Original Article

Cardiac ischemic symptoms among diabetic patients with their exercise tolerance test findings at a tertiary care hospital of Bangladesh

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ABSTRACT

Background: *Cardiovascular disease is the leading cause of death among diabetic patients. Diabetics who experience chest pain should get a full cardiac evaluation. Exercise tolerance test (ETT) is a noninvasive, less costly and relatively accurate test for evaluation of ischemic heart diseases. This study aimed to describe cardiac ischemic symptoms among diabetic patients and their ETT findings.*

Methods: *This cross-sectional study was carried out among 82 diabetic patients with ischemic symptoms, in the Department of Cardiology, BIRDEM General Hospital, Dhaka from July to December 2018.*

Results: *The mean±SD age was 60.91±11.68 years with male predominance (67%). The respondents had diabetes for an average of 8.34±4.92 years. Two-thirds of research participants were on insulin. The majority of the resting ECG results were ST-T changes (86.58%); mostly in anterior leads (54.9%) and 'T' inversion was predominant feature (64.2%) among all ST-T changes. The ETT result was positive in 69.72% of the individuals. During the ETT test, 57.31% of the individuals reached their goal heart rate. Test was terminated owing to tiredness in the majority of the individuals (86.58%). Chest pain and shortness of breath were significantly higher (p 0.042 and 0.011 respectively) in ETT positive participants. Aside from diabetes, the ETT positive participants had risk factors such as dyslipidaemia, hypertension, a family history of IHD and smoking (18.3%, 8.53%, 14.63% and 13.42% respectively).*

Conclusion: *Over two-thirds of the diabetic patients with suspected IHD had positive ETT findings in this study.*

Keywords: *Cardiac ischemic symptom, exercise tolerance test, diabetes mellitus, ischemic heart disease.*

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INTRODUCTION

Diabetes mellitus (DM) is a chronic, severe metabolic disorder that causes functional and structural changes in a variety of organs, most notably the vascular system, over time.[1] According to the Federation of International Diabetes[2], the latest worldwide forecasts for diabetes are 591 million (1 out of every 10 people) by 2035. According to World Health Organization (WHO) estimate from 2016, diabetes impacted 8% (12.88 million) of the total population of Bangladesh, accounting for 3% of all-age deaths.[3] Over time, there has also been an increase in the prevalence of diabetes among the Bangladeshi population.[4]

Cardiovascular disease (CVD) is a primary cause of mortality worldwide. According to WHO, 17.7 million

people died from CVDs in 2015, accounting for 31% of worldwide deaths[5], a figure predicted to rise.[6,7] According to a systematic review and meta-analysis, the prevalence of CVD is growing in Bangladesh. Socioeconomic progress, rapid urbanization and habituation of a sedentary lifestyle (changing food habits, including increased access to and demand for processed food, inconsistent meal times, reduced physical activity, increase in tobacco consumption, an increase in body weight and an increase in the population's rate of diabetes, hypertension and dyslipidemia) may increase the chronic disease burden, particularly coronary artery disease (CAD). [8-11]

Diabetes and cardiovascular disease have a strong correlation. CVD is the leading cause of death among diabetic individuals. Across the United States, the CVD mortality rate for adult diabetic people revealed a 1.8 percent increase in the risk of a heart attack and infarction of myocardia compared to those without DM.[12,13] The Framingham Heart Study discovered a considerable increase in diabetes-related peripheral arterial disease, congestive heart failure, CAD, myocardial infarction (MI) and sudden cardiac death.[14]

Diabetics usually experience less chest pain (known as "silent ischemia") and have a worse prognosis for CAD than non-diabetics. The interplay of hyperglycemia with other cardiovascular risk factors appears to be connected to the growth in cardiovascular morbidity and mortality.[15]

The exercise tolerance test (ETT) is a non-invasive, risk-free way to evaluate cardiac function. Because of its high output of diagnostic (specificity 85 to 95 percent, sensitivity 65 to 75 percent),[16] prognostic and functional importance, ETT remains a crucial test modality, both alone and in combination with other modalities for diagnosis in patients with risk of developing CAD.[14]

