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Analysis of 24-hour urinary sodium excretion and its co-relation with 24-hour blood pressure in healthy subjects, chronic kidney disease patients and maintenance dialysis patients

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ABSTRACT

Background: Hypertension is one of the most important modifiable risk factors for progression of CKD and also cardiovascular events in CKD patients. Accurate blood pressure (BP) measurement aids in the diagnosis and treatment of hypertension. ABPM has been successful in identifying hypertensive CKD patients at increased risk. The present study investigated correlation of 24-hour urinary sodium excretion and 24-hour ambulatory blood pressure in various stages of CKD patients and healthy population.

Materials & Methods: 100 patients fulfilling the criteria were recruited from the nephrology wards. Patients were divided into 3 groups. Group 1: healthy subjects, Group 2: chronic kidney disease patients not on dialysis and Group 3: maintenance dialysis patients. Data on medical history, laboratory test results and current therapy were collected. The24-hourambulatorybloodpressure and 24-hour urine sodiumofallpatients were measured.24-hour ambulatory blood pressure of all patients measured with automated, programmable, oscillometric ambulatory blood pressure monitor with LCD display device named ABPM – 05, manufactured by Meditech Ltd. 1184 Budapest, MikszáthKálmánutca 24, Hungary. ABPM was obtained while patient was receiving regular antihypertensive therapy. Measurement of 24-hour urine sodium was done by Indirect Integrated Multisensor Technology (IMT) by Ion Selective Electrode method. Results thus obtained were assessed statistically.

Results: The mean 24-hour urine sodium (mmol/day) was 112.5 ± 44.6 in group I, 107.7 ± 61.9 in group II and 74.8 ± 26.1 in group III, eGFR (ml/min/1.73 m2) was 102.8 ± 20.9 in group I, 34.6 ± 32.4 in group II and 6.6 ± 4.2 in group III. SBP (mm Hg) was 125 ± 12.5 in group I, 137.6 ± 20.7 in group II and 146.7 ± 18.7 in group III. DBP (mm Hg) was 76.7 ± 7.3 in group I, 82 ± 13.2 in group II and 88.3 ± 13.1 in group III. 24-hours mean MAP (mmHg) was 92.8 ± 8.5 in group I, 100.5 ± 14.2 in group II and 107.8 ± 13.9 in group III. inCKDpopulation,thereisnocorrelation of 24-hour blood pressure with 24-hour urinary sodium excretion

Conclusion: There is a positive but not statistically significant correlation between 24-hoururinarysodiumandmeanSBPinCKDpatientsnotondialysis.

Key words: 24-hourblood pressure, CKD, 24-hour urine sodium.

Introduction

Hypertensionisoneofthemostimportantmodifiableriskfactorsforprogression of CKD and also cardiovascular events in CKD patients.[1]Accurate bloodpressure (BP) measurement aids in the diagnosis and treatment of hypertension. Thisis particularly relevanttoCKD patients,in whom achievementof BPcontrol isdifficult.[2]

High systolic blood pressure (SBP) is the largest contributor to the globaldiseaseburdenthataccountsforannual10.4milliondeathsand218milliondisability- adjusted life years globally.[3]In high-income settings, ambulatory bloodpressuremonitoring(ABPM)isasignificantlybetterpredictoroffuturecardiovascular risk than office or home BP measurement. It is also the only way todetect abnormal nocturnal dipping patterns that are an independent risk factor forfuture cardiovascularevents.[4]

Accumulateddataindicatethatambulatorybloodpressuremonitoringissuperior and better in detecting hypertension compared to office BP measurement.ABPM has been successful inidentifying hypertensive CKD patients at increasedrisk.[5] ABPM help in assessment of circadian BP variation and also short-term BPvariability,whichisusuallyassociatedwithadversecardiovascularandrenaloutcomes. ABPM patterns of normal dipping,non-dipping, extreme dipping, andreversedippingare associated withtargetorgandamageand

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clinicaloutcome.[6] The present study investigated correlation of 24-hour urinary sodium excretion and 24-hour ambulatory blood pressure in various stages of CKD patients and healthy population.

