ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 11, Special issue 1, 2018

Online - 2455-3891
Print - 0974-2441

Research Article

IS URINARY CREATININE ASSOCIATED WITH WASTING IN NEONATES

SRI WIDIA NINGSIH[1]*, NITA ANDRIANI LUBIS[2], ASLIS WIRDA HAYATI[3], ALKAUSYARI AZIS[3]

[1]Department of Pharmacy, Medan Health Polytechnic, Jl. Airlangga No. 20 Medan Indonesia 20112. [2]Department of Health Analyst, Medan Health Polytechnic, Jl. William Iskandar Pasar V Barat No. 6 Medan Estate, Indonesia 20137. [3]Department of Nutrition, Riau Health Polytechnic, Pekanbaru, Indonesia. Email: widianingsih29@gmail.com

Received: 13 October 2017 , Revised: 17 October 2018 and Accepted: 14 February 2018

ABSTRACT

Results: There was no wasting neonates, WH z-score (WHZ) >-2 SD. The concentrations of absolute creatinine urine excretion were about 11.1–167.2 mmol/day, and creatinine urine excretion related to body weight was about 4.08–50.06 mmol/Kg/day. There were negative significant correlation between the absolute creatinine urine with WH (r=−0.357, p=0.035) and creatinine urine – body weight with WH (r=−0.482, p=0.003). Creatinine urine measurement is a sensitive biomarker of renal and total muscle mass that can be used as a child's growth biomarker.

Methods: The study was cross sectional by involving 35 healthy neonates aged 1–3 days that were born at Pekanbaru Andini Hospital, Indonesia, on August to September 2014. Body length gauges, digital weighing scale, family socioeconomic questionnaires, pediatrics urine collection bag, and creatinine urine were used to collect the data. We used two indicators (creatinine urine and weight/height [WH]) as a parameter in this study. Pearson correlation (significance $p<0.05$ and $p<0.01$) was applied for statistical analysis.

Objective: To analyze the correlation between creatinine urine and wasting in neonates.

Conclusion: The creatinine urine was associated with wasting in neonates therefore can be used as a growth biomarker.

Keywords: Biomarker, Creatinine urine, Neonates, Wasting.

 DOI: http://dx.doi.org/10.22159/ajpcr.2018.v11s1.26603

INTRODUCTION

Wasting is a serious public health problem in Indonesia with 12.1% of prevalence [1]. Wasting describes a deficiency in weight for height due to a lack of tissue and fat mass. Children get wasted when they shed weight quickly, consequently of an infectious disease incidence and diets that do not cover nutritional needs. This carries an immediate increased risk of morbidity and mortality in short term and will be impeding children from achieving their full potential development and cognitive performance, for long-term effect will disrupt the country's productivity.

Wasted children have 5–20 times higher risk of dying than nourished children. World health organization (WHO) established wasting standards based on anthropometrics measurement with weight/height z-score (WHZ-score) <−2 SD. Causes of wasting are insufficient access to health care, inadequate caring and feeding practice, lack of food security, and poor sanitary. Currently, some countries report a prevalence of wasting of more than 10% throughout the year, such as Nigeria (10%), Pakistan (15%), and India (20%). The prevalence of wasting in children under five about 6,8% and 5,3% severed wasting in Indonesia [2-4].

Wasting in infants aged under 6 months is often ruled out; particularly, wasting among neonates. Insufficiency of disease prevalence data is the main circumstance aggravating the challenges [5-7]. No certain method has been reported as an indicator. An anthropometric method in determining wasting less accurate because error possibility may occur during measuring such human error. Furthermore, it cannot predict nutrition status in short time and the other factor beyond nutrition.

Creatinine, the biochemical waste product that produced through the catabolism of phosphocreatine, is filtered mainly by the kidney. A high urinary creatinine level can mean a problem in the muscles, moreover, kidneys. The function of the kidney during early fetus in neonates was most affected by amniotic fluid and regulating fetal blood pressure. It will continue through the period after childbirth. The child's kidney perform important function for help the body to maintain the balance of nutrients and minerals, ability to use growth hormone, to correct levels of erythropoietin, to balance the proper levels of mineral and acid-bases in the blood.

