

# NEDITERRANEAN JOURNAL OF Nutrition and Metabolism

Editor-In-Chief Mourizio Battino





ISSN 1973-798X

## **Editorial Board**

#### • • • •

## Editors-in-Chief

Maurizio Battino, PhD, DSc, MD (Hon) (Nutritional Biochemistry) <u>Clarivate Highly Cited Researcher</u> Dipartimento di Scienze Cliniche Specialistiche ed Odontostomatologiche Sez. Biochimica Facoltà di Medicina Università Politecnica delle Marche Ancona, Italy Email: m.a.battino@univpm.it

## **Associate Editors**

R. De Giuseppe (Public Health Nutrition)UNIPV • Laboratory of Dietetics and Clinical Nutrition; Department of Public Health,Experimental and Forensic Medicine, University of Pavia, Italy

T. Forbes (Bioactive Compounds, Obesity and Cancer) Department of Physiology, Institute of Nutrition and Food Technology José Mataix Verdú Center for Biomedical Research University of Granada, Armilla, Spain

F. Giampieri (Nutritional Biochemistry)
 Department of Odontostomatologic and Specialized Clinical Sciences, Sez-Biochimica,
 Faculty of Medicine, Università Politecnica delle Marche, Ancona, Italy (Highly Cited Researcher)

G. Grosso (Nutrition & Dietetics) Department of Biomedical and Biotechnological Sciences. G. Grosso (Nutrition & Dietetics)Department of Biomedical and Biotechnological Sciences,University of Catania, Catania, Italy (Highly Cited Researcher)

E. Espinosa (Internal Medicine) Faculty of Medicine, Università Politecnica delle Marche, Ancona, Italy

M. Petrolo (Dietetics) Karolinska University Hospital Stockholm, Sweden

L. Tomaino (Public Health Nutrition) Emergency Medicine, Università Politecnica delle Marche, Ancona, Italy

## **Co-Editors**

E. Bertoli (Biochemistry) Istituto di Biochimica, Università Politecnica delle Marche, Ancona, Italy

C. Keen (Nutrition) Dept. of Nutrition, University of California, Davis (CA), USA

## **Editorial Committee**

A. Caretto (Clinical Nutrition & Diabetology) Dietetica e Nutrizione Clinica, U.O. di Endocrinologia e Malattie Metaboliche, Azienda Ospedaliera di Summa, Brindisi, Italy

## **Editorial Committee**

A. Caretto (Clinical Nutrition & Diabetology)Dietetica e Nutrizione Clinica, U.O. di Endocrinologia e Malattie Metaboliche,Azienda Ospedaliera di Summa, Brindisi, Italy

F. D'Andrea (Clinical Nutrition & Diabetology) Dietetica e Nutrizione Clinica, Azienda Ospedaliera Maggiore di Novara, Novara, Italy

F. Balzola (Gastroenterology) Azienda Ospedaliera S. Giovanni Battista, Turin, Italy, and Laboratorio Sperimentale di Ricerche Nutrizionali, Istituto Auxologico Italiano, Turin, Italy

E. Del Toma (Nutrition) Scienza dell'Alimentazione, Ospedale S. Camillo Forlanini, Università "Campus Biomedico", Rome, Italy

N. Facchin (Clinical Nutrition & Diabetology) Servizio di Dietetica e Nutrizione Clinica, Ospedale di Bolzano, Bolzano, Italy

G. Fatati (Clinical Nutrition & Diabetology)
Italian Association for Dietetics and Clinical Nutriotion President,
Diabetologia, Dietologia e NutrizioneClinica,
Azienda Ospedaliera, S. Maria, Terni Italy

M.A. Fusco (Clinical Nutrition) Divisione di Dietetica e Nutrizione Clinica, Ospedale S. Camillo-Forlanini, Rome, Italy

M.G. Gentile (Clinical Nutrition) Servizio di Dietetica e Nutrizione Clinica, Azienda Ospedaliera Niguarda, Milan, Italy

J. Godos (Human Nutrition/Clinical Nutrition) University of Catania, Catantia, Italy

L. Lucchin (Clinical Nutrition) Serv. Dietetica e Nutrizione Clinica, Ospedale S. Maurizio, Bolzano, Italy

G. Marelli (Diabetology & Metabolic Diseases) U.O. Diabetologia e Malattie Metaboliche, Ospedale di Desio, Desio (Milan), Italy

F. Muratori (Endocrinology & Pharmacology) Struttura Complessa di Endocrinologia, Ospedale Niguarda Ca' Granda, Milan, Italy

M. Parillo (Clinical Nutrition & Diabetology) UOSD Diabetologia, Malattie del Metabolismo e Nutrizione Clinica,

### **Editorial Board**

G. Adami (Surgery) Dipartimento di Discipline Chirurgiche, Università di Genova, Genoa, Italy

A. Albini (Oncology) Ricerca Oncologica, Polo Scientifico e Tecnologico, IRRCS Multimedica, Milan, Italy

J. M. Alvarez-Suárez (Nutrtional Biochemistry) Grupo de Biotecnología Aplicada a Biomedicina (BIOMED), Universidad de Las Américas, Quito, Ecuador (Highly Cited Researcher)

M. Arca (Internal Medicine) Dip. di Clinica e Terapia Medica, Università di Roma La Sapienza, Rome, Italy

J.M. Argilés (Oncology) Barcelona, Spain

A.G. Atanasov (Biotechnology) Prof. and Head of Molecular Biology, Department: IGAB PAS, Poland

