Original Article

Serum Potassium and Angiographic Severity of Coronary Artery Disease in Non-ST Elevation Myocardial Infarction

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Abstract:

Background: Non-ST elevation myocardial infarction (NSTEMI) patients like other patients with acute coronary syndrome (ACS) need assessment of severity of coronary artery disease (CAD) for prognostication and management. The available scoring systems are complex and include invasive parameters. On the other hand, potassium is a key element and its blood level has been shown to reflect health and disease of vasculature including in some ACS. Objective: The study was conducted to find out the relationship between serum potassium level and angiographic severity of CAD in NSTEMI.

Method: A total of 200 cases of NSTEMI patients undergoing coronary angiography (CAG) were included. Patients getting medications that alter potassium homeostasis (e.g., diuretics, glucocorticoids, intravenous insulin), having renal impairment, haematological or liver disease, congenital or valvular heart disease, cardiomyopathy, prior percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) were excluded. Serum potassium was measured soon after admission with NSTEMI, and the patients were divided: mid to high normal (4 to 5.5 mmol/L) constituted the group I and low normal (3.5-3.9 mmol/L) constituted the group II. CAG was done during index admission, SYNTAX score calculated and compared between 2 groups.

Results: High SYNTAX score was significantly more commonly found in group I than in group II (62.1% vs. 14.7%, p<0.001). Mean SYNTAX score was higher in group I than in group II (24.3±8.2 vs. 15.3±7.8, p<0.001). There was a linear relationship between serum potassium level and SYNTAX score. Mid to high normal serum potassium, hypertension and dyslipidemia were found to be significantly related to higher SYNTAX score with odds ratio being 10.44, 4.37 and 2.12 respectively.

Conclusions: Within physiological limits, higher serum potassium level correlates with severe coronary artery disease in NSTEMI patients. It may be used as an additional tool in conjunction with other scoring systems to assess the severity of CAD in this subset of ACS patients.

Key words: *Potassium, Coronary Artery Disease, Non-ST Elevated Myocardial Infarction, Coronary Angiography*

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Introduction:

Cardiovascular diseases (CVDs) are the leading cause of death in the world and a major barrier to sustainable human development.[1] The 2013 Global Burden of Disease (GBD) study estimates that CVD caused 17.3

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million deaths globally.[2] Eighty percent of deaths occur in low- and middle-income countries. Among the CVDs, ischemic heart disease (IHD), or the coronary artery disease (CAD) accounts for almost 1.8 million deaths annually and 20% of all deaths in Europe.[3] Estimates from the GBG suggests that by the year 2020, the South Asian region will have more individuals with atherothrombotic CVD than any other region.[4] The exact prevalence of CAD in Bangladesh is not known. Only a limited number of small-scale epidemiological studies are available. A recent review has estimated the prevalence of CAD in Bangladesh to be 4-6%.[5]

Risk evaluation is important for the management of patients with CAD. Clinicians need simple, reliable, reproducible, and quantitative tools to identify patients' risks and recommend prevention strategies. The Thrombolysis in Myocardial Infarction (TIMI) score and the Global Registry of Acute Coronary Events (GRACE) score used for the risk stratification of acute coronary syndrome (ACS) patients are primarily based on multivariable models that include components of the medical history, admission electrocardiogram (ECG), and cardiac biomarkers.[6]

Potassium is a key mineral that is crucial for life. The normal range for serum potassium is narrow (3.5 to 5.5 mmol/L) and minor deviation from this range (by less than 1.0 mmol/L) is associated with significant morbidity and mortality. Also, measurement of serum potassium is rapid, simple and reproducible. However, potassium level in serum may be raised erroneously due to tight tourniquet, vigorous exercise, hemolysis, thrombocytosis or leukocytosis.[7] It is well-known that changes in serum potassium ion concentration result in changes in the heart rate and myocardial contractility. Beyond this, there are some evidence that serum potassium significantly affects vasodilatation, and atherosclerosis for-mation.[8] These effects on vasculature may be due to a compensatory mechanism medi-ated by the renin-angiotensin system or may result from the pathophysiologic process of myocar-dial ischaemia.[8] Besides the established risk factors of CAD, i.e., age, diabetes mellitus, male gender, hyperlipidaemia, smoking, family history of CAD, and peripheral artery disease[9], serum potassium level tends to correlate with the severity of coronary artery lesions as assessed by Gensini score[8], and serum potassium level on admission was found to be an independent risk factor for target lesion revascularization.[10]

