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Accuracy of equations for predicting 24-h urinary potassium excretion from spot urine samples in Chinese children

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Abstract

Accurate assessments of potassium intake in children are important for the early prevention of CVD. Currently, there is no simple approach for accurate estimation of potassium intake in children. We aim to evaluate the accuracy of 24-h urinary potassium excretion (24UKV) estimation in children using three common equations: the Kawasaki, Tanaka and Mage formulas, in a hospital-based setting. A total of 151 participants aged 5–18 years were initially enrolled, and spot urine samples were collected in the whole 24-h duration to measure the concentrations of potassium and creatinine. We calculated the mean difference, absolute and relative difference and misclassification rate between measured 24UKV and the predicted ones using Kawasaki, Tanaka and Mage formulas in 129 participants. The mean measured 24UKV was 1193·3 mg/d in our study. Mean differences between estimated and measured 24UKV were 1215·6, −14·9 and 230·3 mg/d by the Kawasaki, Tanaka and Mage formulas, respectively. All estimated 24UKV were significantly different from the measured values in all the time point (all $P < 0·05$), except for the predicted values from Tanaka formula using morning, afternoon and evening spot urine. The proportions with relative differences over 40 % were 87·2%, 32·5% and 47·3 % for Kawasaki, Tanaka and Mage formulas, respectively. Misclassification rates were 91·5 % for Kawasaki, 44·4 % for Tanaka and 58·9 % for Mage formula at the individual level. Our findings showed that misclassification could occur on the individual level when using Kawasaki, Tanaka and Mage formulas to estimate 24UKV from spot urine in the child population.

Key words: **Potassium intake: 24-h urine collection: Children: Blood pressure: Spot urine: Validation study**

Low-potassium diet has been associated with elevation of blood pressure in children[1–3], which poses an increased risk of childhood hypertension and CVD in adulthood[4,5]. Some studies have showed that daily potassium intake in children is commonly less than the recommended levels[6]. Accurate assessment of potassium intake in children is critical for the prevention of low potassium intake associated diseases, such as hypertension and CVD[7]. Currently, dietary assessment tools and 24-h urinary potassium excretion (24UKV) are the two most widely used approaches to measure potassium intake[8]. However, dietary assessment tools method is prone to recall bias and limit its application in children. 24UKV is an alternative tool to measure potassium intake, but this method is costly and burdensome to implement in the real clinical settings. Thus, several formulas were developed to estimate the 24UKV using a spot urine sample, among them Kawasaki[9], Tanaka[10] and Mage[11] are used commonly. These equations were established based on a theoretic framework or designed for Japanese adult population rather than children. Moreover, they all rely on the hypothesis that 24UKV, with a correction for creatinine excretion, would be proportionate to spot urine excretion.

Abbreviations: ICC, intraclass correlation coefficient; 24UKV, 24-h urinary potassium excretion.

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British Journal of Nutrition

Children have distinct metabolic and physiological features from adults, which can be reflected in sex- and age-dependent reference intervals for some paediatric laboratory test index, such as serum creatinine[12]. Whereas using spot urine to predict the 24UKV in adults was previously studied and assessed, these studies got inconsistent results between measured and predicted 24UKV and showed low to moderate accuracy of equations[1,13–16]. We still know little about the accuracy of the three proposed approaches on 24UKV estimation in children, neither on population level nor subgroups with different gender or spot urine timing. The present study aims to validate the accuracy of three commonly used equations for 24UKV estimation among hospital-based child population.

Methods

Study design and participants recruitment

We performed a hospital-based cross-sectional study to evaluate the accuracy of 24UKV estimation using three commonly used equations in children population recruited in 2017–2018, the same population applied to evaluate the accuracy of formulas to estimate Na excretion in previous study[17]. Participants were enrolled from the inpatient wards among department of otolaryngology, orthopaedics and ophthalmology at Beijing Children's Hospital, China. The sample size was estimated using Bland–Altman agreement parameters according to the method described by Lu[18]. Based on the research from Mercado *et al.* (type I error of 5 %, power of 80 %, expected mean of difference of 20 mg/d, expected standard deviation of difference of 40 mg/d, missing data rate of 10 %)[13], a sample size including 118 participants would meet the requirement of Bland–Altman agreement assessment. Given that 24-h urine collection in infants and younger children was unfeasible, this study continuously recruited children aged 5 to 18 years and finally 151 inpatient children were initially enrolled from October 2017 to April 2018.

Qualified subjects must have normal renal function and could complete 24-h urine collection before receiving clinical treatment. Children who were unable to have normal diet, diagnosed with renal insufficiency, heart failure, congenital heart defects, circulatory system disorders, infectious disease and tumours and those treated with diuretics were excluded. This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the Institutional Review Board (IRB) of Beijing Children's Hospital, Capital Medical University (No. 2017–34). Written informed consent was obtained from all participants.

