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Original research article

24 HOUR AMBULATORY BLOOD PRESSURE MONITORING IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Title: 24 Hour Ambulatory Blood Pressure Monitoring In Patients With Chronic Kidney Disease

Abstract

Background and aims: Chronic Kidney Disease (CKD) And Hypertension(HTN) Are Associated With Each Other Invariably And Each Can Cause Or Aggravate The Other.Hypertension Is A Strong Independent Risk Factor For ESRD And Contributes To The Disease Itself, Or Most Commonly, To Its Progression.24 Hour Ambulatory Blood Pressure Monitoring (ABPM) Is Superior To Clinic BP Monitoring In Predicting The Risk In Hypertensive CKD Patients The Aim Of This Study Was To Review The Results Of ABPM In CKD Patients Which Can Guide In Changing The Antihypertensive Therapy .

Material and Methods: This Prospective Observational Study Having 63 Patients. All The Patients Fulfilling The Criteria Of CKD According To The KDIGO Guidelines And Above 18 Years Of Age Were Included In This Study Whose 24 Hour Ambulatory Blood Pressure Was Measured.Detailed History, Clinical Examination And Relevant Investigations Were Recorded Comparisons Of Various ABPM Characteristics WERE Done And P Value <0.005 Was Considered Significant.

Results: Out Of 63 Patients (M:38,F:25)Maximum Patients (25.39%)Were In Age Group 61-70 Years (M:61-70,F:41-45).51(80.95%)Patients Were On Dialysis And 12 (19.04%)Patients Were Not On Dialysis. In This Study 57 Patients Had Hypertension, 44 Had DM,16 Had IHD.In This Study 2(3.17%) Patients Were CKD Stage I,5(7.93%) Were Stage II,1(1.58%) Was Stage lll, 6(9.52%) Were Stage IV And 49 (77.77%) Were Stage V.Out Of Total 16(25.39%) Patients Were Dippers ,21 (33.33%) Were Non Dippers, 21(33.33%) Were Reverse Dippers And 5 (7.93%) Were Extreme Dippers..Mean ABPM Systolic BP ,Mean ABPM Diastolic BP,Mean PTA Systolic BP,Mean Arterial Pressure Were Significantly Higher In Male Patients which were On Dialysis Than Patient Not On Dialysis.

Conclusion: ABPM is Superior Than Clinical Bp Monitoring In Predicting The Future Communications In CKD Patients Especially PTE,HBI MAP And Other Parameter To Guide To Formulate Treatment Protocol Identifying Such Patients Of Hypertension In Earlier Stages Of CKD,Helped In Morbidity Outcomes While Identifying In Later Stages Of CKD Helped In Mortality Benefits.

Keywords: Chronic Kidney Disease,Hypertension Dialysis,Ambulatory Blood Pressure,Diurnal Variation

24 Hour Ambulatory Blood Pressure Monitoring In Patients With Chronic Kidney Disease

INTRODUCTION

Chronic kidney disease (CKD) and hypertension (HTN) are strongly associated with each other and each can cause or aggravate the other [1]. Several large, prospective,observational trials conducted in the general population have demonstrated that hypertension is a strong independent risk factor for ESRD and contributes to the disease itself, or most commonly, to its progression [2,3].

In the Multiple Risk Factor Interventional trial stage 4 hypertension compared to optimal BP (SBP/DBP <120/80 mmHg) was associated with a 20-fold higher relative risk for ESRD [3]. A 17-year follow-up study by Tozawa et al. has demonstrated that high normal blood pressure and mild, moderate, or severe hypertension, when compared to optimal blood pressure, are independent risk factors for ESRD in men and women [4].

It is known that the blood pressure drops during the night time more than it is during the day,a normal phenomenon known as dipping (sleep wake cycle). Non dippers and reverse dippers are those patients whose blood pressure do not drop at night and in turn increase during the night time respectively. Blunting or loss of this diurnal variation of BP (i.e. non-dipping) occurs in CKD patients due to increased sympathetic nervous system activity, volume expansion, sleep apnoea, low level of physical activity during daytime, poor sleep quality, obesity, high salt intake,diabetic neuropathy, chronic kidney disease and old age and use of antihypertensive drugs [6,7] .

