International Journal of Research in Medical Sciences
Avula NR et al. Int J Res Med Sci. 2020 Jun;8(6):2188-2194
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20202264

Original Research Article

Evaluation of role of heart rate variability with holter monitoring in chronic kidney disease

Naveen Reddy Avula, Tushar Dighe*, Atul Sajgure, Charan Bale, Pavan Wakhare

Department of Nephrology, Dr. D. Y. Patil Medical College and Hospital, Pimpri, Pune, Maharastra, India

Received: 29 March 2020
Accepted: 29 April 2020

***Correspondence:**
Dr. Tushar Dighe,
E-mail: naveen23nani@yahoo.com

ABSTRACT

Background: Chronic kidney disease is prevalent disease even in absence of diabetes and hypertension in 12% adults over 65 yrs of age. Autonomic imbalance is not studied in detail which could be a risk factor for chronic kidney disease.
Methods: This Study was observational study in a tertiary care Hospital in pune, india and was conducted for a period of 1 year with sample size of 52. All subjects were known cases of chronic kidney disease from stage III to VD. All individuals of age >18yrs and eGFR ≤60ml/min/1.73m^2 according to CKD- EPI equation were included in the study and who were not giving consent were excluded. 24 hrs Holter monitoring was done in stages from ckd stages III to V, for ckd stage VD on both Hemodialysis day and Non hemodialysis. Analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. The paired t test, analysis of variance (ANOVA) and Chi-square test were used. Level of significance was set at p≤0.05.
Results: In this study when Heart rate variability (HRV) parameters were compared in different stages of ckd from stage III to VD (on Hemodialysis day) SDNN, SDNN Index were found to be statistically significant and on non Hemodialysis day SDNN Index was found to be statistically significant. In each subgroup of ckd stage V when diabetic subjects were compared with non-diabetic subjects, HRV parameters like ratio of P/S which was found to be low and significant in ckd stage V diabetic subjects.
Conclusions: Chronic kidney disease itself can affect the HRV parameters. Causal relationship between HRV and chronic kidney diseases can be vice versa and further needs larger and prospective studies.

Keywords: Chronic kidney disease, Heart rate variability, Hemodialysis

INTRODUCTION

Chronic kidney disease is more common in people suffering from diabetes and hypertension, but 12% of adults aged 65 years also suffer from chronic kidney disease despite the absence of diabetes and hypertension indicating some mechanisms of renal injury may be coming into play in general population.[1]

Autonomic dysfunction is the least explored concept which can cause renal injury. The kidney's vasculature, tubules and juxtaglomerular cells are innervated by sympathetic nerve terminals.[2]

There is no standard method to measure autonomic dysfunction, only one indirect way of measuring would be by Heart rate variability (HRV) with electrocardiographic monitoring.[3]

HRV can be quantified by examining the average heart rate and quantification of beat-to-beat variability (the SD of a patient's RR intervals). In most healthy young adults, resting heart rate will predictably accelerate and decelerate with the respiratory cycle. High resting heart rate and low HRV are associated with a host of adverse cardiovascular outcomes, as well as with precursors of

cardiovascular disease, including features of the metabolic syndrome.[4-6]

Previous studies have found that patients with CKD have decreased HRV relative to those without CKD.[7-10] However, it is not known to what extent autonomic imbalance precedes the development of CKD. If autonomic imbalance precedes the development of chronic kidney disease, it may serve as a marker to identify patients at higher risk of developing ESRD.

Aim of this study is to explore HRV parameters across various stages of CKD from stage III to VD. Objective is to compare HRV in different stages of CKD form stage III to VD and to compare HRV between DM and Non DM in CKD stage V.

METHODS

This Study was observational study in a tertiary care centre in pune, india. Study was conducted for a period of 1 year from January 2018 to January 2019 with sample size was 52. All subjects were known cases of chronic kidney disease from stage III to VD. Study was conducted after informed consent from the subjects and approval from ethical committee. In the study Diabetes mellitus (DM) were considered as with HBa1c≥6.5 or subjects on oral hypoglycemic or insulin.[11] 24 hrs Holter monitoring was done on both Hemodialysis (HD) day and Non hemodialysis (non HD) day of CKD stage VD and in other stages of CKD from III to V.