Urine collection and laboratory testing

All the children were admitted to hospital and had healthy diet provided by the nutrition department of the hospital. During urine collection, participants were reminded of usual drink and regular physical activity. Female menstrual period was avoided during the collection.

The detailed procedures for urine collection were described previously[17]. Briefly, in 24 h, we collected each spot urine at each void except for the first voided urine since all subjects were required to empty the bladder before initiation. The volume of spot urine and 24-h pooled urine was recorded. Researchers (S.C., Z.W., K.L. and Y.Z.) extracted 3-ml urine samples from each void container as spot urine specimens and 4-ml aliquots from the mixed container as 24-h urine specimens. Considering the timing difference on spot urine collection between children and adults[13], we divided all spot urine voids into four durations: morning urine beginning with the second morning urine after awakening and emptying the bladder (08:30–12:30), afternoon (12:31–17:30), evening (17:31–23:59) and overnight urine, which was the first void the next day after the longest period of sleep between 04:00 and 12:00. Random spot urine was chosen by selecting the maximal figures among the randomly generated number of each participant's all urinary samples. A complete collection of 24-h urine sample met the following three requirements: (1) the total volume of 24 h mixed urine $\geq$ 500 ml[19]; (2) leakage of each spot urine $\leq$ 200 ml and (3) missing no more than 1 void during collection.

All urine specimens were stored in the qualified biobank (certificated ISO9001:2015) and were performed under strictly controlled procedures. With the use of automatic biochemical analyser (Roche 5810; Roche), urinary K and Na were measured using the ion-selective electrode method, and urinary creatinine was analysed through the enzymatic method.

Other variables measurement

Height, weight and blood pressure were also collected for each child. The BMI was calculated according to the formula: weight (kg)/height $(m)^2$. All participants were required to rest 5 min before examination. A professional physician recorded their systolic blood pressure and diastolic blood pressure three times using an electronic sphygmomanometer (Omron HEM-7200; OMRON Corporation). Demographic information such as age and gender, clinical data including the serum creatinine level and medication that potentially affect water and electrolyte metabolism were extracted from the electronic medical records. Missing or leakage volume of spot urine, the start and end point of the collection were recorded by case report form.

Twenty-four hour urinary potassium excretion prediction and measurement

The 24UKV was predicted using three formulas based on a single spot urine: Kawasaki[9], Tanaka[10] and Mage[11] methods. Kawasaki and Tanaka equations were developed in Japanese population, whereas the Mage method was a theoretically established formula. Since the Kawasaki method estimated 24UKV using second morning urine spot urine, we compared the timing effect regarding to afternoon, evening and overnight with Tanaka and Mage methods. The formulas are showed in Supplementary Table S1.

The measured 24UKV was calculated by the following formula:

$$\text{Measured 24UKV(mg/d)} = 39 \times \text{concentration of urinary potassium (mmoL/l)} \times \text{24 h urine volume(L/d)}$$

Statistical analysis

We described continuous variables using mean and standard deviation (SD) and categorical variables using proportion rates. The *t* test or Wilcoxon's signed-rank test was used to compare the variable difference between male and female according to the data distribution and skewness.

On the population level, mean 24UKV and SD were calculated for measured and predicted ones by three formulas. Mean differences and 95 % CI between predictive and measured values were obtained to depict the overall accuracy at population level. Paired *t* test or paired Wilcoxon's signed-rank test was conducted to test the significance of mean differences according to the data distribution and skewness. Intraclass correlation coefficient (ICC)[20] and 95 % CI were calculated to evaluate reliability. To conduct an inter-rater reliability analysis using measured 24UKV as the basis of the actual measurement and calculating the estimated values from Kawasaki, Tanaka Mage formulas for each sample, we chose single measurement, absolute agreement (the predicted values equal to the measured ones hypothetically) and two-way mixed-effects model to calculate ICC. Residual mean square was calculated for goodness-of-fit[21] of three equations using paediatric population. The subgroup analysis was conducted on different gender and timing of spot urine. Spearman rank correlation coefficients were calculated between estimated 24UKV and measured values because of the skewed distribution of the 24UKV.

On the individual level, the absolute and relative differences between estimated and measured 24UKV were calculated as follows:

$$\text{Absolute difference (mg/d)} = \text{Estimated 24UKV (mg/d)} - \text{measured 24UKV (mg/d)}$$

$$\text{Relative difference (\%)} = \frac{(\text{Estimated 24UKV (mg/d)} - \text{measured 24UKV (mg/d)})}{\text{Measured 24UKV (mg/d)}} \times 100\%$$

We generated stacked bar charts to show the proportional distribution of 500 mg categories of absolute difference of 24UKV from within ± 500·00 mg/d to beyond ± 2000·00 mg/d and the percentages of five relative difference proportion groups defined within ± 10 %, ±10–19 %, ±20–29 %, ±30–39 %, and over ±40 %. Bland–Altman analysis[22] was further applied to investigate the absolute and relative difference agreement between estimated and measured 24UKV using visualised assessment.

