Journal of Cardiovascular Disease Research

ISSN:0975-3583,0976-2833 VOL13,ISSUE 04,2022

Microalbuminuria in non-diabetic patients with acute coronary syndrome

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Abstract

Background: Ischemic heart disease (IHD) is a multifactorial disorder that is usually associated withhigh morbidity and mortality. Assessment of the individual's cardiovascular risk is frequently needed allowing mediation of preventive measures and enabling early therapeutic intervention. Microalbuminuria (MAU) has been wildly reportedas a risk factor for cardiovascular disease. In non-diabetic patients, MAU is considered a signal for vascular abnormality.

Objectives: To assess the prevalence and predictive role of MAU in non-diabetic patients with acute coronary syndrome (ACS).

Methods: This descriptive study included 75 patients with ACS admitted to the Cardiac Care Unit, Al-Matariya Teaching Hospital, Egypt. The patients were equally categorized into 3 groups based on diagnosis as being unstable angina (UA group), non-ST-elevation myocardial infarction (NSTEMI group), or ST-elevation myocardial infarction (STEMIgroup).Routine laboratory investigations, surface ECG, and conventional echocardiography were performed for all patients. A morning urine sample was collected from each patient for detection of MAU andestimation of albumin/creatinine ratio.

Results: Forty-eight(64%) patients had MAU with significant associations with age, smoking, and hypertension. Additionally, positive MAU was significantly higher among the STEMI group (84%) compared to the UA(56%) and the NSTEMI (52%)groups. Patients with MAU had significantly higher serum creatinine levels as well as lower EF and E/A ratios with larger LVEDD, LVESD, and LAD than those without MAU. Moreover, MAU patients showed significantly higher incidences of congestive heart failure and arrhythmia.

Conclusion: Microalbuminuria was a common findinginnon-diabetic patients with ACS, especially those with STEMI. It was associated with unfavorable echocardiographic findings and poor cardiac outcomes. Hence, MAU may be considered as a biomarker for prediction of ACS in non-diabetic patients.

Keywords: a cute coronary syndrome, microalbuminuria, non-diabetic, STEMI, unstable angina.

Introduction

Coronary artery disease (CAD) is a worldwide leading cause of disability and death.[1, 2]It is a multifactorial disorder with atherosclerosis being the main underlying pathology. Atherosclerosisis associated with increased levels of inflammatory markers, such as the acute-phase proteins and cytokines, which can alter the coronary endothelium. Inflammation at both focal and systemic levels has a major role in the destabilization and rupture of the atherosclerotic plaques, resulting in acute cardiovascular events.[3]

Coronary artery disease has long been linked with several risk factors including advancing age, male sex, hypertension, diabetes mellitus, cigarette smoking, and dyslipidemia.[2]However, these factors do not entirely explain the variation in disease incidence and mortality among populations. Thus, there must have been other factors that could better identify patients at risk of CAD.[4]

Microalbuminuria (MAU) is a common finding in subjects with cardiovascular disease.[5]Ithas been reported to reflectawidespread vascular disease and to be associated with the presence of unfavorable risk profile and target organ damage, especially indiabetic patients.[6]

ISSN:0975-3583,0976-2833 VOL13,ISSUE 04,2022

In non-diabetic patients, endothelial dysfunction has beenincriminated to have the main role in glomerulosclerosis and atherosclerosis. Increased endothelium permeability allows atherosclerotic lipoprotein particles to penetrate the vessel wall, which enhances the development of atherosclerotic plaques. This defective endothelial permeability isproposed to be the origin of the MAU.Microalbuminuriahas also been associated with biochemical indicators of endothelial dysfunction including the increased vonWillebrand factor andplatelet adhesiveness.[7 ,6]

Microalbuminuria as an indicator of endothelial dysfunction and vascular damage might be a predictor for coronary artery atherosclerosis. Therefore, this study was carried out to assess the prevalence and predictive role of MAU in non-diabetic patients with acute coronary syndrome(ACS).

Patients and methods

Patients

This descriptive study enrolled 75 patients with ACSwho were admitted to the Cardiac Care Unit, Al-Matariya Teaching Hospital, Egyptbetween October 2018and April 2019.The study subjectswere categorized into 3 groups (25 participant each) based on diagnosis as being unstable angina (UA group), non-ST-elevation myocardial infarction (NSTEMI group), or ST-elevation myocardial infarction (STEMI group). Patients with diabetes mellitus, renal disease, urinary tract infection, hypertensive crisis, congestive heart failure, or menses were excluded from the study.

