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Research article

VALUE OF ELECTROCARDIOGRAM IN PREDIALYTIC CHRONIC KIDNEY DISEASE PATIENT WITHOUT KNOWN CORONARY ARTERY DISEASE

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ABSTRACT

Chronic Kidney disease (CKD) is a pressing public health burden occurring in about 10% of the population. The majority of them die before reaching End Stage Renal Disease (ESRD) due to cardiovascular disease (CVD). Hypertension (HTN) and anaemia are two reversible factors for progression of CKD. Besides asymptomatic coronary artery disease, the electrolyte abnormalities such as hyperkalaemia and hypocalcaemia also subject these patients to sudden cardiac death. This study is aimed at to see the changes in electrocardiogram (ECG) in hospitalized predialytic CKD patients due to these abnormalities. **Methods:** This is a 6 months cross-sectional study carried out at Chittagong Medical College Hospital in Chittagong, Bangladesh. 50 patients with stages 3, 4 and 5 CKD were recruited from the Nephrology and Medicine wards. Patients with prior history of coronary artery disease, cardiomyopathy, valvular heart disease and dialysis were excluded. All had their standard 12–lead electrocardiogram (ECG) recorded and various findings were critically studied and interpreted independently by two consultant physicians including a cardiologist. **Data analysis** was done using SPSS version 19. **Results:** LVH (left ventricular hypertrophy) (66%), LAE (left atrial enlargement) (30%) and unrecognized myocardial infarction (28%) were very common ECG abnormalities in our predialytic CKD patients. HTN, anaemia, late presentation, and male gender appear to be associated with ECG abnormalities. Though 28 patients (56%) were hyperkalaemic only 9 patients (38%) of them had tall tented T wave in ECG. **Conclusion:** Detection of HTN and anaemia in male predialytic CKD patients will arouse suspicion which will help in early detection of cardiac outcome by ECG abnormality which will help in taking treatment strategy in resource limited country.

Keywords: Chronic Kidney Disease, Electrocardiogram, Cardiovascular disease. Left Ventricular Hypertrophy,

INTRODUCTION

The numbers of patients affected by chronic kidney disease (CKD) are increasing globally[1].The progressive nature of chronic kidney failure and the ensuing end-stage renal disease (ESRD) necessitating renal replacement therapy (RRT) is imposing a substantial burden on global healthcare resources. Only developed countries have sufficient wealth to meet the cost of renal replacement therapy RRT. If pathophysiology of CKD is well understood, it helps in early detection and prevention and so less costly therapy to prevent progression [2]. CKD has an increased risk of not only ESRD, but majority of moderate CKD patients die from CVD before reaching ESRD [3-5]. CKD patients are at high risk of

CVD, which account for 40-50% of the deaths in this population[6,7]. HTN, dyslipidaemia and diabetes (DM) are major risk factors for the development of endothelial dysfunction and progression of atherosclerosis. Elevated Inflammatory mediators and renin-angiotensin system in CKD will also lead to increased prevalence of coronary artery disease, heart failure, stroke and peripheral arterial disease. Prevention and treatment of CVD are a major consideration in the management of individuals with CKD[8]. The cardiovascular risk attributable to CKD is not restricted to those requiring renal replacement therapy, but is evident even in predialytic CKD [9]. Even non diabetic CKD is associated with increased risk of cardiovascular (CV) morbidity and mortality [10,11]. Sudden cardiac death constitutes 62% of the CV mortality in ESRD probably due to CVD resulting from myocardial structural changes, electrolyte imbalance, and autonomic dysfunction[12].The factors contributory to cardiac abnormalities include anaemia, HTN, volume overload, ischaemic heart disease, uraemic cardiomyopathy, electrolyte imbalance, hyperlipidaemia, and arteriovenous fistula[13-15]. Near about 18 million people have CKD in Bangladesh[16]. The occurrence of electrocardiographic (ECG) changes in uraemic patients has been recognized for decade. Electrocardiography is readily available and an inexpensive tool to assess the burden of cardiovascular disease. An association of resting electrocardiographic markers with clinical cardiovascular events could promote 12 lead ECG as a clinical tool for cardiovascular risk stratification in the CKD setting for which reliable markers of subclinical cardiovascular disease are otherwise lacking especially in resource poor nation like Bangladesh. In most of Asian patients, prognosis of patients with advanced CKD is very poor because of late referral and inability to pay for treatment. It is thought that majority of these patients would have died from cardiovascular events in the earlier stages of CKD without access to any health facility. Resting electrocardiographic abnormalities are common in CKD, even in nondialytic patients and independently predict future clinical CV events in this setting [7, 17].

