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AMBULATORY BLOOD PRESSURE MONITORING IN CHRONIC KIDNEY DISEASE

DR. SANMITA RAM. S, DR. R. VEDAVATHI

BACKGROUND:
Hypertension is a global problem, and its incidence and prevalence increase with the declining glomerular filtration rate (GFR) in Chronic kidney disease. It is also the single most powerful predictor of cardiovascular (CV) disease and mortality. ABPM allows a serial BP measurements at specified time intervals throughout a 24-hour period, thereby providing a better assessment of the normal fluctuations in BP levels associated with a person's daily activities and sleep. Hence, ABPM is particularly useful in evaluating the patient with highly variable BP with wide discrepancies between the BP readings obtained in and outside office. The association between masked hypertension and lower eGFR was observed only in those participants with elevated night-time BP. In this study, we aimed to determine the effect of circadian rhythm over hypertension in CKD and non-CKD patients and the associated prognostic value by assessing the target organ damage.
MATERIALS AND METHODS:
This is a prospective observational study after enlisting inclusion and exclusion criteria conducted at a tertiary care centre on 60 patients after obtaining written consent, of whom 30 had CKD and 30 controls were hypertensives not having CKD. ABPM machine was tied to the case and control and blood pressure was measured at intervals of every 30 minutes during the morning hours and hourly during the night.
OBSERVATIONS:
Out of the total 60 patients included in this study, the CKD group showed 53.33% were reverse dippers, 33.33% non-dippers, 13.3% were dippers while the control group showed 76.6%% were dippers, 16.7% were non-dippers, 6.7% being reverse dippers. The Mean SBP being 157.03 + 16.89 in the case group, while it was 136.33 + 10.75 in the control group (p value>0.001), Mean DBP being 85.57 + 13.09, and in the control group being 82.50 (p value<0.331). The mean systolic and diastolic pressure was found to be more in the passive period than in the active period.
CONCLUSION:
ABPM has enabled a more comprehensive estimate of a patient and true BP and its adverse outcomes. Nocturnal BP is superior to day-time BP in predicting CVD outcomes. This study shows both systolic and diastolic pressure variability over 24hrs maximum during night hours (nocturnal hypertension) and non-dipping of early morning BP in CKD. Both Reverse and non-dipping status are associated with increased risk of target organ damage and CV risk.
KEYWORDS: Ambulatory blood pressure monitoring, 24 hours, Continuous, Target Organ Damage, Chronic kidney disease.

INTRODUCTION:

Non-communicable diseases are said to kill 40 million people each year, equivalent to 70% of all deaths globally[1]. Hypertension is a chronic condition of ultimate concern because it plays an important role in the causation of stroke, coronary artery disease (CAD), and other vascular complications. It is one of the most common disease which poses as a major public health problem to the population undergoing a socioeconomic expansion. It is one of the major risk factors for CVD mortality, accounting to around 20-50% of all deaths[1]. According to the NFHS 4-National fact sheet, the prevalence of hypertension is more widespread in men (13.6 %) than in female (8.8%) population and is also said to be higher in the urban subjects than in the rural counterparts[1]. The latest data in India shows that presently the prevalence in urban areas is 33.8% and in rural areas, it is 27.6% with an overall prevalence of 29.8%[2].

Hypertension is commonly encountered in patients with CKD, and its incidence and prevalence increase with declining glomerular filtration rate (GFR)[3]. Also, Amongst the patients with

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hypertension, elevated SBP is associated with incident CKD and a more rapid decline in renal function[1].

Chronic kidney disease is a major public health concern worldwide with regard to the number of individuals affected and therapeutic costs involved. According to the results of the 2013 Global Burden of Disease Study, CKD contributed to 956,200 deaths, a 134% increase from 1990. Studies have reported that CKD affects >10% of the population in several countries and >50% of high-risk subpopulations. In developed countries, CKD affects nearly 7% of all individuals aged ≥30 years, which translates to greater than 70 million individuals. Furthermore, the prevalence of CKD increases with age and exceeds 20% in individuals aged more than 60 years and 35% in individuals aged more than 70 years. Globally, it has been estimated that more than 1.4 million individuals with ESRD receive renal replacement therapy with dialysis or transplantation[4].

