DOI: https://doi.org/10.17816/PED13465-74
Research Article

URINARY BIOMARKERS IN CHILDREN WITH KIDNEY DISEASES TAKING INTO ACCOUNT OBESITY

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For citation: Nastausheva TL, Khan AV, Kulakova EN, Volosovets GG, Chichuga EM, Chubarov TV, Gurovich OV, Grebennikova IV. Urinary biomarkers in children with kidney diseases taking into account obesity. *Pediatrician (St. Petersburg)*. 2022;13(4):65-74. DOI: https://doi.org/10.17816/PED13465-74

BACKGROUND: Overweight and obesity in children are one of the most serious problems of the modern world. There are mane publications devoted to kidney injury in patients with obesity. This injury in developed imperceptibly, without clinical symptoms. Probably the diagnostics of kidney injury in children with obesity may be improved by studying new urinary markers: KIM-1, NGAL, IL-18, β_2-mg.

AIM: Aim of our study was the comparative analysis of urinary markers of tubular kidney injury (KIM-1, NGAL, IL-18, β_2-mg) in children with obesity and kidney diseases.

MATERIALS AND METHODS: We have been studied 78 children aged 7–15 years: 40 children with different kidney diseases and 38 patients with obesity and kidney diseases. The results of the study were presented as markers concentration in urine and as relation to creatinine (normalized indicators).

RESULTS: In children with obesity and kidney diseases the level of KIM-1 was more high in comparison with the children without obesity. The concentration of other markers (NGAL, IL-18, β_2-mg) did not differ in children of two groups. The same results were received when analyzing normalized indicators. It was appeared significant correlation between body mass of patients and NGAL of urine in both groups.

CONCLUSIONS: Investigation of urinary KIM-1 have significance for diagnostics of tubular kidney injury in children with obesity on the background of kidney diseases. Established significant correlation NGAL with body mass can testify about it is diagnostic significance for obesity regardless of kidney diseases.

Keywords: children; kidney diseases; markers of kidney injury; obesity.

Received: 21.06.2022 **Revised:** 22.07.2022 **Accepted:** 30.09.2022

DOI: https://doi.org/10.17816/PED13465-74
Научная статья

МОЧЕВЫЕ БИОМАРКЕРЫ У ДЕТЕЙ С ЗАБОЛЕВАНИЯМИ ПОЧЕК С УЧЕТОМ ОЖИРЕНИЯ

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Для цитирования: Настаушева Т.Л., Хан А.В., Кулакова Е.Н., Волосовец Г.Г., Чичуга Е.М., Чубаров Т.В., Гурович О.В., Гребенникова И.В. Мочевые биомаркеры у детей с заболеваниями почек с учетом ожирения // Педиатр. – 2022. – Т. 13. – № 4. – С. 65–74. DOI: https://doi.org/10.17816/PED13465-74

Актуальность. Многие исследователи описывают повреждение почек при ожирении, в том числе у детей, которое может развиваться незаметно, без клинических симптомов. Возможно, диагностика почечного повреждения на ранних стадиях при ожирении у детей может быть улучшена с помощью исследования таких маркеров почечного повреждения, как KIM-1, NGAL, IL-18, β_2-mg.

Цель — сравнительное определение мочевых биомаркеров тубулярного почечного повреждения у детей при заболеваниях почек, протекающих на фоне ожирения.

Материалы и методы. У 78 детей в возрасте от 7 до 15 лет (40 детей с заболеваниями почек на фоне нормальной массы тела и 38 пациентов с заболеваниями почек на фоне ожирения) была исследована концентрация вышеупомянутых мочевых маркеров повреждения почек и ее отношение к креатинину мочи (нормированные показатели), а также проведен корреляционный анализ.

Результаты. В группе детей с заболеваниями почек на фоне ожирения уровень мочевого KIM-1 имел более высокие значения, а концентрация NGAL, IL-18 и β_2-mg в моче была близкой по значению в обеих группах детей. При анализе «нормированных» показателей достоверность для маркера KIM-1 сохранялась. При корреляционном анализе были выявлены значимые связи между показателями массы тела и концентрацией NGAL мочи, причем в обеих группах пациентов.

