ORIGINAL ARTICLE

Association of Serum Folate and Troponin-I Levels in Acute Myocardial Infarction among Type 2 Diabetic Patients

Rumana Islam[1], Farzana Akonzee Mishu[1], Sayed Rakib Hasan[2], Mariya Tabassum[3], Tamanna Afroz[4], Md. Rakib Al Imran[5], Mohammad Ashraful Alam[6]

ABSTRACT

Acute myocardial infarction (AMI) is a major cause of death and loss of quality of life worldwide. Folate deficiency is an emerging risk factor for AMI. This case-control study was conducted in the Department of Biochemistry and Molecular Biology of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) Hospital, Dhaka, Bangladesh, between July 2021 and June 2022, to determine the possible correlation between serum folate and troponin-I levels in acute myocardial infarction among type 2 diabetic patients. A total 80 type 2 diabetes mellitus (DM) patients were included in the study: 40 patients with acute myocardial infarction (AMI) were in group-I (case) and 40 patients without AMI were in group-II (control). We adopted a convenient sampling technique. After 8-12 hours fasting blood specimens were collected from study participants to estimate serum troponin-I, folate, fasting blood glucose and HbA_1C levels. Serum folate level was significantly lower in group-I compared to group-II (3.87±3.17ng/ml vs. 8.19±3.07ng/ml; P<0.01), while serum troponin-I level was significantly higher in group-I than that of group-II (3035.82±728.16pc/ml vs. 7.58±3.19pc/ml; P<0.01). Regarding glycaemic status, fasting blood glucose (FBG) level was found significantly higher in group-I than that of group-II (10.17±3.56mmol/L vs. 8.64±2.28mmol/L; P<0.01), while HbA1C was also observed significantly higher in group-I compared to group-II (9.81±4.28% vs. 8.45±1.92%; P<0.01). A significant negative correlation was found between serum folate and troponin-I level (r=–0.301; P<0.01). Multiple logistic regression also showed a significant negative association of folate with troponin-I level (P<0.001) To conclude, serum folate level is decreased in AMI in diabetic patients compared to diabetic patients without AMI. Therefore, early detection of serum folate level helps to prevent of AMI and its recurrence in Type 2 diabetic patients.

Keywords: Acute myocardial infarction, type 2 diabetes mellitus, serum folate, serum tropnin-I

International Journal of Human and Health Sciences Vol. 10 No. 01 January'26

DOI: https://doi.org/10.31344/ijhhs.v10i1.902

INTRODUCTION

Acute myocardial infarction (AMI) is one of the leading causes of death in the developed world. The prevalence of the disease approaches three million people worldwide[1]. South Asians have a higher incidence rate compared to western populations[2]. Coronary artery disease is an increasingly important public health problem and is the leading cause of mortality in Bangladesh[3]. Myocardial infarction is one of the most common form of CVD and World health organization forecast an increase of 11% in CVD by 2030[4]. Traditionally there are some conventional risk factors for CAD such as increasing age, male sex, positive family history, hypertension, smoking, obesity, dyslipidemia, metabolic syndrome,

1. Department of Biochemistry and Molecular Biology, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka-1000, Bangladesh.
2. Department of Medicine, Kushtia Medical College Hospital, Kushtia-7000, Bangladesh.
3. Department of Biochemistry, Abdul Malek Ukil Medical College, Begumganj, Noakhali-3820, Bangladesh.
4. Department of Medicine, Dhaka Medical College Hospital, Dhaka-1000, Bangladesh.
5. Department of Internal Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka-1000, Bangladesh.
6. Department of Cardiology, Kushtia Medical College Hospital, Kushtia-7000, Bangladesh.

Correspondence to: Dr. Rumana Islam, Department of Biochemistry and Molecular Biology, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka-1000, Bangladesh. Email: dr.rumanaislam22@gmail.com

