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Original Research Article

ELECTROCARDIOGRAM AS A DIAGNOSTIC TOOL FOR ELECTROLYTE IMBALANCE IN HEMODIALYSIS PATIENTS OF CHRONIC KIDNEY DISEASE

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ABSTRACT

Background: Cardiovascular disease (CVD) including cardiac arrythmia and sudden cardiac death, are the leading causes of about 50% of deaths in patients with CKD specifically during and after hemodialysis session. Arrhythmias in CKD patients may be caused by the rapid changes in intracellular and extracellular electrolytes during the dialysis session. The electrocardiogram, which provides a broad outline of cardiac rhythm and conduction of impulse, so it is obtained routinely as it is a useful diagnostic and prognostic tool in CKD patients. Aim and Objectives: In chronic kidney disease patients, study of the cardiac parameter changes and its correlation to electrolytes. **Materials and Methods:** Our study include 150 patients of CKD who underwent a routine hemodialysis for ≥ 3 months. 12 lead ECG recorded twice over each patient pre and post HD using Cardiart 108T-DIGI. Serum electrolytes were estimated twice using biochemical analyser XL-1000 pre and post HD. **Results:** Statistically significant positive correlation between Heart rate and serum calcium & negative correlation between R-R interval and serum calcium before haemodialysis were observed. There was statistically significant a) Positive correlation of heart rate with serum calcium and serum magnesium b) Negative correlation of Serum magnesium with RR interval c) Negative correlation of QT interval with Serum Magnesium and Serum Calcium after haemodialysis was also observed. **Conclusion:** This study shows that changes in ECG parameters are correlated to serum electrolyte levels which suggest that ECG is a non-invasive marker to detect electrolyte imbalance in CKD patients who undergo haemodialysis. Early detection helps to decrease mortality due to cardiac causes in these patients.

INTRODUCTION

Kidney diseases have risen from the world's 13th leading cause of death to the 10th. Mortality has increased from 813 000 in 2000 to 1.3 million in 2019.[1] CKD and ESRD predictably result in multiple derangements of electrolytes, pH and body fluid which are notable factors leading to disability-adjusted life years and pre-mature deaths. Atrial Fibrillilation is very common in CKD patients and has significant impact on overall clinical outcomes.[2] AF was ascertained by a 12-lead electrocardiogram (ECG) and self-report. (3) ECG-detected AF was present in only 1.2% participants.[3] Hemodialysis works on the principle of diffusion of solutes across the semipermeable membrane utilizing counter-current flow of blood and dialysate fluid and therefore, electrolyte changes are common in patient. Calcium and potassium may contribute to the development of arrhythmias during hemodialysis as these cations play a vital role in genesis of the ventricular action potential and propagation of the electrical impulse. Magnesium being the second most abundant intracellular electrolyte, plays a significant role in regulating vascular tone and heart rhythm. Magnesium balance does not control by any hormone rather dependent on intestinal absorption and renal excretion therefore its imbalance causes cardiovascular mortality in patients of CKD. We look-in that our study analysis will aid to greater attention to CKD in public and spread awareness of early screening for the renal and cardiovascular health. Various studies have reported that sudden changes in serum electrolytes causes arrhythmias in patients of CKD undergoing hemodialysis while some studies suggest no relation between serum electrolytes and ECG changes in patients of CKD undergoing hemodialysis. So, we want to assess and

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explore the effect of hemodialysis on ECG changes associated with serum electrolytes changes in such patients. With this background in mind, we want to discuss the usefulness of ECG as non-invasive biomarker to diagnose electrolytes imbalance before and after dialysis session in patients of CKD to prevent fatal arrhythmias or sudden cardiac death and helps them into decrease morbidity and mortality through early intervention.

MATERIALS AND METHODS

After getting approval by ethical committee (No. GMCS/STU/ETHICS/Approval/10623/2) (Date:06/05/2021), this cross-sectional study was conducted during June-2021 to Dec-2021 at New Civil Hospital, Surat, Gujarat. The study group included total 150 patients with chronic kidney disease and required hemodialysis for maintenance of kidney function. The informed consent was taken from participants after explaining the purpose and procedure of the study.

Inclusion criteria

1) Age >18 years, 2) Diagnosed with Chronic Kidney Disease and required haemodialysis for >3 months and 3) Agreed to volunteer for the study.