Non-ST-elevation myocardial infarction was defined as myocardial necrosis (verified by elevated bloodcardiac markers; troponin I or troponin T and creatine kinase) without acute ST-segment elevation. ECG changes including ST-segment depression, T-wave inversion, or both can be found.ST-elevation myocardial infarctionwas defined as a combination of ischemic symptoms and persistent, ischemic ST-segment elevation.

The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Menoufia University, Egypt (approval number: ……). We obtained written informed consents from all the study participants. Confidentiality of patients' data was maintained by assigning a code number to each patient.

Methods

All the patients were subjected to full History taking, detailed clinical examination, 12-leads surface ECG, and routine laboratory investigations. Conventional echocardiographic examination was performed for all patients using a commercially available system (Vivid 7, General Electric-Vingmed), supplied with a harmonic M5S variable-frequency (1.7-4 MHz), phased-array transducer. A morning urine sample was collected from each patient for detection of MAU and estimation of urine albumin to creatinine ratio (UACR). Microalbuminuria wasdefined as albumin excretion rateof20-200 µg/min in a timed urine collection, albumin excretion of 30-300 mg/day in a 24-hour urine collection, or UACR of 30-300 mg/g creatinine in a spot urine sample.

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (IBM SPSS Statistics) for Windows, version 26 (IBM Corp., Armonk, N.Y., USA). For quantitative data, the Shapiro-Wilk test for normality was performed. For data that followed the normal distribution, values were expressed as mean ± standard deviation. Comparisons between two groups were carried out using the Independent Samples T-test. For data that did not follow the normal distribution, median and interquartile range (IQR; expressed as 25th-75th percentiles) were calculated, and the Mann-Whitney test was used to compare between the two groups. For qualitative data, the variables were summarized as numbers and percentages. Pearson's Chi-square test for independence was used to examine the association between two categorical variables.For continuous variables comparison between the three

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population subgroups was done by One-way ANOVA test for normally distributed data and by Kruskal-Wallis test for abnormally distributed data, followed by Post Hoc analysis whenever significant difference was found.A p-value <0.05 was adopted to interpret the significance of statistical tests.

Results

We found no significant difference between the studied groups regarding demographics, clinical data, or serum creatinine (Table 1). The STEMI group had significantly higher UACRcompared to either UA (P-value = 0.002) or NSTEMI groups (P-value=0.004).Microalbuminuria was noticed in 48 (64%) patients with a significantly higher prevalence among theSTEMI group (84%) compared to UA (56%) and NSTEMI (52%) groups(P-values = 0.028 and 0.014, respectively) (Table 1).

Table 1. Comparison between the studied groups regarding demographic & laboratory data

Parameter	UA (n=25)	NSTEMI (n=25)	STEMI(n=25)	P-value		
Age (years)	55.44 ± 12.84	53.24 ± 10.37	60.28 ± 11.97	0.103		
Gender [No. (%)] Female Male	 10 (40%) 15 (60%)	 5 (20%) 20 (80%)	 7 (28%) 18 (72%)	0.294		
Smoking[No. (%)]	10 (40%)	14 (56%)	12 (48%)	0.525		
Hypertension[No. (%)]	15 (60%)	13 (52%)	14 (56%)	0.850		
Serum creatinine (mg/dL)	1 (0.8, 1.1)	0.9 (0.8, 1.1)	1 (0.9, 1.2)	0.071		
Urinary albumin/creatinine(µg/mg)	35 (20, 85)	40 (20, 92)	120 (55, 220)	0.001*		
				P1>0.999	P2=0.002*	P3=0.004*
Microalbuminuria[No. (%)]	14 (56%)	13 (52%)	21 (84%)	0.037*		
				P1=0.777	P2=0.028*	P3=0.014*

UA: unstable angina; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction; P1: UA vs. NSTEMI; P2: UA vs. STEMI; P3: STEMI vs.NSTEMI; *significant

Table 2 shows that the patients in the STEMI group had statistically significant lower EF but larger LVEDD and LVESDthan those in the UA group (P-values = 0.012, 0.003, and 0.013, respectively).Moreover,the STEMI group patients had a significantly larger LAD than their peers in the NSTEMI group (P-value = 0.047).