N. Battistini (Nutrition) Scienze Tecniche Dietetiche Applicate, Dipartimento di Scienze Igienistiche, Microbiologiche, Facoltà di Medicina e Chirurgia, N. Battistini (Nutrition) Scienze Tecniche Dietetiche Applicate, Dipartimento di Scienze Igienistiche, Microbiologiche, Facoltà di Medicina e Chirurgia, Università degli Studi di Modena e Reggio Emilia, Modena, Italy

R. Belahsen (Nutrition) Training and Research Unit on Nutrition and Food Sciences, Chouaib Doukkali University, School of Sciences, El Jadida, Morocco

Y.N. Berner (Geriatry) Geriatric Medicine, Meir Medical Center, Kfar Saba, Tel Aviv, Israel

G. Biolo (Internal Medicine) Clinica Medica, Ospedale di Cattinara, Trieste, Italy

G. Bodoky (Oncology) Dept. of Oncology, St. Laszlo Hospital, Budapest, Hungary

M. Bozo (Pediatric Gastroenterology) President of the Syrian Society of Pediatric Gastroenterology and Nutrition, Ministry of Health, Damascus, Syria

L. Busetto (Clinical Medicine) Clinica Medica, Policlinico Universitario, Padua, Italy E. Capanoglu Guven (Food Technology) Food Engineering Department, Istanbul Technical University, Istanbul, Turkey (highly cited researcher)

L. Caregaro (Nutrition) Scuola di Specializzazione in Scienza dell'Alimentazione, Università degli Studi di Padova, Padua, Italy

M. Cascante (Biochemistry) Departament de Bioquimica i Biologia, Molecular Facultat de Quimica Marti i Franques 1, Universitat de Barcelona, Barcelona, Spain

J.S. Castillo Hernández (Nutrition) Facultad de Nutrición, Universidad Veracruzana, Mexico

G. Casu (Cardiology) Head of cardiology department, San Francesco Hospital, Nuoro, Italy

M.G. Ceravolo (Physical & Rehabilitation Medicine) Clinica di Neuroriabilitazione, Università Politecnica delle Marche, Ospedali Riuniti di Ancona, Ancona, Italy

B. Cestaro (Clinical Medicine)Dip. Scienze Precliniche "Lita Vialba", Facoltà di Medicina,Università di Milano, Milan, Italy

## Urinary and dietary sodium to potassium ratio as a useful marker for estimating blood pressure among older women in Indonesian urban coastal areas

Farapti Farapti<sup>a,\*</sup>, Siti Rahayu Nadhiroh<sup>a</sup>, Savitri Sayogo<sup>b</sup> and Nunuk Mardiana<sup>c</sup>

<sup>a</sup>Department of Nutrition, Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia <sup>b</sup>Department of Nutrition, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia <sup>c</sup>Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Received 2 January 2017 Accepted 12 June 2017

#### Abstract.

**BACKGROUND:** Risk factors for hypertension (HT) are age, high sodium (Na) intake, and low potassium (K) intake, as well as the geographical location of a region such us coastal area. Calculation of the sodium-to-potassium (Na/K) ratio was more~strongly associated with blood pressure (BP) than either Na or K alone. Dietary recalls and urine analyses are the most feasible methods for estimating electrolyte intake.

**OBJECTIVE:** This study aims to analyze the association between both urinary and dietary (Na/K) ratio and BP among older women residing at urban coastal in Indonesia.

**METHODS:** The cross-sectional study involved 51 older women aged  $\geq$ 45 y post menopause in urban coastal dwellers. A single 24-h urine collection and food recall 2 × 24 h were used to assess sodium and potassium intake.

**RESULTS:** Of the 51 subjects mean age  $56.98 \pm 5.7$  years completed the study, 37.3% of subjects were classified as hypertensive. The mean of urinary and dietary Na/K ratio were  $5.28 \pm 1.68$  and  $1.12 \pm 0.74$  respectively. Urinary Na/K ratio was independently associated with systolic BP (SBP), meanwhile, the association between dietary Na/K ratio and both SBP and diastolic BP (DBP) showed significant correlation only in the unadjusted model.

**CONCLUSION:** Na/K ratio is a useful marker for estimating SBP and assessing populations at high risk for HT. The slightly low Na and substantially low K intake might cause the Na/K ratio become high enough to induce HT. Since the prevalence of HT is high enough, studies in this field may provide clues for the further understanding of its causes and get effectively ways to decrease Na/K ratio in urban coastal dwellers.

Keywords: Sodium, potassium, blood pressure, urban coastal, hypertension

#### 1. Introduction

A raised blood pressure (BP) is the most common and preventable risk factors for cardiovascular disease both in Western and Asian populations; population living in urban areas have the prevalence of hypertension (HT) 2–3 times higher than in rural areas [1, 2]. The prevalence of HT in developing countries was 32.3%, it means about

<sup>\*</sup>Corresponding author: Farapti Farapti, Department of Nutrition, Faculty of Public Health, Universitas Airlangga, Indonesia, Surabaya 60115, Indonesia. Tel.: +62 857 083 87556; E-mail: farapti@fkm.unair.ac.id.

1 in 3 adults in thoses area is hypertensive [3]. Reducing the burden disease associated with HT has become as a global public health priority and a major public health challenge [1]. Indonesian National Health Survey 2013 reported that 26.5% of the Indonesian adult population have established HT, furthermore, most of (63.2%) HT cases in society were not yet diagnosed [4].

