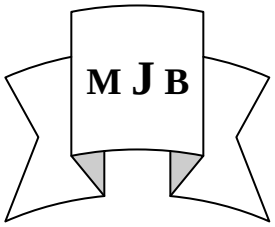
Microalbuminuria and In-Hospital Complications of Acute Myocardial Infarction

Safaa Ali Khudhair
Department of Medicine, College of Medicine, Kufa University, Najaf, Iraq.



Abstract

Back ground: The microalbuminuria happens more often in diabetic patients with acute myocardial infarction (AMI) but it has been reported even in non-diabetic patients with AMI. The microalbuminuria is a considerable predictive factor for in-hospital morbidity and mortality in patients with AMI.

Objectives: To examine whether microalbuminuria has predictive power for early in hospital morbidity and mortality after acute myocardial infarction.

Methods: Sixty patients with acute myocardial infarction were studied, aged (53 ± 5years), 45 male and 15 female. The incidence of early (3-7 days) in-hospital complications and mortality of AMI was related to the first day urinary albumin.

Results: There was significant Interrelationship between microalbuminuria and incidence of early complications of AMI (p value 0.002, RR 2.1).

Conclusions: Microalbuminuria is a significant predictor of in-hospital morbidity and mortality in patients with acute myocardial infarction.

الخلاصة

إن زيادة نسبة تواجد الألبومين في البول وخاصة بكميات صغيرة (مايكروالبومين يوريا) غالبا مايحدث عند مرضى السكري المصابين باحتشاء العضلة القلبية الحاد ،ولكنه تم تسجيل مثل هذه الحالات بعد حدوث احتشاء العضلة القلبية الحاد عند الأشخاص الغير مصابين بداء السكري. إن المايكروالبومين يوريا يعتبر عامل تنبؤي لحدوث المضاعفات التي تحصل للمصابين باحتشاء العضلة القلبية الحاد أثناء تواجدهم في المستشفى وقد أجري هذا البحث لإثبات هذا الغرض.

تم إجراء هذا البحث على ستين مريضا مصابين باحتشاء العضلة القلبية الحاد أعمارهم (٥٣ ± ٥) سنة ،خمس وأربعون رجلا وخمسة عشر امرأة والذين تم فحص نسبة الألبومين في البول لديهم خلال الأربع والعشرين ساعة الأولى من الإصابة باحتشاء العضلة القلبية الحاد.وأظهرت النتائج وجود علاقة هامة بين نسبة الألبومين في البول وحدوث المضاعفات الأولية خلال(٣-٧)أيام من الإصابة باحتشاء العضلة القلبية الحاد إثناء تواجدهم في المستشفى.وهذا يؤيد أهمية نسبة المايكروالبومين يوريا كعامل تنبؤي لحصول المضاعفات الأولية للمصابين باحتشاء العضلة القلبية الحاد.

Introduction

In the healthy kidney over 99% of filtered albumin is reabsorbed by renal tubules. A small increase in glomerular vascular permeability results in an increase in filtered albumin presented to the renal tubules. This cannot be reabsorbed and results in a large increase in urinary albumin [1]. Normal albumin excretion, detected by radioimmunoassay or enzyme immunoassay, is less than 30 mg/day. In healthy volunteers spot testing of urinary albumin shows the mean concentration to be 5.1 mg/l, with 95% of samples having a concentration of less than

29.6 mg/l, regardless of time of collection.[2]

The excretion of abnormal quantities of albumin below the level detectable by the urine dipstick is called microalbuminuria. Microalbuminuria is defined as a urinary albumin concentration of 30-200 mg/l [or a urine albumin (mg/dL)/urine creatinine (mg/dL) ratio of >0.03 –M-]. These values are currently detectable by semiquantitative dipstick tests.[3]

Following the onset of systemic inflammation there is a rapid rise in albumin excretion, peak microalbuminuria being detectable up to two days earlier than other markers of systemic inflammation such as C-reactive protein[4]. Microalbuminuria is thought to reflect the glomerular component of a systemic capillary leak that is fundamental to the pathogenesis of multiple organ failure.[4]

Microalbuminuria is used clinically to monitor incipient diabetic nephropathy, but it is known also to be a non-specific marker of inflammation, both systemic and local, and appears to be useful as a predictor of outcome in several clinical situations. In conditions such as acute pancreatitis and bacterial meningitis microalbuminuria may be detected immediately on hospital admission.[5] Further, microalbuminuria has been implicated as an independent risk factor for cardiovascular disease and increased cardiovascular mortality for patients with type 1 and type 2 diabetes mellitus, for patients with essential hypertension as well as for the general population[6, 7].

