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Serum *β2m level* of coronary artery disease patients in Bangladesh

Abstract

Coronary artery disease (CAD) is one of the most important leading cause of death in Bangladesh. Recent studies suggested that β_2-microglobulin (*β2m*) is an inflammatory marker that may play role in development of coronary artery disease. In this study, effect of β_2-microglobulin (*β2m)* levels with patient of coronary artery disease in Bangladesh was assessed. This cross sectional study was carried out in the Department of Cardiology and Laboratory Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during March 2017 to February 2018. Total seventy four patients who underwent coronary angiography. All patients were enrolled following the inclusion and exclusion criteria. About 4ml blood was collected by venipuncture from each individual and serum β_2-microglobulin(*β2m)*levels were determine by indirect enzyme link immune assay (ELISA) and severity was assessed by SYNTAX score. Serum *β2m* level was significantly higher in coronary artery disease patients (≥3µg/ml, p<0.001). It was also significantly correlated with number of diseased coronary vessels (r=0.562, p<0.001) and SYNTAX score (r=0.547, p<0.001). The study revealed significant correlation of serum *β2m* level in coronary disease suggested that it may be used as a reliable marker for the assessment of coronary artery disease.

Keywords: *β2m*, coronary artery disease

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Introduction

The public health and economic burdens of coronary artery disease (CAD) are substantial. A Large proportion of ambulatory health care visits are for evaluation of patients with suspected CAD. Diagnostic and health care facilities have been improved considerably in Bangladesh during the last two decades. Cardiovascular diseases are becoming a significant burden on health care services in Bangladesh. The exact prevalence of CAD in Bangladesh is not known. It seems to be a rising prevalence of coronary artery disease in Bangladesh. In Bangladesh, coronary disease death reached 50,708 or 6.96% of total death.[1] Cardiovascular disease is an important health problem in Bangladesh. Acute myocardial infraction (AMI) has been reported as the leading cause of death in Bangladesh in 4th decade of life.[2] The prevalence of coronary artery disease in Bangladesh is gradually increasing due to rapid urbanization, migration of people from village to the cities, change in life style and food habits. Several studies showed that inflammatory marker acts as a biomarker of coronary artery disease for help early diagnosis and treatment of disease. One of these markers is β_2-microglobulin that has been proposed to increase in patient with coronary artery disease. Only limited information are available about the risk factors of ischemic heart disease in different age groups in Bangladesh. There is no information available on serum β_2-microglobulin with the relation of Bangladeshi people with coronary artery disease. β_2-microglobulin is the light chain in the major histocompatibility complex (MHC) class I molecules.[3] It is widely distributed in nucleated cells in the body.[4] It is reported that β_2-microglobulin influence tumor cells such as leukemia and myeloma.[5] β_2-microglobulin is also raised in some viral infections such as human immune-deficiency virus (HIV) and cytomegalovirus.[6] Collagen disease may cause deposition of β_2-microglobulin within joint.[7] It is related to carotid intima thickness in haemodialysis patients.[8] Serum *β2*m also predicts cardiovascular events in patients with chronic kidney disease.[9] Recent studies have shown that *β2*m is elevated in peripheral artery disease.[10] Only limited information available on the risk factors of ischemic heart disease in different age groups in Bangladesh. There is no information available on serum β_2-microglobulin with the relation of Bangladeshi people with coronary artery disease. In this study investigated the association of serumβ_2-microglobulin level with coronary disease patients in Bangladesh.