Risk factors for HT include age, high intake of sodium (Na), and low intake of potassium (K), as well as the geographical location of a region [5–8]. Epidemiological study described that female gender, older age, and HT increase the sensitivity to dietary sodium intervention [9]. The association with older age raises concerns about hormonal problems in elderly, which could increase the risk of HT [9]. Moreover, the INTERSALT (International Study of Electrolyte Excretion and Blood Pressure) study reported stronger associations between Na/K ratio and blood pressure with increasing age [10].

Most populations around the world consume less than the recommended intake of K, unfavorably high Na intakes remain prevalent around the world. High Na and low K together had a pivotal role in the pathogenesis of HT [11]. Population studies have reported significant correlation between Na intake and BP, and so have K intake [8,10]. Furthermore, a systematic review have revealed that the sodium to potassium [Na/K] ratio was more strongly associated with HT and BP than either Na or K alone [12].

Several methods were applied by population studies to assess Na and K intake. Urine analyses and dietary recalls are the most feasible methods for estimating electrolyte intake [12–14]. The measurement of 24-hour urinary Na and K excretion is the 'gold standard' and highly reliable method for obtaining data of these intakes in population since it reflects more than 90% of Na and K intake. On the other hand, dietary method is easier to perform and more convenience thoughtless reliable [15, 16].

Studies on Na and K intake using 24-hour urine collection in the healthy population have been applied by many countries in the worldwide [16], although most studies still applied dietary methods to know sodium and potassium intake in society [17]. Several studies demonstrated that region had a significant interaction with the risk of HT [5, 6, 8, 18]. Moreover, Du et al. reported the interaction between the region of residence and Na/K ratio are significant [18].

Community-dwelling in coastal area has a high risk of HT. The tradition of salting and drying fish to preserve fish by coastal communities was a custom and their occupational every day. The high amount of salt used for salting fish can increase the Na intake in these populations and have an undesirable effect on BP [7, 19, 20]. On the other hand, low K intake in urban dwellers was inverse association with BP [8, 21].

Indonesia is an archipelagic country, with high prevalence of HT [4]. Many communities (about 60% of Indonesian people) reside in coastal region [22]. Measuring sodium and potassium intake by 24-hour urinary method at the urban coastal resident in Indonesia is challenging and have never been done. The analysis of relationship between Na/K ratio and BP often uses only one method. This study aims to analyse the association between Na/K ratio and BP among older women residing at urban coastal in Indonesia, using two methods single urinary 24-h and dietary food recall  $2 \times 24$ -hours, and furthermore to assess whether those methods are applicable to identify populations at high risk for HT in this community.

#### 2. Subjects and methods

#### 2.1. Study subjects

Our study assumed that older women related to menopause, so we included healthy old adult women aged  $\geq$ 45 years old and post menopause as participants, although most area use  $\geq$ 60 years to refer to the older population. Since almost of older person in urban coastal in Kenjeran Surabaya (central city of east Java, Indonesia) followed programme of community health care facilitated by government, data was collected on two selected places from five elderly community health care in urban coastal area in Surabaya with cluster random sampling method and subjects recruitment by consecutive sampling. Because of completeness of urine collection,

we recruited all respondents in two places (135 respondents following the strict screening stage) and finally, for one year study (2015), fifty-one subjects met the study criteria.

We recruited only female because most of (88%) participants participating actively at community health care in that place were female. Moreover, there was the difficulty of collecting urinary 24 h in men since they generally worked outside the home (mostly as fishermen). Participants were included in the study if they were postmenopause, permanent resident in coastal area for more than 10 years, and willing to collect a 24-hours urine sample. Participants with cognitive impairment (mini mental state examination score <24), kidney dysfunction (creatinine clearance test (<60 mL/min), consuming tobacco and alcohol, and inaccurate urine collection were excluded.

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures were approved by the Ethics Committee of the Faculty of Public Health, Universitas Airlangga, and written informed consent was obtained from all subjects.

#### 2.2. Study measurements

Data collection in this study including structure questionnaire, food recall  $2 \times 24$  hours, anthropometric measurements, a 24-hours single urine sample, and a blood sample was obtained from all subjects. A structured questionnaire was fulfilled by participants. Body weight, height, and BP were measured. At the end of the first visit, all participants were given plastic bottles complete with written and verbal instructions for a single 24-hours urine collection measured. The sample urine was brought by the researcher to ISO 9001 certificated laboratory to be measured of urinary sodium, potassium, and creatinine. Sodium and potassium were analyzed by ion-selective electrodes method which responds relatively specifically to ions both anions and cations [23]. Creatinine determination in biological fluids was carried out by Jaffe's reaction [24]. Participants were also asked to recall their dietary intake over the previous  $2 \times 24$  hours.

#### 2.3. Anthropometric data

Weight and height were measured by a trained investigator using calibrated electronic scale. Weight and height, to calculate Body Mass Index (BMI), were measured without shoes and heavy clothes. All data were collected following norms set out by the WHO. BMI was computed as the ratio of weight (kg) per square height (m<sup>2</sup>).

#### 2.4. Physical activity

Physical activity of subjects was obtained by interview and the physical activity point was calculated by multiplication score of intensity, duration, and frequency from the questionnaire. It was categorized below the average if total score was less than 40 point [25].

#### 2.5. Blood pressure

Blood pressure was measured on the right arm of seated participants following a 5 min rest period, using standard calibrated mercury sphygmomanometers with regular adult cuffs by trained nurse. Three times measurements were obtained with participants and the average of three readings was used for the analysis. Hypertension was defined by "JNC 7" as a systolic BP (SBP)  $\geq$  140 mm Hg or a diastolic BP (DBP)  $\geq$  90 mm Hg, or a self-report of taking antihypertensive medication or previously diagnosed by a physician.