Exclusion criteria

1) Age < 18 year, 2) Patients having congenital heart disease, pregnancy, pacemaker or cardiopathy, 3) pre-existing endocrine disorder other than Diabetes Mellitus, 4) Patients taking anti arrhythmic drugs, potassium sparing drugs and drugs that cause electrolyte disturbance, antipsychotic, antidepressant, 5) Patients on peritoneal dialysis and 6) Patients with following vital parameters beyond physiological limits were excluded; Respiratory rate, Heart rate and Body temperature.

CARDIART 108T-DIGI electrocardiograph was used to record ECG. ECG was recorded 2 times over each patient. 1st recording was done 15 min prior to haemodialysis and 2nd recording done within 10 min post hemodialysis. The ECG parameters analysed were heart rate, R-R interval, duration and amplitude of QRS complex, QT interval, QTc interval and PR interval.

Two venous samples of each patient were drawn, one 15 min prior to haemodialysis another within 10 min post haemodialysis. XL-1000 fully automated analyser of ERBA Mannheim was used to assess the blood sample. The parameters analysed were Na+, K+, Ca+2, Mg+2, Creatinine and Urea.

The patients fulfilling the inclusion criteria were undergoing maintenance haemodialysis for duration ≥ 3 months at a frequency of 2-3 times/week. Each sitting of haemodialysis lasted for 3.5-4 hr with blood flow rate of 250-300 ml/min and dialysate flow rate 500 ml/min. The 5008-bibag dialysate and Haemodialysis system 4008S containing Hemoflow F6HPS Fresenius polysulfone membrane dialyser was used for haemodialysis.

The data of ECG parameters and serum electrolytes were entered into the Microsoft Excel 2016 and statistical analysis was done by using SPSS version 26 software (Statistical Package for the Social Sciences). For quantitative data, two groups created such as pre-HD and post-HD then Student's paired t test was used to analyse before and after haemodialysis values of serum electrolytes and ECG parameters which were represented as mean, standard deviation and correlation coefficient. Pearson's correlation coefficient was used to correlate between the changes in values of changes in electrolytes and changes in the values of ECG parameters before and after hemodialysis. A p value <0.05 was taken as statistically significant.

RESULTS

Data of 150 diagnosed patients of CKD were collected among them 82 (55%) were male and 68 (45%) were female. Characteristics of the study patients are given in [Table 1].

Table 1: Characteristics of the study patients (n=150)

Groups	Mean ± SD
Age (years)	42.29 ± 13.28
Duration of HD (months)	9.10 ± 5.29
Fluid removed during HD (L)	1.59 ± 0.99
eGFR (ml/min/1.73m^2)	9.69 ± 5.46

In this study, 56% (84) patients have undergone haemodialysis session three times in a week with each session lasting for 3.5 to 4 hours and 16% have undergone haemodialysis two times in a week. Causes of CKD in this study are mentioned in [Table 2].

Table 2: Causes of CKD

Causes of CKD	No	%
HTN and DM	40	26%
HTN	37	25%
Chronic glomerulonephritis	21	14%
DM	20	13%
Idiopathic	13	9%
Renal stone	9	6%
Polycystic kidney disease	6	4%
Chronic pyelonephritis	4	3%

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In our study, out of total 150 patients, 30.7% were hyponatraemic, 23.3% had hyperkalaemia, 37.3% had hypocalcemia and 12% were hypomagnesemic before dialysis. After dialysis, 19% were hypernatremic, 18% were hypokalaemic, 79% were hypercalcemic and 79% had hypermagnesemia.

[Table 3] shows biochemical deviation of serum electrolytes due to haemodialysis. Results depict a significant increase in S. sodium, S. calcium, S. magnesium & a significant decrease in S. potassium, S. creatinine and blood urea as an impact of haemodialysis.