The importance of these findings lies in the possibility that serum potassium level may be useful for stratification of risks in patients with ACS. To date, for risk stratification and to identify the severity of coronary artery lesion, several validated scoring systems are available for use in clinical practice, the SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) score (SX) is a favoured one in this regard.[11] Although these scoring systems have many advantages, they require an invasive method such as coronary angiography to perform the scoring. Therefore, the clinicians are still in search of an easily accessible, cost-effective and noninvasive method to carry out risk stratification to determine the extent and severity of CAD in ACS patients.[12] The present study was planned to find out the relationship between serum potassium level and the severity of CAD in patients with non-ST elevation myocardial infarction (NSTEMI).

Materials and Methods:

This cross-sectional observational study was done in the Department of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh during September, 2018 to August, 2019. A total of 200 patients with NSTEMI who were admitted into NICVD and underwent coronary angiography (CAG), were included for this study. Those getting medications that alter potassium homeostasis (e.g., diuretics, glucocorticoids, intravenous insulin), having renal impairment, haematological or liver disease, congenital or valvular heart disease, cardiomyopathy, prior percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) were excluded. For each patient, relevant history was taken and clinical examination was done and recorded in predesigned structured data collection sheet. For measurement of serum potassium, 2.5 ml of blood was drawn before the day of CAG under aseptic technique from peripheral veins. The collected blood was then directly put into an automated hematology analyzer (Beckman Coulter AU480/ Siemens Dimension EXL LM) to get the values of serum electrolytes including potassium. Other investigations e.g., complete blood count, serum creatinine, lipid profile, blood sugar, were done as per standard protocol. The study patients were divided into 2 groups on the basis of serum potassium level: mid to high normal (4 to 5.5 mmol/L) constituted the group I and low normal (3.5-3.9 mmol/L) constituted the group II. Echocardiography was done before sending the patient to cath lab. CAG was done by conventional method. From the baseline diagnostic CAG, angiographic severity assessment was done by the SYNTAX scoring system by 2 independent experienced interventional

cardiologists blinded to the identities and clinical information of the patients. All coronary lesions with a diameter stenosis e"50% in vessels e"1.5 mm were scored, using the SYNTAX algorithm, which is available on the website www.syntaxscore.com. Patients with SYNTAX scores ≥23 were considered to have moderate to severe CAD according to this definition. For the present study, the patients were divided into 2 groups, those with low SYNTAX scores (≤22) and those with intermediate to high SYNTAX scores (e"23). Comparison of SYNTAX scores between group I (low normal serum potassium) and group II (mid to high normal serum potassium) NSTEMI patients was done.

Data were analyzed by SPSS (Statistical Package for Social Sciences) version 22.0. Continuous data were presented as mean ± SD. Between group comparisons were performed using t-test. Categorical data were presented as percentages and analyzed using chi square test. The correlation between serum potassium level and SYNTAX score was examined by Pearson's correlation analysis. Differences with p values <0.05 were considered statistically significant.

Ethical approval was taken from the Ethical Review Committee of NICVD prior to the commencement of the study. Informed written consent was taken from the participants accordingly.