Creatinine urine measurement is the most widely used to measure renal function [8], which is a sensitive biomarker of renal and total muscle mass. The aim of this study was to assess the correlation between creatinine urine and wasting in neonates therefore can be used as a growth biomarker.

METHODS

Study design Subject and urine collection

It was a cross-sectional study conducted from January to December 2014. Of the 37 neonates that were selected, two individuals removed with missing values of urinary creatinine urine before the analysis. They were healthy neonates that were born at Andini Mothers and Children Hospital at Tuanku Tambusai Street No.55, Pekanbaru, Indonesia, on August to September 2014. Individuals were enrolled around 1–3 days of neonates' life. Criteria for inclusion included normal gestation (36–40 weeks), natural birth, and cesarean section. The study complied with the World Medical Association Declaration of Helsinki–Ethical Principles for Medical Research involving human subjects and approved by the Institutional Review Board of the Faculty of Medicine, University of Riau, Ministry of Education and Culture of Republic Indonesia (certificate number 67/UN19.1.28/UEPKK/2014).

Data collection

All parents gave written informed consent. At the time of informed parental consent, neonates were stratified by gender (male and female), race (Indonesian and expatriate), and feeding (breastfeeding and formula). The 24-h urine was collected by using pediatrics urine collection bag, aliquot to 6 ml, and stored at −20°C until analysis.

Equipment and materials research

Body length gauges, weight scales digital baby, baby urine bags, household socioeconomic questionnaires baby (name, gender, age, race, height parents). The other materials were pediatrics urine collection bag, sanitizing wipe, diaper, urine jar were used in sampling babies wee.

Research procedure

Neonates' urine was collected by a nurse who was trained by researchers at the Andini Hospital. The mother was briefly explained about the implementation of the study and using of pediatrics urine collection bag. The urine is taken as 24-h samples and then stored in the refrigerator at a temperature of −20°C in Prodia Clinical Laboratory Pekanbaru until samples were fully collected. Urine of babies was packed by staff Prodia Pekanbaru and then it was sent to Prodia Centre in Jakarta for analysis. The analysis was carried out simultaneously.

Creatinine urine measurement and standardization

Creatinine measurements were performed with the use of Jaffe method and Spectrophotometer ADVIA 1800: ADVIA, Germany.

Statistical analysis

Statistical analysis and results are reported based on the complete data. Statistical outliers, defined as outside the 95% confidence, limits the normal probability plots. Determination of severely wasted, wasted, normal, and obese was performed according to the classification of WHO. Pearson correlation, with significance *p<0.05 and **p<0.01, was applied for statistical analysis. The analysis was performed by using IBM SPSS Statistics version 20 [9].

RESULTS AND DISCUSSION

Familial socioeconomic characteristic of neonates

The familial socioeconomic characteristic of neonates are presented in Table 1. We met 35 individuals during the study period. Inclusion criteria are medically stable and receiving full enteral feeding (formula and breastfeeding), distribution characteristics (gender, ethnic, gestational age, body weight and body length at birth).

There were different neonates gender in our study population about 74.3% male and 25.7% female. The higher percentage of male neonates than female neonates, due to genital factor. Meanwhile, this was a coincidence that birth rate of male neonates was more than female neonates. Most of the neonates' ethnic were Malay (97.1%), only 2.9% was Chinese [10].

Nutritional status of neonates

The data of individuals' baseline characteristics are presented in Table 2. There was no wasting neonates (WHZ >−2 SD). WHZ of neonates is expected to be optimal. Study from Mgongo *et al*. [4] reported that 24.7% children, aged 0–36 months, were wasting in six districts of Kilimanjaro, Tanzania. In another study, Mahyar *et al*. from Qazvin, Iran indicated that 0.7% from 804 children aged 0–24 months were wasting.

