artery disease (Group I) and score below 36 was termed as absent or mild coronary artery disease (Group II). Association of microalbuminuria with severity of coronary artery disease was determined.*

Results: *Presence of microalbuminuria was found significantly higher (45%) in patients with moderate to severe coronary artery disease than that in patients with absent or mild CAD (4.6%). The Odds of having moderate to severe coronary artery disease in patients with microalbuminuria was observed to be 17 times (95% CI = 4.5 - 63) higher than that in patients without having this condition. Correlation between ACR and Gensini score was also found a significant positive relationship ($r=0.702$, $p<0.001$) with 70% of variation in Gensini score being explained by ACR.*

Conclusion: *Microalbuminuria can be considered as a predictor of the severity of coronary artery disease in non-diabetic myocardial infarction patients.*

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Introduction:

Coronary artery disease (CAD) is a major cause of death and disability in both developed and developing countries.[1] The burden of cardiovascular disease (CVD), especially the CAD is increasing at a greater rate in South Asia than in any other region globally. Among the non-communicable diseases, CVD is probably the most important cause of mortality and morbidity in Bangladesh.[2] Advancing age, male sex, hypertension, diabetes mellitus, dyslipidemia and cigarette smoking are the independent risk factors for CAD,[3] but they do not entirely explain the variation in cardiovascular disease incidence and mortality. Therefore, additional risk factors have been proposed to better identify patients potentially at risk for CAD, and urinary albumin is a promising candidate. Since the first description in 1974,[4] the presence of subclinical increases in urinary albumin excretion has attracted attention, but much remains to be understood about the role of microalbuminuria (MAU) in non-diabetic individuals.

The term microalbuminuria is defined as urinary albumin levels equal to 30 - 300 mg/24 h in 24-h urine collection or albumin/creatinine ratio (ACR)

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of 30 - 300 mg/g in random spot urine sample.[5] It is a surrogate marker for endothelial dysfunction and is independently associated with atherosclerosis in diabetic and in non diabetic patients.[6] Microalbuminuria may be a marker of cardiovascular disease risk because of similar mechanism to renal vascular damage and damage to micro vessels in rest of body. It indicates systemic endothelial dysfunction leading to cardiovascular events. And periodic microalbuminuria screening allows and help to stratify overall CVD risk. Therefore microalbuminuria can be utilized as an important tool to stratify cardiovascular disease risk.[7]

Endothelial dysfunction precedes morphological atherosclerotic alterations and has a major action in lesion progress and simultaneously affects the glomerular endothelial dysfunction. Conditions which are accompanied with impaired endothelial function (for example, DM, hypertension, vascular disease, inflammation, and insulin resistance) also may present as impaired glomerular endothelial function, such that micro albuminuria represents a state of vascular endothelial dysfunction, with the kidney being a window to the vasculature in other tissue parts.[8] So pathophysiological processes associated with MAU are manifold: Local changes in the kidneys such as increased intraglomerular capillary pressure, increased shunting of albumin through glomerular membrane pores and loss of glomerular membrane charge; systemic changes include activation of inflammatory mediators, increased transcapillary escape rate of albumin and vascular endothelial dysfunction.[6] So microalbuminuria developed in myocardial infarction (MI) patients and albuminuria may be an important factors determining the occurrence and the severity of CAD. Recent study reported that there is a strong relationship between the degree of albuminuria and extent and complexity of CAD in patients with type 2 DM or non DM and this association is independent of traditional risk factors.[6,9]

Jha et al., 2017 reported that patients with MAU have more severe angiographically detected CAD than those without MAU, and MAU exhibits a significant association with the presence and severity of CAD.[1] The mortality and morbidity in short term outcome was also significantly increased in patients having microalbuminuria, indicating the significance of microalbuminuria as powerful prognostic biomarker.[10] So that microalbuminuria may have an association with myocardial infarction in absence of traditional risk factors like diabetes and hypertension. Aim of this study is to assess the microalbuminuria and to correlate the findings of microalbuminuria with coronary angiographic severity in Non-diabetic MI patients.

Methods:

This Cross Sectional Analytical Study was conducted in the Department of Cardiology, Sir Salimullah Medical College & Mitford Hospital, Dhaka from April 2018 to March 2019. Non-diabetic MI patients who met the enrolment criteria were consecutively selected and CAG done. A total number of 105 patients who fulfilled inclusion & exclusion criteria were selected for this study as the sample population. According to the coronary angiographic severity the patients were classified into two groups based on Gensini score: Group I (Gensini Score ≥36) consisted with moderate to severe coronary artery disease and Group II (Gensini Score < 36) consisted with absent or mild coronary artery disease. Patients having diabetes mellitus, macroalbumunuria, malignancy, congenital or valvular heart disease, recent urinary tract infection, liver or renal in sufficiency were excluded.

