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Original Research Article

A study of predictive value of microalbuminuria in early outcome of non-diabetic patients of acute myocardial infarction

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ABSTRACT

Background: Excretion of albumin in urine, in the range of 30-300 mg/day is called microalbuminuria, which cannot be detected by routine urine tests. The presence of increased UAE (Urinary albumin excretion) signals an increase in the transcapillary escape rate of albumin and is therefore a marker of micro vascular disease. Thus, microalbuminuria is an early response to myocardial infarction.
Methods: A prospective study of 50 patients of acute myocardial infarction was carried out to find out the sensitivity and the specificity of microalbuminuria in non-diabetic patients of acute STEMI; to verify the association between the level of microalbuminuria and the area of infarcts; and to establish the correlation of microalbuminuria with cardiac biomarkers.
Results: Microalbuminuria test was positive in 92% patients in the study group and 20% subjects in the control group. The sensitivity of microalbuminuria in our study is 92% and the specificity is 80%. The level of Microalbuminuria does not statistically correlate with areas of myocardial infarction.
Conclusions: Microalbuminuria is a non-specific yet highly sensitive marker of myocardial infarction and it can be used as an additional biochemical parameter in non-diabetic patients with acute myocardial infarction. Prognostic marker value of microalbuminuria appears unproved.

Keywords: Acute myocardial infarction, Cardio-vascular risk, Microalbuminuria

INTRODUCTION

Excretion of albumin in urine, in the range of 30-300 mg/day is called microalbuminuria. This range of albumin in urine cannot be detected by routine urine tests. Microalbuminuria has been known to be associated with diabetes mellitus (type I and II over a period of time). In this disease, microalburninuria is an early predictor of renal damage. It takes usually more than 5 years for type I diabetics to have microalbuminuria. These patients go into overt nephropathy later. The presence of increased UAE (Urinary albumin excretion) signals an increase in the transcapillary escape rate of albumin and is therefore a marker of micro vascular disease. Acute myocardial infarction is one of the commonest diseases in hospitalized patients in industrialized countries. The mortality rate of acute myocardial infarction is approximately 30%. 1 in 25 patients who survives the initial hospitalization dies in the first year after acute myocardial infarction.[1] Microalbuminuria has also been implicated as a sensitive indicator of non-renal disease. The association of microalbuminuria with cardiovascular

diseases is very important owing to the burden of cardiovascular morbidity and mortality in this country and abroad. Myocardial infarction is the most significant manifestation of cardiovascular diseases. Microalbuminuria is an early response to myocardial infarction. A study by Berton et al, showed that microalbuminuria occurs in acute myocardial infarction and predicts early mortality.[2,3]

In a cross-sectional study in western India in 2002, microalbuminuria was shown to be associated with carotid intima - media thickening and coronary artery disease.[4] In the mean-time, studies indicate that microalbuminuria is common in non-diabetic population and is considered to be an independent indicator of cardiovascular risk factors and cardiovascular mortality.[5,6] It is perhaps proper to remark that few studies have been conducted to evaluate microalbuminuria in the non-diabetic patients, especially in India. In the present study, an attempt has been made to ascertain if microalbuminuria is associated with acute myocardial infarction, even in non-diabetic local population. Microalbuminuria is defined as the excretion of 30 to 300 mg of albumin per day in urine. It is not a different form or fraction of albumin, but it is just a very small amount of albumin. Albumin molecule is relatively small and it is often the first protein to enter the urine after the kidney is damaged. The table below gives the values which constitute microalbuminuria.[5,7]

Table 1: Range of microalbuminuria.

Category	24-Hour collection (Mg/24 Hour)	Timed collection (µG/MIN)	Spot collection (albumin creatinine ratio)	
			µG/MG	µG/MMOL
Normal	<30	<20	<30	<3.4
Microalbuminuria	30-300	20-200	30-300	3.4-33.9
Macroalbuminuria	>300	>200	>300	>33.9

The objectives of the present studies were to find out the sensitivity and the specificity of microalbuminuria in non-diabetic patient of acute STEMI, to find out the association between the level of microalbuminuria and the area of infarcts, to find out the correlation of microalbuminuria with cardiac biomarkers.