Electrocardiographic abnormalities like Q-T interval prolongation which often occur with left ventricular hypertrophy (LVH) may predispose renal failure patients to various forms of arrhythmias and sudden death [18-20]. An Italian survey has shown that ECG abnormalities (Rhythm abnormalities, intraventricular conduction defects, ventricular repolarization alterations, and left axis deviation) are independently associated with the presence of CKD [21]. Knowledge about CVD in CKD will help in early mortality risk prediction as well as reduction of repeated hospitalization. This study aimed to determine prevalence and pattern of electrocardiographic abnormalities among predialytic CKD patients and its association with anaemia, HTN and electrolyte abnormality in Chittagong Medical College Hospital, a tertiary hospital in southern part of Bangladesh.

MATERIALS AND METHODS

It is a cross sectional observational study carried out in Nephrology and Medicine, Department of CMCH, Chittagong through October 2012 to March 2013**.** The study was approved by Chittagong Medical College ethical review committee. Fifty consecutive predialytic CKD patients irrespective of age were enrolled. Patients on dialysis; with valvular heart disease, cardiomyopathy prior to diagnosis of Chronic Kidney Disease and with known coronary artery disease were excluded. Stages of CKD were defined by Cockcroft-Gault equation[3]. Previous coronary artery disease is defined as history of acute coronary syndrome- STEMI/ NSTEMI/ UNSTABLE ANGINA (as per patients' self documented past medical record); or a history of revascularization (CABG/STENTING). Socioeconomic status (SES) was measured using a scale of Rahman M et al. supported by ICDDRB, after partial modification[22]. LVH was defined as Sokolow-Lyon Criteria **(**S wave in lead V_1 + R wave in lead V_5 or V_6> 3.50 mV or R wave in lead avL 1.1 mV[23]**.** LAE was taken as the Prolonged P wave duration > 120 msec in lead II [23].The Q-T interval is the interval from the beginning of the QRS complex to the end of the T wave. Values more than 0.44 second was considered as prolonged[23]. Corrected QT interval, or Q-Tc, defined as Q-Tc = QT/√R-R. Unrecognized myocardial infarction was defined as the presence of diagnostic Q-wave abnormalities without self-reported. The T waves were normal in more than 50% of patients with hypocalcemia, but decreased T-wave voltage and even negative to deeply negative T waves have been reported. Tall, widened and characteristically shaped tall peaked T wave, widening of QRS complex,

bizarre intraventricular conduction disturbance, progressive diminution and eventual disappearance of P wave were taken as hyperkalaemia. Serum Potassium more than 5.5mmol/l was considered as Hyperkalaemia[24]. Serum calcium less than 2.1 mmol/l or 8.5 mg/dl (after correction with serum albumin) was considered as hypocalcaemia. Haemoglobin level less than 13.5 g/dL (135 g/L) for men and less than 12.0 g/dl (120 g/L) for women (KDOQI 2006**)** was considered as anaemia[6.] Hypertension was defined as systolic BP more than 140 mm of Hg, diastolic BP more than 90 mm of Hg or requiring antihypertensive[6] From all eligible subjects after getting written consent, clinical history was taken and clinical examination was done to elicit findings related to renal diseases and its complication. Related investigations like RBS, S. creatinine, Hb%, Serum K^+, Serum Ca^+, Serum albumin were also done. Urine was collected as a fresh morning sample in a sterile container and 10cc venous blood was collected. All investigations were done in Clinical Pathology and Nephrology departments of CMCH. Resting electrocardiography was done. After explaining the procedure to the subjects to allay anxiety, the upper clothing, and all accessory dressings (watches, necklaces, and rings) were removed. The ECG leads were placed accordingly, in line with the recommendation of the American Heart Association guidelines. The calibrations were 1 mV=10 mm (10 small squares) on the vertical line and ECG speed of 25 and 50 mm/s were used. Lead II was used as the rhythm strip. The ECGs were analysed quantitatively to obtain heart rate, rhythm, QRS axis, P wave, QRS morphology, PR interval. QT intervals in each of the leads were measured. At least three consecutive cycles were measured for each lead and then averaged. All relevant data were noted in the pre tested data sheet. Quantitative data were expressed as mean and standard deviation and qualitative data were expressed as frequency distribution and percentage. **Statistical analysis:** Statistical analysis was performed by using SPSS (Statistical Package for Social Sciences) for windows version 19.0. 95% confidence limit was taken. Probability value <0.05 was considered as level of significance.

