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Relationship of Serum Homocysteine concentration with other Risk Factors in Acute Coronary Syndrome Patients

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ABSTRACT

Introduction: *Acute Coronary Syndrome (ACS) has become a major health problem in the entire world. The aim of the study was to find out the relationship between serum homocysteine level and other risk factors of acute coronary syndrome.* ***Methods:*** *This was a cross-sectional study, conducted in the department of Cardiology, Dhaka Medical College Hospital, Dhaka, during the period of July 2011 to December 2011. In this period, newly diagnosed patients with ACS were taken as cases, and age, sex matched healthy subjects with normal ECG were taken as controls.* ***Results:*** *Smoking, dyslipidaemia, family history (F/H) of premature Coronary arterial disease (CAD) and serum Homocysteine level were found to be significantly ($p<0.05$) associated with ACS-risk, other risk factors (hypertension, diabetes mellitus and obesity) were not significantly associated.* ***Conclusion:*** *Serum total homocysteine concentration (tHcy) is recognized as an independent and important risk factor for ACS patients.Smoking and family history of premature CAD were found significantly associated with elevated tHcy.*

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INTRODUCTION

Acute Coronary Syndrome (ACS) has become a major health problem and is the most common cause of mortality and morbidity in the entire world.[1] In India, 4% (3.15 crore cases in 78.82 crore rural population) rural and 11% (3.71 crore cases in 33.78 crore urban population) urban population suffers from Coronary Artery Disease (CAD). CAD are becoming significant burden on healthcare services in Bangladesh too. The average prevalence of CAD from 3 small scale population based studies in Bangladesh was 6.56/1000.[2,3] The progressively increasing trend of the disease in our country shows that the prevalence was

3.3/1000 in 1976 and 17.2/1000 in 1986 indicating a 5-fold increase in 10 years. Hospital admissions for CAD are increasing rapidly. Socio-economic improvement and changes in life style in respect of increase in tobacco consumption and saturated fat intake, decrease in physical activity, increasing body weight and consequently increasing rate of diabetes mellitus (DM), hypertension (HTN) and dyslipidaemia might have contributed to this increase in our population.

ACS is a multifactorial disease involving well-known risk-factors such as age, male sex, smoking, HTN, DM, obesity, hypercholesterolemia, family history of premature CAD and sedentary lifestyle.[4] ACS develops when a vulnerable or high risk atheromatous-plaque undergoes disruption of its fibrous cap. Following plaque-rupture, a sufficient quantity of thrombogenic substances are exposed, and the coronary artery lumen may become partially or completely obscured by a combination of platelet aggregates, fibrin and red blood cells. Beletic et al.[5] have shown the importance of the novel risk factors like Apolipoprotein B/Apolipoprotein A1 ratio, Lipoprotein (a), fibrinogen, C-Reactive Protein and homocysteine (Hcy) in the pathogenesis of ACS.

Relation of high serum Hcy concentration with other risk factors for acute coronary syndrome has been studied by several authors outside Bangladesh, but this association has not been studied in our population. This study was intended to evaluate whether there is any relation of hyperhomocysteinemia with other risk factors in newly diagnosed Bangladeshi ACS patients.

METHODS

This was a cross-sectional study which was conducted in the department of Cardiology, Dhaka Medical College and Hospital (DMCH), Dhaka, during the period of July 2011 to December 2011. Newly diagnosed patients with Acute Coronary Syndrome (ACS) admitted in the Coronary Care Unit (CCU) of DMCH were taken as cases, age and sex matched healthy subjects (doctors, medical students, nurses and other hospital staffs and patients' attendants from DMCH, Dhaka) with no history of ischaemic heart disease (IHD) and normal ECG were taken as controls. The cases have been diagnosed on the basis of characteristic ischaemic type chest pain, ECG findings of ACS and cardiac bio-marker (Troponin I) findings of ACS, presenting for the first time in the CCU of DMCH, Dhaka. Data were collected by using a pre-tested data sheet. Informed consent was taken from all cases and controls or from their legal guardians. Fasting blood samples were collected for serum homocysteine assay on the morning following the admission day from the cases and the controls and measured from Biochemistry Department of Bangabandhu Sheikh Mujib Medical University (BSMMU).