In addition, we examined the misclassification bias of paediatric potassium intake estimated with 24-h urinary potassium measurements. Considering the average potassium absorption of 77 %[23–27], predicted and measured 24UKV were converted into the amount of potassium intake (g/d), namely, the 24UKV(g/d) was divided by 0·77. Then we divided potassium intake into four categories (≤ 1·00, 1·01–2·00, 2·01–3·00 and > 3·00 g/d). Misclassification analysis of frequency and the fraction of participants misclassified was compared with measured and predicted 24UKV among three equations.

We performed main analyses via SAS 9.4 software (SAS Institute Inc.), and ICC was calculated using MedCalc software v14.12.0 (MedCalc Software bvba). *P* value < 0·05 was considered significant.

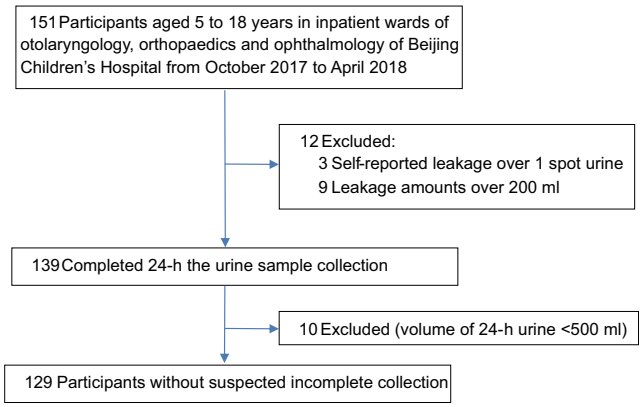

Fig. 1. Flow chart of participants enrollment through the study.

Results

Participant characteristics

This study initially enrolled 151 participants and 129 were included in the final analysis after exclusion of incomplete urine samples (nine subjects were excluded for leakage amount > 200 ml, three for reported leakage of over one spot urine sample and ten for total urine volume < 500 ml; Fig. 1). The mean age of involved participants was 9·7 (SD 2·4) years and 58·1 % (75/129) were male. Systolic blood pressure and diastolic blood pressure showed no difference between male and female, while the BMI and serum creatinine were significantly different between genders. Among all 129 subjects, ten participants voided < 4 times per day had total urine volume ranged from 750 to 2040 ml without leakage or missing, in contrast with one person voided twenty-one times in 24 h had total urine volume of 1880 ml. Overall, the mean void frequency was 7·5 (SD 3·3) times, and the mean 24-h urine volume of all participants was 1349 (SD 628·8) ml. Mean measured 24UKV was 1193·3 (SD 547·9) mg/d and was higher in the male than that in the female (Table 1).

Accuracy of 24-h urinary potassium excretion predictive formulas on population level

The mean predicted 24UKV calculated from Kawasaki, Tanaka and Mage equations were 2426·2 (SD 587·0), 1217·4 (SD 458·6) and 1423·6 (SD 1010·9) mg/d, respectively. The mean bias between predicted and measured 24UKV excretion was showed in Table 2. Mean 24UKV bias (predicted minus measured) for Tanaka equation was −14·9 mg/d (95 % CI: −103, 73·3 mg/d), which was the smallest bias among the three formulas. The largest bias was 1215·6 mg/d

Table 1. Descriptive participant characteristics between male and female
(Mean values and standard deviations)