Hypertension and loss of diurnal BP variation i.e. non-dipping pattern is responsible for rapid progression of cardiovascular and renal disease [24]. Thus warranting an urgent treatment protocol to reduce these complications, the most basic of which is to increase the night time dose of antihypertensive medications in reverse and non-dippers. Such patients can be detected only by ambulatory blood pressure monitoring and based on these patterns newer guidelines can be developed. 24 hour ambulatory blood pressure monitoring (ABPM) is superior to clinic BP monitoring in predicting the risk in hypertensive CKD patients [7].In patients of CKD, those having masked hypertension have a worse prognosis than those having white coat hypertension [10]. ABPM is an invaluable tool to detect masked uncontrolled hypertension (drug resistant hypertension) especially in patients of CKD [11] .

Here the aim of this study was to review the results of ABPM in CKD patients which can guide in changing the antihypertensive therapy [1] .

METHODS

The present study was conducted in the department of medicine and nephrology in a Tertiary care hospital. The study design was prospective

observational study. The study duration was 18 months. All the patients fulfilling the criteria of CKD (Chronic kidney disease) according to the KDIGO guidelines[12] and above 18 years of age were included who were willing to give their consent. Pregnant females and patients with AKI on CKD were excluded. Total 63 patients were included in this study whose 24 hour ambulatory blood pressure was measured. After the Institutional Review Board clearance the study was started. Detailed history, clinical examination and relevant investigations according to a predefined diagnostic algorithm were carried out. The patients were followed through their hospital stay till discharge or death.

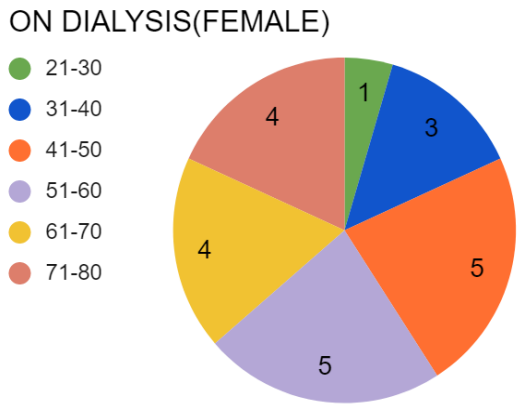
The data obtained was coded and entered into Microsoft Excel Worksheet. Statistical analysis was carried out using Statistical Package for Social Sciences(SPSS) version 20.0 for Windows(IBM Corporation , Armonk , NY). The categorical data was expressed as rates, ratios and proportions and Chi-square or Fisher's exact test was used to compare the data, whichever was applicable. The continuous data was expressed as mean, SD(Standard deviation) and the comparison was done using unpaired t test. To estimate the risk factors for death, Multinomial regression analysis was applied. A probability value ('p' value) of less than or equal to 0.05 was considered statistically significant.

RESULTS

TABLE 1.AGE AND SEX WISE DISTRIBUSTION OF STUDY POPULATION

AGE	NOT ON DIALYSIS (MALE)	ON DIALYSIS(MALE)	NOT ON DIALYSIS(FE MALE)	ON DIALYSIS(FE MALE)	TOTAL
21-30	5(7.93%)	1 (1.58%)	1 (1.58%)	1 (1.58%)	8(12.69%)
31-40	3(4.76%)	2(3.17%)	0	3(4.76%)	8(12.69%)
41-50	1 (1.58%)	4(6.34%)	1 (1.58%)	5(7.93%)	11(17.46%)
51-60	0	6(9.52%)	0	5(7.93%)	11(17.46%)
61-70	0	11(17.46%)	1 (1.58%)	4(6.34%)	16(25.39%)
71-80	0	4(6.34%)	0	4(6.34%)	8(12.69%)
81-90	0	1 (1.58%)	0	0	1 (1.58%)
TOTAL	9(14.28%)	29(46.03%)	3(4.76%)	22 (34.92%)	63
P VALUE	0.001		0.441		

Values are presented as n (%) .



