

# **ORIGINAL ARTICLE**

# Correlation between 24-Hour Holter Monitoring and Clinical Presentation of Arrhythmia in Adults with Type 2 Diabetes Mellitus — A Cross-Sectional Study of 100 Cases

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#### **ABSTRACT**

Background: Cardiac arrhythmias are common in patients with Type 2 Diabetes Mellitus and may present with symptoms like palpitations, dizziness, or syncope. Holter monitoring is a useful tool for detecting arrhythmias in this high-risk population. Methods & Materials: This study employed a cross-sectional design and was conducted at BIRDEM General Hospital, located in Shahbagh, Dhaka. The research was carried out over six months from March 2013 to August 2013. Patients of 18 years of age and above, of either gender, referred for Holter monitoring with symptoms of palpitations, dizziness and syncope were evaluated for types of arrhythmia. Results: The mean age of patients was 58.80±10.98 years. Maximum number of patients with arrhythmia were found in the age group of 60-69 years. Male to female ratio was 1.7:1. There were significant correlation between control in FBG values and arrhythmia in the study subjects (p= <0.001). Statistically significant difference in mean ventricular and supraventricular beats (in 24 hours) was observed between controlled diabetes and those with uncontrolled diabetes (P-value was 0.016 and 0.01 respectively). The complaints for which patients were referred included dizziness in 34%, palpitations in 55% and syncope in 11%. Eighty-eight percent (approx.) patients with dizziness, 72.7% patients with palpitations and 47.4% of patients who presented with syncope had documented arrhythmias (p=0.01). Conclusion: Twenty four hour Holter monitoring is an important investigation for evaluation of patients with palpitation, dizziness and syncope. Arrhythmias were detected frequently in diabetic population in both symptomatic and asymptomatic patients.

**Key words:** 24-hour Holter monitoring, Type 2 Diabetes Mellitus, Cardiac arrhythmia, Palpitations, Dizziness, Syncope, Glycemic control

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# INTRODUCTION

Type 2 Diabetes Mellitus has long been recognized to be an independent risk factor for Cardiovascular disease (CVD). Prospective studies, such as the Framingham, Honolulu, and San Antonio Heart Studies, as well as numerous more recent population studies have documented the excess CVD risk in patients with diabetes from multiple racial and ethnic groups. The United Kingdom Prospective Diabetes Study (UKPDS) demonstrated benefits in decreasing microvascular disease by

controlling hyperglycemia in patients with Type 2 Diabetes Mellitus and also reported that glycemic control also probably reduces macrovascular disease<sup>[1]</sup>.

Cardiovascular disease is the leading cause of morbidity and mortality in patients with diabetes mellitus. Patients with diabetes mellitus have a 2 to 4 time's higher risk of cardiovascular disease and upto 3 times increase in mortality than non diabetics. The accelerated rate of atherosclerosis seen in diabetes mellitus predisposes patients to coronary



artery disease and to higher rates of myocardial infarction and death  $^{[2]}$ . Diabetes has long been recognized as a risk factor for arrhythmia which was subsequently reaffirmed in several studies. It has been established that diabetes causes enhanced susceptibility to arrhythmias. This susceptibility may be based on a combination of nonhomogenous collagen accumulation affecting local conduction and increased electrophysiologic se nsitivity to catecholamines  $^{[3]}$ .

Cardiac Arrhythmia, or an irregular heartbeat, is a serious but treatable condition. Arrhythmias occur when the electrical impulses, in the heart, which coordinate the heartbeats do not function properly, causing the heart to beat too fast, too slow or irregularly. Various types of Arrhythmias include Paroxysmal Supra-Ventricular Tachycardia [PSVT], Atrial flutter, Atrial Fibrillation, Ventricular Tachycardia, Ventricular Fibrillation and various types of heart block. Main causes of arrhythmias are Hypertension, Ischemic heart disease, Valvular heart disease, Cardiomyopathies, Sinus node disease, Pericarditis, COPD (Chronic Obstructive Pulmonary Disease), Thyroid Disease, Alcohol abuse, Vagal stimulation, Smoking, etc.[4] Symptoms are usually palpitation, lightheadedness, history of syncope or near-syncope, vertigo, etc. Common Tests for Arrhythmia are Electrocardiography (ECG or EKG), Holter monitor (continuous ambulatory electrocardiographic monitor), Transtelephonic monitor, Treadmill testing, Head-Tilt Test, Electrophysiologic testing, Echocardiogram., Chest