Meticulous history taking, onset & duration of manifestation, associated medical problem and any complications were noted in detail. A thorough clinical examination and required investigations were conducted. Risk factors for MI like hypertension, DM, smoking, dyslipidemia, obesity and family history of premature coronary artery disease were noted. Baseline laboratory investigation with Urinary albumin and creatinine were estimated and albumin to creatinine ratio (ACR) was calculated.

A morning urine sample was collected from each patient before coronary artery catheterization. Urinary ACR was measured by turbidimetric immunological technique, using Beckman Coulter AU 400 auto-analyzer. The diagnostic procedures were performed by experienced interventional cardiologists by using a SHIMADZU BRANSIST ALEXA system via femoral/ radial artery after

performing local anesthesia with lidocaine. Interpretation of coronary angiogram were reviewed and angiographic severity of coronary artery disease assessed by the Gensini score. Gensini score 36 points is regarded as cut-off value for CAD severity (Gensini score < 36 points – absent or mild coronary atherosclerosis, Gensini score ≥36 points –medium to severe coronary atherosclerosis).[11,12] Then Coronary angiography severity was correlated by microalbuminuria. All the information were properly noted in the preformed data collection sheet. All statistical analysis were performed using the statistical package for social science (SPSS) program, version 25 for Windows. Continuous parameters were expressed as mean ±SD and categorical parameters as frequency and percentage. Comparisons between groups (continuous parameters) were done by Student's t test. Association of microalbuminuria with severity of coronary artery disease was determined by Chi-Square test. Correlation analysis was done by Pearson correlation coefficient. The significance of the results as determined in 95.0% confidence interval and value of $p < 0.05$ was considered to be statistically significant. Results are expressed by appropriate tables and figures and analytical discussion are done. The study protocol was approved by Ethical committee of Sir Salimullah Medical College, Dhaka.

Results:

The present study was intended to find the association between microalbuminuria and angiographic severity of coronary artery disease in non-diabetic myocardial infarction patients. The study included a total of 105 patients (from 32 to 71 years old) based on predefined enrollment criteria. The microalbuminuria was defined as urine albumin to creatinine ratio (ACR) of 30 -300 mg/g, while angiographic severity was measured by Gensini score with score ≥36 was taken as moderate to severe coronary artery disease and score below 36 was termed as absent or mild coronary artery disease. The findings obtained from data analyses are presented below:

Age distribution shows that over 30% of the patients were 41 – 50 years old, 33.3% were 51 – 60 years old and 25.7% were > 60 years old. The mean age of the patients was 50.8 years and the youngest and the oldest patients were 32 and 71 years old respectively. Majority (80%) of the patients were male with male to female ratio being 4:1 (Table I).

Table-I

Distribution of patients by their demography (N = 105).

Demography	Frequency	Percentage
Age* (yrs.)		
≤40	11	10.5
41 – 50	32	30.5
51 – 60	35	33.3
> 60	27	25.7
Sex		
Male	84	80.0
Female	21	20.0

*Mean age = (50.8 ± 9.6) years; range = (32 – 71) years.

Over half (52.4%) of the patients were hypertensive, 29.5% were dyslipidaemic and 42% were smoker. Only 5.7% patients had family history of premature coronary artery disease (CAD) (Table II). The details of smoking status is shown in Fig.1

Table-II

Distribution of patients by their presence of risk factors (N= 105).

Presence of risk factors	Frequency	Percentage
Hypertension	55	52.4
Dyslipidemia	31	29.5
Smoking	44	41.9
Family history of premature CAD	6	5.7

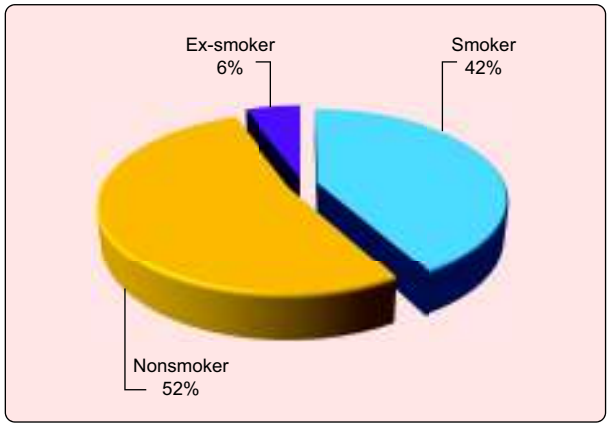

Fig.-1: *Distribution of patients by their smoking status (N = 105).*

The findings of different serum lipids are shown in table III. The mean ACR and the mean serum creatinine are also shown in the table.

