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Electrocardiographic T Wave Abnormality and Associated Factors among Type 2 Diabetic Patients: Multicenter Institution-Based Cross-Sectional Study

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Abstract

Introduction: The T wave on an Electrocardiogram (ECG) represents typically ventricular repolarization. However, various waveform morphologies may indicate benign or clinically significant injury or insult to the myocardium. There is no study about the electrocardiographic T wave abnormalities among type 2 DM patients in Ethiopia. Therefore, this study determined the overall prevalence and the associated factors of T wave abnormalities among people living with T2DM in Amhara National Regional State referral hospitals, Ethiopia.

Methods: A multicenter institution-based cross-sectional study was conducted from January 01st to March 30th, 2022. Simple random sampling and systematic sampling techniques were employed to select the referral hospitals and study participants, respectively. A digital electrocardiograph was used to measure the T wave patterns, and an interviewer-administered questionnaire to collect sociodemographic and some clinical factors. Epi-data version-4.6 and Stata-14 were used for data entry and statistical analysis, respectively. The descriptive statistics were presented with tables and graphs. A binary logistic regression model was fitted to identify associated factors of T wave abnormality. In the final model, statistical significance was decided at $p<0.05$, and the strength of association was indicated using an adjusted odds ratio with 95% CI.

Results: Two hundred and fifty-eight participants (response rate = 99.6%) were included in the analysis. The prevalence of overall T wave abnormality was 21.7% (95% CI: 19, 29.2%). Higher monthly income (>90$) (AOR=0.16 [0.06, 0.46]), hypertension 5.55 (AOR=5.55 [2.12, 14.49]), fasting blood sugar of ≥ 130 mg/dl 6.38 (AOR=6.38 [1.94, 20.94]), were statistically significant factors of T wave abnormality.

Conclusion: Higher income, hypertension, and higher fasting blood sugar were significantly associated with ECG abnormality. The findings of this study suggest the need to institute routine ECG screening for all T2DM patients to reduce silent myocardial ischemia and further complications.

Keywords: T wave abnormalities; Types 2 diabetes mellitus; Ethiopia; ECG

Abbreviations

BMI: Body Mass Index; CAD: Coronary Artery Disease; DM: Diabetes Mellitus; ECG: Electrocardiography; FBS: Fasting Blood Sugar; TWA: T Wave Abnormality

Introduction

Microvascular and macro-vascular complications are the most prevalent causes of mortality and morbidity among people living with DM [1-4]. In diabetic patients, Cardiovascular Disease (CVD) accounts for 24% to 30% of hospitalization and about one-third of deaths [5]. Coronary Artery Disease (CAD) reaches about 75% to 90% of deaths [6].

The T wave on an Electrocardiogram (ECG) represents typically ventricular repolarization. However, various waveform morphologies may indicate benign or clinically significant injury or insult to the myocardium [7]. T wave abnormalities are usually found on ECG and show abnormal ventricular repolarization [8]. The presence and magnitude of T wave abnormality are often associated with cardiovascular disease and mortality in diabetes [8]. Moreover, the abnormal T wave is a highly prevalent condition in Type 2 Diabetes Mellitus (T2DM) patients and is correlated with glycemic control. The risk of ventricular arrhythmias and sudden cardiac death is significantly increased in T2DM individuals [9].

Globally, the abnormal T wave is a very common condition (25%) among people with type 2 diabetes without the manifestation of CVD [10]. In a study in China, the prevalence of T wave abnormality was 26.9% [11], 20.9% in sub-Saharan African individuals [12], 22% in India [13], 21% and 25.4% in Italy [14], and 24.3% in African Americans [15], T wave abnormality is associated with older age, male sex, smoking cigarette, higher BMI, higher fasting glucose, hypertension, and longer duration of T2DM [16]. A study in Italy showed that T wave abnormality in T2DM is associated with age, DM duration, and high HA1c [10]. In China Hong Kong, smoking cigarettes, and hypertension were significantly associated with T wave abnormalities [11]. In the Netherlands, the prevalence of abnormal TWA was related to reduced ejection fraction but not to BMI, DM duration, glycemic control, and insulin use [17]. In Canada, age and sex were associated with T wave abnormality [18].

Common measures that have been done to reduce cardiovascular complications were resting ECG examination every 3-5 years for the duration of diabetes >15 years, >40 years old, end-organ damage, and more than one cardiovascular disease risk factor [19].

In Ethiopia, the prevalence of overall ECG abnormality was conducted among apparently healthy adult T2DM patients [20]. Nonetheless, this study didn't address specific T wave abnormalities in T2DM. Therefore, the current study aimed to assess the prevalence and associated factors of T Wave Abnormality (TWA) among people living with T2DM in selected referral hospitals in the Amhara Region.

