ORIGINAL ARTICLE

Reliability of a portable device for measuring spot urinary Na/K ratios among pregnant Thai women: a cross-sectional study

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Aim: Urinary Na/K ratios are related to the risk of developing cardiovascular diseases. A portable device which rapidly measures urinary Na/K ratios will be useful. This study aimed to test the reliability of a portable device for measuring spot urinary Na/K ratios among pregnant women in southern Thailand.

Methods: Morning spot urine samples were examined with a portable device and automated chemical analyzer independently and blindly. Correlations and predictions were analyzed using Spearman's correlation coefficients and linear regression, respectively. Agreement between the portable device and automated chemical analyzer was examined using the Bland-Altman method.

Results: Measurements from 1,412 specimens revealed that spot urinary Na/K ratios obtained using the portable device had an acceptable level of agreement (mean of difference = 0.78) and strong positive correlation ($r = 0.83$) with those obtained using the automated chemical analyzer. The equation of urinary Na/K ratios obtained with the portable device is required to estimate ratios obtained by the automated chemical analyzer, which had a low proportional error and small constant error.

Conclusion: Portable devices are feasible alternative tools for measuring spot urinary Na/K ratios among pregnant women in clinical settings. Further large-scale studies to assess the reproducibility of measurements from portable devices are warranted.

Introduction

High dietary sodium (Na) and low dietary potassium (K) intake is associated with hypertension and an increased risk of developing cardiovascular diseases. Thus, the World Health Organization (WHO) recommends reducing Na intake at the global level.¹⁾ A recent systematic review suggested that spot urine samples can provide a good indication of mean Na intake.²⁾ A study conducted in the United Kingdom found that preeclamptic women who have high urinary Na/K ratios from 24-hour urine were more likely to have maternal and neonatal morbidities than those with low ratios.³⁾ Furthermore, a study in

Japan found an association between dietary Na/K ratios and cardiovascular diseases.⁴⁾ According to another study, urinary Na/K ratios were consistent with diet consumption within the previous three days.⁵⁾ In addition, a large prospective study of a multiethnic American cohort reported that urinary Na/K ratios obtained from spot urine samples could predict the risk of subsequent major cardiovascular diseases.⁶⁾

A randomized controlled trial tested the utility of a portable hand-sized device for measuring urinary Na/K ratios (HEU-001F; OMRON Healthcare Co., Ltd., Kyoto, Japan) in order to monitor lifestyle behaviors of Japanese people.⁷⁾ Using the same device, another study found

that 99.5% of Japanese subjects had spot urinary Na/K ratios between 0.06 and 11.80, and these ratios were more closely associated with blood pressure than estimated daily salt intake.⁸⁾ Although the portable device was used in two studies in Japan,^{7,8)} its reliability for measuring urinary Na/K ratios is unclear. Moreover, to date, no study has tested the reliability of such portable devices for use among pregnant women whose kidney function differs from that of general healthy volunteers.

The present study aimed to examine the reliability of the same portable device (HEU-001F) for measuring spot urinary Na/K ratios among pregnant women in southern Thailand through comparisons with spot urinary Na/K ratios obtained using an automated chemical analyzer.

Materials and methods

Study design and participants

A cross-sectional study was conducted targeting pregnant Thai women who received antenatal care at two tertiary hospitals in southern Thailand from November 8, 2018 to March 31, 2020. Women who had renal failure or autoimmune disease, or a communication barrier such as deafness or a mental disorder, were excluded. The sample size was calculated based on a 95% tolerance interval with 90% target coverage probability and a 1% error, resulting in at least 1,400 urine samples being required.⁹⁾ This study was part of a cohort study measuring the correlation of spot urinary Na and K levels with blood pressure throughout pregnancy.¹⁰⁾

Data collection

All pregnant women who met the inclusion criteria were invited to participate in this study. After obtaining written informed consent, morning spot urine samples were collected, refrigerated, and transported to the cold storage of the clinical chemistry laboratory unit (Songklanagarind Hospital, Prince of Songkla University, Thailand). Spot urine specimens were independently examined with an automated chemical analyzer (Cobas 8000) using the standard laboratory method for Na and K levels, and a portable device (HEU-001-F; Omron Healthcare Co., Japan) for Na/K ratios. The researchers were blinded to all measurements during the course of the study.

Measurement of urinary Na and K levels with the automated chemical analyzer

Na and K levels of each urine specimen were measured using the Cobas 8000 platform (Roche Diagnostics GmbH, Mannheim, Germany) by the Ion Selective Electrode (ISE) method and expressed as millimoles per liter (mmol/l). Spot urinary Na/K ratios were calculated by dividing urinary Na levels by K levels.

