

# Correlation between Urinary Albumin to Creatinine Ratio and In-hospital Cardiac Events among Patients with Acute Myocardial Infarction

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## Abstract

**Key Words :**  
Myocardial infarction, IHD, Urinary albumin to creatinine ratio, microalbuminuria, macroalbuminuria, MACE.

**Background:** Urinary albumin to creatinine ratio (UACR) is an important predictor of major adverse cardiac events (MACE). However, limited data is available regarding its correlation with in-hospital MACE in patients with acute myocardial infarction (AMI). The aim of the current study was to find out the correlation between UACR and in-hospital MACE among patients with AMI.

**Methods:** 651 AMI patients (mean age:  $54.4 \pm 12.6$  years, male/female: 522/129, STEMI/NSTEMI: 438/213) admitted from November 2013 to December 2014 were enrolled in this observational study. The UACR was measured from spot urine samples collected on admission day. Data on patient's demography, existence of traditional risk factors for cardiovascular diseases (CVD) and baseline clinical parameters were recorded on admission day. The patients were categorized into three groups - normoalbuminuria (UACR less than 30mg/gCr, n = 404), microalbuminuria (UACR between 30 to 299 mg/gCr, n = 215) and macroalbuminuria (UACR equal to or greater than 300 mg/gCr, n = 32). For each enrolled patients, the incidences of specified in-hospital MACE (recurrent angina, acute heart failure, arrhythmia, atrio-ventricular conduction disorders, mechanical complications, cardiogenic shock and cardiac arrest) were recorded throughout the hospital staying period. The comparison of categorical variables between the groups was performed using the chi-square test.  $p < 0.05$  was considered statistically significant.

**Results:** The baseline characteristics (age, male gender, hypertension, hyperlipidemia, diabetes mellitus, family history of CVD, smoking) of three groups were statistically similar. Compared to normoalbuminuria group, the incidences of MACE were significantly higher in micro and macro albuminuria group (p-value: normo vs. micro 0.001 and normo vs. macro 0.006). However, the occurrences of MACE in microalbuminuria group were statistically similar to those of macroalbuminuria group (p-value: micro vs. macro 0.284).

**Conclusion:** Urinary albumin to creatinine ratio, at a level of micro and macro albuminuria, was associated with greater incidence of in-hospital MACE compared to its normal level in patients with AMI.

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## Introduction:

Elevated urinary albumin excretion (UAE) is an independent predictor of major adverse cardiac events (MACE) in the general population and in patients with diabetes, hypertension or coronary artery disease.<sup>1-4</sup> Urinary albumin excretion is reported to be increased in patients with acute myocardial infarction (AMI).<sup>5-7</sup> Gosling et al

observed a transient increase in UAE during AMI attributed to a systemic increase in vascular permeability as part of the early acute inflammatory process accompanying AMI.<sup>5</sup> Other studies confirmed the sharp increase of albumin excretion during AMI.<sup>6,7</sup> UAE is also found to be associated with increased risk for short-term in-hospital mortality in patients with AMI.<sup>7</sup>

However, limited data is available regarding the correlation between UAE and in-hospital MACE in patients with AMI. Therefore, we planned this prospective observational study to find out the correlation between UAE expressed as the urine albumin to creatinine ratio (UACR) and in-hospital MACE among patients with AMI admitted in a national cardiac hospital of Bangladesh.

### Methods:

**Study population:** This prospective study included 651 patients admitted with definite AMI to the coronary care unit of National Institute of Cardiovascular diseases, Dhaka, Bangladesh from November 2013 to December 2014. AMI was diagnosed when at least 2 of the following criteria were present: central chest pain lasting >30 minutes, characteristic changes in serum enzymes (total creatine kinase [CK] and MB isoenzyme of CK), and electrocardiographic changes with pathological Q waves and/or localized ST-T changes in at least 2 contiguous leads.