	All (*n* 129)		Male (*n* 75)		Female (*n* 54)			
	Mean	SD	Mean	SD	Mean	SD	Statistic	*P* value
Age (years)	9·7	2·4	9·8	2·5	9·6	2·2	–0·8	0·4
Height (cm)	140·9	16·4	144·1	16·9	136·4	14·8	–2·4	0·02
Weight (kg)	37·6	15·4	41	16·6	32·9	12·3	–3·0	< 0·01
BMI (kg/m^2)	18·3	4·5	19·1	4·8	17·2	3·8	–2·2	0·03
Systolic BP (mm Hg)	104·1	6·6	104·8	7·5	103·0	4·9	–1·3	0·2
Diastolic BP (mm Hg)	59·9	6·0	60·7	6·1	58·8	5·7	–1·7	0·1
Serum creatinine (μmol/l)	37·8	8·6	39·4	9·3	35·8	7·2	–2·1	0·04
Void frequency (/d)	7·5	3·3	7·6	3·5	7·5	3·2	0·2	0·8
Spot urine								
Random spot urine								
Volume (ml)	202·8	110·7	214·2	124·0	186·9	87·8	–1·0	0·3
Potassium concentration (mmol/l)	31·7	26·1	33·9	27·2	28·6	24·3	–1·1	0·3
Sodium concentration (mmol/l)	115·6	80·6	121·8	86·8	107·0	70·9	–0·7	0·5
Creatinine concentration (μmol/l)	6009·6	5120·7	6368·5	5055·7	5511·1	5215·9	–1·1	0·3
SMU* (*n* 94, male = 54, female = 40)								
Volume (ml)	155·2	96·2	166·0	103·2	140·6	85·0	–1·0	0·3
Potassium concentration (mmol/l)	53·9	38·3	55·8	38·1	51·3	38·9	–0·8	0·4
Sodium concentration (mmol/l)	116·3	73·4	123·1	73·3	107·1	73·5	–1·1	0·3
Creatinine concentration (μmol/l)	7367·1	4836·8	8114·8	5251·0	6357·8	4061·7	–1·5	0·1
Measured 24-h urine								
24-h urine volume (ml)	1349·0	628·8	1403·3	653·4	1273·6	590·7	–1·1	0·3
Potassium concentration (mmol/l)	25·8	14·3	27·1	15·6	23·9	12·0	–0·9	0·4
Sodium concentration (mmol/l)	99·7	54·5	108·0	59·5	88·2	44·6	–1·8	0·07
Creatinine concentration (μmol/l)	5155·1	3580·5	5762·5	4143·1	4311·5	2397·4	–2·0	0·04
Potassium excretion (mg/d)	1193·3	547·9	1296·3	589·5	1050·2	451·6	–2·4	0·01
Sodium excretion (mg/d)	2694·9	1220·3	2974·4	1306·8	2306·8	973·8	–2·9	< 0·01

SMU, second morning urine.
* A total of 94 second morning urine (SMU) samples were analysed for Kawasaki formula, because thirty-five participants, without SMU samples, did not void in the required time duration of Kawasaki equation.

Table 2. Comparison between estimated and measured 24-h urinary potassium excretion (24UKV) using three single spot urine formulas*
(Odd ratios and 95% confidence intervals)

Formulas	24UKV (mg/d)		Mean of absolute difference (mg/d)†	95 %CI	ICC‡	95 %CI	RMS	Correlation§	*P*-value for R
Measured (*n* 129)	1193·3	547·9	Reference		Reference		–	Reference	Reference
Kawasaki (*n* 94)‖	2426·2	587·0	1215·6	1096·1, 1335·1¶	0·12	–0·07,0·38	2·04	0·42	< 0·0001
Tanaka (*n* 117)**	1217·4	458·6	–14·9	–103·0, 73·3	0·53	0·39,0·65	0·33	0·55	< 0·0001
Mage (*n* 129)	1423·6	1010·9	230·3	88·6, 372·0¶	0·47	0·32,0·60	1·11	0·60	< 0·0001

* 24UKV, 24-h urinary potassium excretion; RMS indicates residual mean square.
† Absolute difference (mg/d) = estimated 24UKV (mg/d)-measured 24UKV (mg/d).
‡ ICC, intraclass correlation coefficient, intraclass correlation coefficients and their 95 % CI were calculated using MedCalc by single-measurement, absolute-agreement, two-way mixed-effects model.
§ Correlation referred to Spearman correlation coefficient.
‖ A total of 94 second morning urine (SMU) samples were analysed for Kawasaki formula, because thirty-five participants, without SMU samples, did not void in the required time duration of Kawasaki equation.
¶ The significant difference were detected when comparing estimated values with measured values using paired Wilcoxon test at the 0.05 significance level.
** A total of 117 randomised spot urine (RSU) samples were analysed for Tanaka formula, because the negative bases (12 cases) occurred in the computation procession so that the estimation cannot be computed.

(95 %CI: 1096·1, 1335·1 mg/d) from Kawasaki. Bias was significantly different between Kawasaki and Mage equations ($P < 0·05$).

Moderate, positive correlations were detected between measured and estimated 24UKV using three single spot urine formulas (Spearman correlation coefficient: Kawasaki *v.* Measured: 0·42; Tanaka *v.* Measured: 0·55; Mage *v.* Measured: 0·60, all $P < 0·01$). The ICC and 95 % CI of predicted values from Kawasaki, Tanaka and Mage formulas with measured 24UKV were 0·12(–0·07, 0·38), 0·53(0·39, 0·65), 0·47(0·32, 0·60), respectively. These results indicated all the three formulas had poor reliability to estimate 24UKV. The residual mean square between estimated and measured 24UKV was 0·33 for Tanaka, smaller than those of Mage *v.* measured (1·11) and Kawasaki *v.* measured (2·04) (Table 2, online Supplementary Fig. S1 and Table S2).