Repeatability and intermediate precision of the

automated chemical analyzer were determined using human serum controls in accordance with the CLSI (Clinical and Laboratory Standards Institute), and tested with five replicate analyses in a single run over five consecutive days for two clinically relevant levels of Na and K: L1 (Roche Preci Control Clin Chem Multi1) and L2 (Roche Preci Control Clin Chem Multi2). The precision profile was obtained using serial dilutions of control material. The within-run coefficient of variation for spot urinary Na assays was 0.26 to 0.31%, while the between-run coefficient of variation was 0.60 to 0.81%. For spot urinary K assays, the within-run coefficient of variation was 0.25 to 0.28%, and the between-run coefficient of variation was 0.54 to 0.91%. The Na reference and reportable ranges for spot urine were 54–190 and 60–350 mmol/L, respectively. Likewise, the K reference and reportable ranges for spot urine were 20–80 and 3–100 mmol/L, respectively.

Measurement of urinary Na/K ratios with the portable device

Spot urinary Na/K ratios were measured using the portable device, which measures urinary Na and K levels via ion selective electrodes and displays the urinary Na/K ratio within a minute. The portable device was checked daily for sensor sensitivity and calibrated to assure measurement accuracy.

Statistical analyses

All data were double entered into Epidata version 3.1. Demographic characteristics of participants are presented as frequencies or percentages. Means and standard deviations of spot urinary Na/K ratios as measured by the automated chemical analyzer and the portable device were compared by the paired *t* test. Correlations between spot urinary Na/K ratios as measured by the automated chemical analyzer and portable device were assessed using Spearman's correlation analysis and stratified by different stages of pregnancy (Time 1, ≤ 14 weeks; Time 2, 18–22 weeks; Time 3, 24–28 weeks; and Time 4, 30–34 weeks). Agreement between spot urinary Na/K ratios obtained using the automated chemical analyzer and portable device was examined using the Bland-Altman method. Estimation of urinary Na/K ratios from the automated chemical analyzer by measurements from the portable device was performed using a linear regression model, from which a prediction equation was generated. All statistical analyses were performed with R version 4.0.0 (R Core Team 2020, Austria). $P < 0.05$ was considered statistically significant.

Results

A total of 1,412 urine specimens were collected from

395 women during ≤ 14 weeks, 18–22 weeks, 24–28 weeks, and 30–34 weeks of gestation. Participants' ages ranged from 16 to 45 years (mean $\pm$ sd. = 31.5 ± 5.5). The majority of participants were aged between 20–34 years (70.4%), had an education level of bachelor degree or higher (65.3%), and were employed (76.8%) (Table 1). Spot urinary Na/K ratios from the automated chemical analyzer and portable device ranged from 0.60–14.88 and 0.33–13.20, respectively. Mean spot urinary Na/K ratios as measured by the portable device were significantly higher than those measured by the automated chemical analyzer (Table 2).

Spot urinary Na/K ratios as measured by the automated chemical analyzer and portable device were highly correlated at different stages of pregnancy (Figure 1). The linear regression model yielded a prediction equation of urinary Na/K ratios (y) from the portable device (x) of $y = 0.93x - 0.46$, which explained 71% of the variation and showed a 7% proportional error and 0.46 constant error (Figure 2A). Similar linear regressions were found for different cut-off points when assessing urinary Na/K ratios from the portable device (Figure 2B) and among different age groups (Figure 2C). Proportions of participants with spot urinary Na/K ratios of < 2.00 , 2.00–3.99, 4.00–8.00, and > 8.00 were 16.3%, 43.7%, 36.0%, and 4.0%, respectively.

Differences were not normally distributed (Shapiro-Wilk test, $P < 0.001$), but the skewedness was not serious (Figure 3A). The average difference of spot urinary Na/K ratios was 0.78 units, indicating that, on average, measurements with the portable device were 0.78 units

Table 1. Characteristics of the pregnant women in the study ($n = 395$)

Characteristic	N (%)
Age (years)	
< 20	7 (1.8)
20–34	278 (70.4)
35	110 (27.8)
Religion	
Buddhist	172 (43.5)
Non-Buddhist	223 (56.5)
Education	
Secondary school or lower	98 (24.8)
Vocational school	39 (9.9)
Bachelor or higher	258 (65.3)
Occupation	
No occupation	46 (11.6)
Housewife	46 (11.6)
Farmer/gardener/fisherman/merchant	67 (17.0)
Laborer	56 (14.2)
Teacher	31 (7.8)
Employee	149 (37.8)

Table 2. Descriptive statistics of spot urinary Na/K ratios measured by automated chemical analyzer and portable device ($n = 1,412$)

Machine	Minimum	Maximum	Mean	SD	P value*
Automated	0.6	14.88	3.83	2.03	< 0.001
Portable	0.33	13.20	4.62	1.84	

* Paired t -test for differences between the means of two sets of data.

Figure 1. Correlations of spot urinary Na/K ratios as measured by the automated chemical analyzer and portable device at different stages of pregnancy (Time 1, ≤ 14 weeks; Time 2, 18–22 weeks; Time 3, 24–28 weeks and Time 4, 30–34 weeks).

(A)

(B)

(C)

Figure 2. Linear regression model of spot urinary Na/K ratios using values from the portable device (x-axis) to predict values from the automated analyzer (y-axis).