Inclusion criteria

- All individuals of age >18yrs and eGFR <60ml/min/1.73m^2 according to CKD- EPI equation.[12]

Exclusion criteria

- All individuals of age <18 yrs and eGFR ≥60 ml/min/1.73m^2 according to CKD- EPI equation.[12]
- All individuals not giving consent.

All Subjects were allowed to do daily routine activities and not involve in strenuous exercises or activities. Three -lead electrocardiographic data were recorded for 24 h and were downloaded to the analyser. Holter software version 12.1.0010a was used for analysis. Manual analysis was used to review the ECG data to remove any artefacts. The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. Descriptive statistics included computation of percentages, means and standard deviations.

The paired t test (for quantitative data to compare before and after observations) and analysis of variance (ANOVA) (for quantitative data within groups) with post hoc Bonferroni test (intra-group comparison) were used for quantitative data comparison of all clinical indicators. Chi-square test used for qualitative data whenever two or more than two groups were used to compare. Level of significance was set at p≤0.05.

RESULTS

Of the 52 patients who were enrolled in the study, mean±SD of age in CKD stage III was 42.70±8.01, in CKD stage IV was 47.30±15.00, in CKD stage V was 41.10±14.19, in CKD stage VD was 38.41±11.66. Mean SBP±SD in CKD stage III was 134±9.66, CKD stage IV was 130±16.30, CKD stage V 124.0±12.64, CKD stage VD 139.54±15.57 .Mean DBP±SD in CKD stage III was 85.00±7.07, in CKD stage IV was 84.00±8.43, in CKD stage V 77.00±8.23, in CKD stage VD 86.36±10.93 (Table 1).

In this study 52 patients mean Hemoglobin±SD was lowest in subgroup CKD stage VD with 8.19±1.13, p=0.001. Mean serum creatinine±SD was highest in subgroup CKD stage VD with 8.39±2.0, p=0.001. Mean blood urea±SD was highest in CKD stage VD with 104.4±14.9, p=0.001. Mean albumin±SD was lower in subgroup CKD stage V and not statistically significant. Mean sodium±SD was lower in subgroup CKD stage III and not statistically significant. Mean potassium±SD was higher in subgroup CKD stage VD and not statistically significant.

Mean calcium±SD was lower in subgroup CKD stage VD and statistically significant. Mean phosphorous was higher in CKD stage VD and statistically significant. Mean uric acid±SD was higher in subgroups CKD stage V not statistically significant. Mean cholesterol±SD was highest in subgroup CKD stage V and statistically significant. Mean FBS±SD was higher in CKD stage V, 101.80±19.44 and not statistically significant. Mean PPBS±SD was higher in subgroup CKD stage V and not statistically significant. Mean HBA1C±SD was higher in subgroups CKD stage IV, 6.27±1.21 and not statistically significant (Table 2).

In this study of 52, SDNN (msec) mean±SD was lowest on HD day of CKD stage VD, 61.22±30.62 and statistically significant. SDANN index mean±SD was lowest on HD day of CKD stage VD, 55.27±27.49 and not significant. SDNN Index mean±SD was lowest on HD day of CKD stage VD, 24.54±13.53 and statistically significant. rMSSD (msec) mean±SD was lowest on HD day of CKD stage VD, 14.90±7.70 and not statistically significant. Heart rate/min mean±SD was lowest in CKD stage IV, 81.40±11.86 and not statistically significant. RR mean±SD was lowest in CKD stage V, 697.36±105.90 and not statistically significant. Total power mean±SD in CKD stage VD was lowest, 836.77±1007.15 and not statistically significant. ULF power mean±SD in CKD stage V was lowest, 4.29±3.32 and not statistically significant. VLF power mean±SD on

HD day of CKD stage VD was lowest, 627.99±784.02 and not statistically significant. LF power mean±SD on HD day of CKD stage VD was lowest, 153.31±214.36 and not statistically significant. HF power mean±SD was lowest on HD day of CKD stage VD was 46.97±56.68 and not statistically significant. LF/HF ratio mean±SD was lower in CKD stage IV, 3.03±3.60 and not statistically significant. Ratio P/S mean±SD was lowest in CKD stage III, 11.28±6.83 and not statistically significant. pNN50% mean±SD was lowest on HD day of CKD stage VD, 1.77±3.84 and not statistically significant (Table 3).

Table 1: Base line demographic characteristics.