Results:

The study involved 200 NSTEMI patients undergoing CAG: Group I had 132 NSTEMI patients with mid to high normal serum potassium level (4-5.5 mmol/L), and group II had 68 NSTEMI patients with low normal serum potassium level (3.5-3.9 mmol/L). The mean age of the studied patients was 52.7±8.9 years in group I and 50.9±9.7 years in group II. Out of 200 patients, 172 (86%) were male and 28 (14%) were female. No statistically significant differences were found in age and sex distribution between the groups (p>0.05). Among the CAD risk factors, diabetes mellitus and dyslipidaemia were significantly more in group I than in group II (p<0.05). (Table 1).

The biochemical parameters, including haemoglobin (Hb), RBS, serum creatinine, total cholesterol, LDL cholesterol and HDL cholesterol were almost similar in both the groups, however, TG was found significantly higher in group I than in group II (203.03±63.3 vs. 173.7±52.7 mg/dl, p=0.001). (Table 2) The mean percent of ejection fraction was 52.5±8.2% in group I and 54.4±8.4% in group II, the difference between the two groups was statistically insignificant (p=0.12).

High SYNTAX score was more commonly found in group I than in group II (62.1% vs 14.7%), and the difference between the 2 groups was statistically highly significant (p<0.001). On the other hand, low SYNTAX score was more common in group II than in group I (37.9% vs 85.3%), and the difference was statistically highly significant. Mean SYNTAX score was higher in group I than in group II (24.3±8.2 vs. 15.3±7.8), the difference between the groups was highly significant (p<0.001). (Table 3). Other statistics of SYNTAX score including the 25th and 75th percentile levels, the median, the maximum and minimum values and the inter-quartile ranges of SYNTAX score were higher in group I patients with high serum potassium level than in group II patients with low normal potassium. (Figure I)

Table-I

Distribution of study subjects by coronary artery disease risk factors (N=200)

Risk Factors	Group I (n=132)		Group II (n= 68)		p value
	Number	%	Number	%	
Smoking	78	59.1	36	52.9	0.40^{NS}
Hypertension	80	60.6	48	70.6	0.16^{NS}
Diabetes mellitus	76	57.6	28	41.2	0.03^{S}
Dyslipidaemia	62	47.0	20	29.4	0.02^{S}
Family H/o premature CAD	32	24.2	12	17.6	0.28^{NS}

Group I: NSTEMI patients with mid to high serum potassium level (4-5.5 mmol/L)
Group II: NSTEMI patients with low normal serum potassium level (3.5-3.9 mmol/L)
p value was reached from chi square test. S= Significant (p<0.05), NS = Not significant (p>0.05). CAD = Coronary artery disease

Table-II

Distribution of the study patients by biochemical status (N=200)

Biochemical parameters	Group I (n=132) Mean ± SD	Group II (n= 68) Mean ± SD	p value
Hb (gm/dL)	11.7±1.3	12.0±0.9	0.09^{NS}
RBS (mmol/L)	9.8±4.0	8.9±3.5	0.93^{NS}
Serum creatinine (mg/dl)	1.12±0.25	1.07±0.20	0.21^{NS}
Total cholesterol (mg/dl)	210.2±27.9	202.5±23.5	0.05^{NS}
LDL cholesterol (mg/dl)	87.7±23.5	83.3±18.6	0.18^{NS}
HDL cholesterol (mg/dl)	40.3±4.5	39.3±4.7	0.16^{NS}
TG (mg/dl)	203.03±63.3	173.7±52.7	0.001^{S}

Here, Group I: NSTEMI patients with mid to high serum potassium level (4-5.5 mmol/L)
Group II: NSTEMI patients with low normal serum potassium level (3.5-3.9 mmol/L)
p value was reached from unpaired Student's t test
S= Significant (p<0.05), NS = Not significant (p>0.05), Hb = Haemoglobin, RBS = Random blood sugar, LDL = Low density lipoprotein, HDL = High density lipoprotein, TG = Triglyceride

Table-III

Distribution of the study patients by SYNTAX score (N=200)

SYNTAX Score	Group I (n=132)		Group II (n= 68)		p value
	Number	%	Number	%	
High (e"23)	82	62.1	10	14.7	<0.001^{S}
Low (d"22)	50	37.9	58	85.3	<0.001^{S}
Mean ± SD	24.3±8.2	15.3±7.8	<0.001^{S}		