(A) Prediction equation. (B) Regressions stratified by levels of spot urinary Na/K ratios as measured by the portable device. (C) Regressions stratified by age group.

higher than those of the automated chemical analyzer. The lower and upper limits of difference in spot urinary Na/K ratios were 1.36 units below and 2.92 above, respectively (Figure 3B).

Discussion

Spot urinary Na/K ratios as measured by the portable device HEU-001-F had acceptable limits of agreement and were strongly, positively correlated with those obtained using the automated chemical analyzer Cobas

(A)

(B)

Figure 3. Differences in spot urinary Na/K ratios between the portable device and automated chemical analyzer. (A) Distribution of differences. (B) Bland-Altman plot showing the agreement of spot urinary Na/K ratios as measured by the portable device and automated chemical analyzer.

8000. The predicted equation for urinary Na/K ratios with the portable device had a low proportional error and small constant error when using samples from pregnant women in southern Thailand.

Both the automated chemical analyzer and portable device use the ISE method to measure Na and K levels, which is the standard for measuring urinary Na and K levels.^{11,12} Various machines have been used in the literature to measure Na and K levels, including the Randox Rx Daytona used in a national survey in Ireland,¹¹ the Beckman Synchron DxC800 used in a study in the United States,¹² and the Cobas 8000 used in the present study. Quality assurance analysis with the Cobas 8000 prior to the present study confirmed that its measurements had a low coefficient of variation.

The strong correlation and high agreement of spot urinary Na/K ratios between the automated chemical analyzer and portable device were consistent with the findings of a study from Japan which compared spot and 24-h urine Na/K ratios.⁵ The visualization provided in the Bland-Altman plot is useful to assess true biologic differences not due to sampling error when some values are outside the confidence limits,^{13,14} as well as to identify both systematic and random errors.¹⁵ The present study showed a strong correlation and high percentage of variation (r^2) in the linear regression model of spot urinary Na/K ratios, indicating that measurements using both the automated chemical analyzer and portable device were reproducible.¹³ Given that the Na/K ratios in the present study were not normally distributed, we used Spearman's correlation coefficients to assess the findings, as this method is more robust for data involving outliers than Pearson's correlation coefficients.¹⁶

There were wide variations in spot urinary Na/K ratios based on measurements from both the automated chemical analyzer and portable device. This suggests that our participants consumed diets containing salt varying in levels from low to high based on the findings of a study by Yatabe et al.⁵ In that study, a portable device was used and revealed mean spot urine Na/K ratios of 1.1, 4.2, and 6.6 in healthy volunteers who had normal salt, low salt, and high salt diets. Pregnant women with high salt intake should be concerned, given previous studies reporting that higher urinary Na/K ratios were associated with higher systolic blood pressure levels and stroke rates.^{6,12,17} In the present study, spot urinary Na/K ratios lower than 2 and higher than 4 were found in 16.3% and 40.0% of participants, respectively, consistent with the low- and high-salt diets reported by Yatabe et al.⁵

Mean spot urinary Na/K ratios measured with the automated chemical analyzer were similar to those reported in two Japanese studies using a portable device.^{7,17} Published studies assessing urinary Na/K ratios have targeted many different populations, including

healthy volunteers in Japan,⁵ national populations of Ireland¹¹ and the United States,¹² hypertensive patients in Japan,¹⁷ cirrhotic patients,^{18,19} patients with urinary stone diseases,²⁰ and patients with chronic kidney diseases.²¹ However, the present study is the first to examine spot urinary Na/K ratios in pregnant women. It will be informative to validate the present results with a population of pregnant women at high risk for hypertensive disorders.

This study has some limitations. First, the differences in spot urinary Na/K ratios measured by the automated chemical analyzer and portable device were statistically significant, but the mean differences between the two were generally small and the majority of differences were within the 95% limits of agreement. Therefore, the differences may be in the acceptable range. Second, we could not directly compare our results with previous studies since no study to date has validated spot urinary Na/K ratios in pregnant women measured by a portable device with an automated analyzer. More measurements and studies will be needed to validate these results and their generalizability. Finally, the reliability of the prediction equation for urinary Na/K ratios from the portable device requires further confirmation.

Portable devices are useful for point-of-care testing at antenatal care clinics in women at high risk of developing hypertensive disorders in pregnancy, as they provide fast, reliable results (as confirmed with comparisons using an automated chemical analyzer) and allow pregnant women to monitor their intake of Na and K. Increasing the number of available self-monitoring portable devices to monitor spot urinary Na/K ratios in pregnant women will be beneficial.

Conclusion

Portable devices can offer a feasible, reliable means to measure spot urinary Na/K ratios in pregnant women. Further large-scale studies to confirm the reproducibility of measurements from portable devices are warranted.

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Conflict of interests

The authors declare that there is no conflict of interest.

Contributorship

The authors (TL, SS, KJ, and RM) substantially contributed to the conceptualization and design of the study. TL, SS, and KJ were involved in patient recruitment. TL conducted the data analysis and wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Ethical considerations

We obtained ethical approval for the study, and all participating women provided written informed consent prior to data collection.

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