diabetes, lack of exercise[5]. The Kuopia ischemic heart disease risk factor study (KIHD) showed that dietary intake of folate is associated with a significantly reduced risk of acute coronary events[6]. Folic acid is the parent compound of a family of folate. Human cannot synthesize folic acid; therefore, they have to rely on dietary intake for sufficient levels of this vitamin[7]. Folic acid reduces atherosclerosis and improves endothelial dysfunction. Folic acid also reduces the chemokine response in the endothelial cells which is initiated by homocysteine. This chemokine response initiates the process of atherosclerosis. Poor diet quality is strongly associated with elevated risk of cardiovascular disease morbidity and mortality[8]. Folic acid deficiency below 5.5 ng/ml leads to increase in levels of homocysteine. Homocysteine is an important endothelial aggression factor, which play an important role in the aetiology of atherosclerotic plaque formation[9,10]. However, there is a limited study of serum folate levels in our country especially in diabetic patients with coronary disease like acute myocardial infarction (AMI). The aim of this study is to investigate the possible correlation of between serum folate level and troponin-I levels in type 2 diabetic patients with AMI in a tertiary level hospital in Dhaka, Bangladesh.

METHODS

This case-control study was conducted in the Department of Biochemistry and Molecular Biology of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) Hospital, Dhaka, Bangladesh, from July 2021 to June 2022. A total of 80 type 2 diabetic patients were selected according to inclusion criteria from the coronary care unit (CCU) and outpatient department (OPD) of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) Hospital, Dhaka, Bangladesh. A total 80 type 2 diabetes mellitus (DM) patients were included in the study: 40 patients with acute myocardial infarction (AMI) were in group-I (case) and 40 patients without AMI were in group-II (control). Exclusion criteria were hypothyroidism, malignancy, stroke and genetic disease. Patients taking folic acid supplementation and anticonvulsant therapy were also excluded.

In the data collection sheet, the items included were patients' general (demographic) information, personal history, physical parameters, i.e., height in meters, weight in kg, BMI, temperature, pulse, systolic and diastolic blood pressure (in mm of Hg) and results of biochemical tests (e.g., serum troponin-I, serum folate, plasma glucose, and HbA1c). Baseline and prognostic ECG were done and recorded. With all aseptic precautions fasting venous blood was collected from each patient. Blood was centrifuged at 2500-3000 rpm for 5-10 min. Then blood was separated into two layers, the upper layer called serum and the lower layer consists of formed elements. Then the serum was stored frozen at –40 C^0 in small aliquots until analysis in the laboratory of BIRDEM Hospital. The troponin kit reagent used in this study has a cut-off value of 0.30 ng/ml for diagnosis of acute myocardial infarction. Diagnostic cut-off value for raised troponin indicating myocardial infarction were set at 2µg or higher (according to the ACC/AHA guidelines).[11] Serum troponin-I, serum folate, plasma glucose (fasting) and HbA1c levels were measured using Time-resolved Fluorescence Immunoassay Autonalyzer (Bioscience Axceed P200; made in China). ECG was done by using Fukuda Denshi-FX-2111 EKG Machine (made in Japan).

Collected data were screened through editing, coding, and final verification. Data analysis was performed by using Statistical Package for Social Sciences (SPSS) version 26.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Data was expressed as mean±SD. Comparison between the groups was done using unpaired Student's t-test. P-value <0.05 was considered as statistically significant. Correlation between serum folate and troponin-I levels was determined using Pearson's correlation test. Moreover, multiple logistic regression analysis was done.

RESULTS

Our study showed that serum folate levels were 3.87±3.17 ng/ml and 8.19±3.07 ng/ml in group-I and group-II respectively; folate level was significantly lower in group-I compared to group-II patients ($P<0.001$). Serum troponin-I levels were found 3035.82±728.16 pc/ml and 7.58±3.19 pc/ml in group-I and group-II respectively; troponin-I level was significantly higher in group-I compared to group-II patients ($P<0.001$) (Table-1). Fasting blood glucose

(FBG) levels were found 10.17±3.56 mmol/L and 8.64±2.28 mmol/L, while HbA1C were observed 9.81±4.28% and 8.45±1.92% in group-I and group-II respectively. Both FBG and HbA1C values were found significantly higher significant in group-I as compared to glycaemic status of group-II patients (P<0.001 and P<0.01 respectively) (Table 2). Pearson correlation coefficient showed a significant negative correlation between serum folate and troponin-I levels (r=–0.301; P<0.01) (Figure 1). Multiple logistic regression also showed a significant negative association of folate with troponin-I level (P<0.001) (Table 3).

