Electrocardiogram abnormalities and renal impairment in patients with type 2 diabetes mellitus: a healthcare facilities-based cross-sectional study in Dang district of Nepal

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Electrocardiogram abnormalities and renal impairment in patients with type 2 diabetes mellitus: A healthcare facilities-based cross-sectional study in Dang district of Nepal

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Keywords
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ABSTRACT

Aims/Introduction: The global burden of diabetes mellitus is rising substantially, with a further increase in cardiovascular and kidney disease burden. These public health problems are highly prevalent in low- and middle-income countries, including Nepal. However, there is limited evidence on cardiac and renal conditions among patients with type 2 diabetes mellitus. We determined the status of electrocardiogram (ECG) abnormalities and renal impairment among patients with type 2 diabetes mellitus in Nepal.

Methods: We carried out a cross-sectional study in Tulsipur Sub-Metropolitan City of Nepal using a multistage stratified sampling technique to recruit patients with type 2 diabetes mellitus. We used World Health Organization stepwise approach to surveillance (WHO STEPS) questionnaires and carried out resting ECG to collect data of 345 patients with type 2 diabetes mellitus. Logistic regression analysis assessed the factors associated with ECG abnormalities and renal impairment.

Results: The study showed that 6.1% of participants had major ECG abnormalities (95% confidence interval [CI] 3.8–8.6%), which were associated with hypertension (P = 0.01%) and low socioeconomic status (P = 0.01). The proportion of major and/or minor ECG abnormalities was 47.8% (95% CI 40.5–51%), and were significantly associated with age (odds ratio [OR] 1.04, 95% CI 1.01–1.07), higher education (OR 3.50, 95% CI 1.31–9.33), unemployment (OR 3.02, 95% CI 1.08–8.48), body mass index (OR 1.09, 95% CI 1.02–1.17) and duration of type 2 diabetes mellitus >5 years (OR 2.42, 95% CI 1.19–4.93). The proportion of renal impairment was 3.5% (95% CI 1.5–4.5%) which was associated with older age (OR 1.08, 95% CI 1.00–1.17) and hypertension (OR 12.12, 95% CI 1.07–138.22).

Conclusion: A significant proportion of patients with type 2 diabetes mellitus had ECG abnormalities and renal impairment, which were significantly associated with hypertension. Therefore, hypertension management and early screening are essential to prevent future cardiorenal complications among patients with type 2 diabetes mellitus.

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INTRODUCTION

Diabetes mellitus is a major global public health problem. Approximately half a billion people live with diabetes mellitus worldwide[1]. The burden of diabetes is higher in low- and middle-income countries than in high-income countries. In 2016, there was the highest prevalence of diabetes in poorer nations (12.3%), and the lowest prevalence in wealthier nations (6.6%)[2]. In 2021, the overall prevalence of diabetes in 55 low- and middle-income countries was 9%[3]. It is expected that the number of patients with diabetes will rise by one-quarter in 2030 and by more than half by 2045[1].

The rising prevalence of diabetes mellitus contributes to a parallel increase in cardiovascular diseases (CVD) and chronic kidney disease (CKD) morbidity and mortality. Nearly one-third (32.2%) of patients with type 2 diabetes mellitus have CVD, and 10% of the deaths of patients with type 2 diabetes mellitus are attributed to CVD[4]. Coronary artery disease (CAD), the most prevalent cardiac complication of diabetes, was reported in 8.2% of patients with diabetes from 38 countries[5]. An electrocardiogram (ECG) can predict CAD, other heart conditions and cardiovascular morbidity[6]. Evidence shows that asymptomatic individuals with ECG abnormalities have a higher chance of future cardiovascular events[7]. Similarly, diabetic kidney disease develops in approximately 40% of patients with type 2 diabetes mellitus[8]. There is a 10-fold increase in end-stage renal disease among people with diabetes. According to data from 54 nations, almost 80% of patients with end-stage renal disease had diabetes and hypertension[9]. The presence of heart disease and chronic kidney disease further complicates the management of diabetes mellitus and increases disability and mortality[10].

In Nepal, the prevalence of diabetes mellitus ranges from 6.3% to 16%[11–14], with a pooled prevalence of 8.5% in 2020[15]. Similarly, the CAD burden is increasing in Nepal. CAD prevalence was 5% in 2003[16], and increased to 5.7% in 2009[17]. In 2017, CAD contributed to 16.4% of total deaths and 7.5% of total Disability Adjusted Life Years[18]. Likewise, Nepal has witnessed rising numbers of CKD. A community-based study in 2013 reported a 10.6% prevalence of CKD[19]. This prevalence is even more among specific risk groups, as suggested by a meta-analysis, which determined that 27.6% had CKD. Out of CKD patients included in the meta-analysis, 23% had diabetes mellitus[20]. However, we have scarce information on ECG abnormalities and chronic kidney diseases among patients with type 2 diabetes mellitus. Therefore, we determined the status of ECG abnormalities and renal impairment among patients with type 2 diabetes mellitus visiting primary healthcare facilities in the sub-metropolitan settings of Nepal.