Materials and Methods

Study setting, design, and period

The Gondar specialized referral hospital, Debre Birhan referral hospital, and Debre Markos referral hospital were the three referral hospitals in the Amhara region where this study was carried out between January 01st, and March 30th, 2022. In Amhara Region, seven referral hospitals provide comprehensive diabetic follow-up care. From these, three hospitals were selected to conduct this study. First, Debre Markos referral hospital has provided comprehensive diabetic care services to an estimated catchment population size of more than 3.5 million. The diabetic follow-up clinic in Debre Markos Referral Hospital provides service from Monday to Friday for a total of more than 3,840 type 2 DM patients currently attending follow-up at this Hospital. Second, Debre Birhan referral hospital is situated in North Shewa, which is 130 km away from Addis Ababa, and 516 km away from Bahir Dar. It provides diabetic care follow-up every day from Monday to Friday for a total of 1,634 T2DM patients. Lastly, Gondar specialized referral hospitals found in North Gondar situated 658 km away from Addis Ababa and provides comprehensive diabetic care services to an estimated catchment population size of 6 million. It, also, offers diabetic care follow-up every day from Monday to Friday for a total of 5,312 T2DM patients.

Population and eligibility criteria

All T2DM patients who received follow-up care at the referral hospitals in the Amhara National Regional State comprised the source population. All T2DM patients who visited the chosen referral hospitals in the Amhara National Regional State for a follow-up visit during the study period comprised the study population. The study included all T2DM patients who had received a diagnosis, were at least 18 years old, and who visited for follow-up care during the study period. Patients with T2DM who had a known thyroid condition or symptoms suggestive of one, were on beta-blockers, pregnant, or were critically unwell at the time of data collection, however, were not included.

Sample size determination and sampling technique

With the assumption of a 95% Confidence Interval (CI) and a 5% margin of error (d=0.05), the required sample size was calculated using the single population proportion calculation utilizing an estimated prevalence of 20% (p=0.2) of T wave anomaly from a study done in Senegal [21]. The total sample size was 259 after considering a non-response rate of 5%. In this study, three out of seven referral hospitals in the Amhara Region were chosen using a straightforward random sample procedure. Then, based on the number of T2DM patients at each chosen institution, a proportional allocation of samples was used. In the chosen referral hospitals, there were 1,502 study participants. After determining the Kth interval for each study participant (1502) to each chosen hospital by using the formula: K=N/n: (640/110, 550/94, and 312/55=6), a systematic sampling strategy was then utilized to recruit each study participant from the chosen referral hospitals. Then, using a lottery system, the beginning point was 2, chosen at random from 1 to 6. Every sixth interval, a follow-up individual was chosen to be the next participant.

Operational/Conceptual definitions

The electrocardiographic change was identified deviation of ECG pattern from normal sinus ECG pattern based on Minnesota ECG coding criteria [22].

T wave abnormality was identified when T-wave is inverted, peaked, or flattened [22]. Regular physical exercise is defined as an adult doing moderate physical exercise 2 h to 5 h per week [23].

Higher income is defined as a person earning above 90 US dollars per month according to Ethiopian income distribution [24].

Data collection instruments and procedures

After three days of training, one professional nurse and one supervisor (Nurse) used the World Health Organization's

(WHO) step-by-step standard questionnaire, which includes sociodemographic variables, anthropometric measurement, and clinical aspects, to gather the data. Additionally, ECG parameters were measured using a digital electrocardiograph (CONTEC ECG1200G), blood pressure with a blood pressure monitor, weight with a weighing scale, and height with a height scale. Electrocardiographic T wave abnormalities-related questionnaires were adopted from previously published articles on ECG abnormalities among T2DM [15,21,25]. The ECG measurement was taken by a one-trained person in ECG recording, and interpretation of T wave abnormality was done by a cardiologist.

Measurement variables

Electrocardiographic measurement: The CONTEC ECG1200G, a Chinese-made standard resting 12-lead digital electrocardiographic machine, was utilized in the investigation. Its calibrated paper speed was 25 mm/s, with each large box standing in for 0.2 s and each tiny box for 0.04 s, respectively. The patient was instructed to expose the chest area and remove any electromagnetic objects from his or her body before the measurement was carried out in a supine position with a 45-degree incline. Additionally, instructions were given for the patients to quit talking, moving, and breathe more lightly while the ECG was being recorded. After the transparent gel was applied, ten electrodes (four limb electrodes at the right arm, left arm, and legs, and six chest electrodes, V1-V6) were placed on the participant's arms, legs, and chest, resulting in a total of 12 leads [22]. Finally, the Minnesota coding system was used to identify ECG tracings as having T wave abnormality [26].