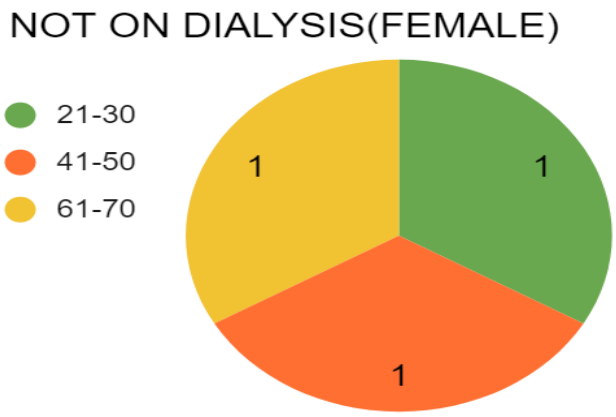


Figure 1. Distribution of female patients on dialysis

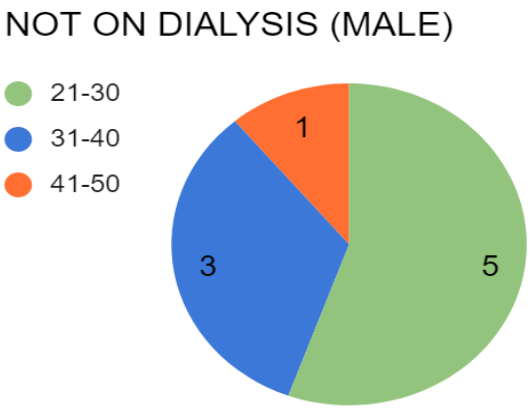


Figure 2. Distribution of female patients not on dialysis

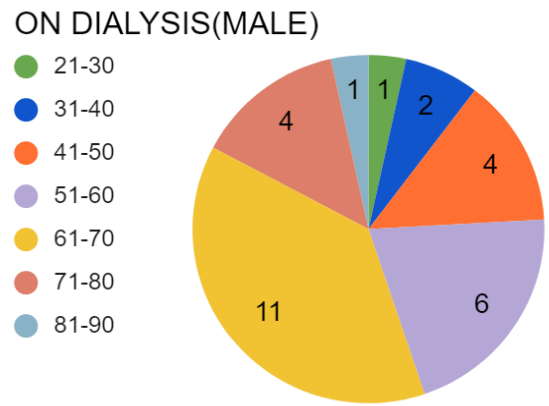


Figure 3. Distribution of male patients on dialysis

Figure 4. Distribution of male patients not on dialysis

TABLE 2. BASELINE CHARACTERISTIC OF STUDY POPULATION

	ON DIALYSIS (n=51)	NOT ON DIALYSIS(n=12)	PROBABILITY(p VALUE)
Mean Age	57.25 ± 13.40	34.41 ± 12.41	P < 0.0001
SEX : MALE FEMALE	29(46.03%) 22(34.92%)	9(14.28%) 3(4.76 %)	P=0.247901
COMORBIDITIES			
HYPERTENSION	49(96.07 %)	8(66.66 %)	P=0.001791
DIABETES	36(70.58%)	8(66.66%)	P=0.789993
OTHERS(IHD)	16(31.37)	0	
SYMPTOMS			
MEAN SYSTOLIC BP	165.41 ± 15.76	146 ± 17.24	P = 0.0004
MEAN DIASTOLIC BP	92.23 ± 8.83	82 ± 7.52	P = 0.0005
MEAN ABPM SYSTOLIC BP	157.50 ± 14.68	136.33 ± 20.45	P = 0.0001
MEAN ABPM DIASTOLIC BP	86.84 ± 8.71	81.33 ± 7.97	P = 0.0498
EGFR CKD STAGE			
>90 I	0	2(16.66%)	
60-89 II	0	5(41.66%)	
30-59 III	0	1(8.33%)	
15-29 IV	4(7.84%)	2(16.66%)	
<15 V(ESRD)	47(92.15%)	2(16.66%)	
Values are presented as n (%) or as mean ± SD.			

Maximum patients were in 61-70 years of Age group (Total 16- 25.39%).

Maximum male patients(total 11-17.46%) were in 61-70 years of age group.

Maximum female patients (total 6- 9.51%) were in 41-50 years of age group.

Maximum OFFICE SYSTOLIC BP IN MALE Patients was in 161-170 mm hg BP group with 11 patients(17.45%) in, out of which 10(15.87%) in on dialysis, 1(1.58%) was not on dialysis.

