Original Research Article

Study of electrocardiographic changes and their comparison in different stages of chronic kidney disease

Akshat Jain[1], Geetanshu Goel[2*], Sujeet Kamtalwar[3]

{[1]SR II, Department of Cardiology} {[2,3]Assistant Professor, Department of Medicine} Government Medical College & J J Hospital, Mumbai, Maharashtra, INDIA.
Email: kamtalwars@yahoo.in

Abstract

Background: Presence of CKD or multiple risk factors associated with it has been shown to confer an increased propensity of developing cardiovascular diseases. ECG abnormalities are quite common in patients with CKD and they independently predict future cardiovascular events. **Aim:** To determine frequency of various ECG abnormalities and their comparison in different stages in patients with CKD. **Material and Methods**: A total of 193 individuals aged between 13 to 60 years, of either gender, who fulfilled the definition of Chronic Kidney Disease as laid down by KDIGO (Kidney Disease Improving Global Outcome) 2012 guidelines or were diagnosed as a case of chronic kidney disease as per history, clinical examination and available investigations were included in this study. All patients underwent 12 lead electrocardiograms (ECG) at the time of admission. Subsequent ECGs if done were not analyzed for study purpose. **Results:** The most common ECG abnormality observed in CKD patients was left ventricular hypertrophy seen in 42 (21.8%) patients followed by ST depression in 38 (19.7%) patients. Ventricular rate increased with increase in CKD stage. Pathologic Q waves were observed only in CKD stage 5 in 10 (14.1%) patients. T wave inversion was observed in higher proportion in patients in stages 4 and 5 of CKD than the lower stages 1-3. Stages 4 and 5 had ST segment depression in 14 (60.9%) and 22 (31%) respectively, which was significantly higher than other stages. **Conclusion:** Almost all of the abnormal ECG findings occurred mostly in the later stages of CKD. Hence, it is imperative to monitor regularly the patients of CKD to assess the changes in ECG. Progression of CKD stage increases the occurrence of abnormal ECG findings, especially in the later stages.

Key Word: Chronic kidney disease, electrocardiography, stages, left ventricular hypertrophy

***Address for Correspondence:**
Dr. Geetanshu Goel, Assistant Professor, Department of Medicine, Government Medical College & J J Hospital, Mumbai, Maharashtra.
Email: kamtalwars@yahoo.in

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INTRODUCTION

CKD has emerged as a major public health problem globally in the past decade.[1] The major reasons being rapidly increasing worldwide incidence of diabetes and hypertension.[2,3]Presence of CKD or multiple risk factors associated with it has been shown to confer an increased propensity of developing cardiovascular (CV) diseases, thus leading to increased morbidity, mortality and rate of hospitalization. ECG abnormalities are quite common in patients with CKD and they independently predict future CV events.[4] Though the prevalence of different ECG abnormalities varies widely in different studies described in literature, of them concluded that resting ECG abnormalities are common in hospitalized CKD patients.[5-7] Also, sudden cardiac death has been accounted for approximately 60% of cardiac-related deaths in patients undergoing dialysis.[6]Common ECG parameters that are automatically recorded during standard ECG acquisition can be considered as independent risk markers for CV death and thus increase the chance of predicting fatal

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outcomes in CKD patients. Also ECG bears a low cost and the facility is widely available, even at most of the primary care centres. Thus, prior and regular use of ECGs amongst individuals with CKD may positively impact the outcome of CV risk reduction strategies in CKD patients.[4] With this background, it appeared logical and essential to study ECG changes and their comparison in different stages in CKD patients, which was lacking in western Indian population.

MATERIAL AND METHODS

This single centre prospective observational study included adult patients admitted in Medicine Wards or Intensive Care Units in a Tertiary Care Centre and diagnosed to have Chronic Kidney Disease (CKD) over a period of two years.Approval from the Institutional Ethics Committee was obtained prior to initiation of the study.

Inclusion criteria

- All individuals aged between 13 to 60 years, of either gender, who fulfilled the definition of Chronic Kidney Disease as laid down by KDIGO (Kidney Disease Improving Global Outcome) 2012 guidelines or were diagnosed as a case of chronic kidney disease as per history, clinical examination and available investigations.
- Patient or his/her Legally Accepted Representative (LAR) willing to give written informed consent.