Ambulatory blood pressure monitoring (ABPM) has become an established clinical tool for the evaluation and management of hypertension both in clinical practice and in the research setting. ABPM allows serial Blood Pressure measurements at specific time intervals throughout a 24-hour period, thereby providing a better assessment of the normal fluctuations in BP levels associated with daily activities and sleep. It has been found that at least 20-25% of patients diagnosed with stage I-II hypertension (DB P 90-104 mm Hg) are normotensive outside the physician's clinic[6]. Hence, ABPM is particularly useful in evaluating the patient with highly variable BP with wide discrepancies between the BP readings obtained.

OBJECTIVE:

To describe ABPM characteristics in a group of CKD and hypertensive patients.

MATERIALS AND METHODS:

Permission to perform study was obtained from the Institutional Ethical committee. A total of 60 patients was subjected in the study and divided into two study groups. Group 1(cases) consists of 30 hypertensive patients having Chronic kidney disease and Group 2(controls) consists of 30 hypertensive patients without chronic kidney disease. A prospective observational study was conducted from January to June 2019 conducted at R L Jalappa Hospital, Tamaka, Kolar. All participants were provided with a written informed consent prior to being enrolled in the study.

Patients who have any Malignancy, Collagen Vascular diseases, Pregnant women or the ones who have had a renal transplant have been excluded from the study.

All data were collected, including demographic history, relevant medical history and previous history of ischemic heart disease or cerebrovascular diseases, lab parameters, medications, 2D echocardiography were noted as per "The WHO-UMC system for standardised causality assessment".

STATASTICAL ANALYSIS:

Analysis done using software - SPSS 16 version. Chi square test used to test qualitative data (BP dipping and ECG changes). Independent t test (student t test) used for comparing quantitative data (for BP).

Graphical representation of data: MS Excel and MS Word was used to obtain various types of Graphs such as bar diagrams or pie charts.

P-value less than 0.05 indicates statistically significant and p value less than 0.001 indicates highly significant.

RESULTS:

In our study a total of 60 hypertensive subjects were taken and were differentiated based on having CKD and not having CKD.

Demographic characters		**CKD group**	**Control**	**Total**
Gender	Male	21 (70%)	18 (60%)	39 (65%)
	Female	09 (30%)	12 (40%)	21 (35%)

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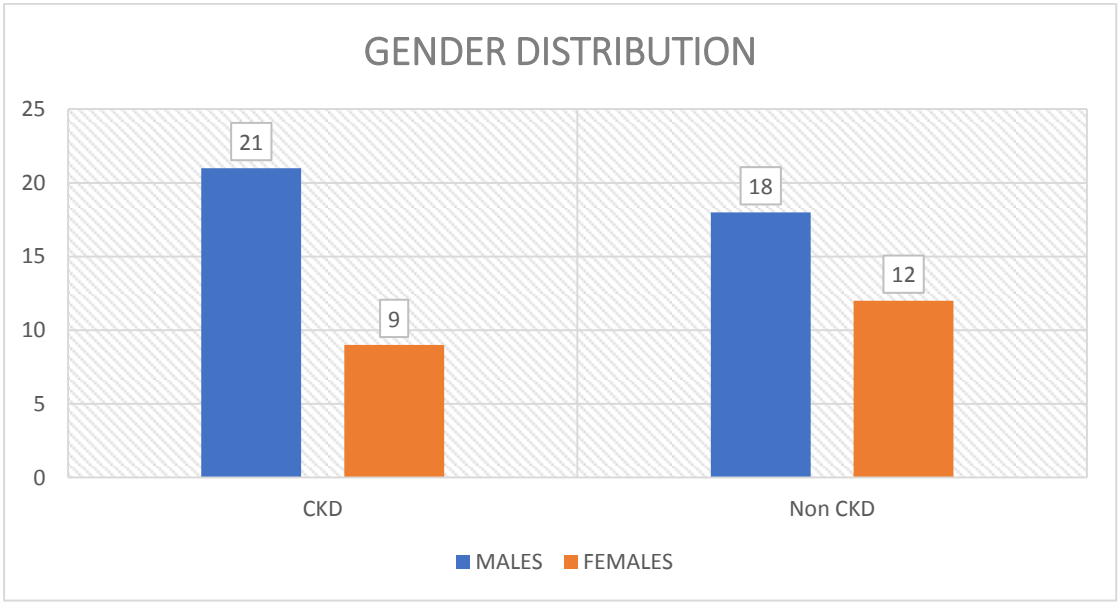