Maximum OFFICE SYSTOLIC BP in FEMALE patients was in 161-170 mm hg BP group with 8 patients(12.69%) , out of which 7(11.11%) were on dialysis, 1(1.58%) was not on dialysis.

Maximum OFFICE DIASTOLIC BP in MALE Patients was in 86- 90 mm hg BP group with total 13 (20.63%) , out of which 11 (17.42%)were on dialysis, 2(3.27%) were not on dialysis.

Maximum OFFICE DIASTOLIC BP in FEMALE patients was in 86-90 mm hg BP group with total 8(12.69%),out of which 7(11.11%)were on dialysis ,1(1.58%)was not on dialysis.

Out of total 63 patients, 51(80.95%) were on dialysis and 12 (19.04%) were not on dialysis.Maximum patients were in CKD STAGE V(ESRD) with EGFR <15 , total 49(77.77%) out of which 47(74.60%) were undergoing dialysis, only

2(3.17%) were not undergoing dialysis.Total 28 male patients were having CKD STAGE V, out of which 27(42.85%) were on dialysis and 1(1.58%) was not on dialysis. Total 21 female patients were having CKD STAGE V, out of which 20(31.74%) were on dialysis and 1(1.58%) was not on dialysis.

TABLE 3. RELATION OF DIPPING PHENOMENON WITH CKD STAGING

CKD STAGING	DIPPERS (MALE)	DIPPERS (FEMALE)	NON DIPPERS (MALE)	NON DIPPERS (FEMALE)	REVERSE DIPPERS (MALE)	REVERSE DIPPERS (FEMALE)	EXTREME DIPPERS (MALE)	EXTREME DIPPERS (FEMALE)	TOTAL
1	0	0	1(1.58%)	0	1(1.58%)	0	0	0	2 (3.17%
2	4 (6.34%)	0	0	0	0	1(1.58%)	0	0	5(7.93%)
3	0	0	1(1.58%)	0	0	0	0	0	1(1.58%)
4	2 (3.17%)	2 (3.17 %	0	0	1(1.58%)	0	0	1(1.58%)	6(9.52%)
5	5(7.93%)	3 (4.76%)	10(15.87%)	9(14.28%)	11(17.46%)	7(11.11%)	2 (3.17%	2 (3.17%	49(77.70%)
TOTAL	11(17.46%)	5(7.93%)	12(19.04%)	9(14.28%)	13(20.63%)	8(12.69%)	2 (3.17%	3 (4.76%)	63(100%)
Values are presented as n (%).									