Anthropometric measurement: Using a body scale, the weight (kg) was measured while wearing only minimal closes, to the nearest 0.1 kg. By utilizing a metric stadiometer and the individuals standing straight without shoes or headgear, height (m) was measured to the nearest 0.1 cm. The formula used to determine the Body Mass Index (BMI) is BMI = wt/(ht)2 (W: Weight in kg, H: Height in meters) [27].

Blood pressure measurement: After five minutes of rest, a standard sphygmomanometer blood pressure instrument was used to take the patient's blood pressure while they were sitting comfortably with their left arm parallel to their heart. The average of the two successive blood pressure readings, taken at intervals of no less than five minutes, was calculated.

Data quality control

The questionnaire underwent pre-testing at Burie General Hospital in Northwest Ethiopia to ensure data quality. Data collectors received three days of instruction on the purpose of the study, the procedures of data collection, and how to gather information from those chosen participants. The principal investigator and supervisor also evaluated and verified the data during the data collection period to ensure its accuracy.

Variables

Dependent variable: T wave abnormality (binary; dichotomized as Yes or No).

Independent variables: Age, sex, marital status, residence, educational status, occupation, income, history of heart disease, history of kidney disease, body mass index, fasting blood sugar, blood pressure, duration of diabetes, physical activity, cigarette smoking, khat chewing, type of drug for DM.

Data processing and analysis

The collected information was verified as accurate before being entered into Epi-data version 4.6 and exported into Stata-14 for analysis. Following a check for normal distribution, descriptive statistics such as mean, standard deviation (for continuous variables), and frequency with percentages were applied to categorical variables depending on the nature of the data. Binary logistic regression was used to ascertain the relationship between independent variables and T wave anomalies. Model fitness was examined using the Hosmer-Lemeshow test ($p>0.05$). The first step was to do a bivariable analysis of each of the chosen indicators for the dataset. Then, to find variables that had a statistically significant association with TWA ($p=0.05$), any variable with a P-value of $p<0.2$ was added to multivariable regression analysis. Crude Odds Ratio (COR) and Adjusted Odds Ratio (AOR) computations with a 95% Confidence Interval (CI) were used to assess the strength of the association.

Result

Sociodemographic characteristics

In this study, a total of 258 (males=133) T2DM patients participated, making a 99.6% response rate. The mean age of the respondents was 56.7(+12.7, range = 28-80) years. The mean monthly income was $112.9 (+$65.6) (Table 1), and the mean duration of DM was 6.6 (+5.24) years, ranging from 6 months to 25 years (Table 2). Moreover, the mean fasting blood sugar was 154.4+50.6 mg/dl. The mean Body Mass Index (BM) was 25.8+4 kg/m^2 and, one hundred and nine (42.3%) of the respondents were hypertensive. BMI of 25 kg/m^2 and above, duration of DM above 10 years, and hypertension were associated with T wave abnormality in Chi-square analysis.

The distribution of T wave abnormalities in type 2 diabetes mellitus

The overall prevalence of T-wave abnormalities among people living with T2DM was 21.7% (95% CI: 19, 29.2%). The most commonly encountered T wave abnormality was inverted T wave 38 (14.7%).

Associated factors of T-wave abnormality in T2DM

T wave abnormality was associated with age, educational status, occupation, income, body mass index, duration of DM, hypertension, and, fasting blood sugar in the bi-variable analyses at a 5% level of significance. In this regression model, factors with $p<0.2$ were entered into multivariable binary logistic regression. Therefore, from socio-demographic factors, income was statistically significant with T wave abnormality. The odds of developing T wave abnormality with a one-unit increase in income were reduced by 30%. The odds of T wave abnormality in fasting blood sugar of ≥ 130 mg/dl was 6.38 times (AOR=6.38, 95% CI; 1.94, 20.94) higher than those who had a fasting blood sugar of <130 mg/dl. Those who had hypertension were 5.5 times (AOR=5.5, 95% CI; 2.12-14.5) more likely to acquire T wave abnormality compared to their counterparts (Table 3).

Discussion

This study determined the prevalence of T wave abnormality and its associated factors. From this, the most commonly encountered T wave abnormality was the inverted T wave. The overall prevalence of T-wave abnormalities among people living with T2DM was 21.7% (95% CI: 19, 29.2%) which is consistent with studies in China at 26.9% [11], India at 22% [13]), Italy at 21%, and 25.4% [14], Sub-Saharan 20.9% [12], and 24.3% in African Americans [15]. The

Table 1: Sociodemographic characteristics of T2DM patients grouped by T wave abnormalities using Chi-square among selected Referral Hospitals in Amhara National Regional State, Ethiopia, 2022 (n=258).