Exclusion criteria

- Individuals with valvular Heart Disease, Congenital Heart Disease, Acute Coronary Syndrome or known case of Ischemic Heart disease.
- Individuals on Class I and Class III anti-arrhythmic Agents.
- Individuals who are known case COPD and Pulmonary Hypertension.
- Individuals with cardiac Implantable Pacemaker in situ.
- Individuals with severe anaemia (Haemoglobin<7.0 gm/dl).
- Individuals with electrolyte imbalance at the time of ECG recording.
- Individuals with thyroid disorders.
- Refusal of re-consent from patient on recovery despite initial consent from the LAR.
- Participants who want to withdraw from the study at any point of time due to any reason.

Sample size: A duration specific non-probability sampling method was used. In a study by Ramanan *et al*,[8] ECG was normal in 14% CKD patients, and ECG findings were thus observed in 86%. Sample size was calculated keeping confidence level as 95%, power of the study as 80%,Sample size = $4pq/l^2$, where p=prevalence=86%, q=100-p=100-86=14%, l=precision error =5. Thus, sample size = 4x86x14/5x5 = 4816/25=192.64=193 (rounded off).Thus, for the purpose of the study we need to study at least 193 patients with CKD. During the period of data collection, 193 patients were enrolled in the study. All patients underwent 12 lead electrocardiograms (ECG) at the time of admission. Subsequent ECGs if done were not analyzed for study purpose. ECG was interpreted by a qualified physician trained in interpretation of ECG abnormalities. ECG abnormalities were defined based on accepted standard criteria.

RESULTS

In the study, majority of patients were in CKD stage 5 (36.8%), followed by those in stage 2 (25.9%) and 1 (22.3%). Very few patients were in stage 3 (3.1%).

Table 1: Distribution of patients as per stage of kidney disease

Stage of kidney disease	Frequency	Percentage
1	43	22.3
2	50	25.9
3	6	3.1
4	23	11.9
5	71	36.8
Total	193	100

In all patients, ECG abnormalities were present in 113 (58.5%) patients. The most common ECG abnormality observed in CKD patients was left ventricular hypertrophy seen in 42 (21.8%) patients followed by ST depression in 38 (19.7%) patients, while the least observed ECG abnormality was QRS duration >120 ms in 4 (2.1%) patients.

Table 2: ECG abnormalities in all CKD patients

ECG abnormality	Frequency*	Percentage*
Left ventricular hypertrophy	42	21.8%
ST depression	38	19.7%
Primary T wave inversion	30	15.5%

Conduction disturbances	30	15.5%
Slow R wave progression	28	14.5%
VPCs or APCs	24	12.4%
QTc>440 ms	18	9.3%
Low QRS voltage	11	5.7%
Pathologic Q waves	10	5.2%
Tachyrrhythmia(atrial fibrillation)	9	4.7%
Short PR interval	7	3.6%
QRS duration >120 ms	4	2.1%

*values are mutually exclusive of each other

Ventricular rate increased with increase in CKD stage. Atrial fibrillation was observed in 2 (4%), 5 (21.7%) and 2 (2.8%) patients in CKD stages 2, 4 and 5, respectively. VPCs or APCs were observed in 4 (9.3%), 3 (13%) and 17 (23.9%) patients in CKD stages 1, 4 and 5, respectively. P wave morphology was normal in all patients, except in patients with atrial fibrillation in whom P wave was absent. Low QRS voltage was observed in 6 (26.1%) and 5 (7%) patients in CKD stages 4 and 5, respectively. Pathologic Q waves were observed only in CKD stage 5 in 10 (14.1%) patients. Slow R wave progression was observed in 4 (17.4%) and 24 (33.8%) patients in CKD stages 4 and 5, respectively. Primary T wave inversion was observed in 6 (12%) patients in stage 1 CKD, 4 (17.4%) patients in stage 2 and 19 (26.8%) patients in stage 3.T wave inversion was observed in higher proportion in patients in stages 4 and 5 of CKD than the lower stages 1-3. Left ventricular hypertrophy was diagnosed in 18 (36%), 4 (17.4%), and 20 (28.2%) patients in CKD stages 2, 4 and 5, respectively. Conduction disturbances were observed in 6 (12%), 2 (33.3%), 4 (17.4%) and 18 (25.4%) patients in stages 2, 3, 4 and 5 of CKD, respectively. Shortened PR interval (<120 ms) was observed in 5 (21.7%) and 2 (2.8%) patients in CKD stages 4 and 5, respectively. QRS duration >120 ms was observed in 4 (5.6%) patients in CKD stage 5. QTc >440 ms was observed in 18 (25.4%) patients in CKD stage 5. Stages 4 and 5 had ST segment depression in 14 (60.9%) and 22 (31%) respectively, which was significantly higher than other stages.