Заключение. Определение мочевого KIM-1 может иметь практическое значение для суждения о наличии тубулярного почечного повреждения у детей с ожирением на фоне заболеваний почек. Установленные значимые корреляционные связи маркера NGAL с показателями массы тела могут свидетельствовать о его диагностическом значении при ожирении у детей, независимо от наличия заболеваний почек.

Ключевые слова: дети; заболевания почек; маркеры повреждения почек; ожирение.

Поступила: 21.06.2022 **Одобрена:** 22.07.2022 **Принята к печати:** 30.09.2022

BACKGROUND

Currently, obesity is one of the most serious problems in Russia and many countries worldwide [1, 12, 15]. Obesity in childhood, as in adults, can be considered a risk factor for the development of chronic diseases, including chronic kidney disease (CKD) [11, 20]. The kidneys correct the metabolism if there is excessive body fat and therefore become one of the main target organs vulnerable to obesity [8, 12]. In adults, the probability of a decrease in the glomerular filtration rate (GFR) to <60 mL/min increases significantly in the case of obesity [10]. The initial kidney damage associated with excessive fat deposition is characterized by glomerular hyperfiltration [18]. In obese pediatric cases, dyslipidemia is considered an independent risk factor for renal tubular injury. In patients with nephropathies against visceral obesity, the lipid spectrum of the blood serum is characterized by an increase in lipid atherogenicity with a decrease in high-density lipoprotein-cholesterol, increase in total cholesterol, very low-density lipoproteins in combination with hyperleptinemia, and impaired glucose tolerance [3]. In patients with obesity and CKD stages III–IV, increased expressions of pro-inflammatory cytokines and infiltration of immunocompetent cells were detected in the adipose tissue, which can accelerate the development of kidney dysfunction and lead to nephron dysfunction [18, 19]. Two main indicators are traditionally used to diagnose CKD, namely, the GFR and the albumin/creatinine ratio. However, the blood concentration of creatinine cannot be used as an ideal marker of kidney pathology because its level varies depending on many non-renal factors [9]. Therefore, biomarkers such as 1/kidney injury molecule (KIM-1), neutrophil gelatinase-associated lipocalin (NGAL), interleukin 18 (IL-18), and beta 2 microglobulin (β_2-mg), which do not depend on the filtration function of the kidneys, are currently proposed as diagnostic criteria for tubular renal injury [7, 9, 11]. These markers have already been studied quite well in kidney diseases; however, they have practically not been considered in pediatric patients with obesity.

This study aimed to determine the level of urinary markers of tubular renal damage (KIM-1, NGAL, IL-18, and β_2-mg) in pediatric patients with obesity-associated kidney diseases.

MATERIALS AND METHODS

The study enrolled 78 children aged 7–15 years, which included 40 pediatric patients with kidney disease and normal body weight (group 1) and 38 patients with obesity and kidney diseases, with body mass index (SDS BMI) ≥+2 (group 2). All children were examined and treated in Nephrology Department of the Voronezh Regional Children's Clinical Hospital No. 1. Kidney diseases included glomerular diseases in 13 patients (group 1, $n = 6$, 15.0%; group 2, $n = 7$, 18.4%), urinary tract infection in 12, pyelonephritis in 37 (group 1, $n = 23$, 57.5%; group 2, n = 14, 36.8%, respectively), and other diseases (without infection) in 16 (group 1, $n = 9.22.5\%$; group 2, $n = 7$, 18.4%, respectively). Prospective examination was conducted in the period from January 2019 to June 2020. In all children examined, in addition to a clinical examination with the determination of physical development, clinical and biochemical blood tests, urine tests, and ultrasound examination of the kidneys and bladder were performed. The parameters of the functional state of the kidneys were assessed using the Zimnitsky test, and the GFR was calculated using the Schwartz equation [17].