Materials & methods

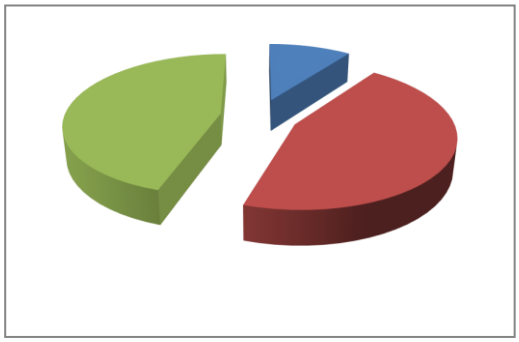
100 patients were recruited from the nephrology wards from 1st January 2019 to 30th November 2020. CKD patients with hypertension were included, if they had monitored their blood pressure for at least 3 months in nephrology OPD.

Exclusion criteria were used such as daily intake of nonsteroidal anti-inflammatory drugs, regular intake of steroids, patients on diuretic initiation in the previous 1 month before taking samples, if the period of urine collection was less than 24 hours, urinary samples in which estimation of sodium, creatinine, cannot be done properly/ undetermined due to technical reasons and inadequate ABPM (Number of BP recordings less than 80%).

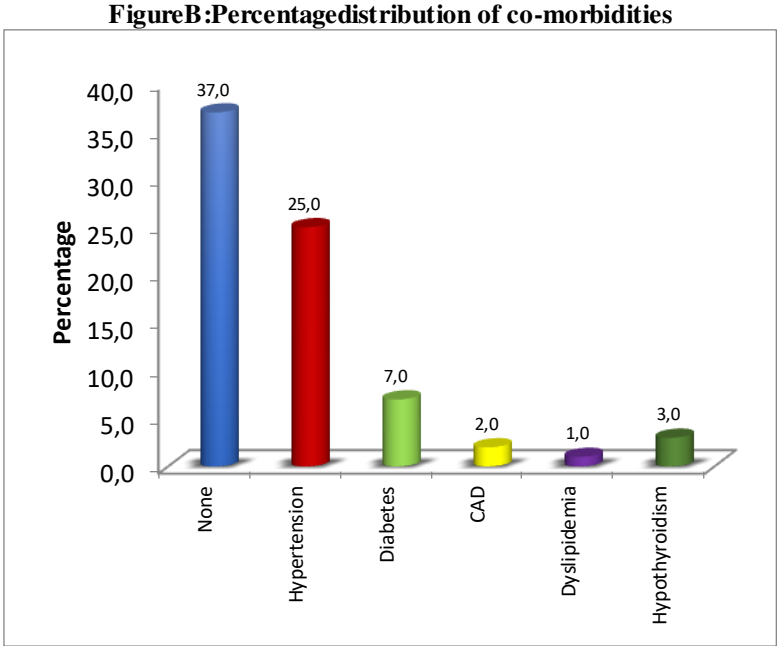
Patients were divided into 3 groups. Group 1: healthy subjects, Group 2: chronic kidney disease patients not on dialysis and Group 3: maintenance dialysis patients. Data on medical history, laboratory test results, and current therapy were collected.The24-hourambulatorybloodpressureofallpatientsmeasuredwithautomated,non-invasive,compact,light-weight,programmable,oscillometricambulatory blood pressure monitor with LCD display device. Results were assessed statistically. 24-hour urine collection was done from 8am to 8am for which Each participant received a 4-L plastic container.