Diabetics who experience typical or uncommon chest pain should get a full cardiac evaluation. ETT is a safe and non-invasive diagnostic tool for detecting CAD in its early stages, aiding in the identification of individuals with high, moderate and low risk.[17] ETT is extremely effective in symptomatic patients with non-diagnostic ECG. Treadmill exercise testing is far less expensive than other costly imaging procedures including stress echocardiography, stress single-photon emission computed tomography (SPECT) myocardial perfusion imaging and coronary angiography.[18] As a result, ETT is a frequently utilized diagnostic test for all types of IHD patients, allowing for diagnosis, risk stratification, prognosis evaluation and functional capacity assessment.[19] The goal of this study was to report on ischemic symptoms in diabetes patients with ETT findings.

METHODS

This cross-sectional study was carried out among 82 diabetic patients in the Department of Cardiology, BIRDEM General Hospital, Dhaka, Bangladesh from July to December 2018. After fulfillment of the eligibility criteria, data were collected from the patients attending in-patient and out-patient service of the Department of Cardiology using convenient sampling.

The objective of the study was discussed in details with the patients or their attendants before enrollment. Clinical examination, baseline ECG and ETT tests were done and data were collected. Demographic information was recorded and substantiated by means of inspection of medical record. Information included was the subject's age, gender, medical history, clinical history of chronic heart failure with diabetes. Data was analyzed by Statistical Package for the Social Sciences (SPSS) version 23. Results were presented in tables, figures and diagrams. P value <0.05 was considered statistically significant.

The Bruce protocol was used in accordance with the established guidelines. Continuous 12-lead ECG monitoring was obtained during each examination. The target heart rate was calculated to be 85% of the maximum predicted heart rate (MPHR = 220 less age). The ETT study was considered positive if at least two leads had upsloping ST depressions of 1.5 mm or downsloping/ horizontal depressions of 1.0 mm, an early positive response within six minutes, ST depression persistence for more than six minutes into recovery, ST segment depression in five or more leads and exertional hypotension or developed typical angina symptoms during the test. Inconclusive or equivocal ETT was defined as failure to achieve > 85% MPHR, atypical chest pain and inappropriate dyspnea despite negative ECG findings and clinically significant rhythm disturbances or ST-segment changes that did not meet criteria for a positive ETT.

The metabolic equivalents were used to calculate peak exercise capacity (METs). One MET is defined as the amount of energy expended at rest, which is approximately 3.5 mL O_2 per 1 kg body weight per minute of oxygen consumption. MET varies according to age and gender. For the purposes of this study, patients with 4 METs were considered to have poor exercise capacity, while those with 5-9 METs were considered to have average exercise capacity. Patients with a high level of exercise capacity (10-13 METs) are expected to fare better. METs greater than 13 were considered to have excellent exercise capacity and expected to be risk free off cardiac disease.

Prior to the commencement of this study, BIRDEM Academy's institutional Review Board granted ethical approval. The aims of this study, as well as the risks and benefits, were properly communicated to the patients in easily understandable local language and each patient provided informed written permission. It was ensured that all information and records were kept private.

Diagnosed diabetic patients having ischemic symptoms suggestive of cardiac disease (e.g. chest pain, shortness of breath, palpitation, pain radiating to shoulder or back, neck, jaw or arm pain, sweating/clamminess, nausea/vomiting, dizziness or lightheadedness), of age between 30 to 65 years, who were willing to participate in the study and had given written consent without previously having established IHD were included. Patients with acute coronary syndrome, severe aortic stenosis, mitral stenosis, hypertrophic obstructive cardiomyopathy, having ECG findings without any ischemic symptoms suggestive of false positive ETT e.g. LBBB, left ventricular hypertrophy, WPW syndrome, digoxin toxicity, confirmed by cardiac specialist, patients with physical and mental incapacity and severe electrolyte imbalance (hypokalemia, hypocalcemia) were excluded from the study.