For the study of urinary markers of tubular kidney damage, the first morning portion of urine was collected in two plastic Vacuette tubes (one tube was intended for urinary creatinine, whereas the other for urinary markers of kidney damage, namely, NGAL, KIM-1, IL-18, and β_2-mg). Urine was stored in a freezer at –70°C for a maximum of 6 months. The study was performed using a Multiskan Go Analyzer (Thermo Fisher Scientific, Finland). The plate was washed using a Wellwash enzyme-linked immunosorbent assay wash plate (Thermo Fisher Scientific), and incubation (if necessary) was performed using a PST-60HL-4 Thermoshaker (Biosan, Latvia). We used a biochemical photometric kinetic analyzer ABhFk-02 NPP-TM with a built-in printer according to TU9443-010-11254896-2002 to determine the creatinine level (Tekhnomedika, Russia).

Urine was centrifuged for 10 min at 3000 rpm to obtain a supernatant, which was used in further work.

Specific markers in the urine were studied using sets of reagents:

(1) Creatinine levels in the urine were determined by the Jaffe method without deproteinization, colorimetric, two-point kinetics. The wavelength was 490–510 nm, and linearity was within the range of 35.4–1350 μmol/L. Sensitivity was 25 μmol/L. Urine was diluted 50 times, and the resulting concentrations were multiplied by 50; Series 0110520, No. 10 102, date of manufacture 05/27/20, Diakon-DS, Russia)

(2) NGAL levels in the urine were quantitatively determined by enzyme immunoassay (set of 96 determinations). The wavelength was 450 nm, and the sensitivity was 0.02 ng/mL. The urine dilution was 1:10 (concentrations obtained multiplied by 10) (Cat. No. RD191102200R, lot E20-031, valid until

03.2021, manufactured by BioVendor Research and Diagnostic Products, Czech Republic).

(3) β_2-mg levels in the urine were measured by indirect enzyme-linked immunosorbent assay, with photometry at a wavelength of 450 nm and sensitivity of 0.1 μg/mL. Dilution was performed 10 times (the resulting concentrations were increased 10 times) (Orgentec Diagnostika GmbH, Cat. No. ORG 5 BM, lot 2003762, valid until 10/06/2021, produced by ORGENTEC Diagnostika GmbH, Germany)

(4) KIM-1 levels in the urine were determined by enzyme immunoassay. Photometry was at a wavelength of 450 nm, the sensitivity was 3.13 pg/mL, and the dilution was 1:4 (the resulting concentrations were multiplied by 5) (Cioud-Clone Corp., Cat. No. SEA785Hu, series 7C20637A38, lot 200826373, valid until 04.2021, China).

(5) IL-18 was quantified in the urine by enzyme immunoassay. Photometry was at a wavelength of 450 nm, the sensitivity was 9 pg/ml, and dilution was not required (Invitrogen, BenderMwdSystems GmbH, Cat. No. BMS267-2, lot 236202-001, valid until 09.2021, Austria).

Statistical research methods

Statistical data analysis was performed using the Microsoft Office Excel 2010, Statistica v.6.0 software package. Data processing was performed with the calculation of the arithmetic mean (M), standard deviation (σ), median, and interquartile range (*Me* [Q_1; Q_3]). For qualitative variables, the values of absolute and relative incidence were calculated. To compare indicators of physical development in pediatric patients, we used *Z*-scores of the body height for age, body weight for age, and BMI for age, calculated according to the standard method of the World Health Organization using WHO programs AntroPlus and WHO Antro [22].

The conformity between the registered distributions and the normal one was tested using the Shapiro–Wilk test. In the case of small samples and refutation of the hypothesis of normal distribution, the nonparametric Mann–Whitney test was used to identify differences between the two groups. Fisher's exact test was used to assess the statistical significance of qualitative indicators. If the expected value was >10, Pearson's χ^2 test was used. Correlation analysis was performed using Spearman's rank correlation coefficient (*R*). Differences between variables were considered statistically significant at $p < 0.05$.