Results

FigureA:Percentagedistributionofsamplesaccordingtogroups



FigureB:Percentagedistribution of co-morbidities



ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

Table ADescriptivestatisticsregarding24-hoururinesodiumbasedongroup

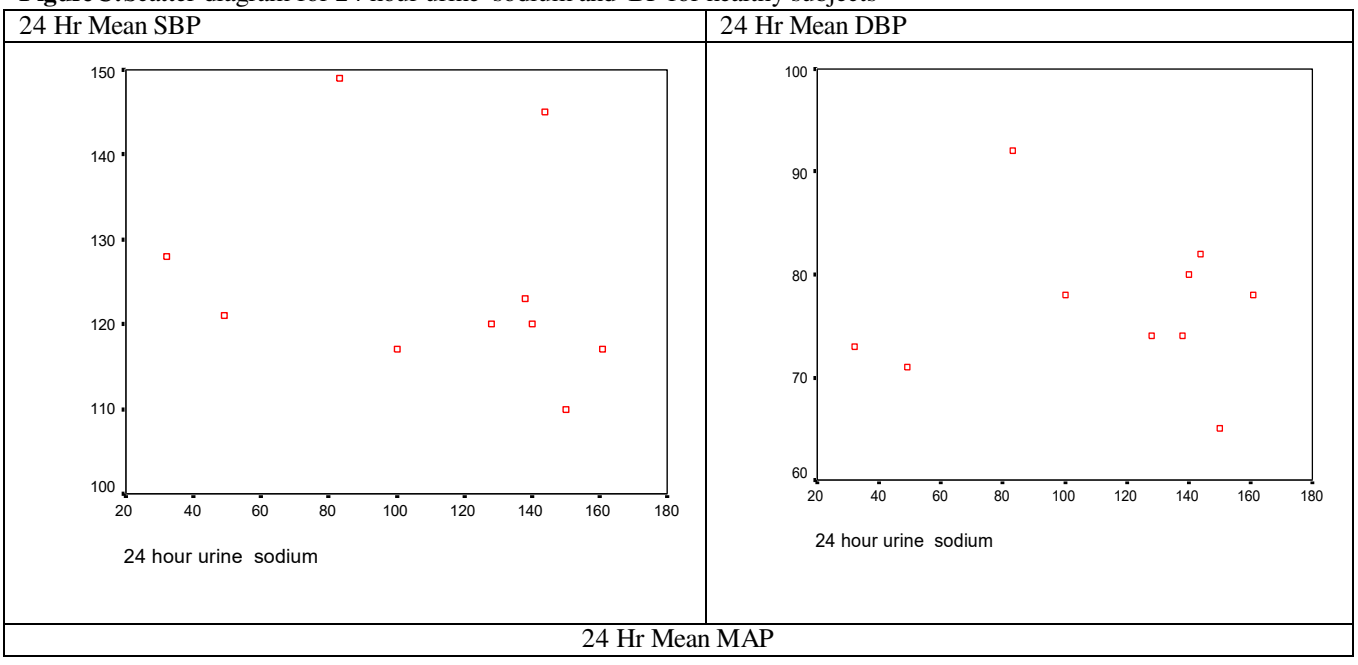
Parameters	Group I	Group II	Group III
24-hour urine sodium(mmol/day)	112.5± 44.6	107.7± 61.9	74.8± 26.1
eGFR (ml/min/1.73 m2)	102.8± 20.9	34.6± 32.4	6.6± 4.2
Mean SBP (mm Hg)	125±12.5	137.6± 20.7	146.7± 18.7
Mean DBP (mm Hg)	76.7± 7.3	82±13.2	88.3± 13.1
24-Hour Mean MAP (mmHg)	92.8± 8.5	100.5± 14.2	107.8± 13.9

Table II shows that mean 24-hour urine sodium (mmol/day) was 112.5 ± 44.6 in group I, 107.7 ± 61.9 in group II and 74.8 ± 26.1 in group III, eGFR (ml/min/1.73 m2) was 102.8 ± 20.9 in group I, 34.6 ± 32.4 in group II and 6.6 ± 4.2 in group III. DBP (mm Hg) was 76.7 ± 7.3 in group I, 82 ± 13.2 in group II and 88.3 ± 13.1 in group III. 24-hours mean MAP (mmHg) was 92.8 ± 8.5 in group I, 100.5 ± 14.2 in group II and 107.8 ± 13.9 in group III.

