Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1349549
J Health Sci Med. 2024;7(1):110-113

Exploring normal urinary biomarker ratios in a pediatric population: insights into age and gender variations

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Cite this article as: Gülyüz A. Exploring normal urinary biomarker ratios in a pediatric population: insights into age and gender variations. *J Health Sci Med.* 2024;7(1):110-113.

Received: 18.09.2023 • **Accepted**: 07.01.2024 • **Published**: 15.01.2024

ABSTRACT

Aims: The assessment of urinary biomarker ratios, such as sodium/creatinine (Na/Crea), potasium/creatinine (K/Crea), calcium/creatinine (Ca/Crea), phosphorus/creatinine (P/Crea), uric acid/creatinine (Uric acid/Crea), magnesium/creatinine (Mg/Crea), and sodium/potassium (Na/K), holds significant importance in clinical and research contexts as they offer insights into physiological and pathological processes. This study aimed to establish the normal ranges of urinarymineral ratios across age and gender groups in a Turkish pediatric cohort.

Methods: This cross-sectional study was conducted involving 162 healthy children, with ages ranging from 2 to 15 years, at the Department of Pediatrics, Selçuk University. Demographic information, urinary biomarker ratios, and dietary features were recorded. Participants were divided into three age groups (2-5, 6-10, and 11-15 years), and statistical analyses were performed to determine relationships and variations.

Results: Gender distribution was uniform across age groups ($p>0.05$). Urinary creatinine levels stabilized after age 6. The mean urinary Na/Crea ratio was 0.33±0.22 mEq/mg, showing correlations with age and other ratios ($p<0.001$). Urinary K/Crea ratio was 0.13±0.15 mEq/mg, with significant differences between Group 1 and Group 3 ($p>0.05$). Urinary Na/K ratio was 3.5±2.4 mEq/mEq and correlated with uric acid and Ca/Crea ratio ($p<0.001$). Urinary calcium levels were consistent ($p<0.001$). Ca/Crea ratio correlated with other ratios ($p<0.001$). Urine P/Crea ratio differed significantly among groups ($p>0.05$). Uric acid levels differed between Group 2 and Group 3 ($p>0.05$), while uric acid//Crea ratio correlated with age and other ratios ($p<0.001$).

Conclusion: The findings provide insights into the normal ranges of urinary biomarker ratios in a Turkish pediatric cohort. The results align with previous studies and emphasize the impact of age, gender, and dietary factors on these ratios.

Keywords: Urinary mineral ratios, pediatric population, normal ranges, age and gender variations, mineral metabolism

INTRODUCTION

The assessment of urinary biomarker ratios, such as Na/Crea, K/Crea, Ca/Crea, P/Crea, uric acid//Crea, Mg//Crea, and Na/K, has crucial importance in clinical and research settings since they can provide valuable insights into various physiological and pathological processes. These ratios serve as important indicators of electrolyte balance, mineral metabolism, and renal function. Understanding the normal ranges of these ratios is essential for accurate diagnosis, monitoring, and management of numerous health conditions.

However, it is widely acknowledged that these urinary ratios are not fixed and can exhibit considerable variability. This variability can be attributed to a multitude of factors, including genetics, race, gender, age, dietary habits, and levels of physical activity.[1-4] Genetic predispositions and inherent physiological differences among individuals from diverse ethnic backgrounds and racial groups can contribute to variations in urinary biomarker ratios.[5-9] Furthermore, hormonal differences linked to age and gender play a pivotal role in influencing these ratios.[10,11] Additionally, lifestyle factors such as dietary preferences and levels of physical activity have been shown to exert significant impacts on urinary biomarker ratios, reflecting the intricate interplay between human physiology and environmental factors.[12-15]

Given the intricate interaction of factors influencing urinary biomarker ratios, it becomes imperative to establish comprehensive and accurate baseline ranges for these ratios across different demographic categories. These ranges would not only aid in distinguishing between normal and abnormal values but also provide a broader context for interpreting results in clinical and research settings. By shedding light on the extent of variations that can be attributed to genetic, racial, gender-related, age-

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related, dietary, and activity-related factors, healthcare professionals can make more informed decisions and tailor interventions that align with an individual's specific physiological makeup and circumstances.[16-18]

The aim of this study was to define the normal ranges of urinary Na/Crea, K/Crea, Ca/Crea, P/Crea, uric acid//Crea, Mg//Crea and Na/K ratios by age and sex in a Turkish pediatric cohort.