The assessment of nutritional status based on birthweight and length is a manifestation of prenatal growth of the infant since individual prenatal growth occurs during the mother's pregnancy. The pattern of prenatal relied on genetic factors but also influenced by environmental factors such as energy and nutrition. The common method to determine nutritional status is the body mass index (BMI) measurement. The BMI is the determination of individual nutritional status by comparing body weight in kilograms (Kg) with height in meters (m) squared.

Mother's BMI before entering pregnancy is one indicator of nutritional status that needs to be considered. Assessment of mother's nutritional status through the calculation of BMI may indicate maternal nutritional quality in the past which may have an impact on maternal and fetal health during pregnancy and the quality of the baby to be born. Therefore, it is established that BMI of a mother before entering pregnancy should be sufficient which is in normal nutrient status category [12].

In our study, we found that mother's BMI of neonates about 65.625% normal, 18.75% underweight, 12.5% overweight, and 3.125% obese, it can be seen in Table 1. Mothers with normal and over nutritional status will affect the neonates' nutritional status not to wasting.

The measurement of daily creatinine excretion is used for the biochemical evaluation of the nutritional status of adults and children which is done by completeness check of 24-h urine collections. The result of measurement absolute creatinine urine excretion of the newborn was about 11.1–167.2 mmol/day, with a negative significant correlation between creatinine urine excretion and WH (r=−0.357, p=0.035), it was presented in (Fig. 1).

The investigation of creatinine urine in infancy is more complicated than other age groups. This is because, during the neonatal period, the renal system has a remarkable role in growth and development. The kidneys itself experience a maturation. Likewise, the condition of the musculoskeletal system at birth is not characterized by a lot of movement, personality, or activity; however, it will be directly affected by the dietary habits. Furthermore, limited references and studies about creatinine urine excretion in infancy give rise to difficulty in interpreting the level of urinary creatinine [8,6].

Several limitations of our study should be considered. First, we did not use a direct comparison to a standard of newborn creatinine urine. Second, we had no information on neonates' illness.

Urinary creatinine excretion related to body weight was about 4.08–50.06 mmol/Kg/day, with a negative significant correlation between creatinine urine-body weight to WH (r=−0.482, p=0.003), it can be seen in (Fig. 2). Based on international clinical reference, normal excretion of creatinine urine in newborns is about 0.11–1.78 mmol/Kg/day [13]. Allegaert *et al*. [14] analyzed creatinine urine about 0.21–2.36 mmol/Kg/day in 84 neonates.

The amount of creatinine formed on a daily basis is related to muscle mass, which varies with diets, ethnicity, age, and gender. According to our study, creatinine urine excretion-body weight was 10–100 times higher

Table 1: Familial socioeconomic characteristics of neonates

Variables	Criteria	Value*
Gender	Male	74.3 (26)
	Female	25.7 (9)
Ethnic group	Malay	97.1 (34)
	Chinese	2.9 (1)
Mother's BMI (Kg/m^2)	Normal	65.625 (21)
	Underweight	18.75 (6)
	Overweight	12.5 (4)
	Obese	3.125 (1)