RESULTS

More than two-thirds of patients were male and only one –fifth were hard workers. Mean age of the patients was 37.24 years. Two-thirds patients came from lower middle class family. Most of the patients were in Stage 5 of CKD [table 1]. Eighty percent of patients had HTN and HTN prevalence in stage 5 is statistically significant than stage 3. The overall prevalence of unrecognized MI in this study was 28% (14 among 50 patients) and distributed in stage 3 to stage 5 CKD patients but not significant [table 2]. 33 patients out of 50 (66%) had anaemia, demonstrated that the prevalence of anaemia in the different stages of CKD was considerably elevated. The prevalence also increased as CKD progressed (fig1).

Among 33 (66%) anaemic patients, 10 patients had unrecognized MI, whereas among 17 (34%) patients without anaemia, 4 patients had unrecognized MI. So it was not significant [table 3].

The overall prevalence of ECG evidence of LVH was 33 (66%) and was found in all three stages of CKD (stage 3 to 5) which is statistically not significant. Among 50 patients, 15 (30%) patients had LAE which was distributed in all three stages (3 to 5) of CKD but more LAE were present in stage 5 CKD patients, i.e. 9 patients (30%). However, this distribution was not statistically significant. There were 11 (22%) patients with prolonged Q-T_C and distributed in stage 3 to stage 5 CKD patients. This distribution was also not significant [table 4].

Among 33 anaemic patients, 28 patients had ECG evidence of LVH. This distribution was significant [table4].

Hyperkalaemia was found in all three stages of CKD, overall prevalence 56% (28 patient out of 50), most of them 18 (36%) in stage 5. It was not significant. There were 14 (28%) patients with biochemical evidence of hypocalcemia and distributed in all three stages of CKD patient, its association with different stages of CKD is not significant (table 5)

28 patients had hyperkalaemia and 22 patients had no hyperkalaemia. Among 28 hyperkalaemic patients 25 patients had serum potassium in the range of 5.5-6.5 and 8 of these patients had tall peaked T wave. On the other hand 3 patients had serum potassium level >6.5 mmol/l, only 1 patient had tall peaked T wave. Among 22 patients with serum potassium < 5.5 mmol/l, only 1 patient had tall peaked T wave (table 7).

Table 1: Baseline characteristics of subjects (n=50)

Characteristics	Frequency	Percent
Sex		
Male	35	70
Female	15	30
Socioeconomic Status*		
Lower class	10	20
Lower middle class	33	66
Upper Middle Class	5	10
Upper Class	2	4
Characteristics		
Stages of CKD		
Stage 3	7	14
Stage 4	13	26
Stage 5	30	60

*Ref: 22

Table 2. Cardiovascular events (n=50)

Characteristics	Frequency	Percent
HTN		
Stage 3	2	5
Stage 4	8	20
Stage 5	30	75*
Unrecognized MI		
Stage 3	2	14.3
Stage 4	4	28.6
Stage 5	8	57.1†
Characteristics		
Stages of CKD		
Stage 3	7	14
Stage 4	13	26
Stage 5	30	60

*p value = .001; †p value = .962 (compared to sum of stages 2&3)