#### 2.6. Dietary sodium (Na) and potassium (K)

Dietary Na and K were assessed by food recall  $2 \times 24$  hours and performed after the day of urine collection. Subjects were requested to maintain their normal eating habits during the survey period. The nutritionist asked the subjects to recall all foods and beverage consumed in the previous  $2 \times 24$  h. One day of 24-h dietary recalls was selected randomly from Monday to Sunday in each individual, and another day when the day of urinary collection. To clear the portion size, nutritionists demonstrated food models and the photographic manual of household measures. The food recall was analyzed using Nutrition Data System (Nutrisurvey) and reported as mg/day.

#### 2.7. Urinary 24 h

All participants were given written and verbal instructions how to collect 24-hour urine correctly. The first urine of the day was discarded, and all urine over the following 24 hours, including the first urine of the following day, was collected in the bottles provided. When the subjects returned the urine bottles to researchers the following day, they were asked to confirm the accuracy of their 24 h urine collection by asking whether any collection of urine was lost or forgotten and total volume of the collection was measured, Completeness of collection was determined by the subject's records and the output of creatinine in the 24-hours urine. Inaccurate urine collections defined as either a 24-hour urinary volume <500 mL or a urinary creatinine <5.0 mmol/day or extreme outliers for urinary creatinine >3 SD from the mean were excluded [26]. In those cases in which the collection of 24 h urine sample had to be repeated, further meetings were planned. So, each participant who meets study criteria but had inaccurate urine collections can be included again become subject by collecting urinary 24 h correctly.

#### 2.8. Urinary and dietary Na/K ratio

Urinary sodium concentration and potassium concentration were analyzed and expressed as millimoles per liter. Urinary Na/K was calculated by dividing urinary Na by K. Similar to urinary Na/K ratio, dietary Na/K ratio was expressed as milligram per day was calculated by dividing dietary Na by K.

#### 2.9. Statistical analysis

All data were checked for normality using the Kolmogorov Smirnov test. Sample characteristics were compared between HT status using *t* test or Mann Whitney test for continuous data (Table 1). Bivariate analysis to assess the correlation between Na, K, Na/K ratio and SBP/DBP was performed by Pearson or Spearman test (Table 2). Multivariable robust liniar regression models were used to evaluate the association of BP (dependent variable) with urinary and dietary Na/K ratio (independent variable) after adjustment for age, length of stay, BMI, and dietary Na/K ratio (for analysis urinary Na/K) or urinary Na/K ratio (for analysis dietary Na/K). To commit the potential effect of antihypertensive medication, sensitivity analyses with the exclusion of subjects consuming these medications were performed (Table 3). All statistical calculations were performed with Statistical Package for Social Science version 21 with a *p*-value<0.05 was significant.

#### 3. Results

A total of 51 subjects completed the study. They averaged  $56.98 \pm 5.7$  years of age, had a BMI of  $25.96 \pm 4.85 \text{ kg/m}^2$ . Almost all subjects lived in the coastal area since birth, so the mean residence was almost similar to mean age ( $52.8 \pm 12.57$ ) years. From 51 subjects with BP measurements, 19 subjects (37.3%) were classified as hypertensive. Among those with HT, 15 subjects were taking antihypertensive drugs regularly. All subjects have participated actively in elderly community health program for five years.

The mean  $\pm$  SD urinary Na of all subjects was  $104.75 \pm 59.25$  mmol/d, urinary K was  $20.52 \pm 9.72$  mmol/d, and urinary Na/K ratio was  $5.28 \pm 1.68$ . The dietary method showed that the mean Na intake was

#### F. Farapti et al. / Urinary and dietary sodium to potassium ratio

Variable	Total	Normotensive	Hypertensive	р
	<i>n</i> = 51	n=32	<i>n</i> = 19	
Age [years]	$56.98 \pm 5.7$	$57.19 \pm 6.85$	$57.16 \pm 3.45$	0.98
Long time of residence [years]	$52.8 \pm 12.57$	$56.59 \pm 7.16$	$56.53 \pm 3.34$	0.96
SBP [mm Hg]	$132.25\pm17.78$	$121.09\pm9.89$	$151.05\pm10.75$	0.00*
DBP [mm Hg]	$83.63 \pm 10.3$	$77.03 \pm 6.33$	$94.74 \pm 4.24$	0.00*
BMI [kg/m <sup>2</sup> ]	$25.96 \pm 4.85$	$24.26\pm5.24$	$28.82 \pm 1.36$	0.001*
Physical activity index	$21.45 \pm 4.86$	$22.06 \pm 4.81$	$20.42\pm4.89$	0.25
Urinary 24 h				
Volume [ml]	$837.25 \pm 330.13$	$818.75 \pm 279.9$	$868.42 \pm 407.6$	0.61
Sodium [mmol/d]	$104.75\pm59.25$	$94.59 \pm 41.13$	$120.53 \pm 81.03$	0.21
Potassium [mmol/d]	$20.52\pm9.72$	$21.19 \pm 10.18$	$19.50\pm9.08$	0.57
Urinary Na/K ratio [mmol/mmol]	$5.28 \pm 1.68$	$4.74 \pm 1.36$	$6.01 \pm 1.89$	0.015*
Clearance creatinine [ml/mnt]	$94.06\pm22.86$	$90.88 \pm 2.11$	$99.42 \pm 24.38$	0.2
Dietary intake				
Fluid consumption [ml]	$1400.91 \pm 343.61$	$1377.71 \pm 348.33$	$1439.98 \pm 341.23$	0.537
Energy [kkal/d]	$1374.63 \pm 303.13$	$1374.91 \pm 261.82$	$1374.16 \pm 370.38$	0.993
Sodium [mg/d]	$1247.8 \pm 764.17$	$1091.23 \pm 747.6$	$1511.49 \pm 736.59$	0.057
Potassium [mg/d]	$1220.09 \pm 955.8$	$1300.92 \pm 680.61$	$1083.96 \pm 391.11$	0.211
Dietary Na/K ratio [mg/mg]	$1.12 \pm 0.74$	$0.89 \pm 0.55$	$1.5\pm0.87$	0.011*