RESULTS

Smoking, dyslipidaemia and hypertension (HTN) were more common risk factors in both cases and controls. However, smoking and dyslipidaemia were significantly ($p<0.05$) higher in case group. Other risk factors like-Hypertension (HTN), Diabetes Mellitus (DM)/Impaired Glucose Tolerance (IGT), Family History (F/H) of premature Coronary Artery Disease (CAD) and obese/over-weight were higher in number in cases than in controls (Table I).

Table I: Distribution of the study subjects according to different risk factors for Acute Coronary Syndrome (ACS)

Risk factors	Case (n-60)		Control (n-60)		*p* value
	n	%	n	%	
Smoking	26	43.3	14	23.3	0.001
Dyslipidaemia	33	55.0	13	21.7	0.001
HTN	21	35.0	12	20.0	0.065
DM/IGT	14	23.3	7	11.7	0.093
F/H of premature CAD	14	23.3	8	13.3	0.609
Obesity/Over-weight	11	18.3	9	15.0	0.624

HTN-Hypertention, DM- Diabetes Mellitus, IGT-Impaired Glucose Tolerance

According to serum Homocysteine level the total study subjects were divided into two sub groups. Smoking and Family History of premature CAD were found significantly ($p<0.05$) higher in >15 mol/L Homocysteine level group in the total study subjects. Others risk factors like HTN, DM/IGT, smoking and obese/over wt. had no statistically significant difference between the two groups (Table II).

Table II: Distribution of the study subjects according to Serum Homocysteine level and risk factors for Acute Coronary Syndrome (ACS)

Risk factors for ACS	Homocysteine<15 (mol/L) (n-80)		Homocysteine>15 (mol/L) (n-40)		Total (n-120)		*p* value
	n	%	n	%	n	%	
HTN	21	26.3	12	30.0	33	27.5	0.664
DM/IGT	15	18.8	6	15.0	21	17.5	0.610
Smoking	20	25.0	20	50.0	40	33.3	0.006
Obese/Over-wt.	14	17.5	6	15.0	20	16.7	0.729
Dyslipidaemia	26	32.5	20	50.0	46	38.3	0.063
F/H of premature CAD	10	12.5	12	30.0	22	18.3	0.019

HTN-Hypertention, DM-Diabetes Mellitus, IGT-Impaired Glucose Tolerance

According to serum Homocysteine level, cases were divided into two sub groups. Cases with smoking and F/H of premature CAD show significantly ($p<0.05$) higher in >15mol/L Homocysteine level in cases by Chi square test. Others risk factors like HTN, DM/IGT, smoking and obese/over wt. had no statistically significant difference between the two groups (Table III).

Table III: Distribution of the cases according to Serum Homocysteine level (mol/L) and risk factors for Acute Coronary Syndrome

Risk factors for ACS	Homocysteine<15 (mol/L) (n-28)		Homocysteine>15 (mol/L) (n-32)		*p* value
	n	%	n	%	
HTN	11	39.3	10	31.3	0.515
No HTN	17	60.7	22	68.8	
DM/IGT	9	32.1	5	15.6	0.131
No DM/IGT	19	67.9	27	84.4	
Smoking	8	28.6	18	56.3	0.030
No Smoking	20	71.4	14	43.7	
Obese/Over-wt.	6	21.4	5	15.6	0.562
No Obese/Over-wt.	22	78.6	27	84.4	
Dyslipidaemia	13	46.4	20	62.5	0.211
No Dyslipidaemia	15	53.6	12	37.5	
F/H of premature CAD	3	10.7	11	34.4	0.031
No F/H of premature CAD	25	89.3	21	65.6	

HTN-Hypertention, DM-Diabetes Mellitus, IGT-Impaired Glucose Tolerance, CAD-Coronary Artery Disease

Among the smokers the mean serum Homocysteine level was 18.5±7.4 mol/L and 12.5±2.2 mol/L in cases and controls respectively. Similarly, in those with F/H of premature CAD the mean serum Homocysteine level was 15.1±2.9 mol/L in case and 12.5±1.9 in control group. The mean serum Homocysteine differences were statistically significant ($p<0.05$) in smokers and in those with F/H of premature CAD between the two groups by unpaired '*t*'test (Table IV).

