

Microalbuminuria as a Marker of Morbidity and Mortality in Patients with Acute Myocardial InfarctionVivek Gupta¹, Pawan Kumar Gangwal², Ranjita Bansal³, Kusum Khoiwal⁴^{1,2}Assistant Professor, Department of General Medicine, National Institute of Medical Sciences and Research, Jaipur Rajasthan^{3,4}Senior Demonstrator, Department of Pathology, Sawai Man Singh Medical College, Jaipur Rajasthan

Received: 25-06-2023 / Revised: 28-07-2023 / Accepted: 30-08-2023

Corresponding author: Dr. Kusum Khoiwal

Conflict of interest: Nil

Abstract:**Introduction:** Acute myocardial infarction is one of the commonest diseases in hospitalized patients in industrialized countries. Microalbuminuria is common in nondiabetic, nonhypertensive population and is considered to be an independent indicator of cardiovascular risk factors and cardiovascular mortality.**Aim & Objective:** To correlate the quantitative value of microalbumin in urine with the mortality and morbidity in acute myocardial infarction (MI) patients.**Materials & Methods:** Fifty six cases of acute myocardial infarction (MI) and fifty six healthy controls were included in this study. The study was conducted at National Institute of Medical Sciences and Research, Jaipur during June 2021 to May 2022. Biochemical and clinical risk factors assessed for MI. Microalbuminuria is defined as excretion of albumin in urine in the range of 20 to 200µg/min. (30-300mg/day).**Results:** Microalbuminuria level increased with age in both case as well as control group while the A/C ratio tends to decreased with the age in the case group and increased in control group. Mean value of microalbumin was 56.11± 20.69 in males and 61.45± 23.81 in females, while mean value of A/C ratio was 120.46± 91.42 in males and 142.65± 113.07 in females. Presence of Microalbuminuria in patients of acute MI predicts the complication significantly; out of 56 acute myocardial infarcted patients 18 patients develop complications in the form of arrhythmia, conduction defects, pulmonary odema, MI extension and death.**Conclusions:** Microalbuminuria is present in large number of non-diabetic, non-hypertensive Myocardial infarction patients. Level of Microalbuminuria increases with the age but there is no significant correlation with gender. Microalbuminuria level was high in patients of Myocardial infarction with complication. Therefore Microalbuminuria can be used as a marker of morbidity and mortality in the Myocardial infarction patients.**Keywords:** Myocardial Infarction [MI], Microalbuminuria [MA], Albumin/Creatinine Ratio (A/C Ratio).This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Acute myocardial infarction is one of the commonest diseases in hospitalized patients in industrialized countries. Microalbuminuria is defined as excretion of albumin in urine in the range of 20 to 200µg/min. (30-300mg/day). Routine urine tests cannot detect this range of albumin in urine [1].

In the past decades, microalbuminuria was studied as a predictor of incipient nephropathy and coronary vascular diseases in the diabetic patients [2]. Microalbuminuria occurs in response to acute inflammatory conditions such as ischaemia [4,5], trauma and thermal injury [6], surgery[7], pancreatitis [8] and inflammatory bowel disease [9]. In all these conditions the degree of microalbuminuria is proportional to the severity of the inflammatory insult, predictive of outcome and not associated with renal impairment [2]. This

response is reflected and amplified by glomerular capillaries in kidneys, quite distant from the primary source of inflammation.

It gradually became increasingly evident that microalbuminuria is associated with an increased risk of cardiovascular disease even in nondiabetic, nonhypertensive patients [3,4]. Microalbuminuria is an early response to myocardial infarction [5]. It is also proportional to the infarct size [10, 11]. A study by Berton et al. showed that microalbuminuria occurs in acute myocardial infarction and predicts early mortality [12, 13]. It is also associated with carotid intima – media thickening and coronary artery disease [14]. Microalbuminuria is common in nondiabetic, nonhypertensive population and is considered to be an independent indicator of cardiovascular risk factors and cardiovascular mortality [15, 16]. It is

concluded that microalbuminuria $>20\mu\text{g}/\text{min}$ had an independent relation with coronary heart disease, taking diabetes mellitus, impaired glucose tolerance, systolic and diastolic blood pressure, smoking, age, sex, ethnic origin and body mass index into consideration [3]. In this study an attempt has been made to find if microalbuminuria is associated in acute myocardial infarction even in nondiabetic, nonhypertensive population and correlate it to see whether it can predict in-hospital mortality and morbidity.

Aims & Objectives: To correlate the quantitative value of micro albumin in urine with the mortality and morbidity in acute myocardial infarction (MI) patients. To study statistical significance of various parameters in our study population.

Materials & Methods: Patients with clinically diagnosed acute myocardial infarction were selected from the CCU of National Institute of Medical Sciences and Research, Jaipur. Clinical diagnosis was based on clinical history, ECG and the cardiac markers. Age of the patients varied from 25- 80 years. Cases were selected exclusively random.

The exclusion criterion included any systemic infection, urinary tract infection, inflammatory conditions like rheumatoid arthritis and nephropathy (serum creatinine $>1.2\text{mg}/\text{dl}$), at the time of admission to the CCU. Myocardial infarction following surgery and major trauma,

history of diabetes mellitus, hypertension were also excluded from the study.