Table 3: Comparison of ECG changes with different stages of CKD

	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
Ventricular rate	82±5.3	86.4±5.1	61.7±4.3	93.4±9.4	90.4±13.4
Tachyarrhyhmia	0	2 (2%)	0	5 (21.7%)	2 (2.8%)
VPCs or APCs	4 (9.3%)	0	0	3 (13%)	17 (23.9%)
Low QRS voltage	0	0	0	6 (26.1%)	5 (7%)
Pathologic Q waves	0	0	0	0	10 (14.1%)
Slow R Wave Progression	0	0	0	4 (17.4%)	24 (33.8%)
LVH	0	18 (36%)	0	4 (17.4%)	20 (28.2%)
Conduction Disturbances	0	6 (12%)	2 (33.3%)	4 (7.4%)	18 (25.4%)
PR interval	144.3±14.8	144.3±14.8	125.3±5.2	133.6±18.3	144.8±17
QRS duration	84.1±5	85±3.7	85±7.7	87.9±8.6	94.8±11.3
QRS axis (Median)	43 (32-54)	20 (10-47.5)	32 (32-93)	29 (-11 - 75)	53 (33-61)
QTc interval	374.4±15.1	386.4±12.1	412.7±9.8	403±20.4	419.7±33.8
Depressed ST segment	-	2 (4%)	-	14 (60.9%)	22 (31%)
Isoelectric ST segment	43 (100%)	48 (96%)	6 (100%)	9 (39.1%)	49 (69%)

Stages 4 and 5 had higher proportion of patients with ST segment depression compared to other stages. There was significant association of changes in ST segment changes with stage of CKD. ST segment depression was observed in higher proportion in patients in stages 4 and 5 of CKD than the lower stages 1-3.

DISCUSSION

In this study, 193 patients were enrolled, as per sample size calculated and it was found that majority of patients were in CKD stage 5 (36.8%), followed by those in stage 2 (25.9%) and 1 (22.3%). Very few patients were in stage 4 (11.9%) and stage 3 (3.1%). As it was not a population based randomized study the proportion of patients in different stages of CKD cannot be inferred as their prevalence or incidence. The discrepancy in the number of patients in different stages may be attributed to limited duration of study and multiple exclusion factors that were present in the study, so as to avoid the ECG changes occurring secondary to other co- morbidities and drugs. Among all patients in the present study, ECG abnormalities were noted in 58.5%. In a study by Shafi *et al* this prevalence was reported to be high as 78.4%