Table IV: Distribution of the study subjects according to mean serum Homocysteine level and risk factors for Acute Coronary Syndrome

Risk factors for ACS	Case (n-60)				Control (n-60)				*p* value
	n	Mean	SD	(min-max)	n	Mean	SD	(min-max)	
Smoking	26	18.5	7.4	(8.5-38.7)	14	12.5	2.2	(9.1-16.2)	0.005
F/H of premature CAD	14	15.1	2.9	(11.5-20)	8	12.5	1.9	(8.7-15.2)	0.039
HTN	21	21.8	25.4	(7.4-129.1)	12	13.3	7.6	(7.4-31.4)	0.367
DM/IGT	14	15.6	5.1	(10.3-26.1)	7	12.0	2.5	(8-15.1)	0.097
Obese/Over-wt.	11	17.8	11.5	(7.4-50)	9	11.2	2.1	(9.1-15.2)	0.107
Dyslipidaemia	33	20.7	20.4	(7.4-129.1)	13	13.6	2.0	(9.9-14.5)	0.281

HTN-Hypertention, DM-Diabetes Mellitus, IGT-Impaired Glucose Tolerance, CAD-Coronary Artery Disease

A smoker compared to a non-smoker was 4.19 (95% CI 1.61 to 10.85) times more likely to have ACS. For dyslipidaemic subject, the reference group is non-dyslipidaemic subject. A dyslipidemic subject compared to a non-dyslipidemic subject was 5 times more likely to have ACS. For F/H of premature CAD, the reference group is those with no F/H of

premature CAD. A subject with F/H of premature CAD was 3.95 (95% CI 1.11 to 14.02) times more likely to have ACS than those with no F/H of premature CAD. Smoking, dyslipidaemia, F/H of premature CAD and serum Homocysteine level were found to be significantly ($p<0.05$) associated with ACS-risk; other risk factors (HTN, DM/IGT and obese/over-wt.) were not found to be significantly associated with ACS-risk (Table V).

Table V: Risk factors analysis for Acute Coronary Syndrome, (multiple logistic regression models) (n-120)

Risk factors for ACS	OR	95.0% CI for Odd ratio (OR)		R^2	*p* value
		Lower	Upper		
HTN	2.71	0.98	7.47	0.17	0.054
DM/IGT	1.68	0.54	5.22	0.11	0.371
Smoking	4.19	1.61	10.85	0.41	0.003
Obese/Over-wt.	1.29	0.44	3.79	0.09	0.646
Dyslipidaemia	5.94	2.16	16.35	0.35	0.001
F/H of premature CAD	3.95	1.11	14.02	0.29	0.033
S. Homocysteine level	6.70	2.48	18.06	0.44	0.001
Constant	0.129				0.000

HTN-Hypertention, DM-Diabetes Mellitus, IGT-Impaired Glucose Tolerance, CAD-Coronary Artery Disease

DISCUSSION

In this study it was observed that smoking (43.3% versus 23.3%) and dyslipidaemia (55.0% versus 21.7%) were significantly ($p<0.05$) higher in both cases and control group. However, other risk factors like- Hypertension (HTN) (35% versus 20%), Diabetes Mellitus (DM) /Impaired Glucose Tolerance (IGT)(23.3% versus 11.7%). Family History (F/H) of premature Coronary Artery Disease (ACD) (23.3% versus 13.3%) and obese/over-weight (18.3% versus 15%) were higher in number in cases but not significantly ($p>0.05$) higher than controls. Tungsubutra et al.[6] observed that risk factors such as tobacco use and a positive family history were more frequent in the ACS patients, whereas diabetes and hypertension were less frequent. Badran et al.[7] showed that cigarette smoking, positive family history and dyslipidaemia were the most common risk factors in patients with ACS, while hypertension and diabetes mellitus were less frequent. These findings were in agreement with the observation from Avezum et al.[8] All these findings suggest that neither diabetes nor hypertension are major risk factors for ACS. In our country, Khan et al.[9] concluded that dyslipidaemia and family history were more prevalent. Almost similar findings were also observed by Majumder et al.[10] and Haque et al.[11] In the present study, it was found that smoking and family history of premature Coronary Artery Disease (CAD) were significantly ($p<0.05$) higher in >15 mol/L homocysteine level in the total study subjects. Other risk factors like HTN, DM/IGT, dyslipidaemia and obese/overweight were not significantly associated with high serum homocysteine level. Similar results were also observed among the case subjects. In this study, mean serum homocysteine level was significantly ($p<0.05$) higher in smokers and in those with F/H of premature CAD among the cases compared to controls; but regarding the other risk factors the mean serum homocysteine differences were not significant ($p>0.05$). In