The results were compared with equal number of normal, healthy randomly selected individuals, after obtaining due consent. The controls were age and sex matched.

The investigations carried out included random blood sugar (RBS), serum glutamate oxaloacetate (SGOT), SGPT, creatine kinase –MB (CK- MB) in serum, microalbumin and creatinine in urine. The same were compared with the controls. The random, mid-stream urine samples (10ml) were collected in sterile containers without preservative and assayed for microalbumin. The level of albumin protein produced by microalbuminuria can be detected by special albumin-specific urine dipsticks.

To compensate for variations in urine concentration in spot-check samples, it is helpful to compare the amount of albumin in the sample against its concentration of creatinine.

This is termed the albumin/creatinine ratio (ACR)[5] and microalbuminuria is defined as $\text{ACR} \geq 3.5 \text{ mg}/\text{mmol}$ (female) or $\geq 2.5 \text{ mg}/\text{mmol}$ (male),[6] or, with both substances measured by mass, as an ACR between 30 and 300 μg albumin/mg creatinine.[4] An early morning sample is preferred.

Definitions of microalbuminuria

	Individual	Lower limit	Upper limit	Unit
24h urine collection		30	300	mg/24h (milligram albumin per 24 hours)
Short-time urine collection		20	200	$\mu\text{g}/\text{min}$ (microgram albumin per minute)
Spot urine albumin sample		30	300	mg/l (milligram albumin per litre of urine) or $\mu\text{g}/\text{g}$ (microgram albumin per gram of urine)
Spot urine albumin/creatinine ratio	Women	3.5	25 35	mg/mmol (milligram albumin per millimole creatinine)
		30	300	$\mu\text{g}/\text{mg}$ (microgram albumin per milligram creatinine)
	Men	2.5 3.5	25 35	mg/mmol
			30	300

Results

The study included total 112 number of patients who fulfilled our selection criteria, 56 were in cases and 56 in control group. Case group was patients of acute MI and Control group was normal persons.

On analysing the data collected from case sheets of these patients the following results were observed:

Table 1: Sex distribution in case and control:

	Male (N)	Female(N)
Cases	37 (66.07%)	19 (33.93%)
Control	31 (55.35%)	25 (44.64%)

N: Total number of patients. In both case and control group there was a male preponderance.

Table 2: Average age in different case and control groups:

	Average Age (In Year)
Case Group	52.07 ± 12.56
Control Group	56.28 ± 10.45

There was no significant age difference in both case and the control group.

Table 3: Age wise microalbumin and albumin/creatinine values of cases and control

Age Group (In Year)	Microalbuminuria Level		A/C Ratio	
	Case	Control	Case	Control
30-40	74.34 ± 32.63	15.32 ± 6.14	253.43 ± 165.45	13.58 ± 6.55
41-50	56.10 ± 14.15	16.30 ± 8.72	108.14 ± 80.19	16.74 ± 10.96
51-60	48.22 ± 10.79	18.85 ± 8.38	158.50 ± 98.15	17.21 ± 10.43
61-70	56.53 ± 28.78	19.01 ± 9.74	89.59 ± 54.36	18.40 ± 12.85
71-80	60.85 ± 15.55	27.03 ± 4.90	88.03 ± 38.96	27.36 ± 5.74
> 80	73.90 ± 9.78	21.26 ± 10.41	153.58 ± 84.70	24.04 ± 12.37

A/C RATIO: Albumin to creatinine ratio; ±: Standard Deviation. In our study the microalbuminuria level increased with age in both case as well as control group while the A/C ratio tends to decreased with the age in the case group and increased in control group.

Table 4: Mean value of microalbumin and A/C ratio in male and female patients of case group:

Sex	Case Group	
	Male (N = 37)	Female (N = 19)
Microalbuminuria Level	56.11 ± 20.69	61.45 ± 23.81
A/C Ratio	120.46 ± 91.42	142.65 ± 113.07

N: Number of patients; ±: Standard Deviation. The above table shows that the microalbuminuria is found slightly higher in females as does the A/C ratio though it is not statistically significant (p value = <0.001).

Table 5: Group wise percentage of complications and average microalbuminuria level

	No Complications	Complications
Case Group (N=56)	38(67.85%)	18 (32.14%)
Microalbuminuria Level	57.21 ± 20.12	59.67 ± 18.94

Table 6: Complications in patients with acute MI

Complications	Total	MICROALBIMINURIA	
		Present	Absent
Arrhythmia	6	5	1
Conduction Defects	5	4	1
Pulmonary Odema	3	3	0
MI Extension	3	3	0
Death	1	1	0
Total	18 (32.14%)	16 (88.88%)	2 (11.11%)

There was one mortality in the study, the MA value was 5th highest of all the cases (the lowest value in the study was 17.14 and the highest value in the study was 143.6) and 2nd highest of complicated cases. The A/C ratio was 14th highest of all the cases and 4th highest of complicated cases (the lowest value in the study was 23.73 and the highest value in the study was 439.42).