The results of subgroup analysis for timing of spot urine and gender were showed in Supplementary Table S3. Except for the predicted values from Tanaka formula using morning, afternoon and evening spot urine, all other estimated 24UKV were significantly different from the measured values in all the timepoint (all $P < 0·05$).

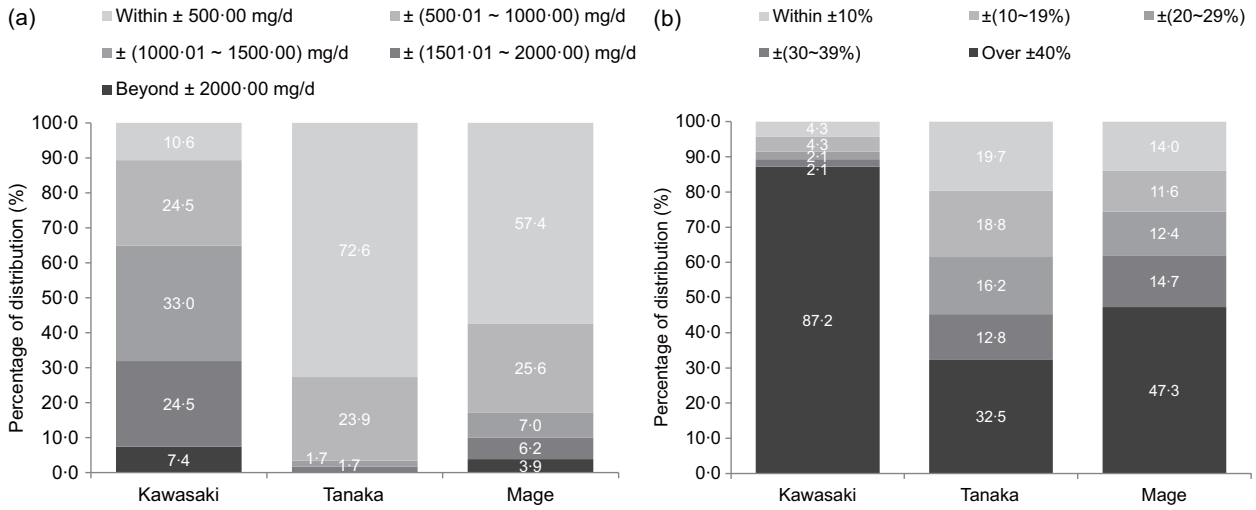

Fig. 2. Absolute and relative difference distribution of Kawasaki, Tanaka and Mage formulas for estimation of 24-h urinary potassium excretion. (a) Absolute difference distribution of Kawasaki, Tanaka and Mage formulas for estimation of 24-h urinary potassium excretion; (b) Relative difference distribution of Kawasaki, Tanaka and Mage formulas for the estimation of 24-h urinary potassium excretion.

Accuracy of 24-h urinary potassium excretion predictive formulas on individual level

The proportions of categories for absolute and relative difference between predicted and measured 24UKV were depicted in Fig. 2. The proportions of absolute difference within ±500·00 mg/d group among Kawasaki, Tanaka and Mage equations were 10·6%, 72·6% and 57·4 %, respectively. On the contrary, the groups with the highest absolute difference (> ±2000·00 mg/d) accounted for 7·4 %, 0·0 % and 3·9 % for Kawasaki, Tanaka and Mage equations, respectively. Tanaka formula had the lowest proportions in each absolute difference category except for the ±500·00 mg/d group among the three formulas. The proportion distribution of relative difference between predicted and measured 24UKV showed similar trends for all the three formulas. The proportion with relative differences within ±10 % was 4·3%, 19·7% and 14·0 %, whereas those > 40 % were 87·2%, 32·5% and 47·3 %, for Kawasaki, Tanaka and Mage, respectively.

Bland–Altman plots in Fig. 3 showed 24UKV prediction using Tanaka equation had the least bias [14·9 mg/d (95 % CI: 103·3, 73·3)] compared with those using Kawasaki and Mage formulas. Values calculated by Kawasaki formula obviously overestimated, while those from Mage formula demonstrated a highly dispersive distribution with wider limit range (upper limit: 1872·3 mg/d; lower limit: –1411·7 mg/d). Moreover, some values were out of the wide limit of Mage formula. Bland–Altman plots showed the least relative difference between estimated and measured 24UKV was from Tanaka formula, while the widest limit range was from Kawasaki formula (upper limit: 343·2 %, lower limit: –78·6 %).

Misclassification analysis

As shown in Table 3, the misclassification rate for 24-h potassium intake calculated from Kawasaki, Tanaka and Mage formulas using single spot urine were 91·5%, 44·4% and 58·9 %, respectively. The misclassification by Kawasaki formula occurred more frequently in the children with lower level of potassium intake (<1·00 g). In contrast, the misclassification mainly happened in children with higher level of potassium intake for Tanaka and Mage formulas (>3·00 g).