Table-III

Distribution of patients by their biochemical findings (N=105).

Biochemical findings	Mean	SD	Range
ACR (mg/g)	19.5	11.8	3.3-59.4
Serum creatinine (mg/dl)	1.1	0.2	0.69-1.36
T. Cholesterol (mg/dl)	181.5	25.7	135-266
HDL (mg/dl)	35.3	4.2	23-41
LDL (mg/dl)	120.0	29.6	44-217
TG (mg/dl)	129.4	44.1	55-325

Out of 105 patients, microalbuminuria (ACR ≥ 30 mg/g) was found in 21(20%) patients (Table IV).

Table-IV

Distribution of patients by microalbuminuria (ACR ≥30)

Microalbuminuria	Frequency	Percentage
Present (ACR ≥30 mg/g)	21	20.0
Absent (ACR < 30 mg/g)	85	80.0

Out of 105 patients, 40 (38.1%) had moderate to severe coronary artery disease (Gensini score 36 or > 36). Neither age nor sex was found to be associated with severity of coronary artery diseases (p = 0.718 and p = 0.315 respectively) (Table V).

None of the conventional risk factors were found to be associated with severity of coronary artery diseases, although dyslipidemia was considerably higher in patients with moderate to severe CAD (p = 0.065) (Table VI).

Of the biochemical variables serum total cholesterol were observed to be significantly higher in patients with moderate to severe CAD compared to those with less severe CAD (p = 0.043). ACR was demonstrated to be staggeringly higher in the former group than that in the latter group (p < 0.001). (Table VII).

Presence of microalbuminuria was staggeringly higher (45%) in patients with moderate to severe coronary artery disease (Gensini score ≥36) than that in patients with absent or mild coronary

Table-V

Association between severity of CAD and baseline characteristics.

Baseline characteristics	Group I Gensini score ≥36 (n = 40)	Group II Gensini score < 36 (n = 65)	p-value
Mean Age# (yrs.)	51.2 ± 8.5	50.5 ± 10.2	0.718^{NS}
Sex*			
Male	34(85.0)	50(76.9)	0.315^{NS}
Female	6(15.0)	15(23.1)	

Figures in the parentheses indicate corresponding %;
#Data were analyzed using Unpaired t-Test and were presented as mean ± SD.
*Chi-squared Test (χ^2) was done to analyze the data.
NS= Not significant (p > 0.05)

Table-VI

Association between conventional risk factors and severity of CAD.

Risk factors	Group I Gensini score ≥36 (n = 40)	Group II Gensini score < 36 (n = 65)	p-value
Hypertension*	23(57.5)	32(49.2)	0.410^{NS}
Dyslipidemia*	16(40.0)	15(23.1)	0.065^{NS}
Smoking*	18(45.0)	26(40.0)	0.235^{NS}
Family history of premature CAD#	3(7.5)	3(4.6)	0.415^{NS}

Figures in the parentheses indicate corresponding %;
*Chi-squared Test (χ^2) was done to analyze the data.
#Fisher's Exact Test was done to analyze the data.
NS= Not significant (p > 0.05)

Table-VII

Association between biochemical variables and severity of CAD.

Biochemical variables	Group I Gensini score ≥36 (n = 40)	Group II Gensini score < 36 (n = 65)	p-value
ACR (mg/g)	29.2 ± 12.6	13.9 ± 6.9	< 0.001[S]
Serum creatinine (mg/dl)	1.2 ± 0.2	1.2 ± 0.1	0.319 [NS]
Serum total cholesterol (mg/dl)	187.7 ± 24.8	177.3 ± 25.8	0.043 [S]
HDL cholesterol (mg/dl)	34.6 ± 4.1	35.8 ± 4.2	0.154 [NS]
LDL cholesterol (mg/dl)	126.8 ± 27.3	116.1 ± 29.3	0.065 [NS]
Triglyceride (mg/dl)	135.4 ± 50.6	126.1 ± 39.5	0.293 [NS]

Figures in the parentheses indicate corresponding %;
#Data were analyzed using Unpaired t-Test and were presented as mean ± SD.
NS= Not significant (p > 0.05); S= Significant (p < 0.05)

Table-VIII

Risk of severe coronary artery disease in patients with MAU.