Table 2. Comparison of conventional echocardiographic parameters between the studied groups

Parameter	UA (n=25)	NSTEMI (n=25)	STEMI (n=25)	P-Value		
EF(%)	57 (54, 68)	56 (50, 62)	50 (37, 58)	0.014		
				P1=0.980	P2=0.012*	P3=0.174
LVEDD (cm)	4.4 (4.3, 5.5)	4.8 (4.31, 5.7)	5.59 (5.1, 6.2)	0.004*		
				P1=0.775	P2=0.003*	P3=0.092
LVESD (cm)	3.1 (2.6, 3.9)	3.4 (2.9, 4.1)	4.2 (3.5, 5.4)	0.012*		
				P1>0.999	P2=0.013*	P3=0.099

ISSN:0975-3583,0976-2833 VOL13,ISSUE 04,2022

LA diameter(cm)	3.8 (3.3, 4)	3.8 (3.5, 3.9)	3.9 (3.8, 4.9)	0.028*		
				P1>0.999	P2=0.076	P3=0.047*
E/A	0.97 ± 0.33	0.91 ± 0.29	0.78 ± 0.26	0.090		

UA: unstable angina; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction; P1: UA vs. NSTEMI; P2: UA vs. STEMI; P3: STEMI vs.NSTEMI; EF: ejection fraction; LVESD: left ventricular end systolic diameter; LVEDD: left ventricular end diastolic diameter; LAD: left atrial diameter; *significant

PositiveMAUwas significantly associated with older age (P-value < 0.001), smoking (P-value 0.009), and hypertension (P-value < 0.001). Serum creatinine level weresignificantly higher among patients with MAU (P-value <0.001) (Table 3).

Table 3. Comparison between patients with and without micro albuminuria regarding demographic data and risk factors

Parameter	Without MAU (n=27)	With MAU (n=48)	P-Value
Age(years)	47.7 ± 9.9	61.17 ± 10.26	<0.001*
Gender [No. (%)] Female Male	 12 (44.4%) 15 (55.6%)	 10 (20.8%) 38 (79.2%)	 0.059
Smoking [No. (%)]	7 (25.9%)	29 (60.4%)	0.009*
Hypertension[No. (%)]	5 (18.5%)	37 (77.1%)	<0.001*
Serum creatinine (mg/dL)	0.9 (0.8, 1)	1.1 (0.9, 1.2)	<0.001*

MAU: microalbuminuria; *significant

Patients with MAU had significantly lower EF and E/A ratiosbut larger LVEDD, LVESD, and LAD compared to those without MAU (P-value<0.001) (Table 4).

Table 4. Comparison of conventional echocardiographic parameters between patients with and without MAU

Parameter	Without MAU (n=27)	With MAU (n=48)	P-Value
EF (%)	58 (56, 62)	53 (38, 60)	<0.001*
LVEDD (cm)	4.31 (4.25, 4.8)	5.5 (4.5, 6.1)	<0.001*
LVESD (cm)	2.9 (2.85, 3.4)	4 (3.1, 4.8)	<0.001*
LA diameter (cm)	3.5 (3.2, 3.65)	3.9 (3.8, 4.1)	<0.001*
E/A	1.1 (0.95, 1.3)	0.7 (0.6, 0.8)	<0.001*

MAU: microalbuminuria; EF: ejection fraction; LVESD: left ventricular end systolic diameter; LVEDD: left ventricular end diastolic diameter; LAD: left atrial diameter; *significant

Table 5 reveals thatMAU patients had significantly higher prevalence of congestive heart

ISSN:0975-3583,0976-2833 VOL13,ISSUE 04,2022

failureand arrhythmia than non-MAU patients (P values <0.001 and 0.005, respectively). Although all patients who were complicated by cardiogenic shock and death had MAU,we found no significant differences between both groups.