METHODS

Study design and study settings

This was a cross-sectional study carried out as a part of a mixed-method design in primary-health facilities of Tulsipur Sub-Metropolitan City in the Dang district of Nepal[21]. This city has a population of 1,41,528[22] and a range of primary healthcare facilities. There are eight health posts, 11 urban health centers, two community health units, six hospitals, two Ayurvedic hospitals, and 23 polyclinics[22].

Inclusion and exclusion criteria

For the quantitative part of our original study, we included patients with type 2 diabetes mellitus diagnosed (verified from previous medical records) at least 1 month before the data collection, who visited the outpatient department of the study centers. However, we did not include pregnant women and mentally ill patients.

Sample size and sampling

We estimated the sample size based on the expected prevalence of significant ECG abnormalities (13%) among patients with type 2 diabetes mellitus from the Netherlands[23]. Based on a 5% level of significance and a 5% margin of error, the sample size required for estimating proportion in one sample situation was 173. This sample was inflated to 306 to adjust the design effect (1.5) for cluster design, and a 15% non-response rate. A multistage cluster sampling technique was used to include representative samples from all healthcare centers of Tulsipur Sub-Metropolitan City. Using a computer-generated random selection technique, we randomly selected primary health centers. Every third patient from the outpatient department of the selected healthcare facilities was included in the study between December 2021 and February 2022.

Data collection

We trained local health professionals and medical students on the consent form, and data collection tools and techniques. A written form was used to obtain informed consent from the participants. To collect information related to sociodemographic, behavioral and anthropometric data, we used World Health Organization stepwise approach to surveillance (WHO STEPS) questionnaires. This tool was validated and has been applied in Nepal[13]. In the present study, we pre-tested this tool among 15 patients before implementation. A biochemical test was carried out using a semi-automated machine in the Provincial Ayurveda Hospital in Dang, Nepal, in the early morning after 12 h of fasting for fasting blood sugar, fasting lipid profile and creatinine. A blood sample for postprandial blood sugar was withdrawn 2 h after patients had their usual meal. Creatinine was measured by the Jaffe method. Creatinine was used to estimate the glomerular filtration rate[24]. This Provincial Ayurveda Hospital was chosen as it is located equidistant from all health facilities. We carried out a resting 12-lead ECG in a supine position for ECG measurement. We carried out a standard ECG of every patient after 30 min of rest for approximately 10 s. ECG paper was set at a standard format at 10 mm/mV amplitude and 25 mm/s speed with standard lead positions. The machine recorded and printed the ECG, providing automatic Minnesota coding. The printed ECG was stored

and independently read by a medical officer, a consultant physician and a cardiologist. Disparities in any report were resolved by consensus. We followed standard definitions (Appendix S1) and a manual for the Minnesota ECG criteria.[25]

Study variables

Sociodemographic, behavioral and anthropometric variables

The level of education was categorized as illiterate, primary (grade 1–5), secondary (grade 6–10) and more than secondary (>10 grade). We re-categorized caste into Brahman, Kshetri, Janajati (Chaudhary, Magar, Gurung and other indigenous castes) and Dalit. The occupation was stratified as employed, self-employed, household work and unemployed (student, non-paid worker or retired). For economic status, we defined the poor if a participant had a household income of 19,262 Rupee ($158) per person per year[26]. We defined a smoker if a patient who was smoking at least 1 month before the data collection. We defined an alcohol user if a participant consumed alcoholic beverages within the past month. For fruit and vegetable intake, we considered as sufficient if a patient consumed at least five servings of fruit and vegetables per day (400 g). We defined a low level of physical activity (physical inactivity) as <600 metabolic equivalents of task minutes per week of physical activity[27]. For body mass index (BMI), we classified participants as underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2) or obese (>30 kg/m^2)[28].

Blood pressure and biochemical measurements

Two blood pressure readings were obtained in the sitting position from the left arm using an aneroid sphygmomanometer to the nearest 2 mmHg, first after at least 15 min rest and the second 3 min after the first reading. We took the average of two readings for the final analysis. Hypertension was defined as average systolic blood pressure ≥140 mmHg and/or an average diastolic blood pressure ≥90 mmHg and/or self-reported use of antihypertensive medication in the past 2 weeks[29]. Poor glycemic control was defined as fasting blood sugar >130 mg/dL and/or postprandial blood sugar ≥180 mg/dL[30]. Dyslipidemia was defined as having either one of the following: high total cholesterol (200 mg/dL), high triglyceride (150 mg/dL), high low-density lipoprotein (130 mg/dL), low high-density lipoprotein (40 mg/dL in men and 50 mg/dL in women) and/or use of antilipidemic drugs[31]. Low-density lipoprotein was calculated using the Friedewald formula[32]. The estimated glomerular filtration rate (eGFR), expressed in mL/min/1.73 m^2, was calculated using the Chronic Kidney Disease Epidemiological Collaboration formula specified for sex, race and serum creatinine[33]. We defined renal impairment if eGFR was <60 mL/min/1.73 m^2[33].