 Table 1

 Baseline characteristics stratified by hypertensive status<sup>1</sup>

<sup>1</sup>Hypertensive subjects significantly different than normotensive subjects. \*t-test. Significant, p < 0.05.

Variable	Systolic BP		Diastolic BP	
	r	р	r	р
Urinary 24 h				
Sodium	-0.053	0.713	-0.118	0.41
Potassium	-0.184	0.195	-0.153	0.283
Na/K ratio	0.377	0.006*	0.263	0.062
Dietary intake				
Sodium	0.196	0.169	0.16	0.27
Potassium	-0.19	0.182	-0.184	0.196
Na/K ratio	0.278	0.048*	0.232	0.101

 Table 2

 Bivariate analysis: Correlation between sodium. Potassium and blood pressure

\*Pearson correlation. Significant. p < 0.05.

 $1247.8 \pm 764.17$  mg/d, dietary K was  $1220.09 \pm 955.8$  mg/d, and dietary Na/K ratio  $1.12 \pm 0.74$ . Based on hypertensive status, the mean urinary and dietary Na/K ratio in hypertensive subjects were higher significantly than normotensive subjects with p = 0.015 and p = 0.011 respectively. Baseline characteristics stratified by hypertensive status are summarized in Table 1.

Independent variable <sup>†</sup>	Ν	Systolic BP	P value	Diastolic BP	P value
	Change [95% CI]			Change [95% CI]	
Urinary Na/K ratio					
Model 1		3.99[1.18–6.81] <sup>†</sup>	0.006*	1.48[-0.223-3.19]	0.087
Model 2		3.89[1.18-6.6]	0.006*	1.28 [-0.37-2.93]	0.125
Model 3		4.89[1.93-7.84]	0.002*	1.72[-0.189-3.63]	0.076
Dietary Na/K ratio					
Model 1		7.79[1.29–14.3]	0.020*	4.39[0.614-8.17]	0.024*
Model 2		4.25[-2.25-10.74]	0.195	2.26[-1.69-6.22]	0.256
Model 3		3.28[-0.38-2.14]	0.309	1.76[-2.43-5.94]	0.397

Table 3 Robust linier regression to show the association of BP [dependent variable] with urinary and dietray Na/K ratio [independent variable]

Model 1: Univariate model. Model 2: Multivariate model adjusted for age. Long time of residence. BMI. and dietary Na/K ratio [for analysis urinary Na/K] or urinary Na/K ratio [for analysis dietary Na/K]. Model 3: Model 2 with sensitivity analysis excluding subjects consuming antihypertensive medication (the number of subjects using antihypertensive medicine is 15 subjects). <sup>†</sup>Unit for change in BP is expressed as the percentage per each 1-unit change in the urinary and dietary Na/K ratio. \*Significant, p < 0.05.

#### 3.1. Bivariate correlation between sodium, potassium, and blood pressure

The analysis of bivariate correlation using Pearson or Spearman test demonstrated either Na or K alone in urinary and dietary did not correlate significantly with BP. However urinary and dietary Na/K ratio correlated significantly with SBP (Table 2).

#### 3.2. The association of urinary and dietary Na/K ratio with Blood Pressure

Urinary Na/K ratio was independently associated with SBP. In the unadjusted model [model 1], SBP increased by 3.99 [95% CI:1.18, 6.81]; p = 0.006] for each 1-unit increase in urinary Na/K. This association remained significant event after adjustment for age, length of stay, BMI, dietary Na/K ratio (for analysis urinary Na/K) or urinary Na/K ratio (for analysis dietary Na/K), SBP increased by 3.89 [95% CI 1.18, 6.6] for each 1-unit increase in urinary Na/K (model 2). Furthermore, urinary Na/K ratio was changed 4.89 with significance by excluding subject with antihypertensive medicine. In other hands, the association between urinary Na/K and DBP reported that no significant correlation both for the unadjusted model and adjusted model.

The association between dietary Na/K ratio and SBP/DBP showed that significant correlation only in the unadjusted model. However, it became not significantly in model 2 and model 3. Furthermore, associated with SBP in the univariate model, dietary Na/K increased almost twice than those in urinary Na/K. There were 7.79 (95% CI 1.29, 14.3) versus 3.99 (95% CI 1.18, 6.81).

#### 4. Discussion

The present findings indicate that two methods both dietary and urinary Na/K ratio were correlated with SBP in older women in the urban coastal area. Moreover, findings in our study corroborate a systematic review of population studies that Na/K ratio was more strongly associated with HT and/or systolic and diastolic BP outcomes than either Na or K alone [12]. Our study also reported that either Na or K alone in both urinary and dietary did not correlate significantly with BP (p > 0.05). Some studies which applicable Na/K ratio more strongly associated with BP than Na and/or K alone were Mente et al. [6], Hu et al. [27], Yamori et al. [28], Ruixing et al. [29], Huggins et al. [26], Schroder et al. [30], and Xie et al. [31] studies.