Traditionally, ambulatory monitoring has been used to determine the cause of palpitations and syncope and to a lesser degree, to identify ventricular ectopy or nonsustained ventricular tachycardia in patients at potential risk for sudden cardiac death<sup>[6]</sup>. Atrial fibrillation has become an increasingly important indication for ambulatory monitoring, predominantly as a tool to monitor the efficacy and safety of pharmacological and nonpharmacological therapies<sup>[7,8]</sup>. A substudy of the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial showed patients with new-onset DM had a significantly higher event rate of new-onset Atrial fibrillation with a hazard ratio of 1.49 compared with patients without DM, and there was a trend toward more AF in patients with DM at baseline[9].

The duration of monitoring largely depends on symptom frequency. In the evaluation of palpitations, patients who experience daily symptoms can be evaluated with a Holter monitor. More often, palpitations are sporadic and require slightly longer monitoring<sup>[10]</sup>. The value of arrhythmia monitoring for syncope is both to identify an arrhythmia as a cause for syncope and to document a syncopal event without a corresponding arrhythmia, thus suggesting a nonarrhythmic cause<sup>[11]</sup>.

In the vast majority of circumstances, ambulatory monitors are used to identify a direct correlation between symptoms and the presence or absence of an arrhythmia. Prolonged asymptomatic pauses can be a clue to the cause of syncope but caution must be used in the interpretation of the significance of these rhythms<sup>[7,12,13]</sup>.

The objective of this study was to determine association between patient's symptoms and incidence of arrhythmia by

24-hour electrocardiographic Holter monitoring in Diabetic population.

# **METHODS & MATERIALS**

This study employed a cross-sectional design and was conducted at BIRDEM General Hospital, located in Shahbagh, Dhaka. The research was carried out over six months from March 2013 to August 2013. Departments involved in the study included Internal Medicine, Cardiology, and Neurology. The study involved a total of 100 adult patients with Type 2 Diabetes Mellitus (T2DM) who were referred for 24-hour Holter ECG monitoring due to symptoms suggestive of arrhythmia. Patients were selected from the inpatient departments of the aforementioned units.

# Sample Selection

#### **Inclusion Criteria**

- Age 18 years or older.
- Both male and female patients.
- Diagnosed with Type 2 Diabetes Mellitus.
- Referred for Holter monitoring due to symptoms suggestive of arrhythmia.

# **Exclusion Criteria**

- Patients with Type 1 Diabetes Mellitus.
- Non-diabetic patients.
- Patients with permanent pacemaker implantation.

Data Collection and Study Procedure: Participants were enrolled based on inclusion and exclusion criteria. Clinical evaluations, laboratory investigations, and 24-hour Holter ECG monitoring were conducted. During Holter monitoring, patients were instructed to log any episodes of palpitations, dizziness, or syncope. Demographic and clinical dataincluding age, gender, medical history, comorbidities, and glycemic control-were collected using a structured data collection sheet and validated against patient medical records. Arrhythmia types were documented and classified per standard diagnostic criteria. Lown classification was used for ectopic beats (Grades 2, 3, and 4 included). Additional arrhythmias identified included sinus bradycardia, sinus arrest, AV blocks, supraventricular tachycardia (SVT), ventricular tachycardia (VT), and atrial fibrillation. Comorbidities such as hypertension, dyslipidemia, ischemic heart disease (IHD), stroke, thyroid disorders, etc., were also evaluated based on clinical and diagnostic parameters.

**Ethical Considerations:** The study was approved by the Ethical Review Board of BIRDEM Academy and the Bangladesh College of Physicians and Surgeons (BCPS). The objectives, benefits, and risks of participation were clearly explained in the local language. Written informed consent was obtained from all participants. Confidentiality was maintained throughout the study.

**Statistical Analysis:** Data were analyzed using SPSS for Windows, version 10. Descriptive statistics such as frequencies and percentages were used to describe baseline characteristics. Inferential statistics, including chi-square tests, were employed to evaluate relationships between variables. A p-value of <0.05 was considered statistically



significant. Data visualization was done using Microsoft Office Chart tools.