Group I: NSTEMI patients with mid to high serum potassium level (4-5.5 mmol/L)
Group II: NSTEMI patients with low normal serum potassium level (3.5-3.9 mmol/L)
p value was reached from chi square test and unpaired t test
S= Significant (p<0.05), NS = Not significant (p>0.05)

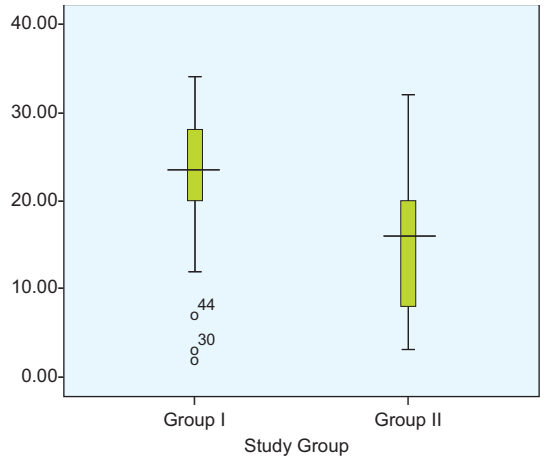

Fig.-1: *Relationship between serum potassium level and SYNTAX score by box plot diagram*

Group I: NSTEMI patients with mid to high serum potassium level (4-5.5 mmol/L)

Group II: NSTEMI patients with low normal serum potassium level (3.5-3.9 mmol/L)

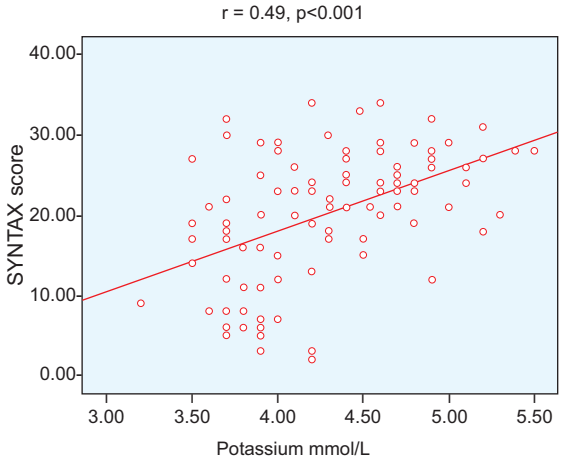

Fig.-2: *Scatter diagram showing correlation between serum potassium level and SYNTAX score*

Also, a positive correlation was found between serum potassium level and SYNTAX score with correlation coefficient, r=0.49, p<0.001. As serum potassium level increases, SYNTAX score also increases. (Figure II)

Table-IV

Multivariate logistic regression for determinants of severity of coronary artery disease as assessed by high SYNTAX score

Variables of interest	Regression coefficient (β)	p value	OR	95% CI
Agee"50 years	0.437	0.27^{NS}	1.54	0.714 – 3.354
Smoking	0.575	0.12 ^{NS}	1.77	0.856 – 3.691
Diabetes mellitus	0.420	0.25^{NS}	1.52	0.739 – 3.135
Hypertension	1.477	<0.001^{S}	4.37	2.024 – 9.474
Dyslipidemia	10.755	0.03^{S}	2.12	1.062 – 4.260
Family history of CAD	0.634	0.13^{NS}	1.88	0.817 – 4.351
Mid to high serum potassium level	2.346	<0.001^{S}	10.44	4.547 – 23.993

Dependent variable: high SYNTAX Score;
Independent variables: age e"50 years, smoking, diabetes mellitus, hypertension, dyslipidemia, family history of CAD and mid to high normal serum potassium level (4-5.5 mmol/L)
S = Significant, NS = Not significant