RESULTS

The mean± SD age of the study subjects was 60.91±11.68 years with male (67%) predominance. The average BMI was 26.06±10.46 Kg/m^2. The mean pulse rate, systolic and diastolic blood pressures were 82±24 beats per minute, 145±35 mm of Hg and 80±20 mm of Hg respectively (Table I). The respondents had diabetes for an average of 8.34±4.92 years. The mean fasting blood glucose and $HbA1_C$ levels were shown in Table II.

Table I. Clinical information of the subjects (N = 82)

Variables	Mean ± SD	Maximum- Minimum
Age	47.36±16.38	63-31
BMI (Kg/m^2)	26.06±10.46	38.13-15.76
Pulse (per minute)	82±24	120-60
Systolic blood pressure (mm of Hg)	145±35	170-100
Diastolic blood pressure (mm of Hg)	80±20	100-60
Gender		
• Male	55 (67.07%)	
• female	27 (32.93%)	

Table II. Glycemic status and lipid profile of patients (N=82)

Variables	Mean ± SD	Maximum- Minimum
Duration of diabetes (years)	8.34 ±5.92	1-19
Glycaemic status		
• FBG (mmol/l)	10.23±5.2	21.7-6.2
• Hb A_1C%	9.4±3.5	13.4-5.9
Lipid status		
• Cholesterol (mg/dl)	184±93.5	285-180
• Triglyceride (mg/dl)	228±137	521-132
• HDL (mg/dl)	51.22±29.67	83-31
• LDL (mg/dl)	122±45.5	171-61.7

Two-thirds of research participants were on insulin and 18.29 percent were on combination of antidiabetic medications. The majority of study participants were getting ACE inhibitor or ARB (Table III). Almost 70% had a ETT positive results. Chest discomfort and shortness of breath were significantly higher in ETT positive participants (Table IV). Aside from diabetes, the ETT positive participants had a statistically significant greater number of risk factors such as dyslipidaemia, hypertension, a family history of IHD and smoking (Table V).

The majority of the resting ECG results were ST-T changes (86.58%). Only 12.19% of the individuals had normal ECGs (Figure 1). The ETT result was positive in 69.72% of the individuals and negative in 8.53 percent. Rest 21% had inconclusive or equivocal results. The ETT machine calculated exercise capacity based on the number of metabolic equivalents (METs) obtained. During the ETT test, 57.31% of the individuals reached their goal heart rate (Table VI). Test was terminated owing to tiredness in the majority of the individuals (86.58%) (Table VII).

Table III. Ongoing medications of the study subjects (N = 82)

Drugs	Frequency	Percentage
Anti-diabetic		
• Insulin	63	75.60
• Oral hypoglycemic agents	24	29.26
• Combined	15	18.29
Anti-hypertensive		
• ACE inhibitor	43	52.43
• ARB	32	39.02
• Beta blocker	18	21.17
• Calcium channel inhibitor	06	07.31
Anti-ischemic		
• Glyceryl trinitrate	59	71.95
Diuretics		
• Frusemide	67	81.70
• Combination of frucemide and spironolactone	15	18.3

*Multiple responses were elicited

Table IV. Symptoms of the study subjects (N = 82)

Pre-existing symptoms	ETT (+) ve subjects (n/%)	Other than ETT (+) ve subjects (n/%)	P value
Typical chest pain	38(46.36)	23(28.03)	**0.042**
Atypical chest pain	10(12.19)	09(10.98)	**0.026**
Breathlessness	22(26.82)	12(14.64)	**0.011**
Palpitation	13(15.85)	15(18.29)	0.073

*Multiple responses were elicited

Table V. Pre-existing risk factors of the study subjects (N = 82)

Pre-existing risk factors	ETT positive subjects (n/%)	Other than ETT positive subjects (n/%)	P value
Dyslipidaemia	40 (48.78)	25 (30.48)	0.024
Hypertension	33(40.24)	26(31.71)	0.014
Positive family history of IHD	33(40.24)	21(25.61)	0.035
Smoking	25(30.49)	14(17.07)	0.043