RESULTS

According to the statistical comparison, the two examined groups did not differ by sex and age (Table 1), but differed in BMI *Z*-scores. Group 2 exceeded the reference ranges and those of group 1. Group 2 had exogenous constitutional obesity. The body height *Z*-scores did not differ between the two groups; the *Z*-scores were normal (*Z* = –1 to +1). Table 2 presents the clinical and laboratory parameters of the patients.

As shown in Table 2, the two groups did not differ significantly in most of the laboratory parameters of blood and urine and in the level of both systolic and diastolic blood pressures. In the general blood test, only the level of hemoglobin showed difference; it was significantly higher in patients with obesity. However, all the laboratory parameters did not exceed the norm in any child.

Table 3 presents the data of kidney damage markers KIM-1, NGAL, IL-18, and β_2-mg in the urine of the two study groups.

The KIM-1 levels were higher in group 2 than in group 1 (Table 3). No statistically significant differences in the indices of the remaining three urinary markers were found between the two groups.

Since the studied markers were presented not only as their concentration in the urine, but also as their ratio to the amount (mg) of creatinine in the urine (normalized values), they were also compared. The differences between the two groups were statistically significant in relation to KIM-1/Cru (pg/mg). Normalized indicators of other markers did not reveal significant differences between the two groups (Table 4).

Table 1 / Таблица 1

Gender, age, *Z*-scores of height and body mass index (BMI) of examined children
Пол, возраст, *Z*-оценки длины и индекса массы тела (ИМТ) обследованных детей

Groups of children / Группа детей	Boys / girls / Мальчики/девочки	Age / Возраст *Me* [Q_1; Q_3]	*Z*-score of height (HAZ) / *Z*-оценки длины тела (HAZ) *Me* [Q_{25}; Q_{75}]	*Z*-score of BMI (HAZ) / *Z*-оценки ИМТ (BAZ) *Me* [Q_{25}; Q_{75}]
Group 1 / Группа 1 (*n* = 40)	18/22 (45.0% / 55.0%)	11.00 [7.00; 14.00]	0.39 [–0.45; 1.06]	–0.26 [–1.20; 0.65]
Group 2 / Группа 2 (*n* = 38)	16/22 (42.2% / 57.8%)	13.00 [7.00;15.00]	0.46 [–0.04; 1.55]	2.35 [1.8625; 2.82]
p	0.49 **	0.49 *	0.81 *	0.000000 *

Note. Me — median; [Q_1; Q_3] — interquartile range. *Mann–Whitney *U*-test; **χ^2 Pirson test.
Примечание. Me — медиана, [Q_1; Q_3] — интерквартильный размах. * *U*-критерий Манна – Уитни; ** критерий χ^2 Пирсона.

Table 2 / Таблица 2

Comparison of some clinical and laboratory parameters in examined children, *Me* [Q_1; Q_3]
Сравнение некоторых клинико-лабораторных показателей у обследуемых детей, *Me* [Q_1; Q_3]