Table 1: Comparison of serum folate and troponin-I between two groups (N=80)

Variables	Group-I Case (n=40) Mean± SD	Group-II Control (n=40) Mean± SD	P-value
Serum Folate (ng/ml)	3.87±3.17	8.19±3.07	<0.001^S
Serum Troponin-I (pg/ml)	3035.82±728.16	7.58±3.19	<0.001^S

P-value reached from unpaired Student's t-test; S=significant.

Table 2: Comparison of glycaemic status between two groups (N=80)

Variables	Group I Case (n=40) Mean± SD	Group II Control (n=40) Mean± SD	P-value
Fasting Blood Glucose (mmol/L)	10.17±3.56	8.64±2.28	<0.001^S
HbA_1C (%)	9.81±4.28	8.45±1.92	<0.01^S

P-value reached from unpaired Student's t-test; S=significant.

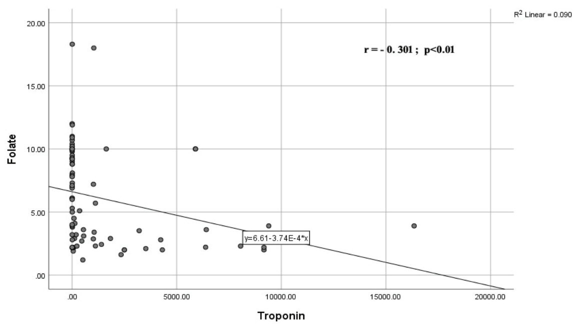

Figure 1: Scatter plot showing a significant negative correlation between of serum folate and troponin-I levels (r=–0.301; P<0.01).

Table 3: Association of serum folate with troponin-I levels

Variable	Beta	P-value	95.0% CI
Serum Folate (ng/ml)	–1.146	<0.001	–406.37, –37.12

Multiple logistic regression analysis done; dependent variable Troponin-I; beta for standardized regression coefficient.

DISCUSSION

Acute myocardial infarction (AMI) is a dreadful medical emergency. There are many risk factors for myocardial infarction (MI) identified to date. Now-a-days, serum folate deficiency has been reported emerging risk factors for MI[12].

In our study, the mean serum folate concentration in group-I and group-II were found 3.87±3.17 ng/ml and 8.19±3.07 ng/ml respectively (P<0.001), which indicated that serum folate level was significantly lower in type 2 diabetic patients with AMI compared to type 2 diabetic patients without AMI. This study also showed a significant negative correlation of folate with troponin-I levels in AMI, i.e., low levels of folic acid are significantly correlated with high levels of troponin-I in AMI patients. Similarly, Ma et al. observed serum folate levels as 7.08±3.43 nmol/L and 12.86±5.85 nmol/L in AMI patients and controls respectively (P<0.001), which supports our findings[13]. Moreover, they showed significant correlations of coronary artery disease (CAD) categories with folic acid (–0.297; P<0.001), which also supports our data[13]. In another study done by Nusier & El-Dwairi reported that AMI patients were significantly deficient in serum folate (70.95%)[14]. This high prevalence of folate deficiency in AMI patients may be due to insufficient consumption of fresh fruits and overcooking of the vegetables.

In the current study, mean fasting blood glucose (FBG) in group-I and group-II patients were 10.17±3.56 mmol/L and 8.64±2.28 mmol/L respectively. HbA1C values were 9.81±4.28% and 8.45±1.92% in group-I and group-II respectively. It was also revealed that fasting blood glucose and HbA1C levels were significantly higher in type 2 diabetic patients with AMI compared to non-AMI group. Similar results on glycemic status (having association with AMI and other coronary events) were reported in several previous studies[14-17].

Our study limitations include small sample size and short duration due to budget constraint. Besides, data derived from a single-centre hardly represents the general population. The larger sample number of multicenter study and longer prospective investigation are necessary to further observe changes in serum homocysteine and folate levels and consequential incidence of adverse cardiovascular events by supplementation of folic acid in high-risk patients.

CONCLUSION

Our data suggests that serum folate level was found decreased in type 2 diabetic patients with acute myocardial infraction. Moreover, it showed a significant negative correlation between serum folate and troponin-I levels in AMI. It also indicated that serum folate level was independently associated with AMI in type 2 diabetic patients.

Conflict of Interest: None declared by the authors.

Funding Source: Self-funding.

Ethical Approval: This study was approved by the Institutional Review Board of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) Hospital, Dhaka, Bangladesh.