Figure 1

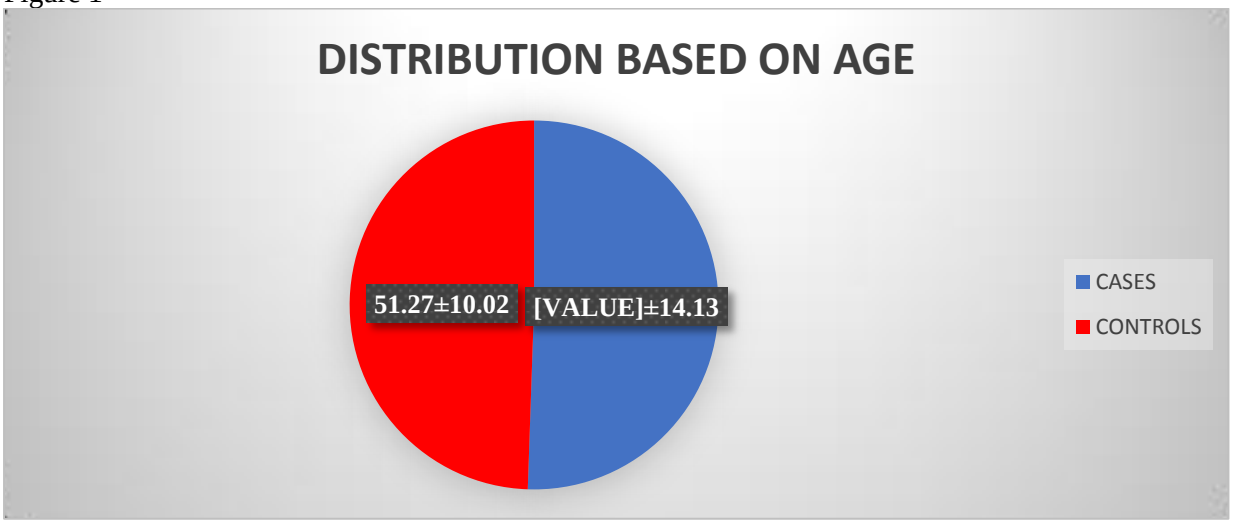

Figure 2

The following is the example of the graph obtained in a patient after 24 hours of ABPM.

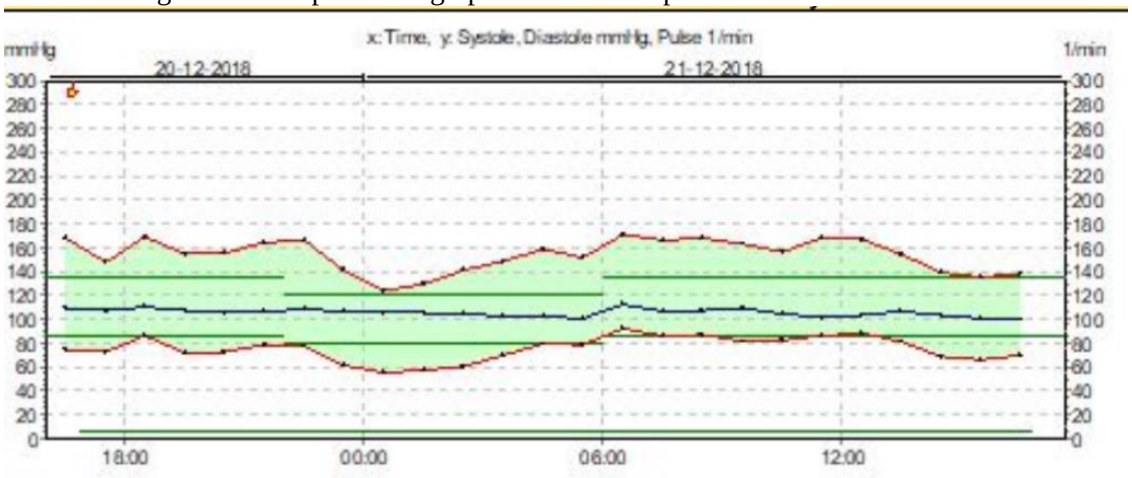

Figure 3

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The following table shows the overall mean of the blood pressure with its p value recorded in 24 hours:

Blood pressure	CKD group	Control	P value
Mean SBP (mmHg)	157.03 + 16.89	136.33 + 10.75	<0.001
Mean DBP(mmHg)	85.57 + 13.09	82.50 + 11.05	0.331
Maximum SBP(mmHg)	190.67 + 24.27	166.17 + 17.15	<0.001
Maximum DBP(mmHg)	102.37 + 18.61	101.20 + 10.89	0.768
Minimum SBP(mmHg)	122.13 + 26.06	109.93 + 13.02	0.025
Minimum DBP(mmHg)	65.63 + 19.96	63.07 + 13.22	0.559

Table 1

Table 2 shows blood pressure recorded during active period (during normal physical activity and morning hours). The mean systolic and diastolic pressure recorded was 153.07+17.03mmHg and 82.90+12.33mmHg respectively in case group, while the control group showed mean systolic and diastolic pressure recorded of 140.20+ 10.26 and 84.47+ 9.97 mmHg, respectively.

Blood pressure	CKD group	Control	P value
Active period mean SBP	153.07 + 17.03	140.20 + 10.26	0.001
Active period mean DBP	82.90 + 12.33	84.47 + 9.97	0.590

Table 2

Table 3 shows blood pressure recorded during passive period (during rest, late night and early morning hours). The mean systolic and diastolic pressure recorded was 154.20+24.41mmHg and 80.83+14.96 mmHg respectively in case group, while the control group showed mean systolic and diastolic pressure recorded of 128.20+ 12.42 and 76.2+ 10.25 mmHg, respectively.

Blood pressure	CKD group	Control	P value
Passive period mean SBP	154.20 + 24.41	128.83 + 12.42	<0.001
Passive period mean DBP	80.83 + 14.96	76.20 + 10.25	0.167

Table 3

Target organ damage was assessed in each group and the results are as follows.

Target organ damage	CKD group	Control	Total
NPDR	3 (10%)	1 (3.3%)	4 (6.7%)
Proliferative diabetic retinopathy	5 (16.7%)	2 (6.7%)	7 (11.7%)
HTN retinopathy	11 (36.7%)	10 (33.3%)	21 (35%)
Mixed retinopathy	5 (16.7%)	3 (10%)	8 (13.3%)
LVH	16 (53.3)	7 (23.33%)	23 (38.33%)

Table 4

The following table shows the dipping pattern observed in our study group including both cases and controls and the different patterns seen in them.

		CKD group	Control	Total	P value
BP dipping	Dipper	3 (10%)	23 (76.6%)	26 (43.33%)	<0.001
	Non dipper	10 (33.3%)	05 (16.7%)	15 (25%)	
	Reverse dipper	16 (53.3%)	02 (6.7%)	18 (30%)	
	Extreme dipper	1(3.33%)	0	1(3.33%)	