Discussion

All the cases in the present study had a normal renal function (Urea ≤ 40 mg/dl; creatinine ≤ 1.2 mg/dl). Microalbuminuria, in these patients was therefore not related to renal dysfunction. Our study in this respect agrees with the views of Peter Gosling, who considered it to be a sensitive indicator of non-renal disease [2]. Haffner et al. considered microalbuminuria as a cardiovascular risk factor in the nondiabetic patients [4].

Gosling et Al. also considered it to be an emerging cardiovascular risk indicator though he felt more studies are required to come to a conclusion [11]. Our study agrees with these studies as it shows a significant microalbuminuria in the acute myocardial infarction patients even in the nondiabetic and the non-hypertensive. It is evident from literature that microalbuminuria holds a lot of promise not only as a predictor of myocardial infarction but also as a predictor of mortality and probable morbidity following such episodes. Berton et.al, considered microalbuminuria to be an early predictor of mortality in acute myocardial infarction [12]. However in our study there was one mortality and the level of microalbuminuria was 5th highest of all the cases and our study agrees with theirs in this respect, though a larger sample size is advisable.

The microalbuminuria was found slightly higher in females as does the a/c ratio, though it is not statistically significant. This needs further validation as the population size was small.

Since microalbuminuria is a simple investigation and relatively inexpensive test and we may propose the use of microalbuminuria as an adjunct biochemical parameter in nondiabetic, nonhypertensive acute myocardial infarction patients and also in diabetics and hypertensive patients. Microalbuminuria can predict in-hospital mortality and its pathophysiology in this clinical setting is systemic inflammatory response and not any renal dysfunction.

Summary & Conclusion

Microalbuminuria is present in large number of non-diabetic, non-hypertensive Myocardial infarction patients. Level of Microalbuminuria increases with the age but there is no significant correlation with gender. Microalbuminuria level was high in patients of Myocardial infarction with complication. Therefore microalbuminuria can be used as a marker in the Myocardial infarction patients as a marker for morbidity and mortality.

References

1. Geleijnse JM. Vitamin D and the prevention of hypertension and cardiovascular diseases: a review of the current evidence. *Am J Hypertens.* 2011; 24:253-262.
2. Zittermann A, Schleithoff SS, Koerfer R. Putting cardiovascular disease and vitamin D insufficiency into perspective. *Br J Nutr.* 2005; 94:483-492.
3. Penckofer S, Kouba J, Wallis DE, Emanuele MA. Vitamin D and diabetes: let the sunshine in. *Diabetes Educ.* 2008; 34:939-940, 942.
4. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. *J Clin Endocrinol Metab.* 2007; 92:2017-2029.
5. Judd SE, Tangpricha V. Vitamin D deficiency and risk for cardiovascular disease. *Am J Med Sci.* 2009; 338:40-44.
6. O'Connell TD, Berry JE, Jarvis AK. 1, 25-DihydroxyvitaminD 3 regulation of cardiac myocyte proliferation and hypertrophy. *Am J Physiol.* 1997; 272:H1751-H1758.
7. Thygeson K, Alpert JS, Jaffe AS. Third universal definition of myocardial definition. *J. Am. Coll. Cardiol.* 2012; 60:1581
8. Bonaca MP, Wiviott SD, Braunwald E. American College of Cardiology, American Heart Association, European Society of Cardiology, World Heart Federation, Universal definition of myocardial infarction, classification system and the risk of cardiovascular death, Observation from the TRITON-TIMI 38 trial, *Circulation* 2012;125:577.
9. Scragg R, Sowers M, Bell C. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third National Health and Nutrition Examination Survey. *Diabetes Care.* 2004; 27:2813– 8.
10. Riachy R, Vandewalle B, Moerman E. 1,25-Dihydroxyvitamin D3 protects human pancreatic islets against cytokine-induced apoptosis via down-regulation of the Fas receptor. *Apoptosis.* 2006; 11: 151–9.
11. Goswami R, Kochupillai N, Gupta N. Presence of 25 (OH) D deficiencies in a rural North Indian village despite abundant sunshine. *J Assoc Physicians India.* 2008; 56:755-757.
12. Marwaha RK, Tandon N, Garg MK. Vitamin D status in healthy Indians aged 50 years and above. *J Assoc Physicians India.* 2011; 59:706-709.
13. Harinarayan CV, Ramalakshmi T, Prasad UV. Vitamin D status in Andhra Pradesh: a population-based study. *Indian J Med Res.* 2008; 127:211-218.
14. Giovannucci E, Liu Y, Hollis BW. 25-Hydroxyvitamin D and risk of myocardial infarction in men: a prospective study. *Arch Intern Med.* 2008; 168:1174-1180.
15. Scragg R, Jackson R, Holdaway IM. Myocardial infarction is inversely associated with plasma 25-hydroxyvitamin D 3 levels: a community based study. *Int J Epidemiol.* 1990; 19:559-563.
16. Ayman El-Menyar, study of low Vitamin D and cardiovascular risk factors in males and females from a sunny, rich country. *The open cardiovascular medicine journal,* 2012, 6, 76-80.