The prognosis associated with myocardial infarction remains unfavorable, despite successes in treatment recorded in the last decades, considering the necessity of the precision of the risk in patients with myocardial infarction, many authors pay a lot of attention on the role and prognostic significance of new, non-traditional factors related to the clinical course and the outcome of myocardial infarction (for shorter or longer periods) such as the level of the natriuretic peptide, C reactive protein, condition of the metabolic control before and during hospitalization and microalbuminuria.[8]

It is shown that microalbuminuria happens more often in diabetic patients with acute myocardial infarction (AMI) but it has been reported even in non-diabetic patients with AMI. The microalbuminuria is a considerable predictive factor in intra-hospital mortality coronary incidents and the death over longer periods after myocardial infarction.[9,10]

Microalbuminuria during AMI peaks at the first day and has a rapid decline throughout the first week after AMI.[11] . Gosling et al [12] found an early rise in urinary albumin concentration useful in distinguishing myocardial infarction from angina. Unfortunately, it was not sufficiently sensitive or specific unless combined with measurement of urinary gammaglobulin (IgG), when the sensitivity rose to 79.6% and specificity to 96.2%.

From clinical practice point of view the investigation of microalbuminuria as a prognostic factor is of considerable importance since a lot of tests show that the microalbuminuria is a factor that could be modified.[13] Some medicines and especially the inhibitors of Angiotensin Converting Enzyme, Angiotensin receptor blockers and statines can decrease its level, which can turn out to be a value in finding therapeutic strategies about diminishing the cardiovascular disease mortality,

including patients with myocardial infarction.[14, 15]

The primary aim of this study is to examine whether microalbuminuria has predictive power for early in hospital morbidity and mortality after acute myocardial infarction.

Patients and Methods

This is a prospective cohort study conducted at the coronary care unit of Al-Sader teaching hospital in Al-Najaf province, from March to November 2009. Sixty randomly selected patients with acute myocardial infarction were studied, aged (53 ± 5years), 45 male and 15 female. The incidence of early (3-7 days) in-hospital complications and mortality of STEMI was related to the first day urinary albumin.

All patients had acute myocardial infarction (STEMI) diagnosed on the bases of typical clinical presentation, ECG changes and enzyme and troponin levels, 31 patients had inferior STEMI and 29 patients had anteroseptal or anterolateral STEMI. Urinary albumin was assessed in the first 24 hour after onset myocardial infarction (12±3hr).

A urine sample was collected from each patient after admission to the CCU and sent for microscopic examination to exclude urinary tract infection and hematuria that may cause false proteinuria. Urine samples with no active sediments were tested for microalbuminuria by special kits(MICRAL-TEST®) that was calibrated to detect microalbuminuria between 30-200 mg/l. Patients with urinary tract infection, hematuria, congestive heart failure, renal impairment, febrile illness, menstruation, vaginal discharge, hypertensive patients treated with angiotensin converting enzyme inhibitors or angiotensin receptors blockers, were excluded.

Other factors, which may affect the prognosis of acute myocardial infarction, like DM, hypertension, smoking and total serum cholesterol were also studied in relation to microalbuminuria and complications of myocardial infarction.

For statistical study the variables were analyzed by Chi-square test of association and goodness of fit, also we used Fisher's Exact Probability Test. P-value of 0.05 considered to be statistically significant.

Results

The results presented in this paper are based on the study of sixty randomly selected patients with acute myocardial infarction (STEMI) aged (53 ± 5years), 45 male and 15 female. The early complications reported for STEMI patients are listed in table 1.

There was significant relation between microalbuminuria and incidence of early complications of STEMI table 2.

The relative risk (RR) of microalbuminuria on outcome of STEMI was 2.1, which is higher than the relative risk of all other confounding factors including age, hypertension, DM, smoking and anatomical site of the infarction. (Tables 3,4, 5, 6, 7)

Table 1 Early complications of STEMI.

Type of Complications	Inf. STEMI	Ant. STEMI
Pulmonary edema	10	11
Post MI angina	4	1
Extension of MI	2	----
Arrhythmias	10	8
Conduction defects	4	3
Death	1	1
Total	31	24

Table 2 Effect of microalbuminuria on the outcome of STEMI.

Albuminuria	STEMI		Total
	complicated	Uncomplicated	
micro-albuminuria	36	10	46
normo-albuminuria	5	9	14
Total	41	19	60
p-value	X^2 =8.9 df=1 p-value 0.002 RR=2.1		

Table 3 Effect of age on the outcome of STEMI.