ECG abnormalities

A range of conditions, including congenital, metabolic, arrhythmia, coronary, rheumatic and hypertensive diseases, can cause changes in ECG[34]. We considered pathological Q wave, ST-segment changes and T wave inversion as major ECG abnormalities, which might suggest CAD. Similarly, bradycardia, tachycardia, irregular rhythm, prolonged PR interval, left ventricular hypertrophy, axis deviation, right or left bundle branch block, arrhythmia, and prolonged QTc were minor ECG abnormalities (Appendix S1).

Statistical analysis

Paper-based data were entered in EpiData version 3.1 (EpiData Association, Odense, Denmark) and exported to SPSS V.20.0 (IBM Corp., Armonk, NY, USA) for analysis. Sociodemographic and clinical characteristics are presented as descriptive statistics. Continuous variables are presented as the mean and standard deviation. Similarly, categorical variables are reported in percentages. We used the χ^2-test or Fisher's exact test to compare categorical variables, and independent *t*-tests to compare continuous variables, respectively. The Mann–Whitney *U*-test was carried out for non-normally distributed continuous variables. Using logistic regression models, we estimated the crude and adjusted odds ratio (adjusted for sociodemographic and clinical variables). For logistic regression, we recoded both major and minor ECG abnormalities and low eGFR as yes (1) and normal as (0). We entered sociodemographic (sex, age, level of education, occupation, occupation), behavioral (smoking, alcohol intake, fruit and vegetable intake, physical activities in metabolic equivalents of task minutes per week), anthropometric (BMI, hypertension), biochemical (fasting blood sugar, dyslipidemia) and clinical (duration of type 2 diabetes mellitus, treatment of diabetes mellitus, family history of diabetes mellitus) variables in the logistic regression model. We used a two-tail test. We considered $P < 0.05$ to be statistically significant.

Ethical consideration

The research proposal was reviewed and approved by the Ethical Review Board of the Nepal Health Research Council (reference number 1430). During data collection, our data collectors read the consent form in Nepali, describing the study objectives, procedures of data collection, risks and benefits of the study, and the confidentiality of their personal information. All participants signed or provided a thumb impression (if unable to write) on the consent form, before participation.

RESULTS

Out of 366 participants, 11 did not have a blood sample collection and ECG measurements. An additional 10 patients refused to have an ECG done. Therefore, only 345 data were available for final analysis. No patients with type 2 diabetes mellitus reported a previous history of heart and kidney diseases.

Sociodemographic characteristics of participants

Overall, 57.4% were men. The mean age was 54.3 ±10.8 years. The majority of participants had either primary or secondary education and were married. More than three-quarters of patients were from Brahman and Kshetri castes. In total, nearly half of the participants were homemakers. One-quarter of the

participants belonged to a class below the poverty line. The median duration of type 2 diabetes mellitus was 3 years (interquartile range 5 years). Approximately one-third of patients (35.7%) had a family history of diabetes (Table 1).

Clinical characteristics and cardiovascular risk factors of participants

A total of 43% of participants were taking only a single antidiabetic medication. The majority were taking metformin as an oral hypoglycemic drug. Of the total, 17.7% were smoking cigarettes, with a significantly higher proportion of men (16.5% vs 1.2%, $P < 0.001$). Similarly, alcohol consumption was 14.2%, with a significantly higher percentage in men (13.3%) compared with women (0.9%, $P < 0.001$). Almost all (98%) were not eating adequate fruit and vegetable servings. Approximately one-tenth (9.9%) were physically inactive. The proportion of overweight and obese people was 47%, with significantly different proportions among the sexes ($P = 0.01$). A total of 60% were hypertensive, and 65.2% had poor glycemic control. Overall, 67.2% had dyslipidemia, with a significantly higher proportion among men than women (42.6% vs 24.6%, $P = 0.001$; Table 2).

ECG abnormalities of patients with type 2 diabetes mellitus

The proportion of major ECG abnormalities was 6.1% (95% confidence interval [CI] 3.5–8.6%). Similarly, 45.8% (95% CI 40.5–51.0%) had minor ECG abnormalities. When both major and minor abnormalities were combined, 47.8% had at least one ECG change (95% CI 42.5–5%). When data were stratified by sex, the proportion of both major and minor ECG abnormalities was higher among men (29.9%) compared with women (18%), despite being statistically non-significant (Table 3). Both major and total ECG abnormalities were the lowest among the patients with type 2 diabetes mellitus with higher education (0.6% and 9%), although statistically non-significant. There were significantly different proportions of ECG abnormalities among patients with various occupations, with household workers having the highest prevalence (26.1%).