		CKD stage III n=10	CKD stage IV n=10	CKD stage V n=10	CKD VD n=22
Age(mean±SD)		42.70±8.01	47.30±15.00	41.10±14.19	38.41±11.66
Gender	Male	5 (50%)	7 (70%)	6 (60%)	17 (77.3%)
	Female	5 (50%)	3 (30%)	4 (40%)	5 (22.7%)
SBP(mmHg) (mean±SD)		134±9.66	130±16.30	124.0±12.64	139.54±15.57
DBP(mmHg) (mean±SD)		85.00±7.07	84.00±8.43	77.00±8.23	86.36±10.93
eGFR(ml/min/1.73m^2) (mean±SD)		41.90±9.55	20.70±4.05	10.10±2.28	7.22±2.04
Diabetes mellitus		5 (50%)	4 (40%)	5 (50%)	6 (27.2%)
Hypertension		0	2 (20%)	3 (30%)	15 (68.2)

Table 2: Lab parameters.

Lab parameters (mean±SD)	CKD stage III n=10	CKD stage IV n=10	CKD stage V n=10	CKD VD n=22	p value
Hemoglobin(g/dl)	9.91±1.11	8.30±1.09	8.60±1.24	8.19±1.13	0.001(S)
Serum creatinine(mg/dl)	1.76±0.17	3.25±0.62	5.93±1.22	8.39±2.00	0.001 (S)
Blood urea(mg/dl)	59.40±10.01	82.20±11.96	97.50±13.41	104.40±14.95	0.001 (S)
Sodium(meq/l)	139.00±3.65	142.80±3.25	141.10±3.54	142.31±4.24	0.1
Potassium(meq/l)	4.31±0.41	4.41±0.44	4.79±0.47	4.48±0.51	0.14
Calcium(mg/dl)	8.93±0.41	8.19±0.63	8.14±0.34	8.12±0.49	0.001 (S)
Phosphorous(md/dl)	4.70±0.76	6.50±1.91	5.89±1.44	6.31±0.63	0.03 (S)
Uric acid(md/dl)	5.85±1.43	6.16±1.15	7.14±2.22	6.24±1.33	0.82
Serum albumin(g/dl)	3.50±0.48	3.52±0.30	3.34±0.40	3.40±0.35	0.66
Serum cholesterol(mg/dl)	139.30±38.91	152.00±27.99	175.30±41.15	140.59±17.28	0.02 (S)
FBS	97.30±18.83	99.00±15.87	101.80±19.44	93.00±17.63	0.59
PPBS	152.30±38.54	160.80±34.63	164.20±34.11	154.86±32.93	0.84
HBA1C	6.02±1.03	6.27±1.21	6.26±1.07	6.00±1.01	0.87

Table 3: Inter group comparison of heart rate variable parameters in different stages of CKD.

HRV variables	CKD stage III	CKD stage IV	CKD stage V	CKD stage VD Hd day	p
SDNN	98.30±26.41	80.30±45.98	69.90±19.48	61.23±30.62	0.02 (S)
SDANN index	73.90±27.30	66.80±39.35	57.10±19.77	55.27±27.49	0.34
SDNN index	43.50±16.60	34.80±24.16	29.30±11.63	24.54±13.53	0.02 (S)
rMSSD	21.60±7.57	22.80±15.13	20.50±10.33	14.90±7.71	0.12
Mean HR/min	81.90±9.92	81.40±11.86	81.60±3.53	86.68±11.23	0.37
Mean RR	788.13±92.87	726.16±128.84	697.36±105.90	701.71±120.48	0.22
Total Power	1386.99±680.350	1675.47±2077.21	1023.62±590.03	836.77±1007.15	0.27
ULF power	7.87±8.28	13.57±11.62	4.29±3.32	8.8136±9.60363	0.15
VLF power	959.59±392.70	1118.32±1472.42	688.86±388.47	627.99±784.02	0.43
LF	320.26±221.50	253.04±381.85	247.44±205.67	153.31±214.36	0.35
HF	99.26±86.67	190.53±311.53	83.01±44.97	46.97±56.68	0.09
LF/HF	4.12±2.64	3.03±3.60	3.89±2.71	3.77±4.73	0.92
Ratio of P/S	11.28±6.83	21.18±26.97	16.24±10.25	20.47±22.74	0.61
PNN50	3.90±4.75	6.90±10.98	5.10±5.59	1.77±3.84	0.17