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Table 5

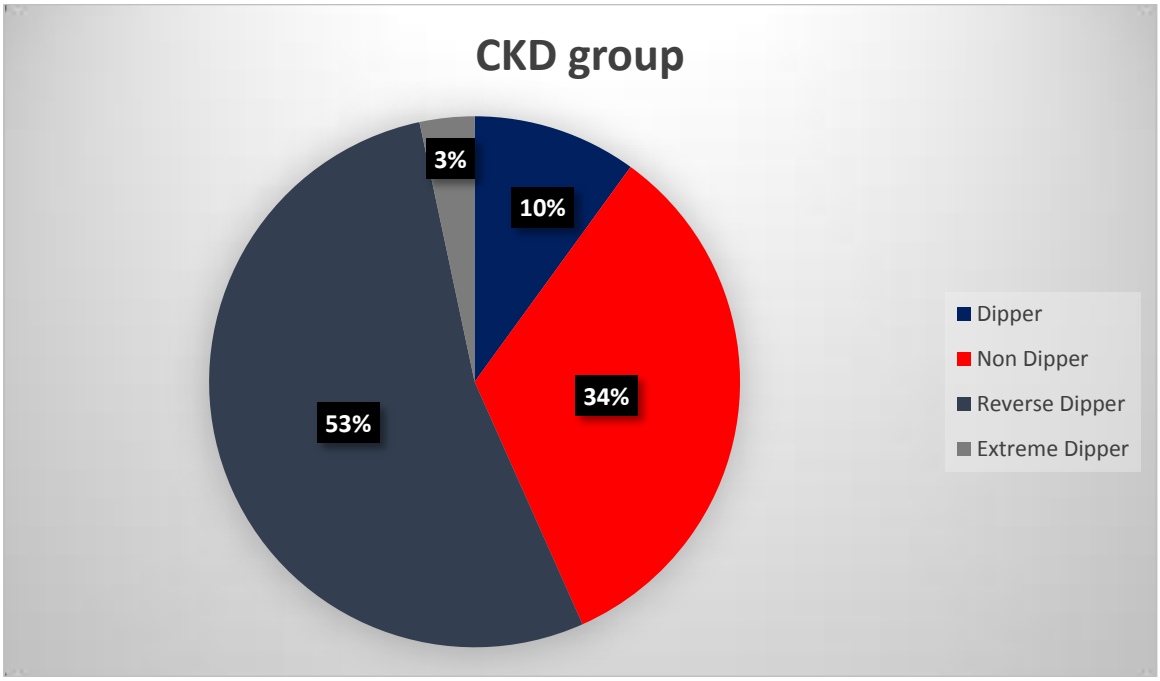

Figure 4

DISCUSSION:

A 24-h BP profile helps to determine the absence of nocturnal dipping status and evaluate BP control in patients on antihypertensive therapy. Not only the ability to detect white-coat or masked hypertension is enhanced by Ambulatory blood pressure monitoring (ABPM) but also has been found to be clinically useful in the identification of nocturnal hypertension (non-dippers), resistant hypertension, episodic hypertension, evaluate the effect of antihypertensive drugs and in individuals with hypotensive episodes while on antihypertensive medication. Current Thresholds for Hypertension Diagnosis Based on ABPM for 24-hour average is >130/ 80 mmHg, while Awake (daytime) average being ≥135/85, Asleep (night-time) average is >120/ 70 mmHg[4].

ABPM is a better predictor of Hypertension-mediated organ damage (HMOD) than office BP. Furthermore, 24 h ambulatory BP mean has been consistently shown to have a closer relationship with morbid or fatal events and is a more sensitive risk predictor than office BP of CV outcomes such as coronary morbid or fatal events and stroke[5]. ABPM might better define the relationship between BP, target organ damage (TOD), and clinical outcomes.

Also, the definitions of the different dips known were laid down, as follows,

Dipping Nocturnal BP- Fall of about 15% of daytime values in normotensive and hypertensive patients

Non-dipping- Absence of nocturnal fall in BP by at least 10%

Extreme dipping- A marked fall in BP during the night by >20%

Reverse dipping or rising- Increase in BP levels during sleep to levels higher than in daytime[7].

In our study, the dipping population correlated with the older studies in the control group. But the cases group showed varied results. In the past, Reverse dipping hasn't been described in many studies which could have been the reason for lack of mention. Reverse dipping was prevalent in patients with Chronic kidney disease which also is a risk factor for the development of cardiovascular morbidity and mortality as suggested by Kumar SS et al.