Discussion

Elevated blood pressure in childhood is an important risk factor for hypertension and cardiovascular metabolic diseases in adulthood[28,29]. Considering the recent well-documented association between abnormal potassium intake and cardiovascular disorders, such as blood pressure[27,30] and stroke[31], as well as the evidence that potassium intake is critically important for children with chronic kidney disease as hyperkalaemia can be life threatening[32], many international authorities, including USA National Academy of Medicine[33] and the European Food Safety Authority[34], have recommended proper potassium intake to prevent hypertension and CVD.

Salt and Other Nutrient Intakes in Children study showed potassium intake was far less than the recommended level in the schoolchildren of Victoria, Australia[24]. Developing healthy dietary habits and tastes in early childhood is critical and has far-reaching influence throughout children's whole lives. Family-based and institutional nutrition interventions can improve children's diet and health[35]. Generally, due to the lack of accurate and simple evaluation approaches, parents do not know their own daily potassium intake or that of their children. Furthermore, given that parents pay more attention to children's health, they are more willing to develop healthier dietary habits and tastes for their children. Therefore, accurate and convenient monitoring of this nutrient during childhood is an important public health strategy to prevent the adverse outcomes mentioned above.

The 24UKV is widely accepted as the gold standard for assessing 24-h potassium intake, though it has poor practicability in children. Spot urine potassium measurements turned out to be a substitute for 24-h urinary potassium excretion and be a

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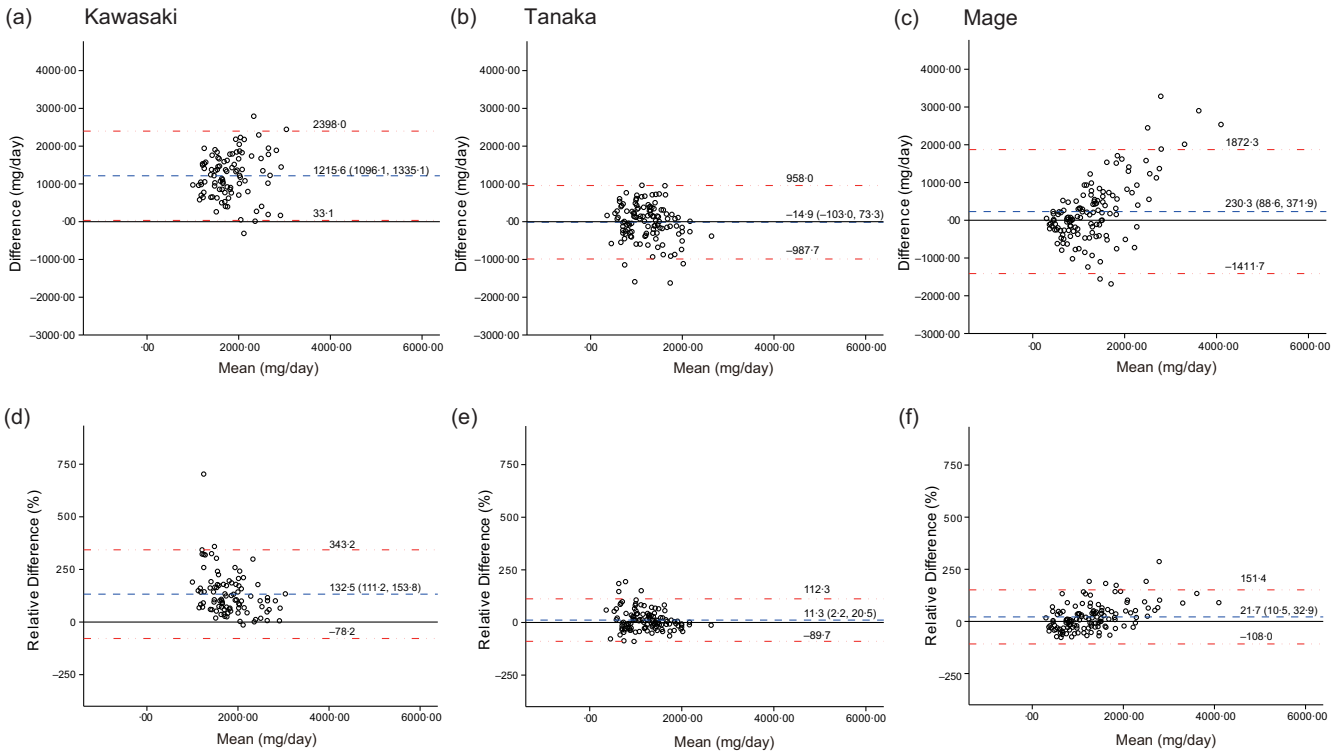

