Original Article

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Analysis of Spot Urine Sodium/Creatinine Ratio and its Correlation with 24-Hour Ambulatory Blood Pressure in Chronic Kidney Disease Cohorts and Healthy Subjects

John Abraham Tharayil, Tushar Dighe, Nilesh Shinde, Pavan Wakhare, Charan Bale, Syed Mohd Azhar Hassan, Atul Sajgure

Department of Nephrology, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Pune, Maharashtra, India.

Abstract

Background: 24-hour ambulatory blood pressure monitoring(ABPM) facilitates better prescription patterns among known hypertensive patients. The present study was a pilot study conducted to determine whether a spot urine sample of sodium/creatinine ratio can accurately reflect blood pressure in chronic kidney disease patients on maintenance dialysis as well as not on dialysis and healthy subjects. **Subjects & Methods:** 100 patients of both genders were divided into 3 groups. Group 1: healthy subjects, Group 2: chronic kidney disease patients not on dialysis and Group 3: maintenance dialysis patients. Measurement of spot urine sodium was done by Indirect Integrated Multisensor Technology (IMT) by Ion Selective Electrode method and spot urine creatinine by Jaffe's kinetic method without deproteinization. Results thus obtained were assessed statistically. **Results:** There was no statistically significant correlation between spot urine sodium/creatinine ratio (USCR) with 24-hour BP in healthy subjects, chronic kidney disease patients not on dialysis and CKD patients on maintenance dialysis. **Conclusion:** There is no correlation of 24-hour ambulatory blood pressure with early morning urine spot/sodium creatinine ratio in CKD population. Hence, USCR cannot be considered as a valuable tool for determining hypertension in CKD patients.

Keywords: ABPM, urine spot sodium/creatinine ratio, Chronic kidney disease.

Corresponding Author: Pavan Wakhare, Department of Nephrology, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Pune, Maharashtra, India.
E-mail: med.nephro@dpu.edu.in

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Introduction

Use of 24-hour ABPM facilitates better prescription patterns among known hypertensive patients.[1] ABPM identifies patients with masked hypertension and those with abnormal dipping patterns who would otherwise be missed when using casual BP measurement methods.[2] The increased diagnostic performance of ABPM makes it cost effective in both primary and specialist care in developed world settings.[3]

Salt intake is linked to pathogenesis of hypertension. Increased salt intake has been linked to change arterial wall structure and function.[4] Excessive salt intake has been associated with arterial stiffness. Some studies have suggested that dipping pattern has been linked to arterial stiffness and salt intake.[5] High sodium intake is an established risk factor for hypertension and cardiovascular disease. Sodium excretion in 24-hour urine indicates the daily salt consumption. 24-hour urine sodium excretion is generally regarded as the gold standard for assessing dietary sodium in population and epidemiological studies.[6] 24- hour urine collection is an appropriate method for assessing average dietary sodium in a healthy population or people with chronic stable health risks. Studies in healthy population have reported that 24- hour urine sodium excretion accounts for 61-107% of ingested sodium.[7]

Currently, the most reliable and readily used method in clinical and epidemiological studies is the 24-hour urine collection. Nonetheless, it is considered more cumbersome by research participants and patients.[8] It has also been suggested that daily sodium excretion may vary from day to day which would further require the collection of multiple samples. In contrast, spot urine collections are considered less reliable but more suitable for participants in clinical practice and large studies.[9] The present study was conducted to determine whether an early morning spot urine sodium/creatinine ratio (USCR) can accurately reflect blood pressure in chronic kidney disease patients on maintenance dialysis as well as not on dialysis and healthy subjects. So far, there are no large studies or trials, which investigate correlation of an early morning spot

USCR with 24-hour ambulatory blood pressure in various stages of CKD patients and healthy population. Hence, we assessed relationship between ambulatory BP and sodium excretion in healthy subjects, CKD patients not on dialysis and on maintenance dialysis independent of baseline salt consumption.

Subjects and Methods

The present study comprised of 100 in-patients of both genders. Consent from all patients was obtained before starting the study. Exclusion criteria was 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, inadequate ABPM (Number of BP recordings less than 80%), age < 18 years, mentally incapacitated, current pregnancy, actively menstruating women and patients with carcinoma and/or undergoing treatment for the same

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. 24-hour ambulatory blood pressure monitoring (ABPM) was done on the day of collection of urine samples. ABPM device was installed at 8 A.M, and first BP recording was taken manually which accounted for office BP recording and ABPM device was removed next day after completing 24 hours. ABP was recorded half hourly from 8:00 A.M. to 10.00 P.M. which accounted for daytime blood pressure and hourly from 10:01 P.M. to 7:59 A.M (night- time blood pressure). Specific adult cuff size 25-32 cm was used which was chosen according to the patient's arm circumference and fixed to the nondominant arm in healthy subjects and CKD patients not on dialysis and non AVF arm in maintenance dialysis patients. All participants were instructed to transfer a portion of first morning void to a 15-mL tube. Voided urine sample was transported to central laboratory within 30 mins to 1 hour for processing and analysis. Measurement of spot urine sodium was done by Indirect Integrated Multisensor Technology (IMT) by Ion Selective Electrode method and spot urine creatinine by Jaffe's kinetic method without deproteinization.