In this study of 52, SDNN (msec) mean±SD on non HD day of CKD stage VD was lowest, 69.09±25.76 and not statistically significant. SDANN index mean±SD in CKD stage V was lowest, 57.10±19.77 and not statistically significant. SDNN Index mean±SD was lowest in non HD day of CKD stage VD, 26.36±10.70 and statistically significant. rMSSD (msec) mean±SD was lowest on non HD day of CKD stage VD,18.59±11.91 and not statistically significant. Heart rate/ min mean±SD was lowest in CKD stage IV, 81.40±11.86 and not statistically significant. RR interval mean±SD was lowest on non HD day of CKD stage VD, 683.49±93.02 and not statistically significant Total power ±SD was lowest on non HD day of CKD stage VD, 728.66±612.64 and not statistically significant. ULF power mean±SD was lowest in CKD stage V was 4.29±3.32 and not statistically significant. VLF power mean±SD was lowest on non HD day of CKD stage VD, 512.65±442.64 and not statistically significant. LF power mean±SD was lowest on non HD day of CKD stage VD, 145.55±178.08 and not statistically significant. HF power mean±SD was lowest on non HD day of CKD stage VD, 61.49±70.50 and not statistically significant. LH/HF mean±SD ratio was lowest in CKD stage IV, 3.03±3.60 and not statistically significant. Ratio P/S mean±SD was lowest on non HD day of CKD stage VD, 17.83±16.67 and not statistically significant. pNN50% mean±SD in CKD stage V was lowest, 4.12±2.64 and not statistically significant (Table 4). In the subgroup CKD stage V out of 10, when diabetic and non-diabetic subjects were compared, there was no statistical significance in HRV parameters like SDNN,SDANN Index, SDNN index, rMMSD, HR, RR, Total power, ULF power, VLF, LF power, HF power, LF/HF ratio. Ratio P/S mean±SD in non-diabetics was 23.26±8.65 and in diabetics was lower, 9.22±6.19 with p=0.01 and statistically significant (Table 5).

Table 4: Inter group comparison of heart rate variability parameters in different stages of CKD.

HRV parameters	CKD III	CKD IV	CKD V	CKD stage VD Non HD day	P
SDNN	98.30±26.41	80.30±45.98	69.90±19.48	69.09±25.76	0.07
SDANN index	73.90±27.30	66.80±39.35	57.10±19.77	62.18±23.69	0.54
SDNN index	43.50±16.60	34.80±24.17	29.30±11.63	26.36±10.70	0.02 (S)
rMSSD(msec)	21.60±7.57	22.80±15.13	20.50±10.33	18.59±11.91	0.78
Mean HR/min	81.90±9.92	81.40±11.86	81.60±3.53	87.13±11.31	0.3
Mean RR	788.13±92.82	726.16±128.84	697.36±105.89	683.49±93.02	0.7
Total power	1386.99±680.351	1675.47±2077.21	1023.62±590.03	728.66±612.64	0.1
ULF power	7.87±8.28	13.57±11.62	4.29±3.32	8.93±11.82	0.24
VLF power	959.59±392.70	1118.32±1472.42	688.86±388.47	512.65±442.64	0.14
LF	320.26±221.50	253.04±381.85	247.44±205.677	145.55±178.08	0.26
HF	99.26±86.67	190.53±311.53	83.01±44.97	61.49±70.50	0.16
LF/HF	4.13±2.64	3.03±3.60	3.89±2.70	3.75±4.85	0.93
Ratio P/S	11.28±6.83	21.18±26.97	16.24±10.25	17.83±16.67	0.61
PNN50	3.90±4.74	6.90±10.98	5.10±5.59	4.32±8.63	0.82

Table 5: Comparison of non DM with DM in CKD V.