Methodology

The study population was recruited from the Cardiology Department of Bangabandhu Sheikh Mujib (BSMMU), Dhaka from March 2017 to February 2018.Total seventy four patients who underwent coronary angiogram for the evaluation of coronary artery disease were enrolled for this study.Patients of renal dysfunction (creatinine level >1.3mmol/l), patients with Human immunodeficiency viral (HIV) disease, Multiple Myeloma, Leukemia and Collagen diseases were excluded from the study. Fifty eight patients (78.37%) were diagnosed as significant coronary artery

disease (≥50% vessel stenosis) and remaining thirteen (21.62%) were diagnosed as non-significant coronary artery disease (normal angiography or <50% vessel stenosis) coronary artery disease. Samples were collected before coronary angiography procedure of each patient. A total 4.0ml venous blood was taken by venipuncture in a red capped tube and centrifuged to separate serum from cells after clot formation. Samples were stored at -20^{0}C until analysis and β_2-microglobulin was estimated in 4 successive occasions. Measurement of β_2-microglobulin was done by indirect enzyme link immune assay (ELISA) method. Number of disease coronary vessels was assessed by coronary angiographic findings and calculation ofSYNTAX score was done by online calculator. Prior to the commencement of this study, the research protocol was approved by the Ethical Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University, Dhaka. Statistical Package for Social Sciences version 24 (SPSS Inc. Chicago, II, USA) was used for all statistical analysis. Data was presented as mean ± SD. Relationships between variables was tested by Pearson correlation Coefficient analysis.

Results

Total 74 patients were enrolled according to inclusion and exclusion criteria. Serum β_2-microglobulin level was measured. The SYNTAX score was calculated by online calculator to assess the severity of coronary artery disease. Then correlation of β2m with the number of diseased coronary vessels and with the SYNTAX score was done by using Pearson's correlation coefficient test (Table 1).

Table 1 Age distribution of the respondents (n=74)

Age (in years)	Number of patients	Percentage
20-30	1	1.4
31-40	12	16.2
41-50	18	24.3
51-60	25	33.8
61-70	14	18.9
71-80	4	5.4
Mean±SD	52.5±10.7	
Range(min-max)	26-76	

The mean age of the total studied population was 52.5±10.7 years. Higher number ofrespondents was within 51-61 years age range (33.8%). According to the study CAD usually occur in the of 5th decade of age (Figure 1).

It was observed that majority patients were male 61(82.4%) out of total (n=74) study patients. Male are more affected in coronary artery disease (Table 2).

Here β2m level was high (≥3.0µg/ml) in 58(100.0%) significant CAD patients and in 3(18.75%) non-significant CAD patients. Normal β2m level (<3.0µg/ml) was found in 81.25% non-significant CAD. The difference was statistically significant (p<0.001) (Table 3).

β2m levels were significantly higher in coronary artery disease. It was observed that the more number of the coronary artery was involved the greater the level of β2m level (Figure 2).

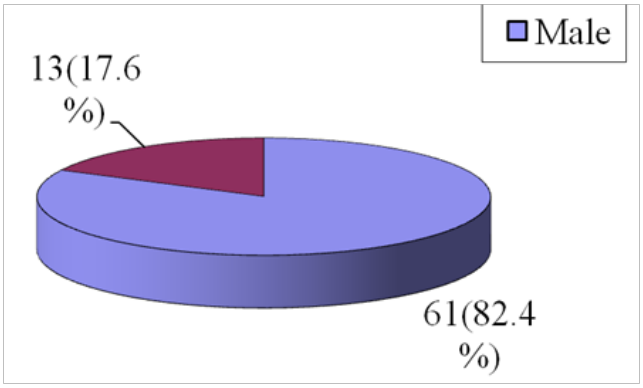

Figure 1 Shows sex distribution of the respondents (n=74).

Table 2 Distribution of serum β2m level into angiographically diagnosed significant and non-significant CAD patients (n= 74)

β2m level (according to Beta-2-Microglobulin ELISA Kits reference)	Significant CAD (≥50% vessel stenosis) (n=58) Subjects		Non-significant (<50% vessel stenosis) CAD (n=16) Subjects		p value
	n	%	n	%	
High (≥3.0µg/ml)	58	100	3	18.75	0.001^s
Normal (<3.0µg/ml)	0	00	13	81.25	

Table 3 Distribution of β2m level according to diseased coronary vessels among the respondents (n=74)

Severity of CAD	Percentage	β2m(µg/ml) Mean±SD	p-value
Non-significant CAD (n=16)	21.61	2.92±0.41	
Significant CAD (n=58)	78.37		
Single vessel disease(SVD) (n=12)	16.21	4.19±0.67	0.001^s
Double vessel disease(DVD) (n=26)	35.13	4.63±0.62	
Triple vessel disease(TVD) (n=20)	27.02	5.11±0.66	

β2m level was found correlated with number of diseased coronary vessels. The positive correlation (r=0.562) was found between β2m level and number of diseased coronary vessels which was also statistically significant (p<0.001) (Table 4).