Results

[Figure 1] shows distribution of ABPM conclusions. hypertensive patients were 3 in group I, 28 in group II and 39 in group III.

[Table 2] shows that there is no statistically significant correlation between spot urine/sodium creatinine ratio and BP for healthy subjects.

[Table 3] shows that there was positive correlation between spot urine/sodium creatinine ratio and BP for CKD patients not on dialysis. However, it is not statistically significant.

[Table 4] there was no statistically significant correlation between spot urine/sodium creatinine ratio and BP for maintenance dialysis patients.

Discussion

We included 100 in-patients after fulfilling the criteria over a span of 2 years. The study population was categorized into 3 groups. 45 subjects belonged to chronic kidney disease patients not on dialysis, 45 subjects were on maintenance dialysis and 10 subjects belonged to healthy population group not having chronic kidney disease.

Mean age of study population was 47.1 ± 16 years with 23% individuals in 41 to 50 years age group, 20 % of individuals in less than 30 years of age and 20% of individuals in 61 to 70 years respectively. In healthy adults, differences in age and kidney function might explain observed differences across cohorts. For example, average age in the PURE study at baseline was 51 years compared to 35 years in GAPP and 44 years in SKIPOGH.[9] Even in PURE study, relationship between blood pressure and sodium excretion was significantly weaker among individuals under the age of 45 years, hinting towards an age-dependent effect.

Currently, the WHO recommends an intake of no more than 2.3 g of sodium per day. The mean sodium excretion in GAPP and SKIPOGH studies were substantially higher. Interventional trials such as DASH (dietary approaches to stop hypertension) have shown that by changing dietary patterns, while maintaining low sodium intake of about 3 g/d, a significant BP reduction can be achieved 249. 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. All maintenance dialysis patients were strictly put on a salt restricted diet (sodium chloride < 5 grams/day) provided from dietary department of hospital. All patients underwent urine spot sodium and urine spot creatinine measurements. The mean urine spot sodium creatinine ratio was 0.18 ± 0.2 mmol/mg. Mean urine sodium creatinine ratio was 0.16 ± 0.07 mmol/mg in healthy subjects, 0.17 ± 0.23 mmol/mg in CKD patients not on dialysis and 0.19 ± 0.18 mmol/mg in maintenance dialysis patients.

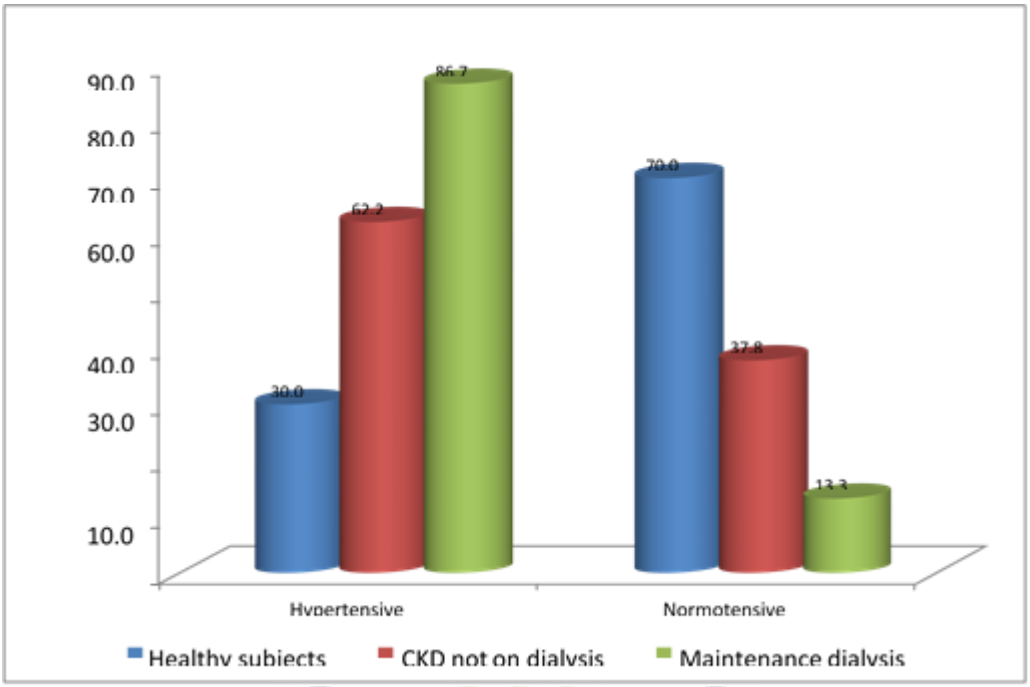

Figure 1: Distribution of ABPM conclusions based on groups

Table 1: Descriptive statistics regarding spot urine/sodium creatinine ratio (USCR) based on groups