#### **RESULTS**

Table - I: Relation between Age distribution of the study subjects and arrhythmia

Age (years)	With arrhythmia (n=75)	Without arrhythmia (n=25)
40-49 (n=18)	16	2
50-59 (n=30)	22	8
60-69 (n=31)	25	6
≥ 70 (n=21)	12	9
Total	75	25

Maximum number of patients with arrhythmia were found in the age group of 60-69 years. (Table I)

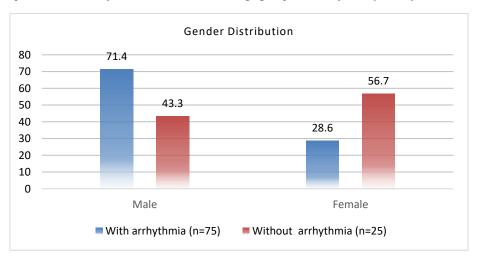


Figure - 1: Bar diagram showing relation between gender distribution of the study subjects and arrhythmia.

Among the study subjects, 71.4% males and 28.6% females had documented arrhythmia (p=0.01) (Figure 1).

Table - II: Relation between clinical presentation and documented arrhythmia

Presentation	Arrhythmia		P value
Presentation	Present No. (%)	Absent No. (%)	P value
Palpitation (n=55)	40 (72.7%)	15 (27.3%)	
Dizziness (n=34)	30 (88.2%)	04 (11.8%)	0.01 <sup>s</sup>
Syncope (n=11)	05 (47.4%)	06 (52.6%)	

p value measured by Chi-square test; s= Significant

Among the study subjects, 55% presented with palpitation, 34% had dizziness and 11% had history of syncope. Their

Holter monitoring revealed arrhythmia in 72.7%, 88.2% and 47.4% respectively(p=0.01) (Table II).

Table - III: Types of Arrhythmia detected in the study subjects

Type of arrhythmia	Number	Percentage
Atrial fibrillation	14	14.00
Atrial flutter	01	01.00
Atrial extrasystoles	47	47.00
Ventricular extrasystoles	52	52.00
SVT	30	30.00
VT	02	02.00
AV block	07	07.00
Sinus bradycardia	11	11.00

<sup>\*</sup>Multiple responses were elicited.

On Holter monitoring, arrhythmia was found in the form of atrial fibrillation in 14%, atrial flutter in 1%, ventricular ectopy in 52%, and supraventricular ectopy in 47%,

ventricular tachycardia (VT) in 2%, supraventricular tachycardia (SVT) in 30%, atrioventricular block (AV block) in 7%, sinus bradycardia in 11% (Table III).



Table - IV: Correlation between glycaemic control and arrhythmia in the study subjects

Glycaemic control	Controlled	Uncontrolled	P value
FBG	35	65	
Arrhythmia	15	55	<0.001s
No arrhythmia	20	10	
2ABF	23	77	
Arrhythmia	13	53	0.27ns
No arrhythmia	10	24	
Hb A <sub>1</sub> C%	28	72	
Arrhythmia	11	22	0.11ns
No arrhythmia	17	15	

P value measured by Chi-square test; S= significant; ns = Not significant

There were significant correlation between control in FBG values and arrhythmia in the study subjects (p = <0.001).

However, control in  $HbA_1C$  and ABF values did not show any significance to incidence of arrhythmia (Table IV).

Table - V: 24 hours holter ECG monitoring findings of ventricular ectopy

Events	Number	Percentage
Single PVC's	41	41.00
Triplets	17	17.00
Couplets	12	12
Ventricular run	08	08.00
Late VE's	02	02.00
Bigeminy	11	11.00
Trigeminy	07	7.00
Mean ± SD total ventricular ectopic beats in 24 hours	7315.98±5289.33	
(Maximum-Minimum)	(18334-17)	

<sup>\*</sup>Multiple responses were elicited.

# 24 hours Holter ECG monitoring findings of ventricular ectopy (n=52)

Regarding ventricular ectopic, it was seen that 8% subjects had ventricular run, 41% had single PVC's. Beside these

findings, triplets (17%), couplets (12%), bigeminy (11%) and trigeminy (7%) were observed (Table V).

Table VI: 24 hours holter ECG monitoring findings of supraventricular ectopy

Events	Number	Percentage
Single PAC's	55	55.00
Atrial pairs	22	22.00
Drop	14	14.00
Late	09	09.00
Atrial run	25	25.00
Bigeminy	12	12.00
Trigeminy	10	10.00
Mean ± SD total supraventricular ectopic beats in 24 hours	6632.23 ±5484.73	
(Maximum -Minimum)	(19340-15)	

<sup>\*</sup>Multiple responses were elicited.