METHODS

A survey of 50 cases of patients clinically diagnosed with acute myocardial infarction, selected from the ICCU, was carried out at Smt. S.C.L. General Hospital, Smt. N.H.L. Municipal Medical College, Ahmedabad, Gujarat, Indiaover a period of 16 months. The age of the patients varied from 35 to 65 years. A permission of Institutional Ethical Committee for conducting the present study was not required as per the policies of the institute.

Selection criteria

Patients clinically diagnosed with acute myocardial infarction, based on ECG finding and cardiac markers were selected for the study. The cases were selected on the basis of simple random sampling method.

Patients with diabetes mellitus, hypertension (BP>140/90 mm Hg), any systemic infection, urinary tract infection, nephropathy (serum creatinine >1.6 mg/decilitre) or inflammatory conditions like rheumatoid arthritis, were excluded from the study.

Patient preparation

The patients were educated about the study and written consent of the patients for participation in the study were obtained.

All the patients were kept and observed in ICCU for initial 2 to 3 days or more depending upon their clinical condition and then in a ward for total of 5 to 7 days. All the patients were treated with standard protocol drugs like antiplatelet agents, analgesics, thrombolytic therapy (if not contraindicated), beta blockers, statins and ACE inhibitors. Other Therapeutic measures were used in complicated cases as per their needs.

The control group consisted of 50 normal, healthy, randomly selected individuals, who were age and sex matched. Due written consent was obtained from the control subjects.

Investigations

- Random blood sugar (RBS)
- Troponin-I
- Creatine phosphokinase (CPK- MB)
- Creatinine in serum
- Microalbuminuria in urine.

Serum samples were collected for RBS and cardiac enzymes as usually done. 3 ml venous blood was drawn aseptically. 1 ml blood was collected in tubes containing

sodium fluoride and ammonium oxalate. 2 ml blood was allowed to clot in separate tubes. These were centrifuged at 5000 rpm for 5 minutes. The plasma and serum thus separated were used for the determination of RBS and cardiac enzymes respectively. The random mid-stream urine samples (10 ml), were collected in sterile containers without preservative and assayed for microalbumin.

RESULTS

Age and sex distribution

The age groups 61-70 years and 41-50 years had the highest number of patients with 13 (26%) patients in each age group. There were 12 (24%) patients in the 51 - 60 years age group, and 10 (20%) patients in the 31-40 years age group. In the present study, only 2 (4%) patients were of ≤ 30 years of age. It shows that acute myocardial infarction is more common in patients between 41 and 70 years of age. Out of 50 patients having acute myocardial infarction, 45 (90%) were male and 5 (10%) were female.

Table 2: Age distribution.

Age group (years)	No. of patients (%)
≤ 30	2 (4%)
31-40	10 (20%)
41-50	13 (26%)
51-60	12 (24%)
61-70	13 (26%)
>70	0 (0%)
Total	**50 (100%)**

Smoking habit and control group distribution

All (100%) the patients with smoking habit had positive level of urine microalbumin, whereas only 66.7% non-smoker patients had positive level of urine microalbumin. Out of 50 patients having acute myocardial infarction, 46 (92%) patients had positive level of urine microalbumin and 4 (8%) patients had negative level of urine microalbumin; whereas among the control group, 10 (20%) subjects had positive level of urine microalbumin and 40 (80%) subjects had negative level of urine microalbumin.

From this data, the sensitivity of urine microalbumin test is 92% while specificity is 80%. Positive predictive value calculated from our data is 83% while negative predictive value is 91%. It shows that urine microalbumin test is very useful simple and inexpensive biochemical parameter in acute myocardial infarction patients.

Microalbuminuria distribution

In the present study, 21 patients had their urine microalbumin level in the range of 201 mg/L to 300 mg/L, 10 patients had their urine microalbumin level in the range of 101 mg/L to 200 mg/L, 15 patients had their urine microalbumin level in the range of 30 mg/L to 100 mg/L, and only 4 patients had their microalbumin level < 30 mg/L.

Table 3: Microalbuminuria distribution.