In case of non-significant CAD the mean ±SD of β2m level was 2.91±0.65µg/ml and mean ±SD of SYNTAX score was 0.13±0.34. On the other hand in case of significant CAD the mean±SD of β2m level was 4.48±0.95µg/ml and mean ±SD of SYNTAX score was 16.27±08.99. Here significant difference was found between β2m level and SYNTAX score among respondents (p<0.001) (Figure 3).

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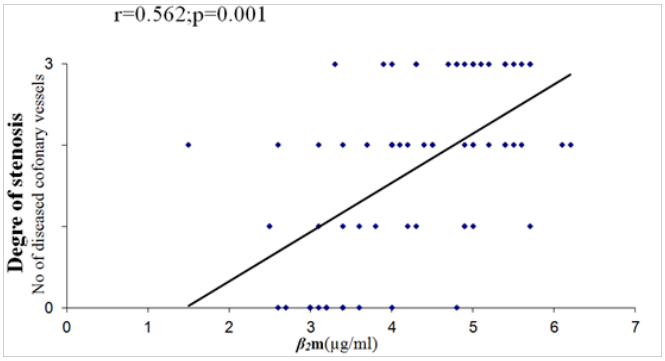

Figure 2 Scatter diagram showing correlation β2m and number of diseased coronary vessels (n=74).

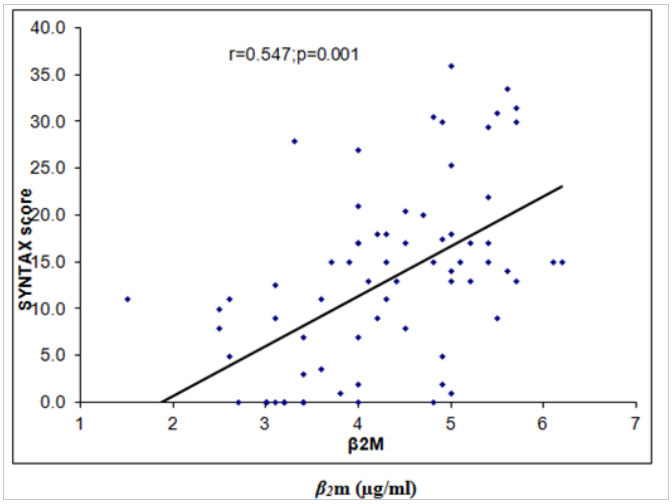

Figure 3 Scatter diagram showing correlation between β2m and SYNTAX score (n=74).

Table 4 Distribution of the respondents by β2m and SYNTAX score (n=74)

Variables	Non-significant (n=16) Mean±SD	Significant (n=58) Mean±SD	p value
β2m (µg/ml)	2.91±0.65	4.48±0.95	<0.001*
SYNTAX score	0.13±0.34	16.27±08.99	<0.001*

Unpaired student t-test

β2m level was correlated with SYNTAX score of respondents. Here the positive correlation (r=0.547) was found between β2m level and SYNTAX score which was statistically significant (p=0.001).