Authors' Contribution: Concept and design: RI, FAM; Patient selection, data collection, and compilation: RI, FAM, SRH, MT, TA, MRAI; Data analysis: RI, MAA; Manuscript writing, critical review, editing and final submission: RI, FAM, SRH, MT, TA, MRAI, MAA.

REFERENCES

1. Reed GW, Rossi JE, Cannon CP. Acute myocardial infarction. Lancet. 2017;389(10065):197-210.
2. Karim MA, Majumder AAS, Islam KQ, Alam MB, Paul ML, Islam MS, et al. Risk factors and in-hospital outcome of acute ST segment elevation myocardial infarction in young Bangladeshi adults. BMC Cardiovasc Disord. 2015;15:73.
3. Islam AKMM, Majumder AAS. Coronary artery disease in Bangladesh: A review. Indian Heart J. 2013;65(4):424-35.
4. Hossain MS, Das PK, Ahsan SA, Bhattacharjee B, Awal A, Das S, et al. Triglyceride to high density lipoprotein cholesterol ratio in acute myocardial infarction and its relationship with angiographic severity. Bangladesh Heart J. 2021;36(2):82-8.
5. Ng KC, Yong QW, Chan SP, Cheng A. Homocysteine, folate and vitamin B_{12} as risk factors for acute myocardial infarction in a Southeast Asian population. Ann Acad Med Singap. 2002;31(5):636-40.
6. Voutilainen S, Virtanen JK, Rissanen TH, Alfthan G, Laukkanen J, Nyyssönen K, et al. Serum folate and homocysteine and the incidence of acute coronary events: The Kuopio Ischaemic Heart Disease Risk Factor Study. Am J Clin Nutr. 2004;80(2):317-23.
7. Yameen M, Maqsood M, Saleh M, Shakir IA, Shuaib A. Association of folic acid deficiency with ischemic heart disease. J Rawalpindi Med Coll. 2018;22(2):108-11.
8. Lichtenstein AH, Appel LJ, Vadiveloo M, Hu FB, Kris-Etherton PM, Rebholz CM, et al. 2021 Dietary guidance to improve cardiovascular health: A scientific statement from the American Heart Association. Circulation. 2021;144(23):e472-87.
9. Mohan A, Kumar R, Kumar V, Yadav M. Homocysteine, vitamin B_{12} and folate level: possible risk factors in the progression of chronic heart and kidney disorders. Curr Cardiol Rev. 2023;19(4):e090223213539.
10. Homocysteine Lowering Trialists' Collaboration. Lowering blood homocysteine with folic acid based supplements: Meta-analysis of randomised trials. BMJ. 1998;316(7135):894-8.
11. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al. ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients with Unstable Angina). J Am Coll Cardiol. 2000;36(3):970-1062.
12. Moysidis DV, Papazoglou AS, Anastasiou V, Daios S, Karagiannidis E, Fyntanidou B, et al. Acute myocardial infarction in patients without standard modifiable risk factors – A state-of-the-art review. Trends Cardiovasc Med. 2025;35(8):506-16.

13. Ma Y, Peng D, Liu C, Huang C, Luo J. Serum high concentrations of homocysteine and low levels of folic acid and vitamin B_{12} are significantly correlated with the categories of coronary artery diseases. BMC Cardiovasc Disord. 2017;17(1):37.
14. Nusier MK, El-Dwairi QA. Effects of vitamin B_{12} and folic acid on hyperhomocysteinemia in patients with acute myocardial infarction. J Health Sci. 2007;53(1):16-22.
15. Khan I, Siddiqui AH, Singhal S, Aslam M, Perwez A, Faraz A. Glycaemic status in patients of acute myocardial infarction: A detailed analysis. Diabetes Metab Syndr. 2016;10(Suppl 1):S140-3.
16. Huda RM, Mozaffor M, Alam MA, Hossain MD. Metabolic syndrome: Its association with acute ST-elevation myocardial infarction and its clinical outcome – A study done in the tertiary level hospital in Bangladesh. Int J Hum Health Sci (IJHHS). 2020;4(3):215-21.
17. Khan MTI, Khan MH, Tabassum M, Hassan M, Mahmud SMT, Naznen F. Association of admission glucose level with arrythmia and heart failure in hyperglycemic patients with non-ST-segment elevation myocardial infarction. Int J Hum Health Sci (IJHHS). 2022;6(3):292-7.