Table 1 | Sociodemographic characteristics of study participants

Variables	Total, *n* (%) (*n* = 345)	Sex		*P*-value
		Male, *n* (%), *n* = 198	Female, *n* (%), *n* = 147	
Age (years)				
Mean (SD)	54.3 (10.8)	56.0 (10.8)	52.0 (10.5)	**0.001**‡
Level of education				
Illiterate	82 (23.8)	24 (7.0)	58 (16.8)	**<0.001**§
Primary	104 (30.1)	48 (13.9)	56 (16.2)	
Secondary	108 (31.3)	84 (24.3)	24 (7.0)	
Higher	51 (14.8)	42 (12.2)	9 (2.6)	
Ethnicity				
Brahman	102 (29.6)	61 (17.7)	41 (12.0)	0.56§
Kshetri	173 (50.1)	102 (29.6)	71 (20.6)	
Janajati	39 (11.3)	19 (5.5)	20 (5.8)	
Dalit	31 (9.0)	16 (4.6)	15 (4.3)	
Marital status				
Married	16 (4.6)	8 (2.3)	8 (2.3)	0.54§
Unmarried	329 (95.4)	190 (55.1)	139 (40.3)	
Occupation				
Employed	45 (13.0)	32 (9.3)	13 (3.8)	**<0.001** §
Self-employed	100 (29.0)	71 (20.6)	29 (8.4)	
Household-work	157 (45.5)	59 (17.1)	98 (28.4)	
Unemployed	43 (12.5)	36 (10.4)	7 (2.0)	
Economic status				
Below poverty line†	72 (20.9)	45 (13.0)	27 (7.8)	0.32†
Above poverty line	273 (79.1)	153 (44.3)	120 (34.8)	
Duration of type 2 diabetes mellitus				
Median (interquartile range)	3 (5.0)	3 (6.0)	3(4.0)	0.25¶
Family history of diabetes				
Yes, *n* (%)	123 (35.7)	73 (21.2)	50 (14.5)	0.58§
No, *n* (%)	222 (64.3)	125 (36.2)	97 (28.1)	

Bold indicates statistical significant value ($p < 0.05$). † Household income per person per year <19,262 Rupee ($158). ‡ Independent *t*-test. § χ^2-test. ¶ Mann–Whitney *U*-test. SD, standard deviation.

Table 2 | Clinical characteristics and cardiovascular risk factors of study participants

Variables		Total n = 345	Sex		P-value
			Male, n (%), n = 198	Female, n (%), n = 147	
Antidiabetic medication					
No	n (%)	101 (29.0)	54 (15.7)	47 (13.6)	0.596‡
Single drug	n (%)	149 (43.2)	86 (24.9)	63 (18.3)	
Two drugs	n (%)	77 (22.3)	48 (13.9)	29 (8.4)	
≥3 drugs	n (%)	18 (5.2)	10 (2.9)	8 (2.3)	
Insulin	n (%)	7 (2.0)	5 (1.4)	2 (0.6)	0.448‡
Current smoker	n (%)	61 (17.7)	57 (16.5)	4 (1.2)	**<0.001**‡
Alcohol users	n (%)	49 (14.2)	46 (13.3)	3 (0.9)	**<0.001**‡
FV (servings/day)	Mean (SD)	2.1 (1.05)	2.1 (0.9)	2.1 (1.1)	0.448†
Inadequate FV intake	n (%)	338 (98)	195 (56.5)	143 (41.4)	0.432‡
MET (min/week)	Mean (SD)	5,898.6 (4348.3)	6,151.9 (4322.3)	5,557.4 (4374.6)	0.21†
Low level of physical activity	n (%)	34 (9.9)	15 (4.3)	19 (5.5)	0.099‡
BMI† (kg/m^2)	Mean (SD)	24.9 (3.6)	24.4 (3.6)	25.6 (3.7)	**0.002**†
Overweight and obesity	n (%)	162 (47.0)	82 (23.8)	80 (23.2)	**0.017**‡
SBP (mmHg)	Mean (SD)	130.7 (17.0)	131.9 (16.7)	129 (17.3)	0.124†
DBP (mmHg)	Mean (SD)	85.2 (10.8)	85.7 (11.2)	84.5 (10.3)	0.291†
Hypertension	n (%)	207 (60.0)	120 (34.8)	87 (25.2)	0.79†
FBS (mg/dL)	Mean (SD)	135.6 (61.7)	134.8 (66.2)	136.7 (55.3)	0.77†
PPBS (mg/dL)	Mean (SD)	217.9 (83.5)	216.1 (87.8)	220.4 (77.6)	0.64†
Poor glycemic control	n (%)	225 (65.2)	125 (36.2)	100 (29.0)	0.34†
TC (mg/dL)	Mean (SD)	151.9 (39.4)	149.8 (39.2)	154.7 (39.7)	0.25†
TG (mg/dL)	Mean (SD)	171.3 (102.9)	170.1 (97.0)	172.9 (110.7)	0.80†
HDL (mg/dL)	Mean (SD)	43.9 (7.4)	41.1 (6.4)	47.7 (7.1)	**<0.001**†
LDL (mg/dL)	Mean (SD)	73.6 (35.3)	74.6 (35.3)	72.4 (35.5)	0.56†
Dyslipidemia	n (%)	232 (67.2)	147 (42.6)	85 (24.6)	**0.001**‡