Fig. 3. Bland–Altman plots of the absolute and relative difference in agreement between estimated and measured 24-h urinary potassium excretion (24UKV). (a), (b), (c) absolute difference of estimated and measured 24 UKV; (d), (e), (f) relative difference of estimated and measured 24UKV; (a), (d) Kawasaki formula using second morning spot urine specimen. (b), (e) Tanaka formula using randomised spot urine; (c), (f) Mage formula using randomised spot urine; The blue mid-dashed line is the mean difference or bias between measured and estimated values. The red dash-point lines represent the 95 % limits of agreement of the absolute or relative difference ± 1·96 SDS.

surrogate to evaluate dietary potassium intake in adults. Previous studies validated the inconsistent accuracy of the predictive Kawasaki, Tanaka and Mage formulas using single spot urine to estimate adult 24UKV; however, we know little about their performance on children.

Our study observed the least mean predicted bias in Tanaka equation [−14·9 (SD 486·4) mg/d (95 % CI: −103·0, 73·3), $P > 0·05$] among the three formulas tested, from whom the point ICC value was the highest [0·53(95 % CI: 0·39, 0·65)] and the residual mean square was 0·33. These results indicated that Tanaka formula seemed to be better to estimate mean 24UKV at the population level. A study involved 2460 Portuguese participants[14] showed that the bias of predicted values from measured ones was significantly different and the ICC of Tanaka formula was lower than 0·47, which did not support the result that Tanaka formula had the least bias. Similarly, the validation from a Chinese adult population showed that the estimated 24UKV using the Kawasaki method and Tanaka method had correlation coefficients of 0·36 and 0·39 (all $P < 0·01$) and ICC of 0·31 and 0·27 (all $P < 0·01$), respectively, while the mean bias for the Kawasaki method in estimating 24UKV was the least among these methods[16]. In the subgroup analysis regarding different gender and timing of spot urine, all other mean absolute difference between estimated and measured values were all significant different, except for those from Tanaka formula using morning, afternoon and evening spot urine. Since the duration of overnight urine collection was relatively long and was influenced by different sleep rhythm of participants, the significant bias was mainly derived from the variants within overnight subgroup rather than the true difference between estimated and measured values. The variation originated from timing of spot urine was also occurred when using Kawasaki and Mage formulas to estimate 24UKV in the adult population[13]. Compared with Masayuki Okuda's study in school-aged children and adolescents which developed equations using the ratios of Na/Cr, and K/Cr to estimate daily urinary Na and K excretion using first-morning spot urine (overnight urine)[36], our research was hospital based, and the population characteristics of non-hospital-based studies, such as age and sex distributions, might lead to different proportion rates, even though the compliance and completeness of 24-h urine collection might be better controlled in hospital-based populations. The variation of Tanaka formulas regarding to timing of spot urine were inconsistent between their study and ours, which may partly because of rhythm of 24-h urinary potassium between adults and children are different[37], thus need more studies to figure out the reasons.

All three formulas failed to get acceptable accuracy on the individual level when using them to estimate potassium excretion in children. Our study showed that the least mean difference between estimated and measured 24UKV in the Tanaka equation was −14·9 mg/d (95 % CI: −103, 73·3 mg/d). However, this accuracy cannot be assessed to be unacceptable

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Table 3. Misclassification analysis of potassium intake based on three formulas at individual level*
(Numbers and percentages)

	≤ 1·00 g (*n* 29)						1·01–2·00 g (*n* 69)						2·01–3·00 g (*n* 27)						> 3·00 g (*n* 4)						All			
	Kawasaki†		Tanaka‡		Mage		Kawasaki		Tanaka		Mage		Kawasaki		Tanaka		Mage		Kawasaki		Tanaka		Mage		Kawasaki		Tanaka		Mage	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
≤ 1·00 g	0§		9§		19§		0		14		16		0		1		2		0		0		0		0		24		38	
1·01–2·00 g	1		12		7		2§		41§		28§		0		11		7		0		2		1		3		66		43	
2·01–3·00 g	13		1		3		28		10		17		3§		14§		5§		0		1		2		44		26		27	
> 3·00 g	4		0		0		26		0		8		14		0		12		3§		1§		1§		47		1		21	
Total	18		22		29		56		65		69		17		26		27		3		4		4		94		117		129	
Misclassified	18	100·0	13	59·1	10	34·5	54	96·4	24	36·9	41	59·4	14	82·4	12	46·2	22	81·5	0	0·0	3	75·0	3	75·0	86	91·5	52	44·4	76	58·9