Variables	Categories	Total (%)	T wave abnormality		X^2 p-value
			Yes (%)	No (%)	
Sex	Male	133 (51.60)	28 (10.9)	105 (40.7)	p=0.793
	Female	125 (48.40)	28 (10.9)	97 (37.5)	
Age (years)	<45	69 (26.80)	2 (0.8)	67 (26)	P<0.001
	46-54	46 (17.80)	8 (3.1)	38 (14.7)	
	55-64	66 (25.60)	20 (7.7)	46 (17.8)	
	>65	77 (29.80)	26 (10.1)	51 (19.8)	
Residence	Urban	195 (75.58)	37 (14.4)	155 (60.1)	P=0.061
	Rural	63 (24.42)	19 (7.4)	44 (17.1)	
Income (USD)	<$57.34	97 (37.6)	41 (15.9)	56 (21.7)	P<0.001
	$57.34-$103.2	32 (12.4)	4 (1.6)	28 (10.9)	
	>$103.2	129 (50)	11 (4.3)	118 (45.7)	
Current marital status	Married	188 (72.87)	35 (13.6)	153 (59.3)	P=0.049
	Unmarried	70 (27.13)	21 (8.1)	49 (19.0)	
Educational status	No formal education	94 (36.43)	29 (11.2)	65 (25.2)	P=0.025
	1^0 and 2^{nd}ry education	15 (5.81)	3 (1.2)	12 (4.7)	
	College and above	149 (57.76)	24 (9.3)	125 (48.4)	
Occupation	Employed	122 (47.29)	21 (8.2)	101 (39.1)	P=0.097
	Unemployed	136 (52.71)	35 (13.6)	101 (39.1)	
Regular exercise	Yes	42 (16.28)	3 (1.2)	39 (15.1)	p<0.05
	No	216 (83.72)	53 (20.5)	163 (63.2)	

USD: United States Dollar

Table 2: Clinical profile of T2DM patients grouped by T wave abnormality using chi-square among selected Referral Hospitals in Amhara National Regional State, Ethiopia, 2022 (n=258).

Variables	Categories	Total (%)	T wave abnormality		X^2 (p-value)
			Yes (%)	No (%)	
Duration of DM (years)	<2	73 (28.2)	7 (2.7)	66 (25.6)	p<0.01
	2-5	64 (24.8)	9 (3.5)	55 (21.3)	
	6-10	64 (24.8)	17 (6.6)	47 (18.2)	
	>10	57 (22.0)	23 (8.9)	34 (13.2)	
FBS	<130 mg/dl	98 (37.98)	4 (5.4)	94 (32.6)	p<0.001
	>130 mg/dl	160 (62.02)	52 (39.5)	108 (22.5)	
Hypertension	Yes	109 (42.25)	45 (17.4)	64 (24.8)	p<0.001
	No	149 (57.75)	11 (4.3)	138 (53.5)	
BMI (kg/m^2)	<25	133 (51.55)	17 (6.6)	116 (45.0)	p<0.001
	25 and above	125 (48.45)	39 (15.1)	86 (33.3)	

BMI: Body Mass Index; FBS: Fasting Blood Sugar; DM: Diabetes Mellitus

physiological condition of oxidative stress brought on by poor glycemic management, obesity, dyslipidemia, insulin resistance, hypertension, and inactivity may be the cause of this prevalence of T wave abnormalities. Then, as a result of elevated Advanced Glycation End products (AGE) and impaired protein kinase C signaling, oxidative stress results in vasoconstriction, arterial inflammation, thrombosis, and atherogenesis, which results in aberrant ventricular repolarization [28-30].

Finally, factors associated with TWA in T2DM patients were identified. Income, hypertension, and fasting blood sugar were factors significantly associated with T wave abnormality. A one $ increase in income reduces T wave abnormality by 30%. Though no previous study was conducted to show this association, the reason for this relationship might be due to increasing self-glucose monitoring practice by easily accessing the glucose monitoring materials, whereas those with low income may not have access to do so. The other reason might be due to increasing health care service receiving practice and the ability to have diet modifications [31].

The odd of T wave abnormality among T2DM with hypertensive patients was 5.6 times higher than T2DM patients with no hypertension. This was consistent with the studies done in China [11], the Netherlands [17], and Senegal [21]. This could be a result

Table 3: Sociodemographic and clinical covariates in bivariable and multivariable binary logistic regression analysis among T2DM in selected Referral Hospitals in Amhara Region, Ethiopia, 2021 (n=258).