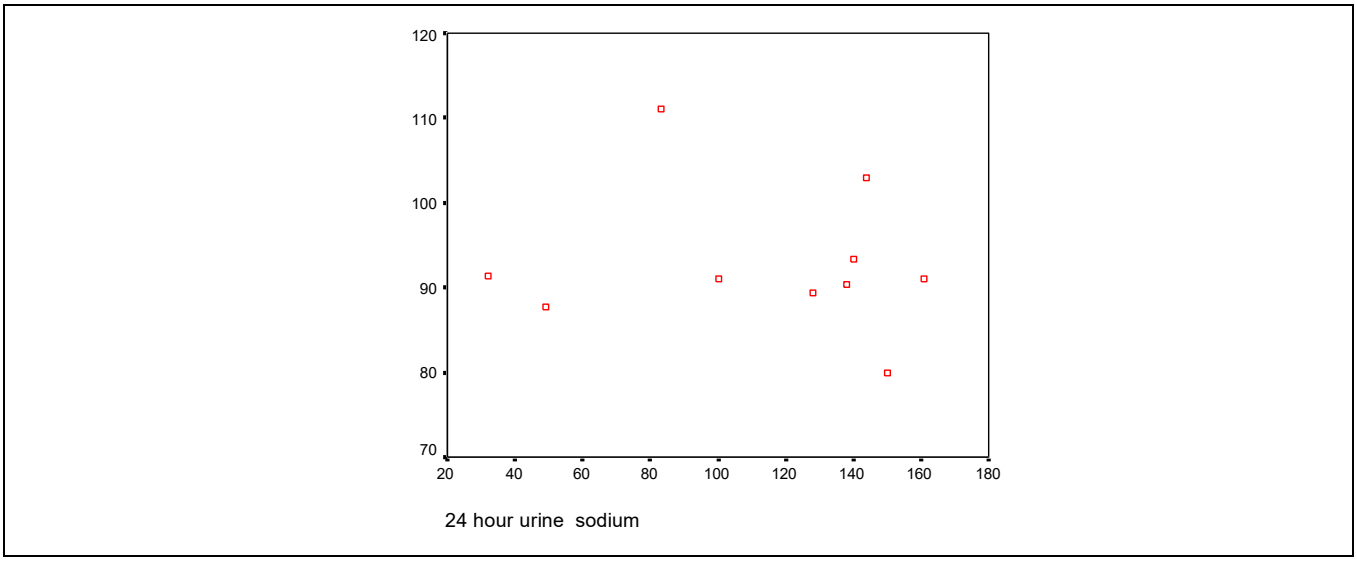
TableB:Comparisonofdippingbasedongroups

Dipping	Healthysubjects		CKD patients notondialysis		Maintenancedialysispatients	
	Count	Percent	Count	Percent	Count	Percent
Dipper	1	10.0	6	13.3	6	13.3
ReverseDipping	0	0.0	15	33.3	14	31.1
ExtremeDipper	1	10.0	0	0.0	0	0.0
No Dipper	8	80.0	24	53.3	25	55.6