24 hours holter ECG monitoring findings of supraventricular ectopy (n=47)

In case of supraventricular ectopy, it was seen that 25% subjects had atrial run, 22% had single atrial pairs and 14%

had drop. Beside these findings, single PAC's (55%), late (09%), bigeminy (12%) and trigeminy (10%) were observed (Table VI).

Table VII: Relation of incidence of supraventricular ectopy with glycaemic control

2AB	level (m	nmol/l)	Mean ± SD total supraventricular ectopic beats in 24 hours (maximum-minimun)	P-value
Below 10	(n=23)		4876.60±5612.26 (14300-15)	- 0.01
10 and m	re (n=77)		8265.88±7011.76 (19340-40)	0.01

<sup>\*</sup>P-value was achieved by t-test.



Significant difference in mean supraventricular ectopic beats (in 24 hours) between subjects with controlled blood sugar and those with uncontrolled one (P-value was 0.01) (Table VII) was seen in the study.

#### DISCUSSION

Cardiac arrhythmia is a heterogeneous group of conditions in which there is abnormal electrical activity in the heart. The heartbeat may be too fast or too slow, and may be regular or irregular. Some arrhythmias are life-threatening medical emergencies that can result in cardiac arrest. In fact, cardiac arrythmias are one of the most common causes of death when travelling to a hospital. Symptoms of arrythmia include palpitation, dizziness, black out, presyncope, syncope. Still others may not be associated with any symptoms at all, but may predispose the patient to potentially life threatening stroke or embolism<sup>[14]</sup>.

Diabetes and cardiovascular disease often appear together. Diabetes mellitus has been said to be equivalent to coronary heart disease, while conversely many patients with established coronary heart disease suffer from diabetes or its pre-states. 20-30% of the patients with an acute coronary syndrome have diabetes and as many as 40% have impaired glucose tolerance. There is evidence that both in-hospital and long-term mortality rates after an acute myocardial infarction are twice as high for patients with diabetes as for those without[14]. Hyperglycaemia, insulin resistance and the consequent cellular shift to increased oxidative stress carry a high risk for the development of co morbidities and cardiovascular risk factors, mainly hypertension, lipid disorders, pro-inflammatory state, and activation of coagulation and thrombosis. As a consequence, the mortality and the incidence of all forms of cardiovascular disease are two- to eightfold higher in persons with diabetes, and coronary artery disease accounts for 75% of all deaths in such individuals[15]. This present cross-sectional study was carried out enrolling 100 subjects aged 18 years and above in the Department of Internal medicine, Cardiology and Neurology, BIRDEM General Hospital, Dhaka. The study subjects were enrolled in this study after fulfillment of the inclusion criteria who were collected from the patients in-patient department of the respective disciplines who were admitted for evaluation of arrhythmia.

The mean age of the study population was  $58.80\pm10.98$  years. No patients were found below the age of 40 years. Majority (31%) of the respondents were found in the age group of 60-69 years. About 30% subjects were found within 50-59 years, 18% in 40-49 years age groups and 21% within 70 years and above. Minimum age and maximum age of the patients were 40 years and 84 years respectively. The mean age of the subjects with arrhythmia was  $59.30\pm10.01$  years. Maximum number of patients with arrhythmia were found in the age group of 60-69 years.

It was observed that 63 (63%) were male and rests 37 (37%) were female. Male to female ratio was 1.7:1. Among male and female subjects, 71.4% males and 28.6% females had documented arrhythmia (p=0.01) (Figure II). These were common epidemiological background of diabetic arrhythmic

subjects. Vinik et al., found that 64% were male and 36% were female with mean age of  $64.4 \pm 7.6$  years in a similar previous study<sup>[16]</sup>. Nichols et al., reported mean age of the study subject was  $58.4 \pm 11.5$  years<sup>[17]</sup>.

Mean Fasting blood glucose (FBG) and Hb  $A_1$ C% level were 15.06±6.40 mmol/l and 10.13±2.59 respectively. There were significant correlation between control in FBG values and arrhythmia in the study subjects (p=<0.001).