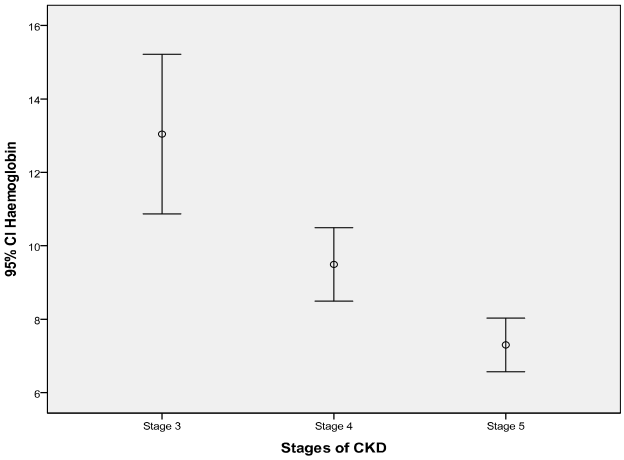

Fig 1: Relation of anaemia (Hb gm/dl) with stages of CKD; as CKD stages progress hemoglobin levels also declining. (p=0.001)

Table 3: Association of anaemia with, un recognized MI:

Anaemia	Unrecognized MI*		Total
	Present†	Absent†	
Present	10(30.3)	23(69.7)	33
Absent	4(23.5)	13(76.5)	17
Total	14(28)	36 (72)	50

*Chi square value = .255, DF= 1, p= 0.613; †parenthesis shows percentage

Table4. Association of LVH, LAE and prolonged Q-Tc with CKD

CKD stage	LVH		LAE		Prolonged Q-Tc	
	Present / Total pts	% within stage	Present /total pts	% within stage	Present /total pts	% within stage
3	5/7	71.4	2/7	28.5	1/7	14.3
4	8/13	61.5	4/13	30.7	5/13	38.5
5	20/30	66.7*	9/30	30 †	5/30	16.7‡

*p = 0.899; †P = 0.995; ‡p=0.247

Table 5: Association of anaemia with ECG evidence of LVH

Anaemia	ECG evidence of LVH*		
	Present	**Absent**	**Total**
Present	28	5	33
Absent	5	12	17
Total	33	17	50

*Chi square value = 15.366, DF= 1, p= 0.00

Table 6. Association of Hyperkalaemia and Hypocalcaemia with different stages of CLKD

CKD stage	Hyperkalaemia		Hypocalcaemia	
	Present / total pts	%within stage	Present/ total pts	%within Stage
3	4/7	57.1	1/7	14.3
4	6/13	46.2	4/13	30.8
5	18/30	60 *	9/30	30†

* Chi square value =.710, DF=2, P= 0.701; † Chi square value = 2.762, DF= 2, p= 0.683

Table 7: Association of tall peaked T wave with serum potassium level

		Hyperkalaemia(n=50)			
		Yes(n=28)		No(n=22)	
		Tall tented T		Tall tented T	
		Present (n=9)	Absent (n=19)	Present (n=1)	Absent (n=21)
		Count	Count	Count	Count
Serum K^+ level (mmol/l)	<5.5	0	0	1(4.5%)	21(95.5%)
	5.5 - 6.5	8(28.5%)	17(60.7%)	0	0
	>6.5	1(3.5%)	2(7.1%)	0	0

DISCUSSION

In this hospital-based study, predialytic CKD patients were evaluated for ECG changes who had no history of coronary artery disease, cardiomyopathy and valvular heart disease.

In the present study male to female ratio was 2.3. The mean age of all patients was 37.24 years like other studies in Nigeria and other parts of Bangladesh but unlike developed countries[25,26,27]. Most of the patients were sedentary and moderate workers (40% each) and belonged to the lower middle class families (66%) [22]. Patients admitting the Government medical college hospital are mostly from lower middle class. Most of the patients (60%) were at stage 5 as classified by Cockcroft and Gault formula. This was due to the fact that in our country patient did not get admitted till they are severely symptomatic.

The leading electrocardiographic abnormalities among our CKD patients were LVH (66%), LAE (30%), unrecognized myocardial infarction (28%), prolonged Q-Tc (22%) and tall peaked T wave (20%). The prevalence of LVH in this study was below the study by Nwankwo et al and higher than that by Chijioke et al possibly due to higher prevalence of HTN and predialytic patients [17,19]. There is gender variation (male preponderance) in proportion of LVH in CKD patients due to differences in body size[28, 29]. It is also true in our study. The very high prevalence of LVH among our patients appears to be related to late presentation and poor control of blood pressure. Costa et al. found sensitivities above 50% for all the electrocardiographic LVH criteria in a study[30]. Paoletti et al stated that left ventricular hypertrophy was the strongest predictor of fatal arrhythmias in ESRD patients [31]. Furthermore, regression of electrocardiographic LVH is associated with reduction in adverse cardiovascular outcomes[32]. Therefore, the ECG-LVH remains of value for the diagnosis and follow-up of target organ damage among patients with CKD.