Microalbuminuria*	Group I Gensini score ≥36 (n = 40)	Group II Gensini score < 36 (n = 65)	Odds Ratio (95% CI of OR)	p-value
Present	18(45.0)	3(4.6)	16.9 (4.5 – 63.01)	< 0.001[S]
Absent	22(55.0)	62(95.4)		

Figures in the parentheses indicate corresponding %;
*Chi-squared Test (c^2) was done to analyze the data.
S= Significant (p < 0.05)

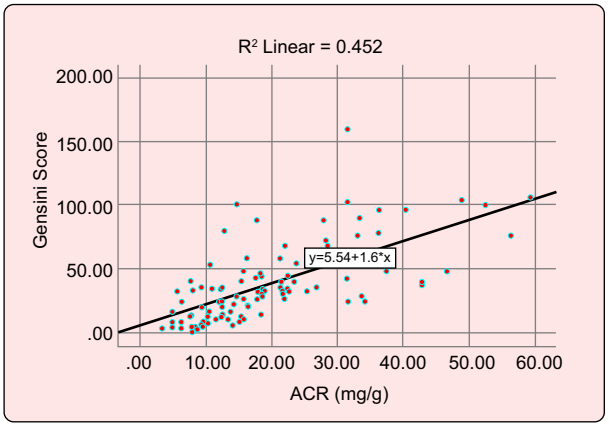

Fig.2: *Correlation between ACR and Gensini Score.*

artery disease (4.6%). The odds of having moderate to severe coronary artery disease in patients with microalbuminuria was observed to be 17 times (95% CI = 4.5 – 63.0) higher than that in patients without having this condition (Table VIII). Correlation between ACR and Gensini score shows that the two variables exhibit a significantly linear relationship (r=0.702, p<0.001) with 70% of variation in Gensini score being explained by ACR (Fig. 2).

Discussion:

Age of majority of the patients were in the range of 41-50 and 51-60 years. The mean age of the studied patients was 50.8 ± 9.6 years ranging from 32- 71 years. The mean age of group I was more than group II but the difference between two groups was not statistically significant. The age distribution of the studied patients were very close to other relevant studies.[1] Male female ratio was 4:1 which indicates male patients were predominant in this study. No significant association was found between the groups in terms of sex distribution which was also relevant to previous studies.[1] As females were given less attention and access them to health care facilities was limited particularly in low socioeconomic

population like our country may contribute this male predominance.

Among the study population, highest percentage had history of hypertension followed by smoking (41.9%), Dyslipidemia (29.5%) and family history of CAD (5.7%). In this study, none of the conventional risk factors was found to be associated with severity of coronary artery diseases, although dyslipidemia was considerably higher in patients with moderate to severe CAD.[13] Kumar, et al.2008 found 45.72% were hypertensive, 16.5% were smokers and 14.54% had family history of CAD in Indian population having MI. These differences might be due to variation in the life style, degree of motivation and level of education.

Albumin excretion in the range of 30 – 300 mg/g of urinary creatinine is referred to as MAU. In the present study urinary ACR in spot urine sample was used to detect MAU, as it was shown to be equally sensitive and specific to 24 hour urine collection method.[14] This study highlights that MAU is more frequent in non-diabetic patients with MI than the general population and may be an important emerging risk marker for CAD. None of the conventional risk factors (Hypertension, Smoking & Family history of CAD) was found to be associated with severity of coronary artery disease between the two groups. Although previous studies have reported the association between hypertension and MAU,[15,16] in this study we were not able to see a similar association. This diversity could be due to differences in sample size, race, and geographic or nutritional factors.

Of the biochemical variables serum total cholesterol was observed to be significantly higher in group I (patients with moderate to severe CAD) than group II. Mean ACR of group I was 29.2 ± 12.6 (mg/g) and that of group II was 13.9 ± 6.9 (mg/g). So ACR was demonstrated to be staggeringly higher in the group I than group II which was also matched with previous studies.

Presence of microalbuminuria was staggeringly higher in patients with moderate to severe coronary artery disease than that in patients with absent or mild coronary artery disease. The odds of having moderate to severe coronary artery disease in patients with microalbuminuria was observed to be 17 times higher than that in patients without having this condition. In this study, Presence of MAU exhibited a significant correlation with the severity of CAD. Previous studies also concluded that there was a positive correlation between severity of CAD and MAU in non-diabetic patients.[17,18]

Conclusions:

In this study, we found microalbuminuria is a predictor of severity of CAD. The results of the present study indicate that non diabetic patients with microalbuminuria have more extensive and complex angiographic coronary artery disease compared to those without microalbuminuria. Since the microalbuminuria is simple and relatively inexpensive investigation, early identification of microalbuminuria may influence the aggressiveness of management and ultimately the outcome of the disease.

Limitation:

There are some limitations in this study. It was a purposive sampling method. Urinary ACR in spot urine sample was used to detect microalbuminuria. For further study, larger, metacentric studies should be carried out to validate the findings of the present study.

Conflict of Interest - None.

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