Albuminuria	Age (yrs)		Total	STEMI		RR
	>40	≤ 40		complicated	uncomplicated	
Micro-albuminuria	39	7	46	36	10	RR (albuminuria) =2.1
Normo-albuminuria	9	5	14	5	9	RR (age) =1.4
Total	48	12	60	41	19	

Table 4 effect of hypertension on the outcome of STEMI

Albuminuria	hypertension		Total	STEMI		RR
	yes	no		complicated	uncomplicated	
Micro-albuminuria	9	37	46	36	10	RR (albuminuria) =2.1
Normo-albuminuria	4	10	14	5	9	RR (hypertension) =1.3
Total	13	47	60	41	19	

Table 5 effect of DM on the outcome of STEMI

Albuminuria	DM		Total	STEMI		RR
	yes	no		complicated	uncomplicated	
Micro-albuminuria	14	32	46	36	10	RR (albuminuria) =2.1
Normo-albuminuria	2	12	14	5	9	RR (DM) =1.1
Total	16	44	60	41	19	

Table 6 effect of smoking on the outcome of STEMI

Albuminuria	smoking		Total	STEMI		RR
	yes	no		complicated	uncomplicated	
Micro-albuminuria	32	14	46	36	10	RR (albuminuria) =2.1
Normo-albuminuria	10	4	14	5	9	RR (smoking) =1.4
Total	42	28	60	41	19	

Table 7 effect of site of the infarction on the outcome of STEMI

Albuminuria	Site of infarction		Total	STEMI		RR
	Inf.	Ant.		complicated	uncomplicated	
Micro-albuminuria	22	24	46	36	10	RR (albuminuria) =2.1
Normo-albuminuria	9	5	14	5	9	RR (site of infarction) =1.1
Total	31	29	60	41	19	

Discussion

In the present study, we found significant association between microalbuminuria and early in hospital complications of acute myocardial infarction for sixty patients with STEMI. At the same time we didn't find such significant correlation with other factors, like age, hypertension, DM, smoking and anatomical site of STEMI.

In Ioannis Lekatsasa, et al. [16] study, the prognostic value of microalbuminuria in two hundred twenty-three (172 men and 51 women) non-diabetic patients with acute myocardial infarction was investigated, a significant proportion of patients (33.6%) had microalbuminuria, and seventy-six patients (34%) developed an in-hospital event (fatal or non-fatal).

Persistent microalbuminuria has been associated with increased risk of atherosclerosis and cardiovascular mortality; neither the mechanism of proteinuria nor an explanation of this association has been found [17]. However the mechanism may be related to increased transvascular leakiness of albumin in systemic as well as renal vessels [6].

Authors examined the relation between microalbuminuria and incident CHD (1993–2002) in a population-based British cohort of 22,368 men and women aged 40–79 years without prevalent baseline CHD and evaluated its prognostic significance in 1,596 participants with baseline CHD. They found microalbuminuria may be useful in identifying persons at increased risk of CHD and subsequent death in the general population [18].

Other researchers correlated microalbuminuria with long term prognosis of myocardial infarction. In a study by Kragelund et al; fasting insulin, blood glucose, HbA1c, and microalbuminuria were measured in a large sample of non-diabetic patients with acute myocardial infarction between the second and the fifth day after admission. All the above markers were associated with global mortality after 7 years of follow up[19].

Although there is controversy about the optimum time for measurement of microalbuminuria after onset of acute myocardial infarction; many authors found highest level of microalbuminuria in the same day of infarction, then it

declines rapidly within seven days[1,11,20,21].

There are different methods used for measurement of microalbuminuria. In this study we did collect a spot urine sample and measured microalbuminuria by dipstick method using special kits(MICRAL-TEST®). The 24-hour urine collection for protein excretion is cumbersome and subject to inaccuracies. A spot urine sample for protein and creatinine can be used to estimate the amount of protein excreted. The ratio may be inaccurate in patients with orthostatic proteinuria [3].

The dipstick for protein is a sensitive assay based on color change induced by the presence of proteins at a given pH. It is most sensitive to the presence of albumin and is much less sensitive to other proteins, such as the light chains of Bence Jones protein. The presence of 1+ protein correlates with about 30 mg/dL of albuminuria, and 3+ protein correlates with greater than 500 mg/dL of proteinuria [3].

Diabetes mellitus and hypertension are well known causes of microalbuminuria, however Current smokers had a higher median albumin excretion than nonsmokers and were more likely to have microalbuminuria and high normal albuminuria [22].

Conclusion

Microalbuminuria is a significant predictor of in-hospital morbidity and mortality in patients with acute myocardial infarction.