Discussion

The measurement of inflammatory markers may be a potent method for identifying individuals with increased inflammation at risk of future cardiovascular events.[11] Several biomarkers like C-reactive protein,[12] high sensitivity C-reactive protein (hs-CRP), intrleukin-6 (IL-6) and tumor necrosis factor (TNF) have been shown to be predictors of coronary artery disease. These markers were not associated with severity of coronary artery disease.[13] Protein markers have potential to enhance the understanding of disease pathogenesis and elucidate biological process that affects the disease risk. The association between β_2-microglobulin (β2m) and cardiovascular disease remain under research.[14] β_2-microglobulin may be participate in the inflammatory process of atherosclerosis. It acts as a chemoattractant for mononuclear cells and potential initiator of inflammation.[15] It may be involved in vascular dysfunction and aortic stiffness in atherosclerosis.[16] It is also related to direct alteration of vascular structure, immunity and response to hypoxia.[17] β_2-microglobulin (11.8kD, protein) also known as β2m is component of major histocompatibility complex (MHC) class1 molecules. It lies below α_1 chain and beside the α_3 chain on the cell surface. It lies on the all nucleated cell. Under normal conditions β2m production is about 0.13mg/h/kg.[18] About 0.9 to 2.5mg/L of free β2m is found in the serum of healthy subjects after shedding from the cell membrane.[19] Ninety percent of β_2-microglobulin is eliminated via glomerular filtration and almost completely reabsorbed by the proximal tubules.[20] β_2-microglobulin was identified as a risk marker for coronary heart disease in a proteomic study on 50 different proteins.[21] Risk stratification is a key issue in treatment of atherosclerosis. Risk stratification was evaluated by Integrated Discrimination Improvement (IDI) and Net reclassification improvement (NRI). It has been reported that β_2-microglobulin improved risk stratification for major cardiovascular events is much better than high sensitivity C-reactive protein (hs-CRP).[22] This cross sectional study was carried out by Department of laboratory medicine in Bangabandu Sheikh Mujib Medical University (BSMMU), Dhaka. We intended to investigated the relation of β_2-microglobulin with coronary artery disease. In this study we investigated 74 patients who underwent selective coronary angiogram for evaluation of coronary artery disease. There is no such type of study done to see the correlation of β2m level and coronary artery disease in Bangladesh. It is our little endeavor to measure and correlate the serum level of β2m with SYNTAX score for the diagnosis and severity assessment of coronary artery disease. It was observed that one- quarter 18(24.3%) of patients was in their 4th decade of life, one third 25(33.8%) in their 5th decade and 14(18.9%) in 6th decade of life. Very few respondents were <40 years and >70 years old. The mean age of the respondents were 52.5±10.7 years (range 26-76 years).That majority patients are male 61(82.4%) out of total (n=74) study patients. A few respondents were female 13(17.6%) with the male and female ratio being roughly 4:1. β_2-microglobulin level was found higher (≥3/ml) in coronary artery disease patients which was statistically significant (p<0.001). β_2-microglobulin was also correlated with number of diseased coronary vessels (r=0.562, p<0.001). Mean β2m level was found 4.48±0.95µg/ml with range from 3-6.1µg/ml and the mean SYNTAX score was found 16.27±08.99 with the range from 1 to 44. Pearson's correlation coefficient was done between β2m level and SYNTAX score. Then the result is r=0.547 and p<0.001. Therefore, there was a positive correlation between β2m level and SYNTAX score.β_2-microglobulin test is safe, rapid, reliable, less expensive and can be measured easily by indirect ELISA method. It may be a noninvasive tool for the assessment of severity of coronary artery disease which may beneficial for patients. Our study revealed that β_2-microglobulin was significantly associated with coronary artery disease. So it may be used as a reliable marker for assessment of coronary artery disease. In the present study, there was a positive correlation between β_2-microglobulin with severity of the coronary artery disease patients.

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Conclusion

It was concluded that serum β_2-microglobulin can be used as a reliable diagnostic tool for early detection and assess progression of coronary artery disease. This may give us a new insight to estimate serum β_2-microglobulin level before invasive coronary angiogram. Limitations of the study the study was done in limited time of span. Cases were collected from only one center, hence may not represent the whole population of the country. The sample size was small. Follow up assessment of the same patient could not be done.Serum β_2-microglobulin can be used as a noninvasive diagnostic screening tool for coronary artery disease. Further studies are need to evaluate the potential benefits of serum β_2-microglobulin level for coronary artery disease in clinical practice. It can also help discover new cases of coronary lesions, follow-up and control of the selected cases.

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None.

Conflicts of interest

The author declares that there is no conflicts of interest.

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