Bold indicates statistical significant value ($p < 0.05$). † Independent t-test. ‡ χ^2-test. BMI, body mass index; DBP, diastolic blood pressure; FBS, fasting blood sugar; FV, servings of fruit and/or vegetable; HDL, high-density lipoprotein; LDL, low-density lipoprotein; METs, metabolic equivalents of task; PPBS, post-prandial blood sugar; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

Table 3 | Prevalence of electrocardiogram abnormalities and renal impairment among study participants stratified by sex (n = 345)

Variables	Total, n (%)	Sex		P-value
		Male, n (%)	Female, n (%)	
Major ECG abnormality				
Yes	21 (6.1)	11 (3.2)	10 (2.9)	0.63
No	324 (93.9)	187 (54.2)	137 (39.7)	
Minor ECG abnormality				
Yes	158 (45.8)	99 (28.7)	59 (17.1)	0.06
No	187 (54.2)	99 (28.7)	88 (25.5)	
ECG abnormality (major and/or minor)				
Yes	165 (47.8)	103 (29.9)	62 (18.0)	0.07
No	180 (52.2)	95 (27.5)	85 (24.5)	
Renal impairment				
Yes	12 (3.5)	9 (2.6)	3 (0.9)	0.2
No	333 (96.5)	159 (55.4)	144 (41.7)	

ECG, electrocardiogram.

Major ECG abnormalities were significantly higher among participants above the poverty line (3.5% vs 2.6%, P = 0.01). Patients with type 2 diabetes mellitus and hypertension had a significantly higher proportion of major ECG abnormalities (5.2%) than patients without hypertension (0.9%, P = 0.01). The prevalence of all ECG abnormalities was highest among participants aged between 46 and 65 years (34%, P = 0.007). Similarly, ECG abnormalities were significantly different among different occupations (P = 0.01), with a higher proportion among household workers (19.4%) compared with those who were employed (4.3%). Participants above the poverty line had higher rates of ECG abnormalities (35.7%, P = 0.04; Table 4). On multivariate analysis, after adjusting for all other variables, age, level of education, occupation, BMI and duration of type 2 diabetes mellitus were significantly associated with ECG abnormalities (Table 5).

Renal impairment of patients with type 2 diabetes mellitus

The proportion of renal impairment among patients with type 2 diabetes mellitus was 3.5% (95% CI 1.5–4.5%). The proportion of renal impairment was higher among men (2.6%) compared with women (0.9%; P = 0.20; Table 3). The proportion of renal impairment was highest (2%) among middle-aged (46–65 years) patients with type 2 diabetes mellitus (P = 0.01). Although non-significant, renal impairment was lower among

Table 4 | Distribution of electrocardiogram abnormality and renal impairment among study participants

Variables	Major ECG abnormality			ECG abnormality (both)			Renal impairment		
	Yes (%)	No (%)	*P*-value	Yes (%)	No (%)	*P*-value	Yes (%)	No (%)	*P*-value
Age (years)									
26–45	0.3	20.9	0.16†	8.1	13	**0.007**	0	21.2	**0.01**†
46–65	4.6	58.8		29.6	33.9		2	61.4	
>65	1.2	14.2		10.1	5.2		1.4	13.9	
Level of education									
Illiterate	1.4	22.3	0.81†	10.7	13	0.21	0.9	22.9	0.97†
Primary	2.3	27.8		14.5	15.7		1.2	29	
Secondary	1.7	29.6		13.6	17.7		0.9	30.4	
Higher	0.6	14.2		9	5.7		0.6	14.2	
Occupation									
Employed	0	13	0.3†	4.3	8.7	**0.01**	0.3	12.8	0.68†
Self-employed	2.3	26.7		16.8	12.2		1.4	27.5	
Household-work	2.9	42.6		19.4	26.1		1.2	44.3	
Unemployed	0.9	11.6		7.2	5.2		0.6	11.9	
Low economic status									
Yes (poor)	2.6	18.3	**0.01**†	12.2	8.7	**0.04**	0.9	20	0.72†
No	3.5	75.7		35.7	43.5		2.6	76.5	
Smoking									
Yes	0.6	17.1	0.31†	8.4	9.3	0.96	0.9	16.8	0.49†
No	5.5	76.8		39.4	42.9		2.6	79.7	
Alcohol use									
Yes	0.3	13.9	0.20†	6.4	7.8	0.65	0.6	13.6	0.8†
No	5.8	80		41.4	44.3		2.9	82.9	
Fruit and vegetable intake									
Inadequate	5.8	92.2	0.35†	46.4	51.6	0.2	3.5	94.5	0.61†
Adequate	0.3	1.7		1.4	0.6		0	2	
Physical activity									
Active	0.6	9.3	0.95†	4.3	5.5	0.64	0.6	9.3	0.42†
Inactive	5.5	84.6		43.5	46.7		2.9	87.2	
Overweight and obesity									
Yes	2.3	44.6	0.4	23.5	23.5	0.44	0.6	46.4	**0.03**†
No	3.8	49.3		24.3	28.7		2.9	50.1	
Hypertension									
Yes	5.2	54.8	**0.01**	31	29	0.07	3.2	56.8	**0.02**†
	0.9	39.1		16.8	23.2		0.3	39.7	
Poor glycemic control									
Yes	4.3	60.9	0.53	33	32.2	0.14	2.3	62.9	0.91†
No	1.7	33		14.8	20		1.2	33.6	
Dyslipidemia									
Yes	3.8	63.5	0.59	32.8	34.5	0.63	2.3	64.9	0.96†
No	2.3	30.4		15.1	17.7		1.2	31.6	