Variables associated with high SYNTAX score were further analyzed by logistic regression analysis to find out the determinants of severity of CAD as assessed by high SYNTAX score. Hypertension, dyslipidemia and mid to high serum potassium level were found to be the significant predictors of high SYNTAX score with ORs being 4.37, 2.12 and 10.44 respectively. (Table 4)

Discussion:

In present study, baseline demographics, i.e., age and sex were statistically similar between patients with low and mid to high normal serum potassium levels. The mean age of patients in group I and II was 52.7±8.9 and 50.9±9.7 years respectively. In a study conducted at Dhaka Medical College by Zahid et al[13] the mean age of NSTEMI patients was 55.9±9.1 years. The majority of the patients of the present study were male (84.8% and 88.2% in group I and group II respectively), such male predominance was also reported by other researchers.[13] The gender disparity in the present study may be multifactorial e.g., lower prevalence of CAD in women, less health-care seeking attitude of females and relative unwillingness for invasive procedures. Regarding CAD risk factors, smoking, hypertension and family history of CAD did not differ significantly between the groups. Diabetes mellitus and dyslipidaemia were found significantly more commonly in group I than in group II (p=0.03 and 0.02, respectively).

In this present study, the SYNTAX score of NSTEMI patients differed between group I and group II. The patients in group II with low normal serum potassium had mean SYNTAX score 15.3±7.8 while, patients in group I with mid to high normal serum potassium had mean SYNTAX score 22.6±7.1. Statistically, this difference was highly significant (p<0.001). Zhao et al[8] demonstrated that serum potassium levels were significantly increased in patients with lower (d" 39 points; 3.90 ±0.02 mmol/L, n=453) and higher (>39 points; 3.9± 0.02, n=194) Gensini scores compared with normal patients (3.82±0.03 mmol/L) (p value<0.05). Furthermore, serum potassium level of the high score group was also significantly higher than that of low score group (p<0.05). In another study[10], Honda et al found serum potassium level on admission as an independent risk factor for target lesion revascularization. Both of the studies had similar findings like the present study in terms of having increased CAD severity with increased serum potassium within normal range. Apart from this, in the USA, serum potassium level was found marginally associated with risk of CVD (hazard ratio per 1mg/dL increment, 1.03; 95% confidence interval, 1.00-1.05; p=.02a multicenter study.[14]

In this study significantly positive correlation was found between serum potassium level within normal range and SYNTAX score (r = 0.49, p value < 0.001). Within normal range as serum potassium level increases, SYNTAX score also increases. Most of the patients with low normal serum potassium had low SYNTAX score, while most of the patients with mid to high serum potassium had high SYNTAX score. Statistically, this correlation was highly significant (p<0.001). Similar significant positive correlation was found by Zhao et al between serum potassium and the severity of CAD assessed by Gensini score (p <0 .05).[8]

In this study, multivariate logistic regression analysis was done to find out the determinants of severe CAD. The analysis revealed that mid to high normal serum

potassium i.e., 4-5.5 mmol/L (odds ratio: 10.44; 95% CI is 4.547-23.993, p<0.001) and hypertension and dyslipidaemia were the independent determinants of increased angiographic severity of CAD (SYNTAX score e" 22). In the study by Zhao et al[8] and Honda et al[10] higher serum potassium level within normal range was demonstrated as independent predictor for severe CAD.

The study has got some limitations. The sample size was relatively small. Also, the sampling method was purposive, so there is risk of selection bias. The study was conducted in a single center, and involved multiple operators. Moreover, coronary artery lesion severity was assessed by visual method, so there was every chance of inter-observer variation.

Conclusion:

Serum potassium within normal range positively correlates with the severity of CAD as assessed by the SYNTAX score in NSTEMI patients. Mid to high normal serum potassium level, along with hypertension and dyslipidaemia, is a significant predictor of high SYNTAX score in patients with NSTEMI. If these findings are validated by larger, multicentric studies, serum potassium level may be added to the existing armamentarium to assess the severity of CAD in NSTEMI patients.

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