Microalbuminuria (mg/L)	No. of patients (%)
< 30	4 (8%)
30-100	15 (30%)
101-200	10 (20%)
201-300	21 (42%)
Total	**50 (100%)**

Area of infarction

Table 4: Correlation between microalbuminuria and the area of infarction.

Micro-albuminuria (mg/L)	A/W MI	I/W MI	Global MI	Total	Data Value
<30	1	2	1	4	X^2 = 3.80 P = 0.702
30-100	11	12	2	15	
101-200	6	4	0	10	
201-300	10	10	1	21	
Total	**28**	**18**	**4**	**50**	

Out of the 21 patients with their urine microalbumin level between 201 mg/L and 300 mg/L; 10 patients had A/W MI, 10 patients had I/W MI and 1 patient had Global MI. Out of the 10 patients with their urine microalbumin level between 101 mg/L and 200 mg/L; 6 patients had A/W MI and 4 patients had I/W MI. Out of the 15 patients with their urine microalbumin level between 30 mg/L and 100 mg/L; 11 patients had A/W MI, 12 patients had I/W MI and 2 patients had Global MI. Whereas out the of 4 patients with their microalbumin level < 30 mg/L; 1 patient had A/W MI, 2 patients had I/W MI and 1 patient had Global MI.

The Chi square value is 3.80 and the p value is 0.702, which is non-significant ($p > 0.05$) in our study.

Among the 21 patients with their urine microalbumin level in the range of 201 mg/L to 300 mg/L, 19 patients had their CPK-MB level between 40 mg/L and 120mg/L; among the 10 patients with their urine microalbumin level in the range of 101 mg/L to 200 mg/L, 7 patients had their CPK-MB level between 40 mg/L and 120 mg/L; among the 15 patients with their urine microalbumin level in the range of 30 mg/L to 100 mg/L, 10 patients had their CPK-MB level between 40 mg/L and 120 mg/L; and among the 4 patients with their urine microalbumin level <30 mg/L, all the 4 patients had their CPK-MB level between 40 mg/L and 120mg/L.

The Chi square value calculated from the above data is 11.8 and the p value is 0.222, which is statistically non-significant in our study.

CPK-MB and Troponin I

Out of the 21 patients with their urine microalbumin level in the range of 201 mg/L to 300 mg/L, 8 patients had their troponin I level > 5.0 ng/dL, out of the 10 patients with their urine microalbumin level in the range of 101 mg/L to 200 mg/L, 6 patients had their troponin I level > 5.0 ng/dL, out of the 15 patients with their urine microalbumin level in the range of 30 mg/L to 100 mg/L, 5 patients had their troponin I level > 5.0 ng/dL, whereas out of the 4 patients with their urine microalbumin level < 30 mg/L, 2 patients had their troponin I level >5.0 ng/dL. The chi square value calculated from the above data is 7.99 and the p value is 0.786, which is statistically non-significant in our study.

Table 5: Correlation of microalbuminuria and creatine phosphokinase-MB.

Micro-albuminuria (mg/L)	CPK-MB				Total	Data value
	<40	40-80	81-120	>120		
<30	0	2	2	0	4	
30-100	3	9	1	2	15	
101-200	2	5	2	1	10	$X^2 = 11.8$
201-300	0	9	10	2	21	P = 0.222
Total	**5**	**25**	**15**	**5**	**50**	

Table 6: Correlation of microalbuminuria and Troponin-I.

Micro-albuminuria (mg/L)	Troponin-I (ng/dl)					Total	Data value
	≤0.45	0.46-5.0	5.1-10.0	10.1-15.0	≥15.0		
<30	0	2	1	1	0	4	
30-100	2	8	3	2	0	15	
101-200	1	3	4	1	1	10	$X^2 = 7.99$
201-300	0	13	4	3	1	21	P = 0.786
Total	**3**	**26**	**12**	**7**	**2**	**50**	

DISCUSSION

All the cases in the present study had a normal renal function (Urea < 30 mg/dl and creatinine < 1.1 mg/dl). Therefore, microalbuminuria was not related to renal dysfunction in these patients. Our study in this respect agrees with the views of Peter Gosling, who considered it to be a sensitive indicator of non-renal disease.