**Data collection and measurement:** In all patients, a thorough medical history was taken from medical records and patient interview. Data on patient's demography, existence of traditional risk factors for cardiovascular diseases (CVD) and baseline clinical parameters were recorded on admission day. The UACR was measured from spot urine samples collected on admission day. For each enrolled patients, the incidences of specified in-hospital MACE (recurrent angina, acute heart failure, arrhythmia, atrio-ventricular conduction disorders, mechanical complications, cardiogenic

shock and cardiac arrest) were recorded throughout the hospital staying period.

**Patient's categorization:** The patients were categorized into three groups according to their UACR value - Normoalbuminuria (UACR less than 30mg/g Cr), microalbuminuria (UACR between 30 to 299 mg/g Cr) and macroalbuminuria (UACR equal to or greater than 300 mg/g Cr).

**Statistical analysis:** All data were analyzed with SPSS statistical software version 19.0 (Chicago, Illinois, USA). Continuous variables (age, blood pressure data, heart rate) were expressed as mean  $\pm$  standard deviation. The comparison of continuous variables between two age groups was performed using the t-test. Categorical variables were expressed as number (n) with regard to percentage (%). The comparison of categorical variables between the groups was performed using the chi-square test.  $p < 0.05$  was considered statistically significant.

### Results:

A total of 651 patients with AMI were enrolled with a mean age of  $54.4 \pm 12.6$  years. Majority of the patients (80.2%) were male (n = 522). Male to female ratio was 4:1. More than one-third of the patients (67.3%) had STEMI (n = 438) and rest of the patients had NSTEMI (n = 213, 32.7%). 62.9% of the patients had normoalbuminuria (n = 404), 33.0% patients had microalbuminuria (n = 215) and 4.9% patients had macroalbuminuria (n = 32).

The incidence of specified in-hospital MACE among the studied population is summarized in Table-II.

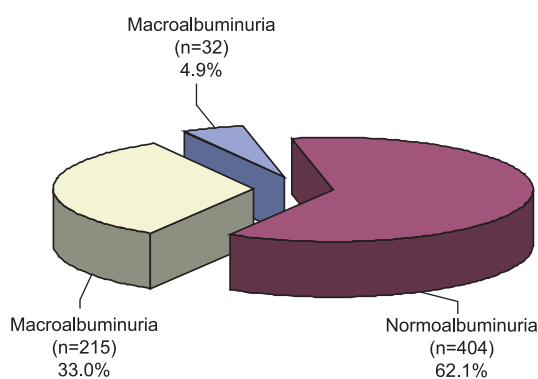
**Table-I**  
*Baseline characteristics of the patients (n=651).*

	Normo- albuminuria (n = 404)	Micro- albuminuria (n = 215)	Macro- albuminuria (n = 32)	p-value		
				Normo- albuminuria versus Micro- albuminuria	Normo- albuminuria versus Macro- albuminuria	Micro- albuminuria versus Macro- albuminuria
Mean age, mean $\pm$ SD, years	53.8 $\pm$ 12.5	55.6 $\pm$ 12.9	54.2 $\pm$ 11.6	0.092	0.861	0.563
Male gender	334 (82.7%)	165 (76.7%)	23 (71.9%)	0.076	0.127	0.547
Hypertension	127 (31.4%)	78 (36.3%)	13 (40.6%)	0.223	0.284	0.634
Hyperlipidemia	83 (20.5%)	57 (26.5%)	6 (18.8%)	0.091	0.808	0.347
Diabetes mellitus	61 (15.1%)	42 (19.5)	8 (25.0)	0.158	0.140	0.473
Family history of CVD	36 (8.9%)	20 (9.3%)	3 (9.4%)	0.872	0.929	0.989