Variables	T-wave abnormality		COR (95% CI)	AOR (95% CI)
	Yes (%)	No (%)		
Age in years	63.6 ± 9.8	51 ± 12.2	1.10 (1.07, 1.12)	1.01 (0.96, 1.05)
Educational status				
No formal education	29 (61.7)	65 (38.3)	1	1
1^0 and 2^{nd}ry education	3 (53.3)	12 (46.7)	0.56 (0.15, 2.13)	1.94 (0.36, 10.48)
College and above	24 (33.6)	125 (66.4)	0.43 (0.23, 0.80)	1.05 (0.28, 4.02)
Monthly income in USD				
<50$	41 (71.1)	56 (28.9)	1	1
50-90$	4 (53.1)	28 (46.9)	0.12 (0.06, 0.60)	0 .13 (0.04, 0.49) *
>90$	11 (23.3)	118 (76.7)	0.13 (0.06, 0.27)	0.16 [0.06, 0.46]) *
Occupation				
Employed	21 (17.2)	101 (82.8)	1	1
Unemployed	35 (25.7)	101 (74.3)	1.70 (0.91-3.06)	0.31 (0.08, 1.22)
Regular exercise				
Yes	3 (7.1)	39 (92.9)	1	1
No	53 (24.5)	163 (75.5)	4.22 (1.26,14.23)	1.58 (0.35, 7.2)
Duration of DM in (years)				
<2	7 (9.6)	66 (90.4)	1	1
2-5	9 (14.1)	55 (85.9)	1.54 (0.54, 4.41)	1.22 (0.32, 4.65)
6-10	17 (26.6)	47 (73.4)	3.41 (1.31,8.87)	0.77 (0.19, 3.09)
>10	23 (40.4)	34 (59.6)	6.40 (2.49, 16.36)	1.04 (0.24, 4.58)
Body mass index kg/m²				
<25	27 (18.9)	116 (81.1)	1	1
25 and above	39 (31.2)	86 (68.8)	3.1 (1.64, 5.83)	0.86 (0.34, 2.15)
FBS				
<130 mg/dl	4 (4.1)	94 (95.9)	1	1
>130 mg/dl	52 (32.5)	108 (67.5)	11.31 (3.94, 32.46)	6.38 (1.94, 20.94) *
HTN				
Yes	45 (41.3)	64 (58.7)	8.82 (4.28, 18.17)	5.55 (2.12, 14.49) ***
No	11 (7.4)	138 (92.6)	1	1

*: p<0.05; **: p<0.01: ***p=0.001, HTN: Hypertension; FBS: Fasting Blood Sugar; 1: Constant, Hosmer Lemeshow Goodness of fit p=0.31

of hypertension reducing blood flow to the heart tissue and causing silent myocardial ischemia [32,33]. On the other hand, it does not line up with the Italian study [14], Netherland [17], and India [13]. This might be due to the effective prevention and treatment of hypertension in this country.

Compared to those with <130 mg/dl of fasting blood sugar, T2DM patients who had ≥ 130 mg/dl were 6.6 times more likely to develop T wave abnormalities. This study was supported by other studies in Italy [14], and Canada [18]. This might be because insulin does not control the transport of glucose across cell membranes, and excessive glucose concentrations harm cells with high intracellular glucose and glucose metabolites levels. These compounds cause the production of reactive free radicals and the deposition of advanced glycation end products by activating auxiliary metabolic pathways such as the sorbitol and protein kinase C pathways [34-36]. However, a study showed in Netherland, that fasting blood sugar was not significantly associated with T wave abnormality [17]. This difference might be due to adherence to diabetic medication, and self-glucose monitoring practice awareness creation for the patients [37].

Strength and Limitations of the Study

This study's key contribution to understanding the burden of T wave abnormalities and related parameters in multi-center settings helped to make it more robust and representative. However, the following restrictions should be considered when interpreting the study's results. It is challenging to demonstrate a cause-and-effect link because the study was a cross-sectional survey. Furthermore, the study did not evaluate how lipid levels affected T wave abnormalities.

Conclusion

Nearly, one-fifth of the study participants had electrocardiographic T wave abnormalities. The most common T -wave abnormality was the inverted T wave. Income, fasting blood sugar, and hypertension were factors that have a statistically significant association with T wave abnormalities. The health sector should institute a routine ECG screening for all T2DM patients to reduce silent myocardial infarction

and further complications.

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