Population studies that investigated the association between urinary Na and K and blood pressure in multiple countries are INTERSALT [10], PURE (Prospective Urban Rural Epidemiology) study [6], and INTERMAP (The International Study of Macro/Micronutrients and Blood Pressure) [26]. Among many countries involved in those studies, Indonesia is not included and there are limited studies about urinary 24 h Na and K intake in Indonesia. Recent study showed among all countries in Southeast Asia until 2013, only Singapore used the gold standard 24-hr urinary Na excretion to estimate intakes [13].

We used two instruments to measure Na and K intake; single urinary 24 h and food recall  $2 \times 24$  h. Urinary excretions of Na and K are considered to adequately reflect the dietary intakes of these electrolytes, meanwhile, dietary Na and K often were reported underestimate or overestimate [13, 16]. However dietary recalls and urine analyses are often the most feasible methods for estimating Na and K intake [13, 14]. Our study demonstrated Na intake from dietary method was less than urinary, otherwise, K intake from dietary method was greater than urinary (Table 1). The Trial of Non-pharmacologic Intervention in the Elderly (TONE) study showed a similar result with our study; dietary recalls yielded estimates of Na and K intake that respectively averaged 22% less and 16% greater than those from urine assays [13]. However, our study differs from the previous study showing that Na intake measured by the dietary method is larger than 24-hour urinary method [14].

The mean of urinary Na/K ratio and dietary Na/K ratio in our study were  $5.28 \pm 1.68$  and  $1.12 \pm 0.74$  respectively and categorized as a high value since dietary guidelines demonstrated the normal range of dietary Na/K ratio was either 0.49 or 0.32 [32]. Most studies using dietary methods to assess Na/K ratio also showed high value of Na/K ratio were Hu et al. with the Na/K ratio of 3.34 [27]; Ruixing et al. of 1.8 [29]; Schroder et al. of 0.62 [30]; Bu et al. of 2 [33]; and Zhang of 1.41 [34]. Meanwhile, several studies applied 24-hours urine collection to assess Na/K ratio in adults [12]. There were Du et al. with the Na/K ratio of 4.9-2.8 [18]; Mirzaei et al. of  $3.69 \pm 1.58$  [21]; Millen et al. of 1.41 [35]; Michel et al. of 3.71 [36]; Huggins et al. of 1.99 [26]; Redelinghuys et al. of 4.27 [37]; Yamori et al. of 4.55 [28]; Xie et al. of 6.1 [31]; Ortega et al. of 2.57 [38]; and Tran et al. of 2.44 [5].

The mean of sodium intake based on 24-h urinary excretion in our subjects was  $104.75 \pm 59.25$  mmol/d. These averages were considerably lower than those reported in many populations in the world. Our result was surprising since the most adult populations have the mean Na intakes >100 mmol/day, and for many Asian countries, the mean intakes are >200 mmol/day [39]. Low sodium intake in our study may be explained by age, education, and energy intake of our subjects. Some countries from epidemiological studies demonstrated that low Na intake presented in women >50 years old, subjects with lower educated and low energy intakes [39, 40]. Furthermore, a coastal area in our study was located in the urban central city so the accessibility of health information and health care could be achieved easily. Following actively in health programme, our subjects might change their behavior by decreasing of salt intake on their food.

Mean dietary intakes of potassium in our subjects were  $1220.09 \pm 955.8 \text{ mg/day}$  and only  $20.52 \pm 9.72 \text{ mg/d}$  based on urinary 24j. It means very low or only 17-25% to compared Recommended Dietary Allowance (RDA). One causes of low potassium intake were the low intake of vegetables and fruits. Analysis fruit and vegetables from data Indonesian National Health Survey 2010 among adult female showed the mean of consuming fruit and vegetables was  $139.7 \pm 55.9 \text{ g/d}$  which were lower than World Health Organization 400 g/d [41]. Moreover, recent study showed low consumption of fruit and vegetable contributed to low potassium intake [42].

The slightly low sodium and substantially low potassium intake in urban coastal dwellers might cause the Na/K ratio among our subjects become high enough to induce HT. It was revealed that both the mean urinary and dietary Na/K ratios in hypertensive subjects were higher significantly than normotensive subjects (Table 1). Moreover, urinary and dietary Na/K ratio correlated significantly with SBP (Table 2). There were similar to Hedayati et al. study at 3303 Dallas heart study age 30–60 years old showed that urinary Na/K ratio in hypertensive subjects was higher than normotensive [43]. Furthermore, INTERSALT study in 40 centers in the worldwide also revealed the relation of urinary Na/K ratio to SBP was highly significant (p < 0.001) [10].

The superiority of this study is we used 24 h urinary to measure Na and K intake because there are limited studies by measuring 24 h urinary Na and K in Indonesia [6, 10, 17, 26]. Furthermore, this study applied Na/K

ratio for assessing dietary and estimating blood pressure at the population level and the previous studies revealed that Na/K ratio is a useful marker for nutrition surveillance in populations and can identify populations at high risk for nutrition-related chronic disease [10,44].

The weakness of our study is about the units of Na/K ratio. For additional note, the units of Na/K differ depending on the measurement method (mg vs mmol), so it may be difficult to compare and to examine the same methods with different units [44]. The assessing of Na and K intake by recent intake and single 24-h urine cannot be regarded to adequately reflect long-term dietary exposure. Multiple 24-hour urine samples collected over a period of several months would yield a better estimate of habitual intake [12, 37]. The results of our study can not be applied to the general population, but generalized only in the population with specific characteristics such as only older women with post menopause dwelling at urban coastal area.