On ECG recordings, atrial fibrillation was found in 16 subjects, atrial flutter in 1, atrial ectopics in 50, ventricular ectopics in 54, features of hypokalaemia in 11, features of hyperkalaemia in 3, sinus bradycardia in 14, atrioventricular block in 9, features of ischaemia in 13, and normal findings in 11subjects. Among the study subjects, 55% presented with palpitation, 34% had dizziness and 11% had history of syncope. Eightyeight percent of the patients with dizziness, 72.7% patients with palpitations and 47.4% of patients who presented with syncope had documented arrhythmias (p=0.01). Irfan et al., showed twenty percent of patients with dizziness had documented arrhythmias, 50% of patients with palpitations had documented arrhythmias and 12% of patients who presented with syncope had documented arrhythmias (p=0.07)[18]. Irfan et al., showed in 100 symptomatic patients who underwent 24-hour Holter monitoring, 82% had documented arrhythmias<sup>[18]</sup>. No specific symptom was more likely than any others to predict the occurrence of significant arrhythmia and no arrhythmia was closely associated with any specific symptom. Zeldis et al., showed that no specific complaint or combination of complaints was more likely to predict a disturbance in rhythm<sup>[19]</sup>. In their study, the overall incidence of arrhythmias was 53% and of major significant arrhythmias were 39%. Sarsin et al., conducted a study on 140 consecutive patients with unexplained syncope who underwent 24-hour Holter monitoring. Nine of the 140 patients had serious arrhythmia during Holter monitoring<sup>[20]</sup>. On Holter monitoring, arrhythmia was found in the form of atrial fibrillation in 14%, atrial flutter in 1%, ventricular ectopy in 52%, and supraventricular ectopy in 47%, ventricular tachycardia (VT) in 2%, supraventricular tachycardia (SVT) in 30% of which 3% had sustained SVT of 2-3 minutes duration, atrioventricular block (AV block) in 7%, sinus bradycardia in 11%. Irfan et al., noted arrhythmias on 24-hour Holter monitoring reports included atrial ectopy in 60%, ventricular ectopy in 54%, ventricular tachycardia in 7% and supraventricular tachycardia (SVT) in 38%, of which 2% had sustained SVT of 2-3 minutes duration[18]. Two percent had paroxysmal atrial fibrillation, 15% had sinus bradycardia, 6% had sinus arrest, 10% had sinus exit block and 5% had varying degrees of AV block. Some patients reported more than one arrhythmia. Nichols et al., revealed Diabetes was significantly correlated with atrial fibrillation<sup>[17]</sup>. Previous study by Binici et al., revealed that atrial fibrillation was seen in 7.22% study subjects which was comparable with the findings of the present study<sup>[21]</sup>.

It was seen statistically significant difference in mean ventricular ectopic beats (in 24 hours) between subjects with controlled blood sugar and those with uncontrolled one (P-value was 0.016).



Regarding supraventricular events, study by Binici et al., revealed that mean total supraventricular beats in 24 hours was 3929, PAC's was observed in 70% subjects and atrial run was observed in 42% patients<sup>[21]</sup>. Regarding ventricular events Adabaq et al., conducted a study where it was seen that mean total ventricular beats in 24 hours was 3256<sup>[22]</sup>. Single premature ventricular contractions were noted in 42% subjects. Statistically significant difference in mean supraventricular beats (in 24 hours) was observed between controlled diabetes and those with uncontrolled diabetes (P-value was 0.01).

#### Limitations of the study

The patient population observed was relatively small. The major limiting factor was the spontaneous frequency of symptom itself, which may not occur during that particular period. If the typical symptom occurs at some time during the study, with or without a concurrent electrocardiographic abnormality, the 24-hour study is still diagnostic and useful. However, this may be complicated by the fact that the same arrhythmia may occur at one time concurrently with symptoms and at other times, asymptomatically. Similarly, the presenting complaint may occur at multiple times during the 24-hour Holter monitoring period and in association with varying electrocardiographic findings. In every case, a cause and effect relationship needs to be established.

#### Conclusion

This cross-sectional study demonstrates that 24-hour Holter ECG monitoring is an effective tool for detecting arrhythmias in adults with Type 2 Diabetes Mellitus presenting with symptoms like palpitations, dizziness, and syncope. A significant correlation was found between poor glycemic control and the incidence of both ventricular and supraventricular ectopics. Potassium imbalance also contributed to arrhythmogenesis. Most symptomatic diabetic patients had documented arrhythmias, indicating that hyperglycemia and associated autonomic dysfunction may play a key role in arrhythmia development. Holter monitoring should be considered an essential part of cardiac evaluation in this high-risk group.

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#### **Conflicts of interest**

There are no conflicts of interest.

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