Bold indicates statistical significant value ($p < 0.05$). † Fisher's exact test. ECG, electrocardiogram.

those patients with higher education, who were employed and had lower economic status. Patients with hypertension had a higher prevalence of renal impairment than those without hypertension (3.2% vs 0.3%, $P = 0.02$). However, patients with type 2 diabetes mellitus and overweight or obesity had a lower rate of renal impairment (0.6% vs 2.9%, $P = 0.03$; Table 4). In multivariate analysis, after adjusting for all other variables, age was significantly associated with renal impairment, with an odds ratio of 1.08 (95% CI 1.00–1.17). Similarly, the odds of having renal impairment among patients with type 2 diabetes mellitus were 12-fold higher if they also had hypertension (95% CI 1.07–138.22; Table 5).

DISCUSSION

Overall, the current study showed that 3.5% of those patients with type 2 diabetes mellitus had renal impairment, and one out of 16 patients with type 2 diabetes mellitus had major ECG abnormalities. Almost half of the patients with type 2 diabetes

Table 5 | Factors associated with electrocardiogram abnormality and renal impairment among study participants

Variables	ECG abnormalities		Renal impairment	
	COR (95% CI)	AOR (95% CI)	COR (95% CI)	AOR (95% CI)
Sex				
Male	Reference	Reference	Reference	Reference
Female	1.48 (0.96–2.28)	0.86 (0.45–1.65)	2.28 (0.60–8.59)	0.73 (0.12–4.41)
Age (years)	1.04 (1.02–1.06)*	1.04 (1.01–1.07)*	1.09 (1.03–1.15)*	1.08 (1.00–1.17)*
Level of education				
Illiterate	Reference	Reference	Reference	Reference
Primary	1.12 (0.63–2.01)	1.14 (0.59–2.19)	1.05 (0.22–4.84)	1.08 (0.18–6.18)
Secondary	0.93 (0.52–1.67)	0.98 (0.47–2.02)	0.75 (1.14–3.82)	0.58 (0.07–4.71)
Higher	1.88 (0.92–3.83)	3.50 (1.31–9.33)*	1.07 (0.17–6.66)	2.25 (0.18–27.11)
Occupation				
Employed	Reference	Reference	Reference	Reference
Self-employed	2.76 (1.32–5.76)*	3.70 (1.52–9.02)*	2.31 (0.26–20.41)	1.41 (0.11–17.04)
Household-work	1.48 (0.74–2.98)	2.09 (0.87–5.01)	1.15 (0.12–10.55)	0.92 (0.07–12.22)
Unemployed	2.77 (1.16–6.60)*	3.02 (1.08–8.48)*	2.14 (0.18–24.57)	0.57 (0.02–11.40)
Economic status				
Not poor	Reference	Reference	Reference	Reference
Poor	1.70 (1.00–2.88)*	1.69 (0.91–3.11)	1.27 (0.33–4.83)	0.77 (0.15–3.74)
Smoking				
No	Reference	Reference	Reference	Reference
Yes	0.98 (0.56–1.71)	0.92 (0.47–9.82)	1.58 (0.41–6.01)	2.48 (0.46–13.39)
Alcohol use				
No	Reference	Reference	Reference	Reference
Yes	0.87 (0.47–1.60)	1.06 (0.50–2.24)	1.21 (0.25–5.72)	2.02 (0.28–14.54)
FV intake (servings/day)	1.09 (0.89–1.34)	1.07 (0.85–1.35)	1.00 (0.58–1.73)	0.96 (0.48–1.91)
MET/min/week	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)
BMI (kg/m^2)	1.04 (0.99–1.11)	1.09 (1.02–1.17)*	0.86 (0.72–1.02)	0.86 (0.69–1.06)
Hypertension				
No	Reference	Reference	Reference	Reference
Yes	1.47 (0.95–2.27)	1.16 (0.69–1.94)	7.68 (0.98–60.24)	12.12 (1.07–138.22)*
FBS	1.00 (0.99–1.00)	1.00 (0.99–1.00)	1.00 (0.99–1.00)	0.99 (0.98–1.00)
Dyslipidemia				
No	Reference	Reference	Reference	Reference
Yes	1.11 (0.71–1.74)	1.00 (0.59–1.69)	0.97 (0.28–3.30)	0.75 (0.17–3.24)
Duration of type 2 diabetes mellitus				
<1 year	Reference	Reference	Reference	Reference
1–5 years	2.06 (1.22–3.46)*	2.32 (1.25–4.31)*	2.39 (0.47–12.08)	3.75 (0.51–27.53)
>5 years	2.55 (1.45–4.49)*	2.42 (1.19–4.93)*	2.25 (0.40–12.59)	1.93 (0.21–17.27)
Treatment of type 2 diabetes mellitus				
No	Reference	Reference	Reference	Reference
Yes	1.51 (0.94–2.41)	1.02 (0.57–1.84)	1.21 (0.35–4.13)	0.51 (0.10–2.56)
Family history of DM				
No	Reference	Reference	Reference	Reference
Yes	1.51 (0.97–2.35)	1.48 (0.88–2.49)	1.30 (0.40–4.19)	1.75 (0.41–7.38)