In conclusion, this study supports the view that Na/K ratio is a useful marker for estimating BP since Na/K ratio is more strongly associated with blood pressure than either sodium or potassium alone. Both urinary and dietary Na/K ratios are potential surveillance tool that can assess and identify populations at high risk for HT in coastal area; assessing by urinary Na/K ratio is more recommended. The slightly low sodium and substantially low potassium intake in urban coastal dwellers might cause the Na/K ratio become high enough to induce HT. Studies in this scope may propose clues for a further understanding of its causes and be getting effective ways to decrease Na/K ratio in our population.

#### Acknowledgments

The authors would like to express our sincere appreciation to the participants of this study. The authors also wish to thank Faculty of Public Health, Universitas Airlangga, for giving a funding support in this research.

#### **Conflict of interest**

The author(s) confirm that this article content has no conflict of interest.

#### References

- Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: Analysis of world-wide data. Lancet. 2005;365:217-23.
- [2] Cifkova R, Fodor G, Wohlfahrt P. Changes in hypertension prevalence, awareness, treatment, and control in high-, middle-, and low-income countries: An update. Curr Hypertens Rep. 2016;18(8):62.
- [3] Sarki AM, Nduka CU, Stranges S, Kandala NB, Uthman OA. Prevalence of hypertension in low- and middle-income countries: A systematic review and meta-analysis. Medicine [Baltimore]. 2015;94(50):e1959.
- [4] Research and Health Development Division, Ministry of Health Republic of Indonesia. Indonesian National Health Survey. 2013.
- [5] Tran TM, Komatsu T, Nguyen TK, Nguyen VC, Yoshimura Y, Takahashi K, Wariishi M, Sakai T, Yamamoto S. Blood pressure, serum cholesterol concentration and their related factors in urban and rural elderly of Ho Chi Minh City. J Nutr Sci Vitaminol. 2001;47:147-55.
- [6] Mente A, O'Donnell MJ, Rangarajan S, McQueen MJ, Poirier P, Wielgosz A. Association of urinary sodium and potassium excretion with blood pressure. EJM. 2014;371:601-11.
- [7] Sihotang UA. The association between risk factors of hypertension and the occurrence of hypertension in coastal communities in District of Belawan Medan. Thesis. 2013.
- [8] Chan TY, Chan AY, Lau JT, Critchley JA. Sodium and potassium intakes and blood pressure in Chinese adults in Hong Kong: A comparison with southern China. Asia Pac J Clin Nutr. 1998;7:33-6.
- [9] He J, Gu D, Chen J, Jaquish CE, Rao DC, Hixson JE, Chen JC, Duan X, Huang JF, Chen CS, Kelly TN, Bazzano LA, Whelton PK, GenSalt Collaborative Research Group. Gender difference in blood pressure responses to dietary sodium intervention in the GenSalt study. J Hypertens. 2009;27(1):48-54.