short, this study showed a significant association of serum homocysteine level with risk factors for ACS like smoking and F/H of premature CAD; but no significant association was found with HTN, DM/IGT, dyslipidaemia and obese/overweight. These findings were consistent with reports from other studies.[12,13] Dey found that serum homocysteine level was significantly higher among the smokers, dyslipidaemics and those with family history of ischaemic heart disease, but no statistically significant association of serum homocysteine level was found with DM and HTN. The findings of the current study were almost consistent with the findings of Puri et al.[1] too. In the multiple logistic regression analysis with ACS as dependent variable and risk factors for ACS as independent variables, it was revealed that, serum total homocysteine level had odds ratio (OR) 6.70 for the development of ACS patients. Among the traditional risk factors-smoking had OR 4.19, dyslipidaemia 5.94, F/H of premature CAD 3.95, HTN 2.71, DM/IGT 1.68 and obese / overweight 1.29. Serum homocysteine level, F/H of premature CAD, dyslipidaemia and smoking were significantly ($p<0.05$) associated with ACS-risk where HTN, DM/IGTand obese/over-weight were not ($p>0.05$). In the current study, very high levels of homocysteine were found in cases (maximum up to 129.05 µmol/L) than in controls (maximum up to 31.4 µmol/L), which can probably explain the high OR associated with homocysteine. Puri et al.[1] showed that patients with elevated serum homocysteine level had a 6.05 times increased risk of CAD. In that study, HTN, smoking, DM and F/H of premature CAD had OR 3.60, 1.30, 7.37 amd 1.80 respectively for CAD-risk. Dey observed significant association of smoking, hypertension, dyslipidaemia and serum homocysteine level with acute myocardial infarction (AMI)-risk. Souissi et al.[14] (OR=2.99; 95% CI=1.18-7.59; p=0.02) also found independent association between high serum homocysteine and increased CAD-risk. The results of the present study regarding the independent association of serum homocysteine level and other risk factors with ACS-risk were also sustained by similar observations made by Taylor et al.[15] and Boushy et al.[16] etc.

CONCLUSION

Acute coronary syndrome (ACS), a multifactorial disease, has become a major health problem and an important cause of mortality and morbidity in the entire world. Serum total homocysteine (tHcy) is increasingly being recognized as an independent and important risk factor for ACS patients. In the present study, an attempt was made to find out the relation between serum homocysteine concentration and other risk factors of ACS patients in Bangladeshi population. Smoking, dyslipidaemia and HTN were more common risk factors in both cases and controls. However, smoking (43.3% versus. 23.3%) and dyslipidaemia (55.0% versus. 21.7%) were significantly ($p<0.05$) higher in the case group. Other risk factors like- HTN, DM/IGT, F/H of premature CAD and obese/over-weight were higher in number in cases but not significantly ($p>0.05$) higher than controls.

In the current study fasting serum homocysteine was significantly ($p<0.05$) higher in cases than controls both in terms of mean concentration (19.5±16.3 versus. 12.6±3.3 mol/L) and hyper-homocysteinemia (>15 mol/L) incidence (53.3% versus 13.3%). High serum homocysteine was strongly associated with ACS-risk in patients having OR=7.43 (95% CI=2.80 to 20.34). Smoking and F/H of premature CAD were found significantly ($p<0.05$) associated with elevated tHcy in this study while other traditional risk factors of ACS like- HTN, DM/IGT, dyslipidaemia and obese/overweight had no such association.

Conflict of Interest There is no conflict of interest

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