*Significant at level of <0.05. AOR, adjusted odds ratio; BMI, body mass index; COR, crude odds ratio; DM, diabetes mellitus; electrocardiogram; FBS, fasting blood sugar; FV, fruit and vegetable intake; MET, metabolic equivalents of tasks.

mellitus had major and/or minor ECG abnormalities. In this way, the current study determined the prevalence of cardiac disease and renal disease using ECG and eGFR.

The proportion of major ECG abnormalities was 6.1%, which is comparable with other studies. In Nepal, among patients with diabetes in the tertiary care center, 4.4% had major cardiac complications diagnosed by ECG[35]. The proportion of the major ECG abnormalities in the present study is comparable with a prevalence of 5.1% in a population-based study in Nepal[17]. However, the current study's findings were slightly lower than a similar study in the Netherlands, which reported that 9% of patients with diabetes had major ECG

abnormalities[23]. The present findings were lower than an African American Heart Study, which reported that 23% of patients with type 2 diabetes mellitus had major ECG abnormalities[36]. The differences between studies could be explained by different study sites, patient enrolment, sample size and inclusion criteria of major ECG abnormalities.

The current study determined that almost 48% had both major and/or minor ECG abnormalities, which is higher than those reported in studies from India (26%)[37], Spain (24.9%)[38] and the Netherlands (29.1%)[23]. However, the current proportion of major and minor ECG abnormalities is lower in other studies from Ethiopia (61%)[39] and among African Americans in the USA (60%)[36]. The different prevalence rates could be due to the study population, study sites and sample size of various studies. Current findings showed that men with type 2 diabetes mellitus had a higher proportion of ECG abnormalities than women. This result is opposite to the previous studies, which found that women with diabetes have a higher risk of having coronary heart disease than men[40,41].

As the present findings were not statistically significant and the number of male participants was higher than female participants, we are not confident about the current findings. Therefore, another study is required to corroborate findings in semi-urban settings. Similarly, the current study found that patients with higher education had a lower proportion of ECG abnormalities. This finding corroborates the result of a study among CAD patients inferring that patients with graduate education had a lower risk of all-cause mortality[42,43]. The current study determined ECG abnormalities were significantly higher among patients above the poverty line and who were only busy with household chores. Previous studies also found that socioeconomic status was inversely related to cardiovascular outcomes[44,45]. Therefore, future policies should include plans to reduce these socioeconomic disparities in cardiovascular outcomes.

The major ECG abnormalities were associated with hypertension in the current study. A similar study in Nepal also investigated the association between hypertension and coronary artery disease[17]. Previous studies suggest that untreated diabetes mellitus and hypertension accelerate coronary artery disease[46]. In the present study, the higher the age, the greater the risk of ECG abnormalities. Our results showed that the proportion of ECG abnormalities was highest among the age group of 46–64 years. Age is an independent predictor of cardiovascular risk factors and diseases[47]. In the current study, we observed that the unemployed and self-employed had higher odds of ECG abnormalities. Many studies suggested that diet, physical activities and other behavioral factors might differ with occupations[48]. The present study also showed that a higher BMI was associated with a higher prevalence of ECG abnormalities. Obesity contributes to dyslipidemia, hypertension and diabetes, which cause CVD development[49]. However, contrary to the previous studies[50,51], the current data showed no significant association between smoking and ECG abnormalities. This might be due to a small sample size, all participants might not have revealed the habit of smoking or may have short duration of smoking. Future studies in similar settings are required to corroborate the findings.