Parameter / Показатель	Group 1 / Группа 1 (n = 40)	Group 2 / Группа 2 (n = 40)	p *
Systolic AP (centile), mm of mercury / Систолическое артериальное давление (центиль), мм рт. ст.	63.00 [41.5; 74.7]	69.00 [41.25; 81.0]	0.21
Diastolic AP (centile), mm of mercury / Диастолическое артериальное давление (центиль), мм рт. ст.	56.00 [35.3; 71.00]	64.00 [49.5; 79.0]	0.62
Blood glucose, mmol/l / Глюкоза крови, ммоль/л	4.99 [4.75; 5.22]	4.9 [4.6; 5.3]	0.64
ALAT, U/L / Аланинаминотрансфераза, Ед/л	13.4 [9.1; 15.0]	17.50 [13.65; 36.8]	0.93
ASAT, U/L / Аспартатаминотрансфераза, Ед/л	30.20 [24.2; 32.5]	20.95 [16.8; 27.1]	0.58
Urea of serum, mmol/l / Мочевина сыворотки крови, ммоль/л	3.90 [3.32; 4.50]	3.8 [3.4; 4.40]	0.65
Serum creatinine, mg/dl / Креатинин сыворотки, мг/дл	0.67 [0.59; 0.85]	0.76 [0.65; 0.89]	0.36
GFR ml/(min · 1,73 m^2) / Скорость клубочковой фильтрации, мл/(мин · 1,73 м^2)	116.5 [104.8; 133.7]	114.89 [104.5; 127.5]	0.1
Total protein, g/l / Общий белок, г/л	74.1 [71.1; 78.1]	75.1 [71.7; 78.0]	0.71
Hemoglobin, g/l / Гемоглобин, г/л	136.0 [128.3; 142.00]	139.0 [133.0; 148.5]	0.04
Blood leukocytes, th/μl / Лейкоциты крови, тыс. мкл	7.0 [5.35; 8.0]	7.2 [5.8; 9.65]	0.06
ESR, mm/h / Скорость оседания эритроцитов, мм/ч	4.0 [3.0; 5.75]	5.0 [2.5; 8.0]	0.22
Max spec. grav. / Максимальный удельный вес мочи	1023 [1015; 1026]	1021.5 [1015.75; 1026.25]	0.74
Ph мочи / Urine PH	5.0 [5.0; 5.75]	5.0 [5.25; 5.88]	0.13
Urine protein, g/l / Белок мочи, г/л	0 [0; 0]	0 [0; 0]	0.46
Urine red blood sells, f/v / Эритроциты мочи, п/з	0 [0; 0.25]	0 [0; 0.25]	0.34
Urine leukocytes, f/v / Лейкоциты мочи, п/з	0.45 [0.1; 5.9]	0.75 [0.1; 5.15]	0.89

Note. Me — median; [Q_1; Q_3] — interquartile range. * Mann–Whitney *U* Test.
Примечание. Me — медиана, [Q_1; Q_3] — интерквартильный размах. * *U*-критерий Манна – Уитни.

Table 3 / Таблица 3

Markers of kidney injury NGAL, KIM-1, IL-18, urine β_2-mg in examined children, *Me* [Q_1; Q_3]
Маркеры повреждения почек NGAL, KIM-1, IL-18, β_2-mg мочи у обследованных детей, *Me* [Q_1; Q_3]

Groups of children / Группа детей	Markers / Маркеры			
	NGAL, ng/ml / нг/мл	KIM-1, pg/ml / пг/пл	IL-18, pg/ml / пг/пл	β_2-mg, μg/ml / мкг/мл
Group 1 / Группа 1 (n = 40)	4.49 [1.53; 7.57]	1419.25 [993; 1888]	109.8 [89.63;134.97]	11.08 [3.30; 19.7]
Group 2 / Группа 2 (n = 38)	4.10 [0.7; 6.1]	2444.0 [1381; 3077]	109.60 [97.4; 136.1]	10.59 [2.86; 19.57]
p *	0.64	0.06	0.34	0.26

Note. Me — median; [Q_1; Q_3] — interquartile range. * Mann–Whitney *U* Test.
Примечание. Me — медиана, [Q_1; Q_3] — интерквартильный размах. * *U*-критерий Манна – Уитни.

Table 4 / Таблица 4

Markers of kidney injury (normalized indicators) NGAL/Cru, KIM-1/Cru, IL-18/Cru, β_2-mg/Cru in examined children, *Me* [Q_1; Q_3]
Маркеры повреждения почек (нормированные показатели) NGAL/Cru, KIM-1/Cru, IL-18/Cru, β_2-mg/Cru у обследованных детей, *Me* [Q_1; Q_3]