* Listed in *n* (%) for cases and proportion.
† A total of 94 second morning urine (SMU) samples were analysed for the misclassification analysis of Kawasaki formula because thirty-five participants, without SMU samples, did not void in the required time duration.
‡ A total of 117 randomised spot urine (RSU) samples were analysed for the misclassification analysis of Tanaka formula because the negative bases (twelve cases) occurred in the computation procession so that the estimation cannot be computed.
§ The number of consistent classification between estimation and measurement values.

because the mean differences are affected by both under- and overestimation, which could be neutralised interactively. This has been indicated from the individual accuracy results of counterpart proportions between under- and overestimation both in the absolute and relative difference distribution (i.e. > +30 % proportion versus > −30 % proportion for Kawasaki, Tanaka and Mage formulas, respectively). In this study, the proportions of relative differences > 40 % were 87·2 %, 32·5 % and 47·3 %, for Kawasaki, Tanaka and Mage, respectively. The proportion within 20 %, which might be considered acceptable in real world, was approximately less than half for all three formulas (only 8·6 % in Kawasaki, 38·5 % in Tanaka and 25·6 % in Tanaka).

The Bland–Altman plots also showed the estimated agreement performance of three formula through visual evaluation. This kind of neutralised interaction is clearly shown in the Tanaka and Mage formulas (Fig. 3(b), (c), (e) and (f)). For Kawasaki formula, the overestimation appeared to be seen in all levels of 24UKV. This result differed from Mercado's study[13], which showed that the individual relative bias between predicted and measured 24UKV varied from low to high levels. These results showed that the direct use of three approaches in child population could lead to a different pattern of bias compared with that occurred in adults.

In addition, we found the average 24UKV of our participants (mean age: 9·7 years) was 1193·3 (SD 547·9) mg/d (≈30·6 (SD 14·0) mmol/d), which is higher than that in the recent systematic review which showed mean potassium excretions was 14·7–25·2 mmol/d for Chinese children aged 3–16 years[38]. Considering the average potassium absorption of 77 %, the average potassium intake of these participants was about 1550 mg, which was lower than the recommended level by the Chinese dietary reference (adequate intake for potassium: 4–6 years: 1200 mg/d; 7–10 years: 1500 mg/d; 11–13 years: 1900 mg/d; 14–17 years: 2200 mg/d)[39]. In our study, the misclassification rates at individual level were high in all the three methods. Thus, direct application of these formulas in paediatric population might not be a good method to estimate potassium intake and explored its association with interested clinical outcome.

Dietary potassium mainly comes from cereal, rice and potatoes in the daily diet in China according to The China Health and Nutrition Survey[40]. Given the cardiovascular disorder risk by consuming too much Na and too little potassium, some studies showed that replacement of regular salt with potassium-enriched substitutes can lower blood pressure in both controlled situations[38,41] and pragmatic population-wide samples[42], especially among people with hypertension and chronic kidney disease. Currently, the common method of measuring potassium excretion in clinical trials or communities-based investigation was collection of 24-h urine samples[31,43], which was inconvenient for people in work and children. Some large global researches used predictive formulas, such as Tanaka and Kawasaki equations, to estimate the 24-h potassium excretion from spot urine[31,44]. Our study provided an evidence that cautions should be taken when using these three formulas to estimate potassium intake from 24UKV on child population for future field investigation, promotion and evaluation of potassium-enriched substitutes.

Our study applied a modified 24-h urine collection method to collect each single-timed urine sample independently for 24 h, facilitating a reasonable selection of spot urine required in each formula. In addition, we developed a series of protocols to assure the quality of samples, including a detailed written and pictorial instruction for urine collection and standard operation procedure for training all researchers, calibration of instrument with standard samples before test and 10 % of double samples for stability measurement. Nevertheless, given this study was hospital-based cross-sectional observational design, several limitations on this research should be noted. First, the participants were from three general surgical wards involving orthopaedics, otolaryngology and ophthalmology in a medical centre; thus, generalisability of our result on the health children may need further evidence. Other confounders, such as dietary intake, physical activity, drinking water amount, environmental temperature, and humidity, and rest circadian rhythm, could be relatively controlled as well because of the in-hospital accommodation and nursery management. However, generalisation of the results and conclusions to a community child population may need further research in community-based child populations. Second, considering the compliance and feasibility of urine collection, we did not collect multiple 24-h urine on continuous days, and thus the influence of consistency and time delay in metabolism could not be analysed. Therefore, future studies should involve healthy children and collect samples covered several days to validate the performance of the three formulas in children.

Conclusions

In conclusion, cautions should be taken when applying the three common formulas to estimate 24UKV, which is an indicator of potassium excretion in children. Given the urgent need to assure reasonable potassium intake in children, we need to develop a feasible and accurate approach to estimate 24UKV for children.

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Supplementary material

For supplementary materials referred to in this article, please visit https://doi.org/10.1017/S0007114521003354

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