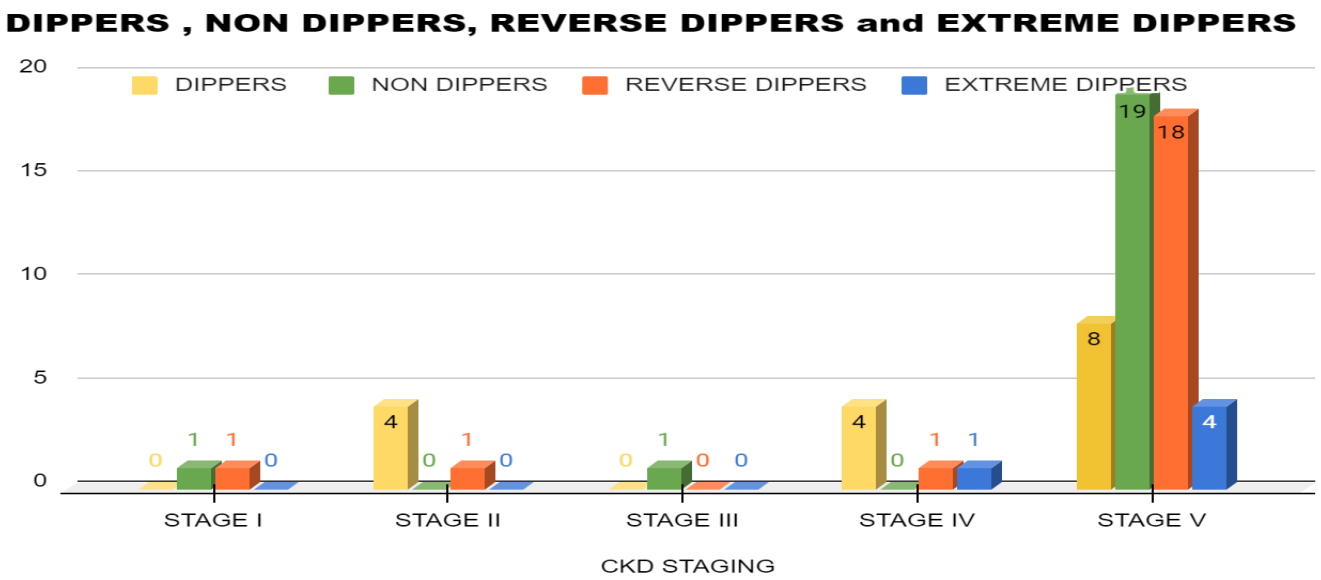


Figure 5. CKD Stages VS Diurnal Index

TABLE 4. ABPM characteristics in CKD PATIENTS

	On dialysis	Not on dialysis	PROBABILITY(p VALUE)	On dialysis	Not on dialysis	PROBABILITY(p VALUE)
	MALE	MALE	MALE	FEMALE	FEMALE	FEMALE
MEAN ABPM SYSTOLIC BP	160.27 ± 14.51	134.88 ± 22.57	P = 0.0003	153.86 ± 14.11	140.66 ± 10.96	P = 0.1355
MEAN ABPM DIASTOLIC BP	89.34 ± 7.14	82 ± 8.64	P = 0.0146	83.54 ± 9.47	79.33 ± 4.98	P = 0.4631
PTE SYSTOLIC BP	77.82 ± 16.70	57.66 ± 29.31	P = 0.0129	77.45 ± 17.58	61 ± 15.29	P = 0.1380
PTE DIASTOLIC BP	48.27 ± 25.04	36.33 ± 34.61	P = 0.2619	46.85 ± 26.25	26 ± 5.65	P = 0.1909
HBI SYSTOLIC BP	694.48 ± 357.33	448.88 ± 357.57	P = 0.0801	553.04 ± 305.45	331.66 ± 329.90	P = 0.2543
HBI DIASTOLIC BP	267.79 ± 211.85	128 ± 192.87	P = 0.0864	261.81 ± 321.82	140.33 ± 160.98	P = 0.5321
MAP	112.98 ± 9.14	99.62 ± 13.24	P = 0.0015	106.98 ± 10.13	99.77 ± 6.77	P = 0.2480
Values are presented as mean ± SD.						

In our study, maximum patients of mean systolic BP were 16 (25.39%) who fell in the 151-160 mm hg range.

Maximum male patients were 9 (14.27%) in 161-170 mm hg 24 hour mean systolic BP range , out of which 8 (12.69%) were on dialysis and 1(1.58%) was not on dialysis

Maximum female patients were 8 (12.69%) in 151-160 mm hg 24 hour mean systolic BP range, out of which 7 (11.11%) were on dialysis and 1(1.58%) was not on dialysis

Maximum patients of mean diastolic BP were 21 (33.33%) who fell in 86-90 mm hg range,

Maximum male patients were 13 (20.63%) in 86-90 mm hg 24 hour mean

diastolic BP range, out of which 11 (17.46%) were on dialysis and 2(3.17%) were not on dialysis.
Maximum female patients were 8 (12.69%) in 86-90 mm hg 24 hour mean diastolic BP range, out of which 7 (11.11%) were on dialysis and 1 (1.58%) was not on dialysis.
PTE (percent time elevation) indicates the duration of the day spent in a high blood pressure state. It is a qualitative measure of high blood pressure. It is measured in percentage with maximum being 100.
In our study maximum number of patients, 15 (23.80%) fell in the 81-90 range of systolic BP PTE , out of which 14(22.22%) were undergoing dialysis. 57 (90.47%) patients had more than 50% systolic PTE which is quite significant compared to 6 (9.52%) patients having less than 50% PTE.
In our study maximum number of patients , 11 (17.46%) fell in the 21-30 diastolic BP PTE. 6 (9.52%) patients fell in the maximum range 91-100 diastolic PTE out of which 5 (7.93%) were o n dialysis.
HBI (HYPERBARIC IMPACT) is a quantitative measure of high blood pressure suggesting how long and how elevated the blood pressure was in the 24 hour ABPM cycle.
In our study we found the maximum number of patients 16(25.39%) had systolic HBI in the
range of 201-400
>1000 HBI was present in 7 patients all of which were undergoing dialysis.