USCR (mmol/mg)	Healthy subjects	CKD patients not on dialysis	Maintenance dialysis patients
Mean ± SD	0.16 ± 0.07	0.17 ± 0.23	0.19 ± 0.18
Median (IQR)	0.16 (0.11 - 0.21)	0.09 (0.07 - 0.19)	0.14 (0.08 - 0.21)
Minimum	0.03	0.02	0.03
Maximum	0.27	1.28	1.00

Table 2: Correlation of spot urine sodium/creatinine ratio and mean BP for healthy subjects

Parameters	r	p
24 Hr Mean SBP	-0.397	0.256
24 Hr Mean DBP	-0.174	0.630
24 Hr Mean MAP	-0.293	0.411

Table 3: Correlation between spot urine/sodium creatinine ratio and BP for CKD patients not on dialysis

Parameters	r	p
24 Hr Mean SBP	0.085	0.580
24 Hr Mean DBP	0.192	0.206
24 Hr Mean MAP	0.16	0.293

Several studies have attempted to highlight the benefits of using a spot urine sample. An epidemiological study conducted by Dyer et al,[10] reported a strong correlation between the late afternoon sodium creatinine ratios of a spot urine sample with the sodium excretion per amount of creatinine in a 24-hour urine sample. Similarly, another

Table 4: Correlation of spot urine/sodium creatinine ratio and BP for Maintenance dialysis patients

	R	p
24 Hr Mean SBP	-0.186	0.220
24 Hr Mean DBP	0.098	0.523
24 Hr Mean MAP	-0.022	0.884

epidemiological study conducted in the Japanese population evaluated the correlation between a spot sample and a 24-hour urine collection for both sodium and potassium. The study established that the urine spot sample was in fact an accurate and time-saving method in measuring the population's mean of sodium and potassium excretion. In addition, the degree of correlation of the measured 24-hour urinary sodium excretion with an estimated 24-hour urinary sodium excretion from a spot sample might be dependent on the degree of the average salt consumption of the population. Excessive dietary sodium intake represents a pathogenic determinant and a key modifiable environmental risk factor for hypertension.

To date, 24-hour urine collection has been recommended as the gold standard for the assessment of salt intake in the population. Nevertheless, many factors, ranging from the mechanisms of sodium absorption to metabolic and environmental factors, can affect urinary sodium excretion. Ando and Fujita,[11] characterized differences in creatinine clearance and renal blood flow (RBF) determined by clearance of 131iodine para-amino hippurate in 6 SS and 14 SR hypertensive subjects in balance on low and high sodium diets. Creatinine clearance did not differ between these 2 groups while on a high sodium diet, but renal vascular resistance (RVR) was greater in the SS subjects, and responses of RVR and MAP to sodium loading were significantly correlated.

The complex mechanisms underlying renal sodium handling could be involved in the inter-individual variability and in the responses of BP to dietary sodium intake. Maintenance dialysis patients had higher 24-hour mean systolic blood pressure (mean 146.7 ± 18.7 mmHg) than CKD patients not on dialysis (137.6 ± 20.7 mmHg) and healthy subjects (125 ± 12.5 mmHg). 24 Hour Mean DBP was 88.3 ± 13.1 mmHg in Maintenance dialysis patients which was higher compared to the other groups. 24 Hour Mean MAP was 107.8 ± 13.9 mmHg in Maintenance dialysis patients. Urinary sodium excretion is used as an assessment tool for salt intake and in the assessment of salt handling. The phenotypical representation of salt homeostasis may result from a dynamic interplay between genes and the environment. One major environmental factor influencing renal sodium handling is dietary salt intake which can be assessed by urine sodium excretion. Schmidlin et al,[12] demonstrated in SS hypertensive subjects that a three week sodium load lowered RBF, increased RVR, and increased filtration fraction from 19.4% to 21.4% ($P \leq 0.001$). SR hypertensive subjects showed no significant changes.

Conclusion

Authors concluded that urine spot sodium/creatinine ratio measured in morning voided urine cannot be used to predict hypertension in healthy subjects, chronic kidney disease patients not on dialysis and CKD patients on maintenance dialysis. Regarding ABPM in CKD population, there is no correlation of 24-hour blood pressure with urine spot/sodium creatinine ratio. Thus, estimation of spot USCR cannot predict hypertension in CKD population. However, more studies are required in CKD population to establish these facts.

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