patients.[7]Sachdeva *et al* reported 75% patients with abnormal ECG finding.[9]Yadla *et al* reported 72.5% patients with ECG abnormality.[10]While Chijioke reported 86% patients with abnormality.[11]Ramanan *et al* observed 86% patients with abnormal ECG.[8] These differences in present study as compared to previous studies can be explained as a result of long lists of comorbidities excluded, in present study, which might contribute to ECG changes directly or indirectly. In the present study, LVH was the most common ECG abnormality seen in 21.8% patients. Shafi *et al* also reported LVH as the most common ECG finding in 40.8% CKD patients.[7]Sachdeva *et al* reported LVH in 33.33% CKD patients.[9]LVH was the most common finding reported by Yadla *et al* in 50% patients.[10]Chijioke *et al* reported a prevalence of 27.6% patients with LVH on ECG.[11] LVH was reported in 30% CKD patients by Ramanan *et al*.[8]Reddy *et al* reported LVH in 62.5% CKD patients.[12] In a study by Bignotto *et al*, LVH was found in 36.3% patients on ECG.[13] Dutta *et al* reported LVH has the most common ECG abnormality present in 66% patients in pre dialytic CKD stages 3, 4 and 5.[14]Left ventricular hypertrophy (LVH) represents a key feature to provide an accurate picture of systolic-diastolic left heart involvement in CKD patients. As a consequence of LVH, myocardial apoptosis, and inter-myocardial fibrosis, the decrease in myocardial capillary density occurs together with diastolic (impaired diastolic filling of the ventricle to increased myocardial stiffness) and systolic dysfunction, disturbances in intra-ventricular conduction, and chamber dilation. Progressively, we might observe more compensatory hypertrophy, dilation and dysfunction of the heart. The severity and persistence of LVH are strongly associated with mortality risk and cardiovascular events in CKD and ESRD patients as reported by Zoccali *et al*. and London *et al*. who observed how a 10% decrease in Left Ventricular Hypertrophy was translated into a 28% decrease in cardiovascular mortality risk in a cohort of patients on hemodialysis.[15-17] Though many of the previous studies have combined the findings of ECG abnormalities in all stages of kidney, it was not hypothesized whether there were any changes with respect to the stage of CKD. There is a lack of literature reporting the differences of ECG findings in various stages of CKD. In the present study, a few such ECG differences were reported. The pulse rate of patients was higher in the stages 3, 4 and 5 compared to earlier stages, and with increase in stage increase in pulse rate was observed. However, the mean pulse rate of the patients was within the normal range. The PR interval was shortened in stages 4 and 5 of CKD while no such observations were noted in stages 1-3. Prolonged QRS and QTc duration was noted in 5.6% and 25.4% patients in CKD stage 5, while other stages of CKD did not report prolonged QRS and QTc duration. The ST segment was much depressed in stages 4 and 5 compared to earlier stages of CKD. Similarly, incidence of primary T wave inversion was higher in stages 4 and 5 of CKD than stage 1. Also, Pathologic Q waves, Slow R wave progression and Low QRS voltage were present in stages 4 and 5 and no such patients were seen in earlier stages. However, increasing trend of LVH occurrence was not reported to increase with the stages of CKD. VPCs or APCs occurrence increased with increase in stage of CKD. Mortality was reported in patients in stages 4 and 5 but not in earlier stages. These ECG changes in different stages of CKD increases the risk of patients to cardiovascular morbidity and mortality. It is important how these ECG changes guide the management of CKD. In earlier stages of CKD, the ECG abnormality findings were lower. In the higher stages of CKD, with ongoing renal failure and dialysis procedures, there is huge potential for electrolyte imbalances which trigger the cardiac arrhythmias as an acute event or on a chronic perspective may predispose to conditions which may result in structural changes in the heart disease. Though presence of ECG abnormalities cautions us about the status of the patient, managing these changes is again another issue. As these ECG changes result from chronic disease status of the patients, appropriate management of the CKD is important. Exact mechanisms why structural disease such as LVH are more common in CKD patients is not exactly known, multiple pathophysiologic mechanisms have been proposed as outlined above. Conduction disturbances and arrhythmias appear to be obvious due to electrolyte imbalances and changes in the myocardium as explained above.

LIMITATIONS OF THE STUDY

Present study had certain limitations. Number of patients found in stage 3 CKD, were comparatively less than the other stages of CKD. Only resting ECGs of patients were taken. Many patients diagnosed as CKD were excluded due to presence of co-morbidities (which might, but not always affects the ECG of the patient).

CONCLUSION

To conclude, resting ECG abnormalities are common in CKD patients. The most common ECG abnormality observed in CKD patients was left ventricular hypertrophy followed by ST depression. It was observed that almost all of the abnormal ECG findings occurred mostly in the later stages of CKD.i.e., stage 4 and 5. Hence, it is imperative to monitor regularly the patients of CKD to assess the changes in ECG. Progression of CKD stage increases the occurrence of abnormal ECG findings, especially in the later stages.

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