HRV parameters	Non DM(n=5)	DM(n=5)	p
SDNN	66.40±24.03	73.40±15.66	0.6
SDANN Index	52.80±24.24	61.40±15.69	0.52
SDNN Index	27.20±12.54	31.40±11.67	0.59
rMMSD	16.20±8.01	24.80±11.38	0.2
Mean HR/min	82.00±5.15	81.20±1.09	0.74
Mean RR	696.48±119.06	698.24±105.15	0.98
Total Power	984.14±626.90	1063.10±621.62	0.84
ULF	2.70±1.28	5.88±4.10	0.13
VLF	677.94±445.69	699.78±374.98	0.93
LF	246.52±159.93	248.36±263.82	0.99
HF	56.96±33.77	109.06±41.39	0.06
LF/HF	5.28±2.42	2.50±2.41	0.1
P/S	23.26±8.65	9.22±6.19	0.01 (S)
pNN50%	2.40±2.88	7.80±6.61	0.13

DM- Diabetes mellitus

DISCUSSION

Almost all subjects of CKD stage VD group were on 1 or more antihypertensive Previous studies suggested that short-acting DHP-CCB (dihyrdopyridine-calcium channel blocker) was associated with increased risk of a cardiovascular event which might be due to reflex activation of sympathetic nerve activity caused by excessive and rapid reduction of BP.[13-15] There still exists controversy whether amlodipine can cause increase HR by activating sympathetic system.[16-18] In this study all subjects were on amolidpine as calcium channel blocker and majority of subjects on antihypertensives were on maintenance hemodialysis.

In this study, when authors compared different stages of CKD with CKD stage VD, on HD day authors found SDNN (msec) mean±SD which was lowest in CKD stage VD and statistically significant. SDNN Index mean±SD which was statistically significant lowest in CKD stage VD. Remaining HRV parameters were not found to be significant. This study was not a long term follow up study and it couldn't comment on cardiovascular mortality. In previous studies done by Longenecker et al, they analysed the association between HRV and atherosclerotic cardiovascular (CV) disease in subjects on chronic HD and found low HRV parameters like SDNN, SDANN were strongly associated with atherosclerotic CV disease.[19] Oikawa et al, showed in their study that low SDNN was related with Cardiovascular mortality in HD patients and LF,HF and LF/HF were low in in patients who died.[20]

A study done by Ferrario et al, had found patients with low hydration status before HD showed an increased in LF after HD, whereas no significant change in LF was seen in high hydration status before HD.[21] This might be due to reduction in central volume in patients during dialysis with lower hydration status, which could lead to increased intensive oscillation of LF.

In previous studies ΔLF% was useful and stronger than other HRV parameters before HD in predicting overall and CV mortality in HD patients. LF component of HRV correlates with the interaction of baroreflexes with peripheral vasomotor activity via the parasympathetic and sympathetic system. Previous studies have reported that low LF before HD was associated with adverse CV outcomes and LF increased after HD procedure.[20,22]

Barnas et al, had found also evaluated the change in autonomic nervous system during HD.[23] They found an increase in LF during non-hypotensive dialysis, but decreased during hypotensive dialysis. In this study there were very few hypotensive episodes for the patients on Hemodialysis and could not be analysed.

Hathway et al, study showed that, there was severe autonomic dysfunction in ESRD patients who were on conservative therapy.[24] Previous study showed that patients stage 5 CKD had a lower LFnu/HFnu ratio than those with stage 3, suggesting that ANS response worsens as the disease progresses. This data is in accordance with the study of Banavandan et al, which studied patients with a median GFR of 23 ml/min/1.73 m2 and identified a positive correlation between ANS dysfunction and low GFR but this study did not show any significance even though LF/HF was progressively declining in only diabetic subjects as the CKD stage progresses.[25]

This study showed HRV parameters were lowest in CKD stage VD and is in concordance with previous studies. Vita et al, studied ESRD patients undergoing hemodialysis and found autonomic dysfunction in 53% of patients by HRV.[26] In this study of 52, authors compared different stages of CKD and CKD stage VD on non HD day authors found Mean SDNN Index mean±SD was 26.36±10.70 with p=0.02 which was significant lowest in CKD stage VD. Remaining parameters were not found to be statistically significant.

In the sample out of 10 patients in CKD stage V, 5 were diabetics Ratio P/S mean±SD in non DM was 23.26±8.65 and in DM was 9.22±6.19 with p=0.01 which was significantly lower in diabetic group.

Previous studies demonstrated a autonomic imbalance in both diabetic and non-diabetic uraemic patients compared with non-uraemic diabetic patients and controls.[24,27,28] The autonomic dysfunction was characterized by constant presence of sympathetic activity which was significantly associated with sudden death and increased mortality after myocardial infarction and the occurrence of ventricular arrhythmia.[29-31]

As previous studies suggest there was an improvement in uraemic neuropathy after initiation of hemodialysis, probably because the toxic effect of uraemia is removed.[32] However, diabetic neuropathy is not improved by haemodialysis.[33] This difference after initiating hemodialysis indicates that non-diabetic CKD subjects have inherently a different autonomic response to hemodialysis. However this study was confined only to exploring HRV parameters in diabetics and not with severity or changes with neuropathy.