The proportion of renal impairment in the present study was 3.5%. This was not dissimilar to a previous study carried out among patients with type 2 diabetes mellitus in 38 countries, which reported a 5% prevalence of chronic kidney disease[5], and a study in India reported a prevalence of 4.2% of low eGFR among the general population[52]. The current study reports a lower prevalence rate than previous studies from Nepal, which reported a prevalence of 6–7% among patients with diabetes mellitus[35,53,54]. Similarly, the current proportion of renal impairment was far less than in other studies carried out in various countries. For instance, a meta-analysis of Ethiopia reported that 14.5% of patients with diabetes had stage 3–5 kidney disease[55]. Similarly, almost 40% of patients with diabetes in Thailand had low eGFR[56]. The latter studies were carried out on hospitalized patients, explaining the higher prevalence rates. Our current study determined that women had a higher proportion of renal impairment than men. These findings are in line with other studies[57,58]. Our study found that renal impairment was lower in patients with higher education and lower economic status, in line with a meta-analysis of 43 articles[59]. Additionally, in the current study, renal impairment was significantly associated with hypertension, as in previous studies[60]. However, the current findings show that renal impairment was higher among non-obese patients compared with obese patients, which is opposite to the earlier studies[61,62]. This finding needs to be explored in future studies.

One critical finding of the current study is that both renal impairment and major ECG abnormalities are significantly associated with hypertension with higher odds. This finding corresponds to a meta-analysis that shows the higher impact of hypertension on renal impairment[60]. Similarly, another recent cohort study found that raised blood pressure is associated with rapid kidney function decline over 30 years of follow up compared with normotensive individuals[63]. This suggests that we must target hypertension to prevent future cardiorenal complications among patients with type 2 diabetes mellitus. Similar to the present findings, one systematic review determined an association between hypertension and long-term cardiovascular events[64]. This result is also supported by another study that showed that controlling blood pressure can have a positive impact on CVD[65]. Therefore, in rural and semi-urban areas with poor resource settings, it is essential to target hypertension to prevent cardiac and renal complications.

The current study showed that the prevalence of hypertension, dyslipidemia and poor glycemic control was >50%, much higher than major ECG abnormalities and renal impairment. In addition, smoking, inadequate amount of fruit and vegetable intake, and physical inactivity were prevalent among diabetes patients in the current study. Therefore, it is also essential to

scale up the health system to minimize behavioral risk factors, deliver treatment to lower blood glucose, manage hypertension and dyslipidemia[3,66,67]. According to a study in 55 low- and middle-income countries, fewer than one out of 10 patients with diabetes mellitus received comprehensive treatment according to guidelines[3]. Critical barriers to effective chronic disease management are insufficient population awareness of disease risk factors, understanding of the disease and its complications; limited access to health services and medication; financial constraints these patients face; and inadequate policies and chronic disease guidelines[67–69]. Therefore, Nepal must strengthen policies and programs to increase awareness, availability, affordability, and accessibility of essential medicines and diagnostics for patients with diabetes, CVD and CKD[66].

There were a few limitations of current study. First, resting ECG is not enough to detect silent ischemia, and there was no possibility of carrying out an exercise ECG. In addition, because of the small sample size and lower proportion of individual outcomes, we could not assess the factors associated with different ECG abnormalities and severity of renal impairment. Third, we could not assess urine albumin/creatinine ratio and microalbuminuria, which could have underestimated the prevalence of nephropathy in the current study population. Additionally, the glycated hemoglobin test could not be carried out in a suburban area. Finally, the present study was carried out in one submetropolitan city of Nepal; therefore, we must be cautious in generalizing the current study's findings to other populations.

A significant proportion of the patients with type 2 diabetes mellitus visiting primary healthcare facilities in Nepal had ECG abnormalities and renal impairment. Hypertension was significantly associated with major ECG abnormalities and renal impairment. Therefore, hypertension management, and early screening by ECG and renal function tests are essential to prevent future cardiorenal complications among patients with type 2 diabetes mellitus. Other evidence-based policies, and locally adaptable guidelines and programs need to be implemented through the primary healthcare facilities to reduce future morbidity and mortality from cardiorenal complications among patients with type 2 diabetes mellitus in Nepal.

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DISCLOSURE

The authors declare no conflict of interest.

Approval of the research protocol: Reviewed and approved by the Ethical Review Board of the Nepal Health Research Council (reference number 1430).
Informed consent: Data enumerators used an informed consent form to describe the study. All participants signed or provided thumb impression on the consent form.
Registry and the registration no. of the study/trial: N/A.
Animal studies: N/A.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusion of this article will be made available by the authors, with undue reservation.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1 Definitions of ECG abnormalities.