*% (n). BMI: Body mass index

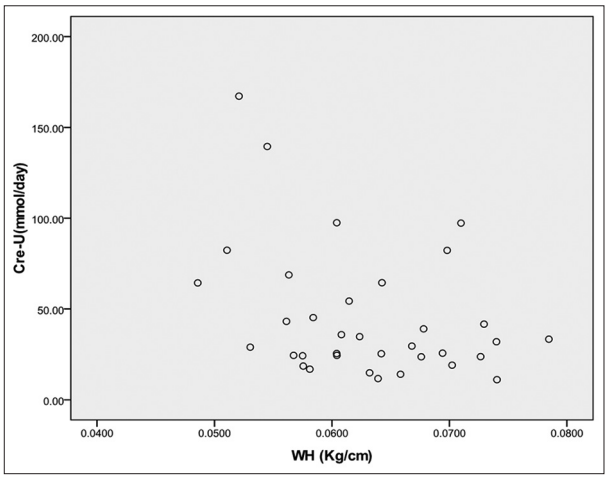

Fig. 1: Absolute creatinine urine excretion in neonates related to weight/height

Table 2: Characteristics of neonates

Variables	Mean±SD	Range
Age (day)	0.6286±0.64561	0–3
Weight (Kg)	3.1203±0.42130	2.38–4.08
Height (cm)	49.5143±1.63368	46–53
WH (Kg/cm)	0.0629±0.0738	0.0521–0.0740
WAZ	0.00000±1.000000	−1.757–2.278
HAZ	0.00000±1.000000	−2.151–2.134
WHZ	0.00000±1.000000	−1.943–2.106
Absolute urinary creatinine excretion (mmol/day)	45.3171±36.04347	11.1–167.2
Urinary creatinine excretion related to body weight (mmol/Kg/day)	45.3171±36.04347	4.08–50.06
Logarithm absolute urinary creatinine excretion (mmol/day)	1.5509±0.29691	1.07–2.22

SD: Standard deviation, WH: Weight/height, WHZ: Weight/height z-score

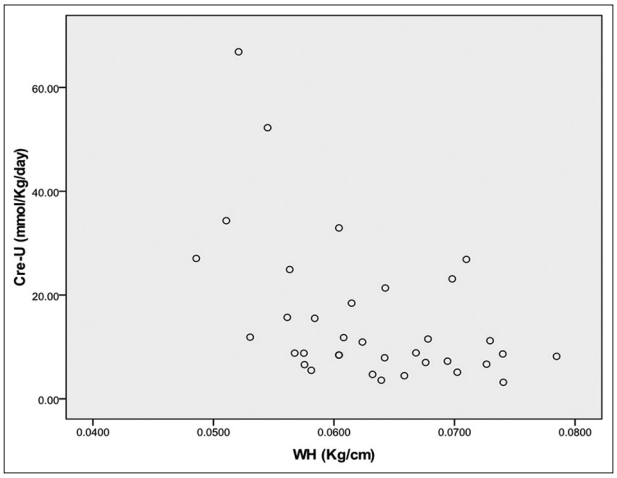

Fig. 2: Creatinine urine excretion – body weight in neonates related to weight/height

than the previous study of Allegaert *et al.* [14] that was conducted in Belgium. This was because of the following: (1) The condition of neonates in dehydration. When the neonates were just born, they were separated from their mother for hours without milk whether breastfeeding or formula. They were given formula milk (10–30 ml), then breastfeeding practice about 2–6 hours later [7,8,15]. Creatinine urine levels were affected by various biological creatinine metabolism [16].

The levels of creatinine urinary-body weight had a different range in different gender. It was about 7.73–21.04 mmol/Kg/day in female neonates and 4.08–50.06 mmol/Kg in male neonates. A study by Remer *et al.* [17] found that urinary creatinine excretion in children aged 3–18 years was about 0.134–0.201 mmol/Kg/day in boys and 0.127–0.182 mmol/Kg/day in girls. Urinary creatinine excretion in males tends to be higher than females. Females usually have lower creatinine levels than males because on average, they have less skeletal muscle mass than males [18].

CONCLUSION

The creatinine urine was associated with wasting in neonates and can be used as growth biomarker. Similar research should be conducted with more sample and cohort through 1000 days of life.

ACKNOWLEDGMENT

Herewith, we convey our thanks and best regards for financial and facilitation support from Riau Health Polytechnic, Prodia Clinical Laboratory, and Andini Hospital.