Like Kajmi et al in our study, 66% of patients had anaemia, which gradually increased with progression of CKD [33]. In this study, we also tried to correlate ECG evidence of LVH with the presence of anaemia; the prevalence of ECG evidence of LVH between those with and without anaemia was statistically significant. Different studies have shown an association between anaemia and hospitalization, quality of life and mortality in CKD patients, with the mortality risk increasing as the haemoglobin level falls below 10gm/dl, [34]

In our study total 40 (80%) patients had hypertension and among them 30 (60%) patients with stage 5. Here we tried to correlate presence of HTN with stages of CKD; it was significantly distributed reflecting prevalence of HTN increases as renal function declines. Natalia Ridao et al showed 60.5% prevalence of HTN[35, 36].

LVH regression is expected to reduce cardiac arrhythmias, new onset cardiac failure and sudden death [37]. Therefore, if we try to intervene LVH by prompt treatment of HTN and anaemia especially in resource poor nations like ours, we can halt progression of CKD and reduce the incidence of cardiovascular mortality.

In our study we found out of 28 hyperkalaemic patients 9 patients had tall T wave whereas 1patient had tall T wave without biochemical evidence of hyperkalaemia. And only out of 3 patients with potassium level above 6.5 mmol/l one patient had tall peaked T wave. In one published series out of 127 patients with serum potassium concentrations ranging between 6 and 9.3mEq/L, only 46% of ECG was noted to have changes suggestive of hyperkalaemia, including peaking of T waves[38, 39]. There are multiple case reports of patients with renal failure who presented without significant ECG changes despite markedly elevated potassium levels[40]. It has been postulated that cardiac and neuromuscular complications of hyperkalaemia are less evident in ESRD patients due to variable serum calcium concentration [41].

Unrecognized myocardial infarction found in 14 patients (28%); 8 of them in stage 5, which is higher than the previous report, which showed that, the prevalence of unrecognized myocardial infarction was 13% compared with 4% in those without CKD[42]. This may be explained by less access of our population to health care facilities, as a result, there is a high prevalence of incident diagnosis of unrecognized MI. Moreover CKD stages 3 to 5 were included in our study rather than CKD stages 4 and 5. We also tried to correlate unrecognized MI with anaemia, but here it was statistically not significant. We overlooked ST-T changes as because there is a high prevalence of non-specific ST-T changes in CKD patient and is thought to be due to LVH, volume overload and electrolyte abnormalities typically seen in CKD patients. Baseline ECG abnormalities are much rarer in the general population, occurring in only 8.5% of men and 7.7% of women[43]. In this study out of 14 (28%) hypocalcaemia patients we found 11 patients (22% of total study population) with prolonged Q-Tc, a substrate for torsades de pointes and ventricular tachycardia which was distributed in all stages of CKD mostly in stage 5 (5 patients) . It is likely that the progression of CKD, probably through its association with heart disease or progressive cardiac calcification, is the main explanation for this tendency toward prolonged Q-Tc[44].

Limitations: Limitations of this study was small sample size, single center study, absence of long term follow up, use of only baseline ECG for evaluation of CVD and use of only self reported documents to exclude previous CVD.

CONCLUSION

In conclusion, LVH, LAE, unrecognized myocardial infarction, were very common ECG abnormalities in our pre dialytic CKD patients which was most commonly found in hypertensive, anaemic and in male patients. An ECG should be enlisted in the initial investigation in CKD patients as a screening test which guides the clinician for further evaluation of cardiovascular disease. We should use biochemical level of serum potassium for management of hyperkalaemia in advanced CKD patient rather than ECG evidence of hyperkalaemia, as ECG evidence of hyperkalaemia is less pronounced in advanced CKD patient.

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Conflict of Interest: Nil

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