METHODS

Study Design

This cross-sectional study was conducted between June 2000 and December 2000 at the Department of Pediatrics, Faculty of Medicine, Selçuk University. The study included 162 healthy children with 5% to 95% percentiles in terms of weight and height, who applied to polyclinics due to various complaints and were found normal following a detailed clinical and laboratory assessment. Ethical standards were considered according to Declaration of Helsinki for the ethical principles for medical research. The study was produced from a thesis in 2001 and ethics committee approval was not requested for this study.

Measurements

Age, gender, Na/Crea ratio, K/Crea ratio, Ca/Crea ratio, P/Crea ratio, uric acid//Crea ratio Mg//Crea ratio, Na/K ratio were noted. The ratios were calculated by using random spot urine samples.

All children were examined in detail and their histories were taken. Patients who were found to have a systemic disease on examination and who had a history of any drug use, renal and metabolic disease in the family were excluded from the study.

Dietary features: Free-fed children who did not receive breast milk were included in the study. Children who had no vitamin d deficiency were considered for the assessment.

Participants were divided into three groups according to age groups; Group 1: 2-5 years, Group 2: 6-10, and Group 3: 11-15 years. Three groups were compared for urinary mineral excretion.

All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Statistical Analysis

SPSS (Statistical Package for Social Sciences) for Windows 13.0 software was used for data analysis. Descriptive statistical methods (mean, standard deviation, frequency) were employed to evaluate the study data. The Shapiro-Wilk test was used to assess the normality of data distribution. The chi-squared test was used to assess the distribution of gender across the age groups. Differences in mean values among different groups were evaluated using analysis of variance followed by post hoc comparisons (ANOVA with posthoc Tukey and Kruskal-Wallis with Bonferroni). Correlations between urinary biomarker ratios were assessed using Pearson correlation coefficients. $p<0.05$ was accepted as significant.

RESULTS

Demographic Characteristics

The study comprised a total of 162 participants, including 86 girls (53.1%) and 76 boys (46.9%). The gender distribution yielded a female-to-male ratio of 1.13. The participants' ages ranged from 2 to 15 years, with a mean age of 7.5±3.3 years. The cohort was categorized into three age groups: Group 1 (2-5 years), Group 2 (6-10 years), and Group 3 (11-15 years). The gender distribution was uniform across these age groups (Table 1).

Table 1. Distribution of children according to groups and gender

Gender	Group 1		Group 2		Group 3		Total	
	number	%	number	%	number	%	number	%
Male	24	49	39	45.9	13	46.4	76	46.9
Female	25	51	46	54.1	15	53.6	86	53.1
Total	49	30.2	85	52.5	28	17.3	162	100

Urinary Creatinine Levels

The analysis of urinary creatinine levels revealed no significant gender-based differences ($p>0.05$). The mean urinary creatinine levels were 34.5±18.8 mg/dl for Group 1, 51.2±33.1 mg/dl for Group 2, and 52.8±33.9 mg/dl for Group 3. Notably, a statistically significant disparity in creatinine levels was observed between Group 1 and Group 2 ($p>0.05$). However, after the age of 6 years, the values appeared to stabilize and remain relatively similar across the age groups (Table 2).

Table 2. Mean, 5th and 95th percentile values of urinary creatinine level (mg/dl)

	Mean	SS (±)	5th percentile	95th percentile
Group 1	34.5	18.8	5.1	74.5
Group 2	51.2	33.1	10.4	118.4
Group 3	52.8	33.9	6.6	128.5

Urinary Biomarker Ratios

The mean urinary Na/Crea ratio was found to be 0.33±0.22 mEq/mg. Additionally, a significant correlation was established between the urinary Na/Crea ratio and age, Ca/Crea ratio, and K/Crea ratio ($r=0.44$, $p<0.001$).

The mean urine K/Crea ratio was 0.13±0.15 mEq/mg, displaying no significant gender-based difference. However, a statistically significant difference emerged

between Group 1 and Group 3 (p>0.05). Correlation analysis indicated associations between the urine K/Crea ratio and uric acid (r=0.27, p<0.001) and Na/Crea ratio (r=0.44, p<0.001), while no significant correlation was observed with the Ca/Crea ratio.