Table 5. Comparison between the patients with and without MAU regarding in-hospital complications

Parameter	Without MAU (n=27)	With MAU (n=48)	P-Value
Congestive heart failure[No. (%)]	0 (0.0%)	22 (45.8%)	<0.001*
Arrhythmia [No. (%)]	1 (3.7%)	17 (35.4%)	0.005*
Cardiogenic shock [No.(%)]	0 (0.0%)	6 (12.5%)	0.141
Death [No. (%)]	0 (0.0%)	6 (12.5%)	0.141

MAU: microalbuminuria; *significant

Discussion

The current descriptive investigated the prevalence and predictive role of MAU in non-diabetic patients with ACS. The results showed that MAU was present in 48 (64%) patients with a significantly higher prevalence among the STEMI group.Similarly, Kumar et al. reported that the mean level of MAU was significantly higher among non-diabetic patients with ACS compared to normal subjects, and the higher values were in patients with STEMI.[8] Al-Saffar et al. assessed MAU in non-diabetic patients with UA/NSTEMI and found that30% of the studied patients had MAU.[6]As well, Vaishali et al.reported asignificantly higher prevalence of MAU among patients with ACS than healthy adults with similar biological features.[5]Surprisingly, Klausen et al. reported that even a low level of MAU (as low as 4.8 µg/min)may be a strong determinant of CAD and death.[9]

In the current study,MAU was significantly associated with age, smoking, and hypertension.Sharing the same point of view, Pradhep et al.detected a high prevalence (88.3%) of MAU in non-diabetic patients withCAD and reported ahigher risk for MAU among smokers and hypertensive patients.[10]Hashim et al. delineated that the frequency of MAU was 37% in non-diabetic patients with IHD and the highest incidence was found among the elderly.[11]The study of Pruijm and co-workers evaluated the presence of MAU among the general population of an African country. They detected that MAU prevalenceat the age of 25–64 years was 5% among non-diabetic and non-hypertensivesubjects, with much higher rates among subjects with either diabetes mellitus or hypertension(20%) and those with both conditions(41%). In addition, MAU was related to age and hypertension stage in multivariate analysis.[12]In patients with severe hypertension that is associated with organ damage, the leak of urinary albumin is the result of glomerular damage. Treatment with angiotensin converting enzyme inhibitors or angiotensin receptor blockers can reduce urine albumin excretion and subsequently reduce the cardiovascular risk. Thus, MAU can be a risk factor for both progressive renal damage and long-term injury to the cardiovascular system.[13] Regarding smoking, Gupta et al. noticed that smokers had urinary albumin and albumin/creatinine ratio that are significantly higher than non-smokers, and both MAU and UACR levels were directly related to the extent of smoking (pack-years).[14] When it comes to the relationbetween MAU and cardiovascular findings, the present study showed that MAU was significantly associated with echocardiographic parameters and hospital complications especially arrhythmia and congestive heart failure. Mok et al. studied the association between the UACR and post-myocardial infarction outcomes ascardiovascular mortality, all-cause mortality, recurrent myocardial infarction, heart failure,and

ISSN:0975-3583,0976-2833 VOL13,ISSUE 04,2022

ischemic stroke. The researchers reported that higher UACR levels were associated with all outcomes except ischemic stroke, andthusalbuminuria was a good predictor of myocardial infarctionoutcomes.[15] In addition, Memon et al.noticed a higher mortality rate in patients with acute myocardial infarctionwho had MAU implyingits significanceas a prognostic biomarker.[16]

The present studyenrolled a small number of participants. In addition, the urine sample was taken once only and the management strategy wasn't includedbecausepercutaneous coronary interventionwasn't available during the period of the study, which may affect the rate of hospital complications.

Conclusion: Microalbuminuria was a common finding in non-diabetic patients with ACS, especially those with STEMI. It was associated with unfavorable echocardiographic findings and poor cardiac outcomes. Hence, MAU may be considered as a biomarker for prediction of ACS and its hospital complication in non-diabetic subjects especially older, smoker,or hypertensive patients.