- [10] Intersalt Cooperative Research Group. Intersalt: An international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. BMJ. 1998; 297:319-28.
- [11] Adrogue HJ, Madias NE. Sodium and potassium in pathogenesis of hypertension. N Engl J Med. 2007;356:1966-78.
- [12] Perez V, Chang ET. Sodium-to-potassium ratio and blood pressure, hypertension, and related factors. Adv Nutr. 2014;5:712-41.
- [13] Espeland MA, Kumanyika S, Wilson AC, Reboussin DM, Easter L, Self M, Robertson J, Brown WM, McFarlane M, TONE Cooperative Research Group. Statistical issues in analyzing 24-hour dietary recall and 24-hour urine collection data for sodium and potassium intakes. Am J Epidemiol. 2001;153:996-1006.
- [14] Sasaki S, Yanagibori R, Amano K. Validity of a set-administrated diet history questionnaire for assessment of sodium and potassium comparison with single 24-hour urinary excretion. Jpn Circ J. 1998;62:431-5.
- [15] Sauberlich HE. Assessment of nutritional status. Second edition. New York: CRC press; 1999. pp. 301-11.
- [16] Kawano Y, Tsuchihashi T, Matsuura H, Ando K, Fujita T, dan Ueshima H. Report of the working group for dietary salt reduction of the Japanese society of hypertension: [2] Assessment of salt intake in the management of hypertension. Hypertens Res. 2007;30:887-93.
- [17] Batcagan-Abueg AP, Lee JJ, Chan P, Rebello SA, Amarra MS. Salt intakes and salt reduction initiatives in Southeast Asia: A review. Asia Pac J Clin Nutr. 2013;22:490-504.
- [18] Du S, Batis C, Wang H, Zhang B, Zhang J, Popkin BM. Understanding the patterns and trends of sodium intake, potassium intake, and sodium to potassium ratio and their effect on hypertension in China. Am J Clin Nutr. 2014;99:334-43.
- [19] Begossi BO, Cavichiolo MP, Gungel M. Blood Pressure and Hypertension among Coastal Fishermen in South-east Brazil. J Community Med Health Educ. 2013;4:1-5.
- [20] Pougnet R, Pougnet L, Lodde B, Canals-Pol ML, et al. Cardiovascular risk factors in seamen and fishermen: Review of literature. Int Marit Health. 2013;64:107-13.
- [21] Mirzaei M, Soltaniz M, Namayandeh M, GharahiGhehi N. Sodium and potassium intake of urban dwellers: Nothing changed in Yazd, Iran. J Health Popul Nutr. 2014;32:111-7.
- [22] Fahrudin A, Yulianto G. The sosio economic characteristics of coastal population. Coastaleco's Webblog. [updated 2008 April26; cited 2016 Jan 15]; Available from https://coastaleco.wordpress.com
- [23] Hilwa WR. Clinical Instrumentation Refresher Series: Ion Selective Electrodes. Med TechNet Online Services; 1998, pp. 1-16.
- [24] Toora BD, Rajagopal. Measurement of creatinine by Jaffre' reaction-determination iof concentration of sodium hydroxide required for maximum color development in standard, urine, and protein free flitrate of serum. Indian Journal of Experimental Biology. 2002;40:352-4.
- [25] Montoye HJ, Kemper HCG, Saris WHM, Washburn RA. Measuring Physical Activity and Energy Expenditure. Champaign, IL: Human Kinetics, 1996.
- [26] Huggins CE, O'Reilly S, Brinkman M, Hodge A, Giles GG, English DR, Nowson CA. Relationship of urinary sodium and sodiumto-potassium ratio to blood pressure in older adults in Australia. MJA. 2011;195:128-32.
- [27] Hu G, Tian H. A comparison of dietary and non-dietary factors of hypertension and normal blood pressure in a Chinese population. J Hum Hypertens. 2001;15:487-93.
- [28] Yamori Y, Liu L, Mu L, Zhao H, Pen Y, Hu Z, Kuga S, Negishi H, Ikeda K, Japan-China Cooperative Study Group: Chongqing P. Diet-related factors, educational levels and blood pressure in a Chinese population sample: Findings from the Japan-China Cooperative Research Project. Hypertens Res. 2002;25:559-64.
- [29] Ruixing Y, Jinzhen W, Shangling P, Weixiong L, Dezhai Y, Yuming C. Sex differences in environmental and genetic factors for hypertension. Am J Med. 2008;121:811-9.
- [30] Schroder H, Schmelz E, Marrugat J. Relationship between diet and blood pressure in a representative Mediterranean population. Eur J Nutr. 2002;41:161-7.
- [31] Xie J, Liu L, Kesteloot H. Blood pressure and urinary cations in a low fat intake Chinese population sample. Acta Cardiol. 2001;56: 163-8.
- [32] Drewnowski A, Maillot M, Rehm C. Reducing the sodium-potassium ratio in the US diet: A challenge for public health. Am J Clin Nutr. 2012;96:439-44.
- [33] Bu SY, Kang MH, Kim EJ, Choi MK. Dietary Intake Ratios of Calcium-to-Phosphorus and sodium to potassium are associated with serum lipid level in healthy Korean adults. Prev Nutr Food Sci. 2012;17:93-100.
- [34] Zhang Z, Cogswell M, Gillespie C, Fang J, Loustalot F, Dai S, Carriquirry AL, Kuklina EV, Hong Y, Merritt R, et al. Association between usual sodium and potassium intake and blood pressure and hypertension among U.S. adults: NHANES 2005–2010. PLoS ONE. 2013;8:e75289.
- [35] Millen AM, Norton GR, Majane OH, Maseko MJ, Brooksbank R, Michel FS, Snyman T, Sareli P, Woodiwiss AJ. Insulin resistance and the relationship between urinary Na+/K+ and ambulatory blood pressure in a community of African ancestry. Am J Hypertens. 2013;26:708-16.

- [36] Michel FS, Norton GR, Majane OH, Badenhorst M, Vengethasamy L, Paiker J, Maseko MJ, Sareli P, Woodiwiss AJ. Contribution of circulating angiotensinogen concentrations to variations in aldosterone and blood pressure in a group of African ancestry depends on salt intake. Hypertension. 2012;59:62-9.
- [37] Redelinghuys M, Norton GR, Scott L, Maseko MJ, Brooksbank R, Majane OH, Sareli P, Woodiwiss AJ. Relationship between urinary salt excretion and pulse pressure and central aortic hemodynamics independent of steady state pressure in the general population. 2010;56:584-90.
- [38] Ortega RM, Lo'pez-Sobaler AM, Ballesteros JM, Perez-Farinos N, Rodriguez E, Aparicio A, et al. Estimation of salt intake by 24h urinary sodium excretion in a representative sample of Spanish adults. Br J Nutr. 2011;105:787-94.
- [39] Brown IJ, Tzoulaki J, Candeias V, Elliott P. Salt intakes around the world: Implications For public health. International Journal of Epidemiology. 2009;38:791-813.
- [40] Geleijnse JM. Sodium, potassium, and blood pressure studies in the young and the old. Haveka B.V Alblasserdam, 1996.
- [41] Muharram Z, Hardinsyah. The Analysis of fruits and vegetables consuming in Indonesia female. JPG. 2013;8(Suppl 1):36.
- [42] Farapti. Tender coconut water as alternative food to increase potassium intake among prehypertension adult female? Health science Journal of Indonesia. 2015;1:12-6.
- [43] Hedayati SS, Minhajuddin AT, Ijaz A, Moe OW, Elsayed EF, Reilly RF, Huang C. Association of urinary sodium/potassium ratio with blood pressure: Sex and racial differences. Clin J Am Soc Nephrol. 2012;7:315-22.
- [44] Yi SS, Curtis CJ, Angell SY, Anderson CA, Jung M, Kansagra SM. Highlighting the ratio of sodium to potassium in populationlevel dietary assessments: Cross-sectional data from New York City, USA. Public Health Nutr. 2014;17:2484-8.