Table 3: Comparison of Biochemical analyses of serum electrolytes, Creatinine and urea pre & post HD

Biochemical findings	Pre-HD	Post-HD	p value
	Mean ± SD	Mean ± SD	
serum Na^+ (mmol/L)	137.6 ± 5.45	142.45 ± 2.84	< 0.00001
serum K^+ (mmol/dl)	4.37 ± 1.07	3.63 ± 0.6	< 0.00001
serum Ca^{+2} (mg/dl)	8.94 ± 1.71	11.46 ± 1.9	< 0.00001
serum Mg^{+2} (mg/dl)	2.54 ± 0.71	3.2 ± 0.66	< 0.00001
Urea (mg/dl)	110.85 ± 49.39	50.41 ± 27.48	< 0.00001
Creatinine (mg/dl)	7.58 ± 3.04	2.95 ± 1.3	< 0.00001
p value < 0.05 statistically significant; M – male; F – female; SD – standard deviation			

[Table 4] represents the study of ECG and blood pressure changes before and after haemodialysis. There was a statistically significant a) Increase in QRS amplitude, b) Decrease in T wave amplitude, c) Increase in Heart rate, and QT interval d) Decrease in R-R interval, e) Decrease in PR, f) Decrease in DBP. In our study, 49.3% patients were having increased heart rate >100 bpm, 43.3% were have raised SBP >140 mmHg, 8% patients had hypotension, 7.3% were have DBP > 90 mmHg, 74% were have QT interval >0.44 sec, 42% were have QTc interval > 0.46 sec and 2% were have PR interval > 0.2 sec after haemodialysis.

In [Table 5], statistically significant positive correlation between Heart rate and serum calcium & negative correlation between R-R interval and serum calcium before haemodialysis are observed. Rest of the serum electrolytes and ECG parameters correlations are statistically insignificant.

[Table 6] shows statistically significant a) Positive correlation of heart rate with serum calcium and serum magnesium b) Negative correlation of Serum magnesium with RR interval c) Negative correlation of QT interval with Serum Magnesium and Serum Calcium after haemodialysis.

Table 4: Comparison of changes in BP and ECG parameters pre & post HD

ECG parameters and BP	pre-HD	post-HD	p value
	Mean ± SD	Mean ± SD	
HR (beats/min)	86.21 ± 12.53	107.18 ± 30.51	**< 0.00001**
R-R interval (sec)	0.68 ± 0.16	0.6 ± 0.16	**< 0.00001**
QRS complex (sec)	0.1 ± 0.02	0.11 ± 0.09	0.21
QRS complex (mV)	1.97 ± 0.7	2.13 ± 0.69	**0.0001**
PR interval (sec)	0.13 ± 0.04	0.12 ± 0.04	**0.0001**
QT interval (sec)	0.38 ± 0.06	0.47 ± 0.06	**< 0.00001**
QTc interval (sec)	0.46 ± 0.08	0.47 ± 0.06	0.83
SBP (mmHg)	144.39 ± 26.14	141.85 ± 20.55	0.05
DBP (mmHg)	85.88 ± 10.3	83.99 ± 6.6	**0.003**
HR – heart rate, **SBP –** systolic blood pressure, **DBP** – diastolic blood pressure ***p value** <0.05 statistically significant; **SD** – standard deviation			

Table 5: Correlation between serum electrolytes and ECG parameters pre- HD

Pre-HD correlation	HR		R-R interval	
	r	p	r	p
Na^+	-0.0031	0.97	-0.0003	1
K^+	-0.117	0.15	0.11	0.18
Ca^{+2}	0.196	0.02	-0.164	0.045
Mg^{+2}	0.07	0.39	-0.095	0.25
*r – Pearson's correlation coefficient *p value <0.05 statistically significant				

Table 6: Correlation between serum electrolytes and ECG changes post-HD

Post-HD correlation	HR		R-R interval		QT interval	
	r	p	r	p	r	p
Na^+	-0.12	0.14	0.07	0.39	0.15	0.07
K^+	0.05	0.55	-0.04	0.58	-0.11	0.16
Ca^{+2}	0.16	0.04	-0.14	0.1	-0.21	0.01
Mg^{+2}	0.18	0.03	-0.19	0.02	-0.19	0.02
*r – Pearson's correlation coefficient *p value <0.05 statistically significant						

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DISCUSSION

In this study, we observed that some electrocardiographic parameters and serum electrolytes have changed after hemodialysis. Haemodialysis is a preferred therapy in the patients with chronic kidney disease over other replacement therapies. Mortality incidence is higher amongst CKD patients who undergo hemodialysis. Mortality is due to cardiovascular complications amongst which, cardiac arrest is most common cause of death due to cardiac changes as a result of changes in serum electrolytes. ECG changes, suggestive of cardiac disease, observed in patients before haemodialysis are due to variations in specific serum electrolyte levels which remain for some time even after haemodialysis. Cardiac monitoring is highly mandatory amongst these patients and is done by screening with ECG machine. Most of manifestations in ECG are correlated with serum electrolyte levels of Sodium, Potassium, Calcium and Magnesium.