Limitations of the study was a single centered study and with a small sample size. This study was not a long term follow up study to establish the association of autonomic dysfunction in CKD and its prognosis. Majority of subjects were on anti-hypertensive medication which could have affected the HRV.

CONCLUSION

Hemodialysis itself could have affected HRV parameters. However there was no significant difference between hemodialysis day and non hemodialysis day even though lower HRV was found on hemodialysis day. In chronic

kidney disease diabetes may be a significant factor which may affect autonomic balance as this study suggests.

Recommendation

A large sample size and long term follow up study would have given a better understanding of effect of Heart rate variability in chronic kidney disease.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Coresh J, Byrd-Holt D, Astor BC, Briggs JP, Eggers PW, Lacher DA, et al. Chronic kidney disease awareness, prevalence, and trends among US adults, 1999 to 2000. J Am Soc Nephrol. 2005 Jan 1;16(1):180-8.
2. DiBona GF. Physiology in perspective: The Wisdom of the Body. Neural control of the kidney. Am J Physiol Regul, Integrat Comparat Physiol. 2005 Sep;289(3):R633-41.
3. Dibona GF. Neural control of the kidney: past, present, and future. Hypertension. 2003 Mar 1;41(3):621-4.
4. Koomans HA, Blankestijn PJ, Joles JA. Sympathetic hyperactivity in chronic renal failure: a wake-up call. J Am Soc Nephrol. 2004 Mar 1;15(3):524-37.
5. Kudaiberdieva G, Görenek B, Timuralp B. Heart rate variability as a predictor of sudden cardiac death. Anatolian J Cardiol. 2007 Jul 2;7.
6. Carney RM, Blumenthal JA, Freedland KE, Stein PK, Howells WB, Berkman LF, et al. Low heart rate variability and the effect of depression on post-myocardial infarction mortality. Arch Internal Medi. 2005 Jul 11;165(13):1486-91.
7. Bilchick KC, Fetics B, Djoukeng R, Fisher SG, Fletcher RD, Singh SN, et al. Prognostic value of heart rate variability in chronic congestive heart failure (Veterans Affairs' Survival Trial of Antiarrhythmic Therapy in Congestive Heart Failure). Am J Cardiol. 2002 Jul 1;90(1):24-8.
8. Schroeder EB, Chambless LE, Liao D, Prineas RJ, Evans GW, Rosamond WD, et al. Diabetes, glucose, insulin, and heart rate variability: the Atherosclerosis Risk in Communities (ARIC) study. Diabet Care. 2005 Mar 1;28(3):668-74.
9. Levey AS, Coresh J, Bolton K, Culleton B, Harvey KS, Ikizler TA, et al. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002 Mar 9;39(2 SUPPL. 1).
10. James MT, Hemmelgarn BR, Tonelli M. Early recognition and prevention of chronic kidney disease. Lancet. 2010 Apr 10;375(9722):1296-309.
11. Gillett MJ. International expert committee report on the role of the A1c assay in the diagnosis of diabetes. Diabet Care 2009; 32 (7): 1327-34.
12. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Internal Medi. 2009 May 5;150(9):604-12.
13. Alderman MH, Cohen H, Roqué R, Madhavan S. Effect of long-acting and short-acting calcium antagonists on cardiovascular outcomes in hypertensive patients. Lancet. 1997 Mar 1;349(9052):594-8.
14. Furberg CD, Psaty BM, Meyer JV. Nifedipine: dose-related increase in mortality in patients with coronary heart disease. Circulation. 1995 Sep 1;92(5):1326-31.
15. Psaty BM, Heckbert SR, Koepsell TD, Siscovick DS, Raghunathan TE, Weiss NS, et al. The risk of myocardial infarction associated with antihypertensive drug therapies. JAMA. 1995 Aug 23;274(8):620-5.
16. Eguchi K, Kario K, Shimada K. Differential effects of a long-acting angiotensin converting enzyme inhibitor (temocapril) and a long-acting calcium antagonist (amlodipine) on ventricular ectopic beats in older hypertensive patients. Hypertens Res. 2002;25(3):329-33.
17. Grassi G, Spaziani D, Seravalle G, Bertinieri G, Dell'Oro R, Cuspidi C, et al. Effects of amlodipine on sympathetic nerve traffic and baroreflex control of circulation in heart failure. Hypertension. 1999 Feb;33(2):671-5.
18. Hamada T, Watanabe M, Kaneda T, Ohtahara A, Kinugawa T, Hisatome I, et al. Evaluation of changes in sympathetic nerve activity and heart rate in essential hypertensive patients induced by amlodipine and nifedipine. J Hypertens. 1998 Jan 1;16(1):111-8.
19. Longenecker JC, Zubaid M, Johny KV, Attia AI, Ali J, Rashed W, et al. Association of low heart rate variability with atherosclerotic cardiovascular disease in hemodialysis patients. Medi Princi Pract. 2009;18(2):85-92.
20. Oikawa K, Ishihara R, Maeda T, Yamaguchi K, Koike A, Kawaguchi H, et al. Prognostic value of heart rate variability in patients with renal failure on hemodialysis. Int J Cardiol. 2009 Jan 24;131(3):370-7.
21. Ferrario M, Moissl U, Garzotto F, Cruz DN, Tetta C, Signorini MG, et al. The forgotten role of central volume in low frequency oscillations of heart rate variability. PloS One. 2015;10(3).
22. Genovesi S, Bracchi O, Fabbrini P, Luisetto E, Vigano MR, Lucini D, et al. Differences in heart rate variability during haemodialysis and haemofiltration. Nephrol Dialys Transplantat. 2007 Aug 1;22(8):2256-62.
23. Barnas MG, Boer WH, Koomans HA. Hemodynamic patterns and spectral analysis of