Haffner considered microalbuminuria as a cardiovascular risk factor in the non-diabetic 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.[8] Our study agrees with these studies as it shows a significant microalbuminuria in the acute myocardial infarction patients and none of them were diabetic.

Microalbuminuria in the non-diabetic, acute myocardial infarction patients could be an overwhelming response, secondary to acute myocardial infarction. There is however no ambiguity in the fact that microalbuminuria is related to cardiovascular diseases significantly even in non-diabetic patients. We also observed that all (100%) smokers with myocardial infarction had urine microalbumin test positive. While 8 (66.67%) non-smokers had urine microalbumin test positive. The Chi square test is 13.8 and the p value is 0.000. It shows significant association between smokers and microalbuminuria.

This study agrees with the fact that microalbuminuria does occur in non-diabetic, healthy population, but it does not agree with the percentage of patients (prevalence rates) of microalbuminuria found in other studies. The higher values in our study might be the effect of smoking which was present in 66.67% of the subjects in control group.

In this study, microalbumin test was positive in 46 (92%) patients in the study group and 10 (20%) subjects in the control group. It is negative in 4 (8%) of patients and 40 (80%) of the control group. The sensitivity of microalbuminuria in our study is 92% and specificity is 80%. Hence, we can use microalbumin test as an additional screening tool in myocardial infarction.

The chi square value of this comparison is 52.6 and the p value is 0.000. The results of our study indicate that there is highly significant microalbuminuria in non-diabetic, acute myocardial infarction patients. The level of significance (P <0.0001), of microalbuminuria in our study, was comparable to that observed in other international studies.[5]

In this study, the level of microalbumin varies with area of infarction. In patients of anterior wall MI, 16 patients had urine microalbumin level more than 100 mg/L but 12 patients had it less than 100mg/L. Similarly in I/W MI patients, 14 patients had their urine microalbumin level >101 mg/L and 14 patients had their urine microalbumin level ≤ 100 mg/L. In Global MI 1 patient had the urine microalbumin level >101 mg/L and 3 patients had urine microalbumin level ≤ 100mg/L. The Chi square value is 3.80 and the p value is 0.702. Hence, the level of microalbumin does not statistically correlate with areas of myocardial infarction.

From our study, we can observe that there were 16 patients with their urine microalbumin level > 101 mg/L, however their CPKMB value were less than 80 mg/L. Similarly, 5 patients had their CPK-MB level > 80 mg/L, still their microalbumin level was < 100 mg/L. Hence, we can say that the level of microalbumin does not vary with the level of CPK-MB. So, it is statistically non-significant.

Similarly in the study of troponin-I level, 17 patients had their microalbumin level > 101 mg/L, in spite of that they have their Troponin-I value < 5.0 ng/ml. Similarly, 7 patients had their troponin-I level > 5.0 ng/ml, still their microalbumin level was < 100. Hence, we can say that the level of microalbumin also does not vary with the level of Troponin-I. So, it is statistically non-significant.

In this study, the level of microalbuminuria in acute myocardial infarction patients was highly significant (P <0.0001) when compared to that of the control subjects. This does not agree with Gosling et al, study who found significant correlation between microalbuminuria and cardiac enzymes and remarked that microalbuminuria can predict the area of infarction.[5] In their study, hypertension was not excluded but diabetes mellitus was excluded. In our study, we had excluded both the hypertension and the diabetes mellitus and this may be responsible for the lack of correlation between microalbuminuria and cardiac enzymes.

CONCLUSION

In the absence of any renal insufficiency, microalbuminuria is a non-specific yet highly sensitive marker of myocardial infarction. Since microalbuminuria is a simple investigation and relatively inexpensive test, we propose the use of microalburninuria as an additional biochemical parameter in non-diabetic patients with acute myocardial infarction.

In this study, the level of microalbuminuria is higher among smokers as compared to non-smokers but it does not correlate with values of conventional cardiac biomarkers and areas of myocardial infarction. Prognostic marker value of microalbuminuria appears unproved from various studies.

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