Study of Ahmet Korkmaz et al. included total 46 participants out of which 65% were male and 35% were female patients.[4] Study of Erken et al. included 107 CKD patients out of which 51% were male and 49% were female.[5] Out of total 150 participants we observed that 55% were male and 45% were female patients of CKD. These all studies show a higher prevalence of CKD in males over females.

In the study of Clevin Rashmi Rebello et al., mean age of patients was 54.67±10.82 years and mean duration of dialysis was 1.86±1.51 years.[7] While in our study, mean age is 42.29 ± 13.28 years and duration of haemodialysis is 9.10 ± 5.29 months.

Nathan W. Levin et al in their study mentioned the mean of total fluid removed during dialysis that was 2332 ± 230 ml.[8] In their study, hypotensive episodes occurred in 13.5% intra- and post-dialytic evaluations. While in this study, mean of total fluid removed is 1590 ± 990 ml and 8% patients have episode of hypotension post-haemodialysis. The amount of removed fluid and rate of fluid removal play important roles in episodes of intradialytic and post-dialytic hypotension as they reduce blood pressure as well as cardiac output.

Cases of CKD in study of Mitsutoshi Shindo et al. had the following comorbidities, DM (28.3%), HTN (27.8%), chronic glomerulonephritis (7.2%), polycystic kidney disease (6.1%) and idiopathic (9.4%).[9] In the study of Erken et al, the major cases of CKD patient groups were that of DM (39.2%), followed by HTN (33.6%), glomerulonephritis (11.2%) and polycystic kidney disease (7.4%).[5] Compared to these, cases of CKD in present study are patients having HTN and DM (26%), HTN (25%), chronic glomerulonephritis (14%), DM (13%), idiopathic (9%), renal stone (6%), polycystic kidney disease (4%) and chronic pyelonephritis (3%). Other studies show DM as a leading cause of CKD but in this study leading cause is combination of HTN and DM. These variations may be due to difference in age, gender, nutrition, physical activity, various associated diseases and timing of blood sample collection of study population.

Study of Ramazan Astan shows post-haemodialysis decrease in blood urea 53.90 ± 19.19 mg/dl, S. creatinine 3.62 ± 1.29 mg/dl, S. potassium 3.58 ± 0.56 mEq/L.[6] which supports current study while their study shows decrease in S. sodium 135.77 ± 3.49 mEq/L and S. calcium 2.17 ± 0.18 mg/dl,[6] which is against current study findings showing increase in S. sodium and S. calcium post-haemodialysis.

Study of Clevin Rashmi Rebello et al. show changes in Na^+ levels usually doesn't have any effect on the ECG.[7] Hypercalcaemia is commonly associated with shortened QT interval, prolonged QRS duration, bradycardia, increased QRS amplitude, diminished T wave amplitude.[7] Hypocalcaemia is associated with lengthened QT interval, shortened QRS duration, AV block, sinus bradycardia, SA block, ventricular fibrillation.[7] Hyperkalemia is associated with pointed T waves, wider P wave with decreased amplitude, prolonged PR interval, ST segment elevation, wider QRS complex.[7] Hypokalaemia is associated with wider T wave with low amplitude, ST segment depression prominence of U waves along with T wave inversion and increase of amplitude of P wave.[7] ECG changes noted in CKD patients on haemodialysis are due to combined effects of changes in various serum electrolytes level, uraemia, acid-base imbalance.[7] Here, the rise in HR post-haemodialysis was insignificant,[7] but in contrast to this, our study shows significant increase in HR pre- haemodialysis (86.21 ± 12.53 bpm) to post- haemodialysis (107.18 ± 30.51 bpm) and did not show any correlation of serum electrolyte level with P wave and T wave of ECG.

The study of Yuxin Nie et al. showed that the more the serum potassium decreased, the longer the QTc interval was observed post dialysis,[10] which is supportive finding to the present study.