FigureC: Scatter diagram for 24 hour urine sodium and BP for healthy subjects

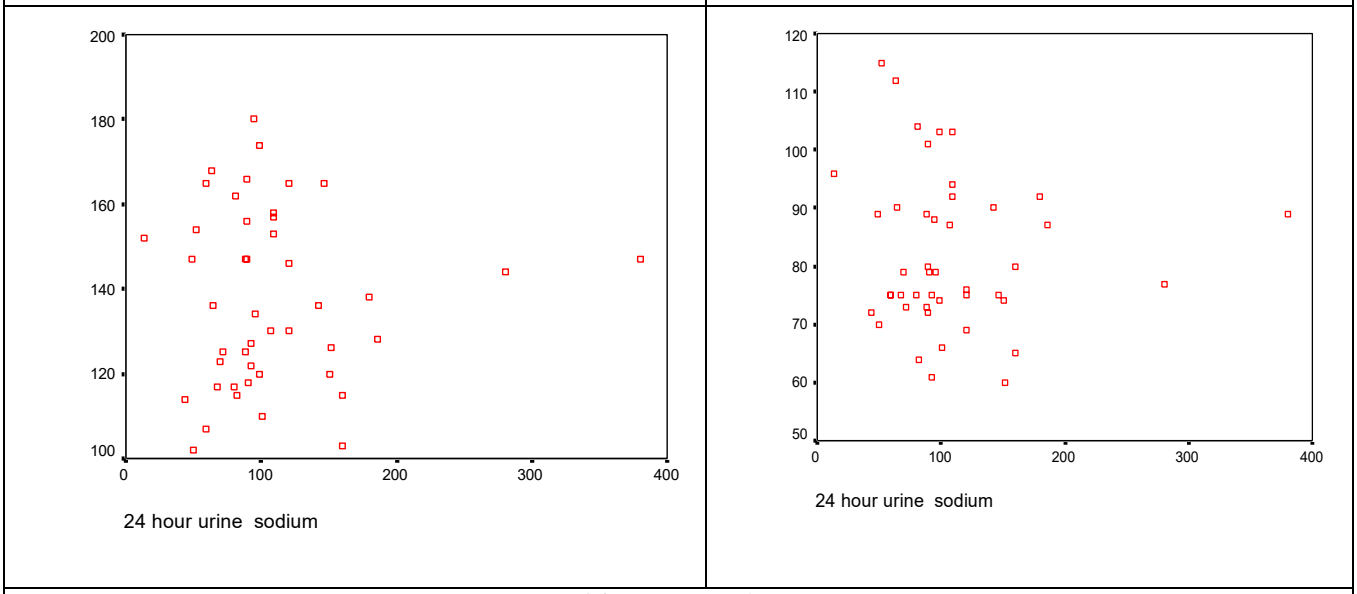


ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021



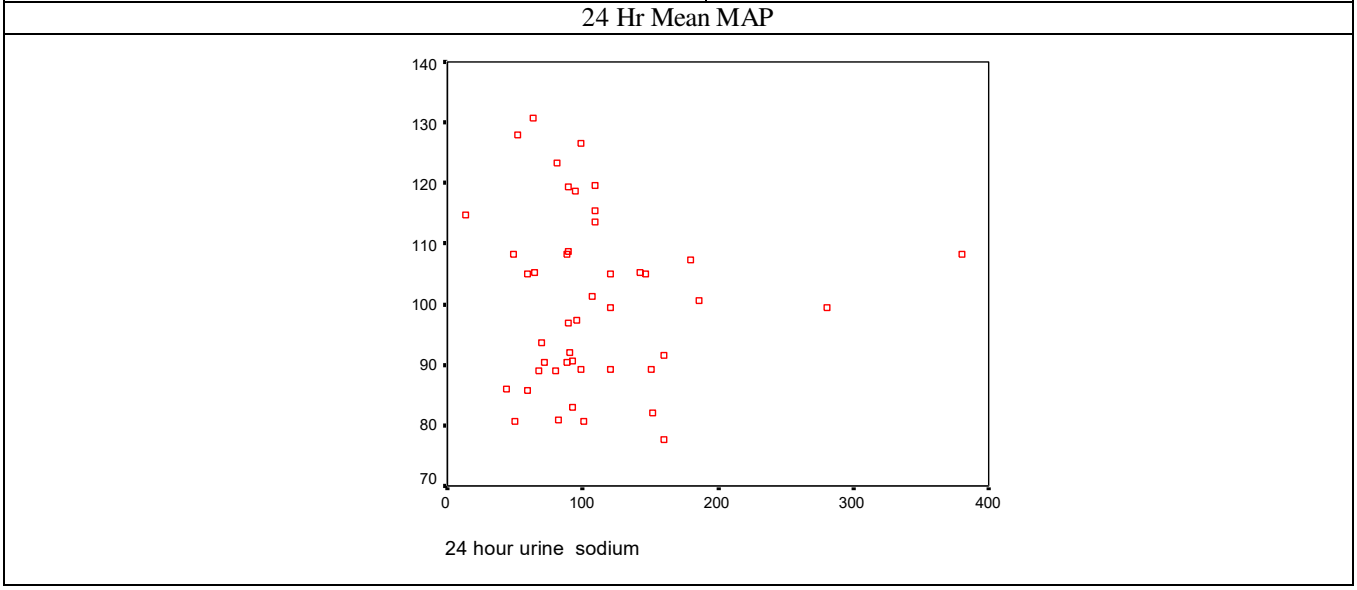
FigureD: Scatter diagram for 24 hour urine sodium and BP for CKD patients not on dialysis