References

1. Gosling P. Microalbuminuria: a marker of systemic disease. Br J Hosp Med. 1995; 54: 285-290.
2. Watts GF, Morris RW, Khan K, Polak A. Urinary albumin excretion in healthy adult subjects: reference values and some factors affecting their interpretation. Clinica Chimica Acta. 1988;172: 191-198.
3. Hasan Bazari. Approach to the patient with renal disease. Goldman: Cecile medicine. 2008; 23rd edition. Chapter 115.
4. Jensen JS, Borch-Johnsen K, Jensen G, Feldt-Rasmussen B. Microalbuminuria reflects a generalised transvascular albumin leakiness in clinically healthy subjects. Clin Sci. 1995; 88: 629-633.
5. Gosling P. Microalbuminuria: a sensitive indicator of non-renal disease? Ann Clin Biochem. 1995; 32: 439-441.
6. Naidoo DP. The link between microalbuminuria, endothelial dysfunction and cardiovascular disease in diabetes. Cardiovasc J S Afr. 2002; 13(4):194-9.
7. Catherine M. Cardiovascular disease. MKSAP 14. 2007.
8. Klausen K., K.Borch-Johnsen, B.Feldt- Rasmussen et al. Very low levels of microalbuminuria are associated with increased risk of coronary heart disease and death independently of renal function, hypertension, and diabetes, Circulation. 2004; 110: 32–35.
9. Lekatsas, I., S. Koulouris, K.Triantafyllou et al., Prognostic significance of microalbuminuria in nondiabetic patients with acute myocardial infarction, Int.J.Cardiol. 2006; 106 (2): 218- 223.
10. Brantsma, A.H., D. de Zeeuw, H.L.Hillege, Letter Regarding Article by Klausen et al, "Very Low Levels of Microalbuminuria Are Associated With Increased Risk of Coronary Heart Disease and Death Independently of Renal Function, Hypertension, and

Diabetes". Circulation. 2005; 111: 110-111.
11. Berton G, Cordiano R, Palmieri R, De Toni R, Guarnieri GL, Palatini P. Albumin excretion in diabetic patients in the setting of acute myocardial infarction: association with 3-year mortality. Diabetologia. 2004; 47:1511–1518.
12. Gosling P, Hughes EA, Reynolds TM, Fox JP. Microalbuminuria is an early response following myocardial infarction. Euro Heart J. 1991; 12: 508-513.
13. Otter,W., S.Kleybrink, W.Doering et al. Hospital outcome of acute myocardial infarction in patients with and without diabetes mellitus, Diabet.Med. 2004; 21(2): 183-187.
14. Asselbergs, F.W., G.F. Diercks, H.L.Hillege et al., Prevention of Renal and Vascular Endstage Disease Intervention Trial (PREVEND-IT) Investigators.Effects of fosinopril and pravastatin on cardiovascular events in subjects with microalbuminuria, Circulation. 2004; 110: 2809 –2816.
15. Douglas, K., P.G.O`Malley, J.L.Jackson, Meta-Analysis: The Effect of Statins on Albuminuria , Ann. Int. Med. 2006; 145(2): 117-124.
16. Ioannis Lekatsasa,Spyridon Koulourisa, Konstantinos Triantafyll, Prognostic significance of microalbuminuria in non-diabetic patients with acute myocardial infarction. Inter J cardio. 2006; 106: 218-223.
17. Goddrad J, Trner A.N, Coming A.D, et al. kidney and urinary tract disease. Davidson's principles and practice of medicine. 2006; 20th edition.
18. Matthew F. Yuyun, Kay-Tee Khaw, et al. A Prospective Study of Microalbuminuria and Incident Coronary Heart Disease and Its Prognostic Significance in a British Population. Am J Epidemiol. 2004;159:284-293.
19. Kragelund C, Snorgaard O, Kober L, et al. Hyperinsulinaemia is associated with increased long-term mortality following acute myocardial infarction in non-diabetic patients. Eur Heart J. 2004; 25:1891–1897.
20. Wiegmann TB, Chonko AM, Barnard MJ, et al. Comparison of albumin excretion rate obtained with different times of collection. Diabetes Care. 1990; 13:864–871.
21. Berton G, Citro T, Palmieri R, et al. Albumin excretion rate increases during acute myocardial infarction and strongly predicts early mortality. Circulation. 1997; 96:3338–3345.
22. Sara-Joan Pinto-Sietsma,Jaap Mulder; Wilbert M.T. Smoking Is Related to Albuminuria and Abnormal Renal Function in Nondiabetic Persons.Annals. 2000; 133:585-591.