*Multiple responses were elicited

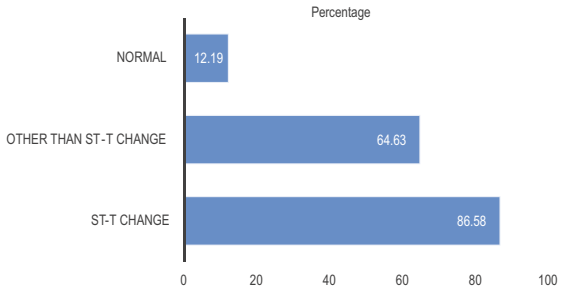
Table VI. Exercise result of the study subjects (N=82)

	Frequency	Percentage
ETT result		
• Negative	07	08.53
• Equivocal/Inconclusive	18	21.75
• Positive	57	69.72
Exercise capacity		
• Poor	26	31.70
• Average	23	28.04
• Good	29	35.36
• Excellent	04	04.90
Achievement of target heart rate		
• Yes	47	57.31
• No	35	42.69

Table VII. Reasons for termination of ETT test in study subjects

Reasons for termination	Frequency	Percentage
Exhaustion	71	86.58
ST changes	49	59.75
Angina	57	69.51
Dyspnoea	46	56.09
Dizziness	28	34.14
Pain in legs	19	23.17
Fall in BP	17	20.73
Arrhythmia	11	13.41

* Multiple responses were elicited



* Multiple responses were elicited

Figure 1. Resting ECG findings of the study subjects (N=82)

DISCUSSION

Concurrent with developments in diabetes care, particularly in terms of cardiovascular risks, there has been an astounding growth in the number of technologies available for identifying and treating coronary artery disease (CAD). This has resulted in a significant reduction in CAD-related mortality. [13, 20, 21]

A fully normal ETT has been demonstrated to be a predictor of a positive prognosis in diabetic individuals.[22] Diabetic patients are at high risk for CAD. But those with comorbidities may provide a challenge to traditional ETT because of limitations. Some findings, however, imply that well-judged patient selection is linked to safe and accurate ETT evaluation. There have been several research undertaken to investigate the presence of undetected asymptomatic CAD among diabetics.[23] Individuals with diabetes mellitus are more likely to have CAD at an advanced stage, with extensive atherosclerosis and a bad prognosis, yet CAD is usually overlooked in its asymptomatic stages. [13, 24, 25] Diabetic patients with asymptomatic CAD had a higher risk of cardiac mortality than symptomatic.[26]

In current study, the average age was 60.91±11.68 years, with a range of 47 to 64 years. The majority of patients (48%) were between the ages of 49 and 59. The prevalence of IHD increased with age. Males were affected somewhat more than females (2.03:1).

Diabetics are prone to the onset and rapid progression of atherosclerosis, as well as the onset of ischemic heart disease (IHD) and diffuse involvement of the coronary arteries.[23] Diabetics are found to have a two to fivefold increased risk of developing angina, MI, and heart failure in the Framingham study.[27] When compared to the general population, the risk of CVD in people under 45 years old is more than 11 times higher.[28] In the presence of preexisting diabetes, mortality after myocardial infarction or even post-revascularization deaths are increased.[29, 30]

Obscure and atypical symptoms delay diagnosis in the majority of diabetic patients.[31] Diabetic patients have even more extensive CAD.[32] Hyperglycemia, hypertension, dyslipidemia, and hyperinsulinemia all cause early endothelial damage.[33] Diabetes patients may have silent myocardial ischemia without typical recognized associated symptoms, particularly chest discomfort.