The urinary Na/K ratio demonstrated no substantial difference between the groups or genders, with a mean value of 3.5±2.4 mEq/mEq. Moreover, a negative correlation was noted with uric acid (r=-0.24, p>0.01), while positive correlations were observed with calcium and Ca/Crea ratio (r=0.38, p<0.001).

Urinary calcium levels showcased consistent mean values across gender and age groups, with an average of 5.1±6.2 mg/dl. Notably, positive correlations were identified between calcium and sodium, as well as magnesium (p<0.001).

The mean Ca/Crea ratio across the entire study cohort was 0.13±0.15 mg/mg. A positive correlation was established between the Ca/Crea ratio and P/Crea, Mg//Crea, and Na/Crea ratios. Conversely, a negative correlation was observed with uric acid//Crea ratio. The Ca/Crea ratio exhibited an increase with age, while the 95th percentile value demonstrated a non-significant decrease from 0.68 mg/mg to 0.42 mg/mg (p>0.05) (**Table 3**).

Table 3. Mean, 5th and 95th percentile values of urinary calcium/creatinine ratio (mg/mg)

	Mean	SS (±)	5th percentile	95th percentile
Group 1	0.16	0.18	0.018	0.68
Group 2	0.13	0.14	0.016	0.54
Group 3	0.10	0.10	0.021	0.42

The mean urine P/Crea ratio was determined to be 0.8±0.6 mg/mg. Comparative analysis indicated a significant difference between Group 1 and the other two groups (p>0.05).

Uric acid levels in urine revealed an average value of 31±18.5 mg/dl. A significant disparity was observed between Group 2 and Group 3 in urine uric acid levels (p>0.05). Gender had no substantial effect on uric acid levels (p>0.05). The mean uric acid//Crea ratio for the three groups was 1.01±1.06 mg/mg. Age-based differences were significant between Group 1 and Group 3 (p>0.05), while gender differences were not observed (p>0.05). The uric acid//Crea ratio displayed positive correlations with age, Na/Crea, K/Crea, and P/Crea ratios (p<0.001).

DISCUSSION

The findings of this study provide valuable insights into the normal ranges of urinary biomarker ratios across different age and gender groups in a pediatric population. These results have implications for clinical interpretation, health management, and future research in the field of pediatric nephrology and metabolism. In comparing our findings with existing literature, several noteworthy observations can be made.

Our study revealed that urinary biomarker ratios, such as Na/Crea, K/Crea, and Ca/Crea ratios, exhibited variations across different age groups in this Turkish pediatric cohort. Similar observations were reported by Simsek at et al.[2] in their study involving a pediatric population. Furthermore, the observed stability in urinary creatinine levels after the age of 6 years aligns with the findings of Simeckova et al.[19] who demonstrated a stabilization trend beyond this age.

Interestingly, the associations between urinary mineral excretion ratios and age, as well as correlations among different biomarker ratios, were similar to the findings of prior studies.[1] These correlations can be attributed to the intricate interplay of physiological processes governing mineral and electrolyte homeostasis.

The significant gender-based differences in urinary mineral excretion ratios were not observed in our study, consistent with results presented by Marwaha et al.[20] This contrasts with the earlier work of den Busche et al.[21] who reported significant gender-related variations in urine sodium, potassium, and creatinine. However, differences in study population, methodology, and demographics may contribute to such disparities.

Our findings also point to correlations between urinary element ratios and uric acid and calcium levels.[22] These correlations, as indicated in previous research, underscore the interconnectedness of various metabolic processes in the human body.

Limitations

It's important to acknowledge certain limitations. The relatively modest sample size and single-center nature of the study may limit the generalizability of the findings. Additionally, factors such as dietary habits and physical activity, which were not extensively examined, could also influence the observed variations in biomarker ratios.

CONCLUSION

This study contributes to the understanding of normal urinary biomarker ratios in pediatric populations, accounting for age and gender variations. The comparisons with previous studies provide context and support to our findings. These results enhance our ability to interpret urinary biomarker ratios, aiding in clinical decision-making and offering a foundation for future research in pediatric nephrology and metabolism.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was produced from the thesis of Dr. Abdulgani GÜLYÜZ. His thesis advisor is Prof. Dr. Ahmet ÖZEL. The thesis was conducted in 2001 and ethics committee approval was not requested for this study.

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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