Groups of children / Группа детей	Markers / Маркеры			
	NGAL/Cru, ng/mg / нг/мг	KIM-1/Cru, pg/mg / пг/мг	IL-18/Cru, pg/mg / пг/мг	β_2-mg/Cru, μg/mg / мкг/мг
Group 1 / Группа 1 (n = 40)	1.67 [0.686; 13.24]	1064.45 [632.78; 1635.74]	8.72 [5.33; 16.31]	4.92 [2.56; 12.92]
Group 2 / Группа 2 (n = 38)	2.47 [0.82; 4.26]	1630.564 [839.33; 3318.95]	13.50 [4.71; 23.47]	7.93 [5.44; 13.16]
p *	0.52	0.002445	0.12	0.06

Note. Me — median; [Q_1; Q_3] — interquartile range. * Mann–Whitney *U* Test.
Примечание. Me — медиана, [Q_1; Q_3] — интерквартильный размах. * *U*-критерий Манна – Уитни.

Then, a correlation analysis was performed between the studied urinary markers and some clinical and laboratory parameters of the two groups. The results of the analysis are presented in Tables 5 and 6, respectively.

Significant correlations were detected between the concentration of KIM-1 in the urine and body height *Z*-scores, KIM-1 and GFR, KIM-1 and diastolic blood pressure centiles, and direct associations were found between urinary β_2-mg concentration and body height *Z*-scores, between urinary IL-18/Cru concentration and body height *Z*-scores, and between urinary NGAL concentration and body weight and BMI.

In group 2, significant relationships were found between KIM-1/Cru concentration and systolic blood pressure centiles and between urinary NGAL concentration and body weight, BMI, and body height. Moreover, an inverse relationship was noted between the concentrations of IL-18 and IL-18/Cru in the urine with serum urea (Table 6).

Thus, the BMI and BMI Z-scores correlated only with the NGAL concentration in the urine of both groups. However, direct correlation was found in group 1, and an inverse correlation was observed in group 2. The significant correlations of the urinary markers with various parameters in the two groups may indicate their different diagnostic value in obesity.

Table 5 / Таблица 5

Spearman's correlation coefficients (*R*) of urinary markers with body height mass, BP and GFR in children with kidney diseases without obesity

Коэффициенты корреляции Спирмена (*R*) мочевых маркеров с показателями массы и длины тела, артериального давления и скорости клубочковой фильтрации у детей с заболеваниями почек на фоне нормальной массы тела

Parameter / Показатель	Markers / Маркеры				
	KIM-1	KIM-1/Cru	β_2-mg	NGAL	IL-18/Cru
Body mass / Масса тела	–0.03	–0.1	0.05	0.34 (0.03)	–0.13
BMI / Индекс массы тела	0.002	–0.06	–0.07	0.34 (0.03)	0.1
Z-score of height / *Z*-оценка длины тела	–0.35 (0.02)	–0.37 (0.01)	0.34 (0.03)	–0.08	0.34 (0.03)
DAP (centile) / Диастолическое артериальное давление, центиль	0.39 (0.02)	–0.01	0.14	–0.18	–0.19
GFR / Скорость клубочковой фильтрации	0.02 (0.01)	–0.24	0.27	–0.3	–0.21

Note. The values of *p* are given in parentheses only for statistically significant correlation coefficients.
Примечание. В скобках приведены значения *p* только для статистически значимых коэффициентов корреляции.

Table 6 / Таблица 6

Spearman's correlation coefficients (*R*) of urinary markers with body weight, BMI, *Z*-scores in children with kidney diseases and obesity

Коэффициенты корреляции Спирмена (*R*) мочевых маркеров с показателями массы и длины тела, артериального давления и скорости клубочковой фильтрации у детей с заболеваниями почек и ожирением

Parameter / Показатель	KIM-1/Cru	NGAL	NGAL/Cru	IL-18	IL-18/Cru
Body mass / Масса тела	–0.07	–0.53 (0.002)	–0.47 (0.007)	–0.12	0.06
BMI / Индекс массы тела	–0.14	–0.62 (0.0002)	–0.59 (0.0004)	–0.07	0.08
Body length / Длина тела	–0.12	–0.41 (0.02)	–0.34	–0.16	0.004
SAP, centile / Систолическоое артериальное давление, центиль	0.39 (0.04)	–0.05	–0.01	0.09	0.38
Urea / Мочевина	–0.28	–0.09	–0.19	–0.41 (0.02)	–0.51 (0.003)

Note. The values of *p* are given in parentheses only for statistically significant correlation coefficients.
Примечание. В скобках приведены значения *p* только для статистически значимых коэффициентов корреляции.