24 Hr Mean SBP



24 Hr Mean DBP

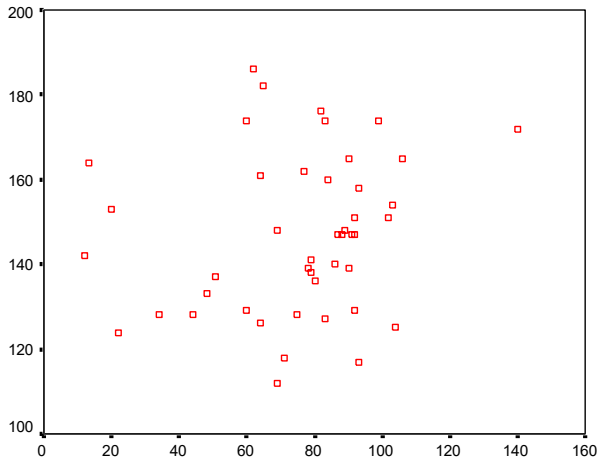
24 Hr Mean MAP



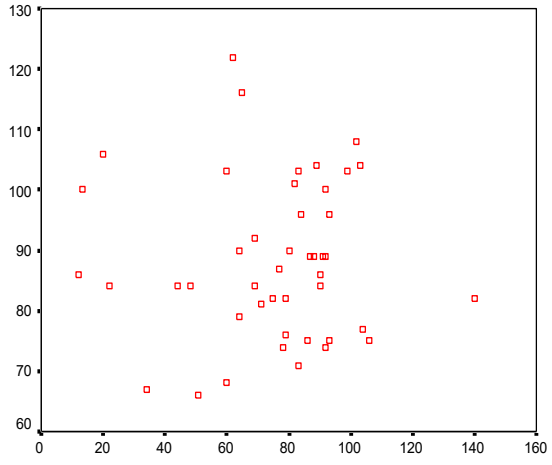
ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

FigureE: Scatter diagram for 24 hour urine sodium and BP for Maintenance dialysis Patients

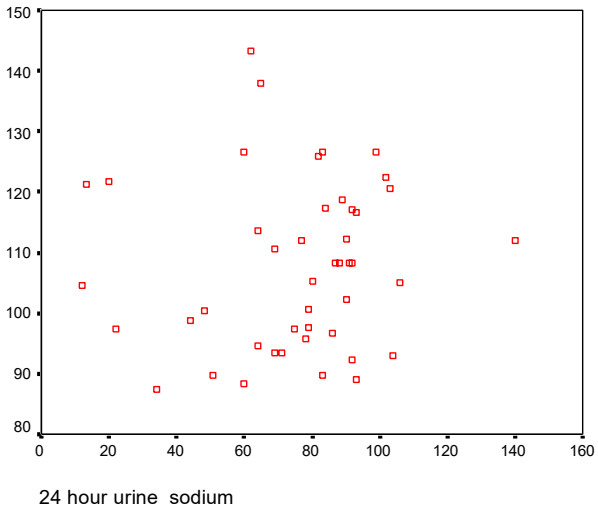
24 Hr Mean SBP



24 Hr Mean DBP



24 Hr Mean MAP



Discussion

We suggest that non-dipping of blood pressure, enhanced nocturnal sodium excretion, and sodium sensitivity of blood pressure are manifestations of an intermediate stage in the evolution of hypertension during aging. When young subjects, who are normotensive and with normal renal function, are challenged with a sodium load, sodium balance is quickly restored by suppression of renal tubular reabsorption. This is by humoral and paracrine mechanisms without any rise in blood pressure. These responses are essentially the mirror image of those evolutionarily preserved responses adapted for sodium conservation.