In our study we observed that maximum number of patients 13 (20.63%) had diastolic HBI in the range of 101-150. 10 patients (15.87%) had diastolic HBI of >400 out of dich 9 patients were undergoing dialysis which was significant.

Mean arterial pressure is calculated by
MAP| = DBP + [(SBP-DBP)/3] where DBP and SBP are diastolic blood pressure and systolic blood pressure. The means of systolic and diastolic blood pressures are taken into the formula.The normal range should be 70-110mmhg.

In our study we found that 36 (57.14%) patients had mean arterial pressure fall in the 70-110mmhg range out of which 27 (42.85%) were on dialysis.27(42.85%) patients had mean arterial pressure >110mmhg out of which 24 (38.09%)
were undergoing dialysis which was significant.

DISCUSSION

Our study had 63 patients whereas Catia et al.[1] Chaudhary et al.[7] Agarwal et al [13] and Satoshi et al [14] had 54,80, 217, 1075 patients respectively. In our study. 38 (60.31%)were males which was comparable with other studies,which is showing CKD is more common in males compared to females[15].

In our study 44 (69.84%) patients had history of diabetes which was significantly higher compared to other studies whereas Catia et al had 42.6%, Agrawal et al 41.9%,Satoshi et al had 35.44% diabetics, showing long standing diabetes being underlying cause of CKD [16].

In Catia et al 100% patients had hypertension whereas in our study 90.47% patients were hypertensive,which is comparable.

In our study 16(25 39%) had a history of ischemic heart diseases whereas in Catia et al and Agarwal et al it was 11.1% and 38.2 respectively,which is comparable.

Average age in our study was 52.9 years whereas in Catia et al, Chaudhary et al.,Agarwal et al it was 59.48 and 67 respectively.

Most common age group in our study was 61-70 years,favouring that CKD developed at a higher age in our geographic region where Hypertension and Diabetes are the leading causes [14].

Duration of our study was 18 months whereas Catia et al, Chaudhary et al, Agarwal et al it was 4 years, 13 months and 3.5 years respectively.

In our study total 51(80.95%) patients were on dialysis and 12 (19.04%) were not on dialysis whereas Catia et al included only patients who were not on dialysis. There was a significantly higher number of patients undergoing dialysis in our study due to the fact that we have a fully functional nephrology department having a state of the art dialysis unit .

In our study 2(3.17%) patients were CKD stage I,5(7.93%) patients were CKD stage II,1(1.58%) patient was stage llll, 6(9.52%) patients were stage IV and 49 (77.77%) were stage V. In Catia et al stages I, Il included 11(20.4%) patients, stage lll included 25(46.3%) and stages IV, V included 18 (33.3%),which is can be due to higher number of patients presented to us at late stage or higher number of patients in our study were on dialysis [17] .

Out of 63 patients 16(25.39%) patients were dippers ,21 (33.33%) were non dippers, 21(33.33%) were reverse dippers and 5 (7.93%) patients were extreme dippers. In Chaudhary et al 32 (40%) were dippers and 48 (60%) were non dippers. In Agarwal et al 105 (48,38%) patients were dippers and 112 (58.62%) were non dippers. In Satoshi et al 395 (36.73%) were dippers. 408(37.94%) were non dippers which was comparable

to our study which had 33.33% of nondippers, 105 (9.76%) were extreme dippers which was comparable to our study which had 7.93% of extreme dippers and 167(15.53%) were reverse dippers,showing that no dipping is more common in patients with CKD [18] .