heart rate variability during dialysis hypotension. J Am Soc Nephrol. 1999 Dec 1;10(12):2577-84.
24. Hathaway DK, Cashion AK, Milstead EJ, Winsett RP, Cowan PA, Wicks MN, et al. Autonomic dysregulation in patients awaiting kidney transplantation. Am J Kidney Dis. 1998 Aug 1;32(2):221-9.
25. Bavanandan S, Ajayi S, Fentum B, Paul SK, Carr SJ, Robinson TG. Cardiac baroreceptor sensitivity: A prognostic marker in predialysis chronic kidney disease patients?. Kidney Int. 2005 Mar 1;67(3):1019-27.
26. Vita G, Bellinghieri G, Trusso A, Costantino G, Santoro D, Monteleone F, et al. Uremic autonomic neuropathy studied by spectral analysis of heart rate. Kidney Int. 1999 Jul 1;56(1):232-7.
27. Ewing DJ, Martyn CN, Young RJ, Clarke BF. The value of cardiovascular autonomic function tests: 10 years experience in diabetes. Diabet Care. 1985 Sep 1;8(5):491-8.
28. Ewing DJ, Winney R. Autonomic function in patients with chronic renal failure on intermittent haemodialysis. Nephron. 1975;15(6):424-9.
29. Weise F, London GM, Pannier BM, Guerin AP, Elghozi JL. Effect of hemodialysis on cardiovascular rhythms in end-stage renal failure. Kidney Int. 1995 May 1;47(5):1443-52.
30. Algra A, Tijssen JG, Roelandt JR, Pool J, Lubsen J. Heart rate variability from 24-hour electrocardiography and the 2-year risk for sudden death. Circulation. 1993 Jul;88(1):180-5.
31. Kleiger RE, Miller JP, Bigger Jr JT, Moss AJ. Decreased heart rate variability and its association with increased mortality after acute myocardial infarction. Am J Cardiol. 1987 Feb 1;59(4):256-62.
32. Campese VM, Romoff MS, Levitan D, Lane K, Massry SG. Mechanisms of autonomic nervous system dysfunction in uremia. Kidney Int. 1981 Aug 1;20(2):246-53.
33. Heidbreder E, Schafferhans K, Heidland A. Autonomic neuropathy in chronic renal insufficiency. Nephron. 1985;41(1):50-6.

Cite this article as: Avula NR, Dighe T, Sajgure A, Bale C, Wakhare P. Evaluation of role of heart rate variability with holter monitoring in chronic kidney disease. Int J Res Med Sci 2020;8:2188-94.