**Table-II**  
*In-hospital MACE of the patients (n=651).*

	Normo- albuminuria (n = 404)	Micro- albuminuria (n = 215)	Macro- albuminuria (n = 32)	p-value		
				Normo- albuminuria versus Micro- albuminuria	Normo- albuminuria versus Macro- albuminuria	Micro- albuminuria versus Macro- albuminuria
Recurrent angina	41 (10.1%)	31 (14.4%)	5 (15.6%)	0.115	0.332	0.857
Acute heart failure	55 (13.6%)	35 (16.3%)	9 (28.1%)	0.370	0.026	0.102
Arrhythmia	1 (0.2%)	2 (0.9%)	1 (3.1%)	0.244	0.020	0.290
AV conduction disorders	1 (0.2%)	9 (4.2%)	-	0.0002	0.778	0.238
Mechanical complications	4 (1.0%)	-	-	0.143	0.572	-
Cardiogenic shock	4 (1.0%)	5 (2.3%)	1 (3.1%)	0.186	0.275	0.784
Cardiac arrest	3 (0.7%)	4 (1.9%)	-	0.210	0.625	0.437
MACE	109 (27.0%)	86 (40.0%)	16 (50.0%)	0.001	0.006	0.284

27% patients in normoalbuminuria group, 40% patients in microalbuminuria group and 50% patients in macroalbuminuria group had faced any of the specified MACE during their hospital stay. Among all groups of patients, acute heart failure was the most common manifestation of in-hospital MACE. Compared to normoalbuminuria group, the incidences of MACE were significantly higher in micro and macroalbuminuria group (p-value: normo vs. micro 0.001 and normo vs. macro 0.006). However, the occurrences of MACE in microalbuminuria group were statistically similar to those of macroalbuminuria group (p-value: micro vs. macro 0.284).



**Fig 1:** Categorization of the patients according to UACR value.

### Discussion:

Our study demonstrated that UACR, at a level of micro and macro albuminuria, was associated with greater incidence of in-hospital MACE compared

to its normal level in patients with AMI. Our study also found that the occurrences of MACE in microalbuminuria group were statistically similar to those of macroalbuminuria group. Previously, similar findings were reported by Lekatsas I et al.<sup>8</sup> This study included only non-diabetic hospitalized AMI patients. On the other hand, our study enrolled both diabetic and non-diabetic hospitalized AMI patients. The mean age of the patients of this study was higher than our study ( $66 \pm 11$  years versus  $54.4 \pm 12.6$  years). This indicates that Bangladeshi populations are more prone to have an AMI at younger age.

Our results are in agreement to another study performed by Berton G et al.<sup>7</sup> This study included mixed population of diabetics and non-diabetics with AMI like our study. This study found the correlation of UACR with in-hospital MACE and in-hospital mortality. On the contrary, our present study confined to in-hospital MACE only.

Many hypotheses have been proposed in order to explain the high albumin excretion rate during acute myocardial infarction. It is estimated that during the initial two days after acute myocardial infarction, heart failure or hemodynamic alterations,<sup>9</sup> seem to be the main determinant of urinary albumin excretion rate, but endothelial dysfunction and inflammation seem to play the key role from the third day.<sup>10</sup> Inflammation is also an important feature in patients with acute myocardial infarction.<sup>11,12</sup> Ischemia produces a systemic increase in vascular permeability,

including the vessels in the kidney, as part of the acute inflammatory process, thereby increasing the leak of urinary albumin.<sup>13</sup> Several studies support the association of the severity of inflammation with the degree of microalbuminuria.<sup>14,15</sup> However, the possible pathophysiologic mechanism responsible for an association between microalbuminuria and adverse prognosis after acute myocardial infarction remains under investigation.

### Conclusion:

Urinary albumin to creatinine ratio is a significant predictor of in-hospital MACE in patients with AMI. UACR, at a level of micro and macro albuminuria, was associated with greater incidence of in-hospital MACE compared to its normal level in patients with AMI. This data could be useful for explaining the necessity of effective treatment strategy in patients with AMI to keep their UACR within the targeted level during the hospital stay. This data may also suggest that AMI patients with micro and macroalbuminuria may need a more aggressive medical and interventional therapy before their discharge.

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### Conflict of Interest - None.