ETT positivity was considerably higher among individuals with pre-existing risk factors such as dyslipidaemia, hypertension, a positive family history of IHD, and smoking in the current investigation. In another study, only hypertension was significantly higher in the ETT positive group than in the ETT negative group.[34] Previous researches discovered that IHD was linked to risk factors such as smoking, dyslipidaemia, hypertension, and family history.[11, 35, 36]

Unless there are formal contraindications, diabetic patients with ischemic heart disease should always be treated with aspirin, beta blockers, angiotensin converting enzyme inhibitors, and statins, regardless of lipid levels, left ventricular systolic function, or the presence of congestive heart failure.[37] Insulin was used in 75.6 percent of the participants in the current study, whereas combination therapy (Insulin + oral hypoglycemic medicines) was used in 18.29 percent. Of the study participants ACE inhibitor and ARB was used by 52.43% and 39.02% respectively. Beta blockers were given to 21.17 percent of those who took part. Only 7.31 percent of the people were given a calcium channel inhibitor. Glyceryl trinitrate was provided in 71.95 percent of the patients. The great majority of patients received furosemide (81.7 percent). A combination of furosemide and spironolactone were given to 18.3% of people.

In the current study, statistical analysis demonstrated that there was a significant difference in clinical presentation between ETT positive participants and those with other subjects for chest pain (typical and atypical) and dyspnea. Previous studies [1, 11, 36] found that ischemic heart disease was characterized by angina pectoris (chest pain with exercise or emotional stress), acute chest pain, signs of heart failure (cough, dyspnea, oedema), and occasionally heartburn. In contrast, no correlation between ETT and chest discomfort or dyspnea was discovered in the study conducted by Fatima et al.[34] However, among diabetics with neuropathy, chest discomfort may be unusual or entirely nonexistent.

Being a metabolic disorder, diabetes has an impact on basic metabolic processes such as protein, lipid, and glucose metabolism. Diabetes-related lipid abnormalities, known as "diabetic dyslipidemia," are characterized by high total cholesterol (T-Chol), high triglycerides (TG), low high density lipoprotein cholesterol (HDL-C), and higher amounts of tiny dense LDL particles.[38] Similarly those were also reflected in the findings of our investigation.

Normal and abnormal ECG results were seen in diabetic participants with IHD symptoms. The individuals' resting ECG showed ST-T changes in 86.58 percent and other than ST-T change (RBBB, LBBB, LAHB, and Variable ectopics) in 64.63% respondents. Only 12.19% of the individuals had a normal ECG. Tachycardia, shortening of the QRS and QT intervals, increased dispersion of the QT interval, lower amplitudes of depolarization waves, shorter activation time of ventricular myocardium, and flattening of T waves were all seen in DM patients without cardiovascular problems.[39]

Among the participants 57.31 percent of individuals attained their target heart rate during ETT. The ETT test was terminated owing to tiredness in the majority of the individuals (86.58%). The ETT machine calculated exercise capacity based on the number of METs obtained. Thirty one percent participants had insufficient exercise capacity, whereas 69.72 percent had a favorable ETT outcome.

Because of the prevalence of CAD in diabetic patients and the possible problems in evaluating it, the development of precise and cost-effective diagnostic techniques is clearly clinically important. When screening low-risk populations, ETT lacks the specificity to be cost-effective, but it has the sensitivity to be reliably predictive in high-risk groups.[32] As a result, the ETT is most beneficial in individuals with a moderate risk of CAD.[40] The ETT is superior to a pharmacological stress test because it reflects the real strain of the heart and better resembles everyday cardiac activity.[41]

Conclusion

Almost seventy percent of the study subjects had positive ETT findings in this study. Diabetic patients with suspected ischemic heart disease came at a young age and had risk factors such as dyslipidaemia, hypertension, smoking and a family history of IHD. After a baseline ECG, subjects with diabetes and IHD risk factors of any age should be recommended for an ETT test.

Limitations

The sample size was small. A multi-center research in future will aid in the identification and analysis of risk variables.

Authors' contribution: SS planned the study, collected data, drafted manuscript. NS planned the study, collected data. MKC planned study, analyzed data. All authors approved the final manuscript.

Conflicts of interest: Nothing to declare.

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