PR interval was significantly reduced indicating improved conduction of impulses which can be explained based on K level changes post haemodialysis.[7] In contrast to it in my study, there is no significant correlation between PR interval and S. potassium changes (r=-0.14, p=0.09) post-haemodialysis. QRS duration was significantly prolonged which can be explained based on changes in Ca^{+2} levels post-haemodialysis.[7] My study results are opposite to it, there is no significant correlation between QRS duration (r=-0.017, p=0.84) and S. calcium post- haemodialysis in my study.

In my study, QT interval negatively correlated with S. calcium (r=-0.21, p=0.01) and S. magnesium level (r=-0.19, p=0.02) post-haemodialysis. S. Ca^{+2} (r=0.16, p=0.04) and S. Mg^{++} (r=0.18, p=0.03)

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significantly positively correlated with HR post-haemodialysis.

The current study shows significant positive correlation between S. Mg2+ and HR. 41.3% patients had tachycardia (>100 bpm) with S. Mg2 > 2.7 mg/dl after haemodialysis. S. Mg2+ shows significant negative correlation with RR interval (r=-0.19, p=0.02) and QT interval (r=-0.19, p=0.02) after haemodialysis. The study of John Cunningham et al. demonstrated that magnesium concentration of the dialysate is one of the major determinants of haemodialysis patients' magnesium balance.[11] Hemodialysis patients with mild hypermagnesemia exhibited the lowest mortality rate.[12] Magnesium might be useful to prevent phosphate-induced kidney injury.[12] Ionized magnesium levels of hemodialysis patients were mostly within the reference range despite their elevated total serum magnesium.[12] The details of molecular mechanisms involved in the protective effects of higher dietary magnesium on heart still could not be explored.[13]

Bi-variant Pearson's analysis revealed that serum K+ level appeared to be the main determinant of QTc duration before haemodialysis (r=0.699, p=0.001) but showed no influence on R or T waves amplitude (r=-0.088, p=0.729 and r=-0.149, p=0.554 respectively).[14] Pre-haemodialysis Ca2+ had no significant effect on the pre-haemodialysis QTc interval (r 0.083, P 0.743).[14] There was no influence of post-haemodialysis serum K+ and Ca2+ on the changes in post-haemodialysis QTc interval (r=532, p=0.152 and r=0.136, p=0.591).[14] While in my study, S. Ca^{2+} level is the main determinant of heart rate (r=0.196, p=0.02) and RR interval (r=-0.164, p=0.045) prior to haemodialysis but similar to previously mentioned study, S. calcium has no statistically significant effect on QT interval (r=-0.06, p=0.47) or QTc interval (r=0.024, p=0.77) pre-haemodialysis. S. Na^{+} , S. K^{+} and S. Mg^{+2} does not have statistically significant effect on ECG parameters. The study of Erken et al. mentioned that QT prolongation and ventricular arrhythmias may frequently be in association with low magnesium levels.[5] Oddly enough, they found a positive correlation between serum magnesium levels and the length of QT and QTc intervals in patients with CKD (p= 0.012 and 0.019 respectively).[5] Favouring the current study result, which shows significant negative correlation between QT interval and S. Mg2+ after haemodialysis. The study of Tsering Dhondup and Qi Qian mentioned that severe and chronic hypomagnesemia can present with muscle weakness, paraesthesia, tetany, and seizures. It can potentiate cardiac arrhythmias.[15]

The strength of this study include: (1) All patients data were obtained within continuous six months from single centre and (2) All laboratory data obtained from one single laboratory facility. The limitations of this study are data collected from single centre and the role of autonomic nervous system were not considered. Finding of this study cannot be generalized because of small sample size. Larger sample size needed for detailed study. Further studies are required to observe whether abnormal ECG findings predict cardiac activity or mortality in CKD patient population.

CONCLUSION

This study concludes that change in ECG parameters, such as heart rate, RR interval and QT interval are correlated to S. Calcium and S. Magnesium levels which suggest that ECG is a non-invasive marker to detect electrolyte imbalance in CKD patients who undergo haemodialysis as a renal replacement therapy. Although S. Na+ and S. K+ show their effect on ECG parameters, it is statistically not significant. The prolongation of QT interval and alteration in HR and RR interval may be a further non-invasive marker of susceptibility to cardiac electrical disturbances. Screening by ECG is highly recommended to avoid progression to cardiac arrest. ECG would effectively identify patients who have a depolarization and/or repolarization defect before and after haemodialysis. In these patients, a dialysis regimen can be adopted which is less likely to affect cardiac electrical activity and cardiac function.

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