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### References:

- Hillege HL, Fidler V, Diercks GF, van Gilst WH, de Zeeuw D, van Veldhuisen DJ, et al. Prevention of Renal and Vascular End Stage Disease (PREVEND) Study Group. Urinary albumin excretion predicts cardiovascular and noncardiovascular mortality in general population. *Circulation*. 2002;106(14):1777-1782.
- Gerstein HC, Mann JF, Yi Q, Zinman B, Dinneen SF, Hoogwerf B, et al. HOPE Study Investigators. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. *JAMA* 2001; 286: 421-426.
- Olsen MH, Wachtell K, Bella JN, Palmieri V, Gerds E, Smith G, et al. Albuminuria predicts cardiovascular events independently of left ventricular mass in hypertension: a LIFE substudy. *J Hum Hypertens*. 2004;18(6):453-459.
- Solomon SD, Lin J, Solomon CG, Jablonski KA, Rice MM, Steffes M, et al. Prevention of Events With ACE Inhibition (PEACE) Investigators. Influence of albuminuria on cardiovascular risk in patients with stable coronary artery disease. *Circulation*. 2007;116:2687-2693.
- Gosling P, Hughes EA, Reynolds JP, Fox JP. Microalbuminuria is an early response following acute myocardial infarction. *Eur Heart J*. 1991;12:508-513.
- Taskiran M, Feldt-Rasmussen B, Jensen GB, Jensen JS. Urinary albumin excretion in hospitalized patients with acute myocardial infarction. Prevalence of microalbuminuria and correlation to left ventricle wall thickness. *Scand Cardiovasc J*. 1998;32:163-166.
- Berton G, Citro T, Palmieri R, Petucco S, De Toni R, Palatini P. Albumin excretion rate increases during acute myocardial infarction and strongly predicts early mortality. *Circulation*. 1997;96:3338-3345.
- Lekatsas I, Koulouris S, Triantafyllou K, Chrisanthopoulou G, Moutsatsou-Ladikou P, Ioannidis G, et al. Prognostic significance of microalbuminuria in non-diabetic patients with acute myocardial infarction. *Int J Cardiol*. 2006;106(2):218-223.
- Foy SG, Crozier IG, Richards AM, et al. Neurohumoral changes after acute myocardial infarction. Relationships with hemodynamic indices and effects of ACE inhibition. *Eur Heart J* 1995;16:770-778.
- Siminiak T, Dye J, Egdell R, More R, Wysocki H, Sheridan D. The release of soluble adhesion molecules ICAM-1 and E-selectin after acute myocardial infarction and following coronary angioplasty. *Int J Cardiol* 1997;61:113-118.
- Furman MI, Becker RC, Yarzebski J, Savegeau J, Gore JM, Goldber RJ. Effect of elevated leucocyte count on in-hospital mortality following acute myocardial infarction. *Am J Cardiol* 1996;78:945-948.
- Lagrand W, Niessen H, Wolbink GJ, et al. C-reactive protein colocalizes with complement in human hearts during acute myocardial infarction. *Circulation* 1997;95:97-103.
- Suval WD, Duran WN, Boric MP, Hobson RW, Berendsen PB, Ritter AB. Microvascular transport and endothelial cell alterations preceding skeletal muscle damage in ischemia and reperfusion injury. *Am J Surg* 1987;154:211-218.
- Li Vi-Heng, Teng Jeng-Kai, Tsai Wei-Chun, Tsai Liang-Miin, Lin Li-Jen, Chen Jyh-Hong. Elevation of soluble adhesion molecules is associated with the severity of myocardial damage in acute myocardial infarction. *Am J Cardiol* 1997;80:1218-1221.
- Schmidt AM, Crandall J, Hori O, Cao R, Lakatta E. Elevated plasma levels of VCAM-1 in diabetic patients with microalbuminuria: a marker of vascular dysfunction and progressive vascular disease. *Br J Haematol* 1996;92:747-750.