AUTHOR'S CONTRIBUTION

SWN, NAL, ASW, and AA contributed to design the study. SWN prepared the manuscript and research report. ASW and NAL analyzed the data. AA managed the data collection. All the authors reviewed the manuscript before submission. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Indonesian Health Ministry. National Basic Health Research. Jakarta. Indonesian Health Ministry; 2013.
2. Fernandez ID, Hilmes JH, de Onis M. Prevalence of nutritional wasting in populations: Building explanatory model using secondary data. Bull World Health Organ 2002;80:282-91.
3. World Health Assembly Target 2025: Wasting Policy Brief. WHO; 2014. Available from: http://www.who.int/nutrition/topics/globaltargets_wasting_policybrief.pdf.[Last accessed on 2017 Jun 04].
4. Mgongo M, Chotta NA, Hashim TH, Uriyo JG, Damian JD, Pedersen BS, *et al*. Underweight, stunting and wasting among children in Kilimanjaro Region, Tanzania; A population-based cross-sectional. Int J Environ Res Public Health 2017;14:439.
5. Kerac M, Blencowe H, Grijalva-Eternod C, McGrath M, Shoham J, Cole TJ, *et al*. Prevalence of wasting among under 6-month-old infants in developing countries and implications of new case definitions using WHO growth standards: A secondary data analysis. Arch Disease Child 2011;96:1008-13.
6. Manila RM, Bouchard C, Bar-Or O. Growth, Maturation and Physical Activity. 2nd ed. New Zealand: Human Kinetics Publisher; 2004.
7. Andreev E, Koopman M, Arisz L. A rise in plasma creatinine that is not a sign of renal failure: Which drugs can be responsible? J Intern Med 1999;246:247-52.
8. Sulemanji M, Vakili K. Neonatal renal physiology. Semin Pediatr Surg 2013; 22: 195–198.
9. Hayati AW, Aziz A, Ningsih SW. The Pyridinium Crosslinks of Urine is Associated with Body Length in Neonates. Indonesia, Jakarta: Seminar in Responding to the Nutrition Transition in Asia Pacific Region; 2016.
10. Na'im A, Syaputra H. Citizenship, Ethnicity, Religion and Language of the Indonesian Population, the Results of the 2010 Population Census. Jakarta-Indonesia: International Crisis Group (ICG); 2011. p. 36.
11. Mahyar A, Ayazi P, Fallahi M, Javadi TH, Farkhondehmehr B, Javadi A, *et al*. Prevalence of underweight, stunting and wasting among children in Qazvin, Iran. Iran J Pediatr Soc 2010;2:37-43.
12. Ibrahim M, Forsyth JS. Lifestyle and maternal health interaction between mother and fetus. In: Jane BM, John WT, editors. Nutrition in Early Life. Chichester: John Wiley & Sons Ltd.; 2003. p. 1-38.
13. Creatinine Random Urine; 2017. Available from: http://www.questdiagnostics.com/testcenter/TestDetail.action?ntc=8459. [Last accessed on 2017 Aug 25].
14. Allegaert K, Vermeersch P, Smits A, Mekahli D, Levtchenko, Pauwels S. Paired measurement of urinary creatinine in neonates based on a Jaffe and an enzymatic IDMS-traceable assay. BioMed Central Nephrol 2014;15:62.
15. Sharkawy AM, Sahota O, Maughan RJ, Lobo DN. The pathophysiology of fluid and electrolyte balance in the older adult surgical patient. Clin Nutr 2014;33:6-13.
16. Poggio ED, Nef PC, Wang X, Greene T, Van Lente F, Dennis VW, *et al*. Performance of the cockcroft-gault and modification of diet in renal disease equations in estimating GFR in ill hospitalized patients. Am J Kidney Dis 2005;46:242-52.
17. Remer T, Neubert A, Masser-Gluth C. Anthropometry-based reference values for 24-h urinary creatinine excretion during growth and their use in endocrine and nutritional research. Am J Clin Nutr 2002;75:561-9.
18. Howard TE. Clinical Chemistry. New York: John Wiley and Sons; 1989. p. 4, 58-62.