A study by Minutolo et al. evaluated the prognostic role of daytime and night-time systolic and diastolic BP in 436 consecutive CKD patients. Primary end points were taken as time to renal death (ESRD or death) and time to fatal and nonfatal cardiovascular events. Of note, dipping status was based on the night to day ratio of mean ambulatory BP. Patients were stratified as extreme dippers,

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dippers, non-dippers, and reverse dippers when the night to day ratio was less than 0.80, 0.80 to less than 0.90, 0.90 to 1.00, and greater than 1.00, respectively[8].
Target organ assessment done in our study, also revealed that maximum number of patients in the CKD group were associated with LVH as evidenced on ECG and 2D ECHO, also retinopathy was at increased prevalence amongst the group of CKD, which was another strong predictor as a prognostic value to development of cardiovascular morbidity and mortality.
Generally, the association between office BP and Target Organ Damage is relatively poor. On the other hand, the closer correlation between TOD and ambulatory BP is well established regardless of whether the damage is quantified in the heart (LVH or LV dysfunction), brain (cerebral lacunae or white matter lesions at magnetic resonance imaging), small and large arteries, or kidney (progression of CKD, moderately increased albuminuria or overt proteinuria).

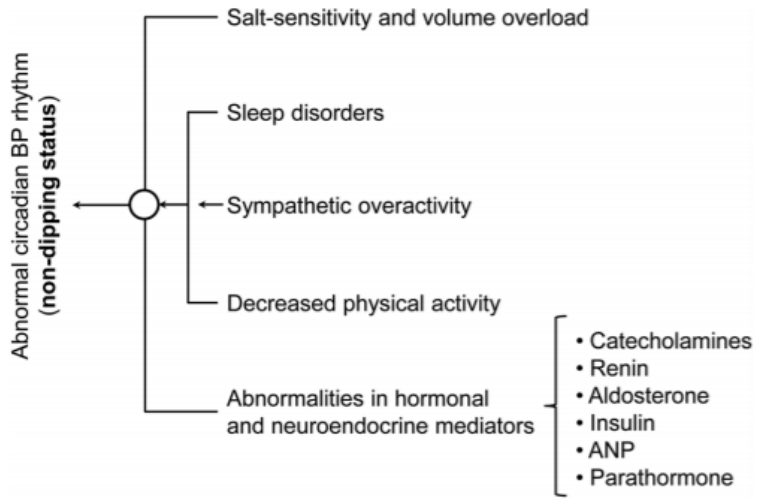

Figure 5- Key elements explaining the abnormal circadian blood pressure rhythms in chronic kidney disease patients. BP- blood pressure, ANP- atrial natriuretic peptide[8].
The figure 5 represents the different mechanisms involved in the reason for the nocturnal hypertension present in the CKD group which is evidenced as a dip in the general population during the night time.
In a 8-week uncontrolled trial, changing the timing of antihypertensive medication dosing from morning to evening decreased the night/day ratio of mean ambulatory BP in 93.7% of 32 CKD patients and restored normal circadian rhythm in 87.5%[9]. Furthermore, proteinuria was also reduced by the evening administration of antihypertensive drugs[9].
Despite several studies conducted in this area, the prognostic impact of ambulatory BP in CKD patients should be better clarified. Future studies should also investigate whether or not re-timing drug treatment according to individual ABP profiles could be advantageous in these patients.

CONCLUSION:

Over the past 30 years, The introduction of ABPM has enabled a more comprehensive estimate of a patient's true BP and its adverse outcomes. Many studies support the use and superiority of ABPM over Office BP measurements. Nocturnal BP is evidenced to be superior to day time BP in predicting the CVD outcomes. This study shows both systolic and diastolic pressure variability over 24hrs maximum during night hours (nocturnal hypertension)- reverse-dipping and non dipping of early morning BP. Both non and reverse-dipping status are associated with target organ damage and CV risk. Management of hypertension in CKD patients should focus on choosing appropriate use of antihypertensive drugs to reduce the level of nocturnal BP and restore diurnal rhythm of BP. In the meantime, ambulatory or some form of home BP monitoring should be used to obtain a more accurate picture of BP control in patients with chronic and ESRD. Office BPs frequently under- or overestimate the true BP in CKD patients and dialysis center BP measurements, although widely used

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to guide therapy, are poor indicators of interdialytic BPs. Tight BP control is needed to limit the progression of renal disease and lessen cardiovascular morbidity and mortality in patients with kidney disease. However, to achieve this goal, BP must be accurately measured. Ambulatory or some form of home BP monitoring should be more widely adopted in patients with chronic and ESRD.

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