Mean clinical systolic BP in our study was 161.71mmhg whereas Chaudhary et al it was 146mmhg, Agarwal et al had 155.2mmhg. In Satoshi et al, mean clinical systolic BP in male was 132 mmhg and in females it was 129.8mmhg.
Mean clinical systolic BP in patients on dialysis was 165.42 in comparison to patient not on dialysis which was 146 which was clinically significant in our study (p: 0.0004)

Mean clinical diastolic BP in our study was 90.28mmhg whereas Chaudhary et al it was 82mmhg, Agarwal et al had 84.7mmhg.In Satoshi et al mean clinical diastolic BP in male was 77.6mmhg and in females it was 76.3 mmhg.
Mean clinical diastolic BP in patients on dialysis was 92.23 in comparison to patient not on dialysis which was 82 which was clinically significant in our study (p: 0.0005)

Mean 24 hour systolic BP in our study was 153.47mmhg. In Calia et al it was 137.3mmhg. In Chaudhary et al it was 136mmhg and in Agarwal it was 133 mmhg.
Mean 24 hour systolic BP in patients on dialysis was 157.50 in comparison to patient not on dialysis which was 136.33 which was clinically significant in our study (p: 0.0001)

Mean 24 hour diastolic BP in our study was 85.79mmhg. In Catia et al it was 76.6mmhg. In Chaudhary et al it was 78mmhg and in Agarwal it was 73.1 mmhg.

Mean 24 hour diastolic BP in patients on dialysis was 86.84 in comparison to patients not on dialysis which was 81.33 which was clinically significant in our study (p: 0.049).
MAP was higher in patients on dialysis (Male:112.98,Female:106.98) in comparisons to patients not on dialysis(Male:99.62,Female:99.77).In male it was statistically significant (p: 0.0015)and in female it was not statistically significant ,which can be due to low number of female patients in comparison to male.

PTE systolic and diastolic BP are higher in our study ,which coincides with elevated blood pressure in CKD patients [19] .

PTE systolic BP was higher in patients on dialysis (Male: 77.82,Female: 77.45) in comparisons to patients not on dialysis(Male: 57..66,Female: 61.).In male it was statistically significant (p: 0.0129)and in female it was not statistically significant ,which can be due to low number of female patients in comparison to male.

PTE diastolic BP was higher in patients on dialysis (Male:48.27,Female:46.85) in comparison to patients not on dialysis(Male: 36.33,Female: 26),which was statistically insignificant.

HBI systolic and diastolic BP are higher in our study ,which coincides with elevated blood pressure in CKD patients [19].

HBI systolic BP was higher in patients on dialysis (Male:694.48,Female:553.04) in comparison to patients not on dialysis(Male:448.88,Female:331.66),which was statistically insignificant.

HBI diastolic BP was higher in patients on dialysis (Male:267.79,Female:261.81) in comparison to patients not on dialysis(Male:128,Female:140.33),which was statistically insignificant.

LIMITATIONS

The study of 63 patients cannot be extrapolated to the general population

Moreover this study was done in a single centre So, it cannot be correlated differences observed because of regional variations.

Due to the small sample size of our study, statistical significance could not be gemid the general population

CONCLUSION

ABPM is an invaluable tool in predicting the future communications in CKD patients.

Identifying such patients of hypertension in earlier stages of CKD,helped in morbidity outcomes while identifying in later stages of CKD helped in mortality benefits.

Also dose modification is of utmost importance in newly diagnosed hypertensives as well as known cases of CKD as it will prevent complications in newly diagnosed and also help in delaying the worsening of CKD stages.Treatment guideline can vary depend on whether patient is on dialysis or

not on dialysis [20,21,22] .

Diurnal index is the main parameter depicting the current state of hypertension control in patients of CKD. The number of patients having abnormal dipping patterns are invariably in late stages of CKD and undergoing dialysis.

Treatment protocols must be made for non dippers and reverse dippers as they are at highest risk of cardiovascular risk factors. Such patients should receive night time anti-hypertensive dose
Morning surge is itself a strong predictor of cardiovascular risk factors and measures should be taken to keep that in check [6,10] .
PTE should be kept under 50% for optimal treatment goals as it is a strong predictor for worsening hypertensive status especially in CKD patients.

As HBI is a quantitative measure of hypertensive status measures should be taken to keep that as low as possible.

MAP should be kept in the suggested range as even slight changes (high or low) are detrimental to the patient.

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