DISCUSSION

Among urinary markers of tubular kidney injury analyzed in this study, only KIM-1 was significantly elevated in patients with both obesity and kidney disease compared with non-obese patients with kidney disease. Previously, we published similar data [14]. KIM-1 is a transmembrane glycoprotein involved in T-helper differentiation, belonging to the immunoglobulins, and it is not expressed in healthy cells of the renal epithelium and is an early marker of kidney damage [13]. An increase in the concentration of KIM-1 in the urine was confirmed in response to renal ischemia, when the kidneys are exposed to nephrotoxic drugs, and in CKD [21]. Few studies have examined KIM-1 in pediatric patients with obesity, where its increase was detected compared with healthy children [11]. Essentially, the authors established the diagnostic value of urinary KIM-1 for kidney damage in the early stages of obesity in pediatric patients.

Other urinary markers (NGAL, IL-18, and β_2-mg) did not show a clear diagnostic significance in obesity in pediatric patients with pre-existing kidney pathologies because their values were comparable to those of non-obese children with nephropathies. This apparently indicates that in obesity, the proximal tubules are primarily involved in the pathological process because KIM-1 is a marker of damage to the proximal tubules of the kidney [11]. This statement requires confirmation and thus further research.

However, the revealed correlations of BMI and BMI *Z*-scores with NGAL may also indicate the diagnostic significance of this urinary marker in pediatric patients with obesity, but may be independent of kidney disease. NGAL is expressed and secreted by various cells under stress, for example, due to an inflammatory process and ischemia. In general, in humans, in response to damage to the renal tubules, both the blood plasma and urine levels of NGAL increase sharply [5, 6]. Moreover, the excretion of NGAL in the urine is 24–48 h ahead of the increase in the blood serum concentration of creatinine.

Some authors note that urinary NGAL, compared with KIM-1, as a more sensitive biomarker in kidney diseases, can reveal tubulointerstitial damage in patients with arterial hypertension or kidney disease at an early stage [4]. According to these authors, urinary KIM-1 is a more inert biomarker and was unable to detect this damage in hypertensive patients with mild renal dysfunction; however, it identifies early tubulointerstitial kidney damage in hypertensive patients with chronic pyelonephritis. However, KIM-1 is a clear diagnostic marker for obesity in pediatric patients with kidney diseases. That is, NGAL is a marker for obesity regardless of kidney disease, and KIM-1 is a marker for obesity-associated kidney disease. Other authors have revealed a significant negative correlation between NGAL and GFR and a positive correlation with daily proteinuria in patients with diabetes mellitus and CKD. Thus, the NGAL level can be a useful and non-invasive factor in diagnosing diabetic nephropathy and assessing the degree of renal damage [2, 16].

Together with the data obtained, the findings reveal the value of these urinary markers in pediatric patients with obesity, both with an independent disease and in combination with another pathology.

CONCLUSIONS

1. In children with obesity-associated kidney disease, the values of urinary KIM-1, especially normalized ones, were statistically significantly higher than those of non-obese children with kidney diseases.

2. The values of urinary NGAL, IL-18, and β_2-mg showed no statistically significant differences between obese pediatric patients with kidney diseases and pediatric patients with kidney disease without obesity.

3. Statistically significant correlations (from 0.34 to –0.62) were found between the concentration of urinary NGAL and body weight indicators, namely, BMI and BMI *Z*-scores in both groups.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Consent for publication. Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Информированное согласие на публикацию. Авторы получили письменное согласие официальных представителей пациента на публикацию медицинских данных.

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