References

1. Sanchis-Gomar, F., Perez-Quilis, C., Leischik, R., & Lucia, A. (2016, July 1). Epidemiology of coronary heart disease and acute coronary syndrome. *Annals of Translational Medicine*. AME Publishing Company. doi:10.21037/atm.2016.06.33
2. Carnethon, M. R., Pu, J., Howard, G., Albert, M. A., Anderson, C. A. M., Bertoni, A. G., et al. (2017, November 21). Cardiovascular Health in African Americans: A Scientific Statement from the American Heart Association. *Circulation*. doi:10.1161/CIR.0000000000000534
3. Sharma, R. S. (2017). Correlation between Benign Prostatic Hyperplasia and Coronary Artery Disease. *International Journal of Scientific Study*, *5*(5), 191–196. doi:10.17354/ijss/2017/420
4. Sadaka, M., Elhadedy, A., Abdelhalim, S., & Elashmawy, H. (2013). Albumin to creatinine ratio as a predictor to the severity of coronary artery disease. *Alexandria Journal of Medicine*, *49*(4), 323–328. doi:10.1016/j.ajme.2013.01.005
5. Vaishali, B., & Gayatri, G. (2016). Correlation of Microalbuminuria and Multiple Risk Factors in Acute Coronary Syndrome. *International Journal of Science and Research (IJSR)*, *5*(3), 187–191. doi:10.21275/v5i3.nov161805
6. Al-Saffar, H. B., Nassir, H., Mitchell, A., & Philipp, S. (2015). Microalbuminuria in non-diabetic patients with unstable angina/non ST-segment elevation myocardial infarction. *BMC Research Notes*, *8*(1). doi:10.1186/s13104-015-1347-x
7. Jensen, J. S. (1995). Renal and systemic transvascular albumin leakage in severe atherosclerosis. *Arteriosclerosis, thrombosis, and vascular biology*, *15*(9), 1324–9. doi:10.1161/01.atv.15.9.1324
8. Kumar, T. S., Mantur, P. G., Bidri, R. C., Popuri, S. K., bhavirisetty, V., & Prasad, D. P. D. (2018). Microalbuminuria in Non Diabetic Acute Coronary Syndrome Patients. *Annals of International medical and Dental Research*, *4*(3). doi:10.21276/aimdr.2018.4.3.me3
9. Klausen, K., Borch-Johnsen, K., Feldt-Rasmussen, B., Jensen, G., Clausen, P., Scharling, H., et al. (2004). Very low levels of microalbuminuria are associated with increased risk of coronary heart disease and death independently of renal function, hypertension, and diabetes. *Circulation*, *110*(1), 32–35. doi:10.1161/01.CIR.0000133312.96477.48
10. Pradhep, R. L. S., Janakiram, N., Benjamin, V. P., & Natarajan, S. (2017). A Study of Microalbuminuria in Coronary Artery Disease among Non-Diabetic Individuals. *International Journal of Current Microbiology and Applied Sciences*, *6*(1), 344–361. doi:10.20546/ijcmas.2017.601.042
11. Hashim, R., Nisar, S., Khalil ur Rehman, & Naqi, N. (2006). Microalbuminuria: association with ischaemic heart disease in non-diabetics. *Journal of Ayub Medical College, Abbottabad : JAMC*,

ISSN:0975-3583,0976-2833 VOL13,ISSUE 04,2022

18(1), 40–43.

12. Pruijm, M. T., Madeleine, G., Riesen, W. F., Burnier, M., & Bovet, P. (2008). Prevalence of microalbuminuria in the general population of Seychelles and strong association with diabetes and hypertension independent of renal markers. *Journal of Hypertension*, *26*(5), 871–877. doi:10.1097/HJH.0b013e3282f624d9
13. Dawnay, A. (2014). Proteinuria. In M. Lapsley, A. P. Day, & R. M. B. T. Ayling (Eds.), *Clinical Biochemistry: Metabolic and Clinical Aspects* (3rd ed., pp. 152–167). Elsevier. doi:10.1016/B978-0-7020-5140-1.00008-0
14. Gupta, R. K., Gupta, R., Maheshwari, V. D., & Mawliya, M. (2014). Impact of smoking on microalbuminuria and urinary albumin creatinine ratio in non-diabetic normotensive smokers. *Indian Journal of Nephrology*, *24*(2), 92–96. doi:10.4103/0971-4065.127893
15. Mok, Y., Ballew, S. H., Sang, Y., Grams, M. E., Coresh, J., Evans, M., et al. (2019). Albuminuria as a Predictor of Cardiovascular Outcomes in Patients with Acute Myocardial Infarction. *Journal of the American Heart Association*, *8*(8). doi:10.1161/JAHA.118.010546
16. Memon, A. G., Ansari, Z. A., Devrajani, B. R., & Baloch, S. (2016). Microalbuminurea in diabetic patients with Acute MI. *Rawal Medical Journal*, *41*(2), 166–170.