Because the range of most individual's sodium excretory capacity is great, the bulk of any dietary sodium ingested is excreted during the day, and a normal diurnal rhythm of sodium excretion is maintained.[7] With aging or renal damage or because of inter-individual genetic or developmental differences in renal sodium excretory capacity, the plasticity of renal responses declines, but sodium balance can be efficiently maintained by raising blood pressure. Blood pressure dependent natriuresis is initially limited to night time and manifests as non-dipping of blood pressure, an increased rate of nocturnal sodium excretion, and a reversal in the diurnal rhythm of sodium output.[8]

When sodium balance can no longer be maintained by humoral and transient nocturnal pressor mechanisms, the operating set point of pressure natriuresis shifts to a higher range throughout the day and night, and hence sustained hypertension results.[9] We, therefore, propose that more attention should be paid to the nexus of sodium excretion, non-dipping, and sodium sensitivity in studies of how genetic and environmental determinants initiate the development of hypertension. Prevalence of hypertension increases with falling

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

glomerular filtration rate (GFR) and reaches an estimated 86% in patients with end-stage renal disease (ESRD. With progressive decline in GFR, sodium and water retention maybe related to high prevalence of hypertension. However, many other factors such as activation of sympathoadrenal system, renin-angiotensin system, and circulating inhibitors of nitric oxide (NO) are also responsible for the high prevalence of hypertension.[9.10]

Ambulatory blood pressure monitoring (ABPM) has been the most important clinical tool for the evaluation and treatment of hypertension both in clinical practice and in research setting. Throughout a 24-hour period, serial BP measurements at specific time intervals can be known. Hence, 24-hour ABPM provide a better assessment and understanding of fluctuations in BP levels during day and night.[11,12]

Ours is the first study to analyze 24-hour urinary sodium excretion correlation with 24-hour blood pressure in healthy subjects, chronic kidney disease patients and maintenance dialysis patients. We measured 24-hour urine sodium, spot urine sodium and spot urine creatinine along with 24-hour ambulatory BP in all participants fulfilling the criteria. Renal function tests were done in all participants. We also analyzed the correlates of fall in BP with sleep (the dipping phenomenon), which is an independent predictor of poor renal outcomes in the CKD population.

We found that group I had 10, group II had 45 and group III had 45 subjects each. We found that mean 24-hour urine sodium (mmol/day) was 112.5 ± 44.6 in group I, 107.7 ± 61.9 in group II and 74.8 ± 26.1 in group III, eGFR (ml/min/1.73 m2) was 102.8 ± 20.9 in group I, 34.6 ± 32.4 in group II and 6.6 ± 4.2 in group III. USCR (mmol/mg) was 0.16 ± 0.07 in group I, 0.17 ± 0.23 in group II and 0.19 ± 0.18 in group III. SBP (mm Hg) was 125 ± 12.5 in group I, 137.6 ± 20.7 in group II and 146.7 ± 18.7 in group III. DBP (mm Hg) was 76.7 ± 7.3 in group I, 82 ± 13.2 in group II and 88.3 ± 13.1 in group III. 24-hours mean MAP (mmHg) was 92.8 ± 8.5 in group I, 100.5 ± 14.2 in group II and 107.8 ± 13.9 in group III.Timio et al[13] prospectively studied 27 normotensive, 41 hypertensive patients with stable CKD, 28 matched healthy subjects and 47 patients with essential hypertension without kidney disease. 72 % of our study population was males. Mean BMI was 22.8 ± 4 kg/m2 and 5% of individuals were classified obese as per WHO BMI Classification. In obese population, 3 belonged to chronic kidney disease patients not on dialysis and 2 patients were on maintenance dialysis. 37 % of study population had no comorbid conditions.

In our study, 25 % of study population was hypertensive, 7% were diabetic, 3% had hypothyroidism, 2% had underlying coronary artery disease and 1% had hypothyroidism. ABPM concluded that 30% of healthy subjects were detected to have hypertension. 62.2 % of CKD patients not on dialysis were hypertensive and 86.7 % were hypertensive in maintenance hemodialysis group.

Conclusion

From results of present study it is concluded There is a positive but not statistically significant correlation between 24-hourinarysodiumandmeanSBPinCKDpatientsnotondialysis.

RegardingABPMinCKDpopulation,thereisnocorrelation of 24-hour blood pressure with 24-hour urinary sodium excretion. Thus,estimation of 24-hourinesodium excretioncannot predict hypertension in CKD population. A study with larger sample size and long term follow up would give a better understanding between relation between 24-hour urinary sodium excretion and 24-hour ambulatory blood pressure in chronic kidney disease population.

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