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Evaluation of adipocytokines in children with chronic kidney disease

Ocena stężenia adypocytokin u dzieci z przewlekłą chorobą nerek

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Abstract

Introduction: Adipose tissue through the many secreted adipocytokines creates a highly active metabolic and endocrine organ. The evaluation of serum adipocytokine concentration in children with chronic kidney disease (CKD) could serve as a marker of cardio-vascular complication progression and an index of outcome in adulthood and after kidney transplantation.
Material and methods: The aim of the study was to evaluate simultaneously the serum concentrations of six different adipocytokines: adiponectin, apelin, chemerin, omentin, resistin, and vaspin, in 28 children with CKD stage 5 on haemodialysis and peritoneal dialysis.
Results: The concentration of apelin, omentin, and resistin in children with CKD was significantly higher and the concentration of vaspin, adiponectin, and chemerin was significantly lower than in the control group. After adjusting to body mass index (BMI), the same results were obtained. After adjusting to body surface area (BSA), the concentration of vaspin, adiponectin, and chemerin did not differ between children with CKD and the control group. In analysis of the correlation between serum total adipocytokine levels in children with CKD we found a negative relationship in pairs: omentin–apelin and omentin–vaspin, and positive in pairs: adiponectin–chemerin and adiponectin–resistin.
Conclusions: Our results show that changes in serum adipocytokines concentration are associated with the kidney dysfunction in CKD in children. Longitudinal studies on larger groups of paediatric cohorts would be helpful in investigating whether adipocytokines play a harmful role in the development of CKD and would enable further understanding of the risk factors for CKD progression.
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Key words: *adipocytokines; children; chronic kidney disease; adiponectin; apelin; chemerin; omentin; resistin; vaspin*

Streszczenie

Wstęp: Tkanka tłuszczowa poprzez wydzielane liczne adipocytokiny tworzy narząd bardzo aktywny metabolicznie i hormonalnie. Ocena stężenia adipocytokin w surowicy krwi u dzieci z przewlekłą chorobą nerek (CKD) może służyć jako marker progresji powikłań sercowo-naczyniowych i wskaźnik rokowniczy w wieku dorosłym i po przeszczepie nerki.
Materiał i metody: Celem pracy była ocena stężenia w surowicy krwi jednocześnie sześciu różnych adipocytokin: adiponektyny, apeliny, chemeryny, omentyny, rezystyny i waspiny u 28 dzieci z CKD w stadium 5. leczonych hemodializami i dializą otrzewnową.
Wyniki: Stężenie apeliny, omentyny i rezystyny u dzieci z CKD było znacząco wyższe, stężenie waspiny adiponektyny, chemeryny było znacząco niższe niż w grupie kontrolnej. Po skorygowaniu do wartości BMI uzyskano takie same wyniki. Po skorygowaniu do wartości powierzchni ciała stężenia waspiny, adiponektyny i chemeryny nie różniły się u dzieci z CKD i w grupie kontrolnej. W analizie korelacji pomiędzy całkowitym stężeniem adipocytokin w surowicy krwi u dzieci z CKD stwierdzono ujemną zależność w parach: omentyna–apelina i omentyna–waspina i pozytywną w parach: adiponektyna–chemeryna, rezystyna–adiponektyna.
Wnioski: Wyniki przedstawionego badania wskazują, że zmiany stężenia adipocytokin w surowicy krwi są związane z upośledzeniem czynności nerek w CKD u dzieci. Długoterminowe badania w większych grupach pediatrycznych byłyby pomocne w wyjaśnieniu, czy adipocytokiny odgrywają niekorzystną rolę w rozwoju CKD, oraz umożliwiłyby dalsze zrozumienie czynników ryzyka progresji CKD.
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Słowa kluczowe: *adipocytokina; dzieci; przewlekła choroba nerek; stężenie adiponektyny; apelina; chemeryna; omentyna; rezystyna; waspina*

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Introduction

It is well known that adipose tissue through secreted adipocytokines creates a complex and highly active metabolic and endocrine organ. Solely adipocytokines with their receptors could act in endocrine and paracrine mode expressing their abnormalities in obesity conditions and as well as in wasting disorders. The data on various adipocytokines concentrations and their role in children with chronic kidney disease (CKD) are not abundant. The evaluation of adipocytokines concentration in children with CKD is extremely important since it could serve as a marker for cardio-vascular complication progression and final outcome in adulthood and after kidney transplantation [1–4].

Adiponectin described almost 20 years ago is a unique adipocyte-derived hormone, which represents antidiabetic, anti-inflammatory, and anti-atherogenic properties [5]. Mills et al. found that adult patients with higher adiponectin levels have greater odds of CKD in their study on cohort of 201 patients [6]. They documented the simultaneous influence of older age, higher BMI value, gender, and cardiovascular events history on the likelihood of CKD in logistic regression analysis. Adiponectin also exerts renoprotective effects by albuminuria inhibition, which was documented in rodents [7].

Apelin, the next adipocytokine, plays a role in the regulation of cardiovascular, gastrointestinal, and immune functions, and it has an influence on bone metabolism, fluid homeostasis, and intrauterine development of the cardiovascular system [8–10]. This hormone is expressed in different tissues; kidney and endothelial cells among them. Zhang et al. found that apelin induced the proliferation of glomerular endothelial cells in a dose-dependent manner. They also described increased permeability in diabetic glomeruli, which could be associated with a role of apelin in the pathogenesis of diabetic nephropathy [11]. Silva et al. found in their study that apelin levels showed a negative correlation with cardiovascular risk factors and positive correlation with estimated glomerular filtration rate (eGFR) [12].

Chemerin is one of the newly recognised adipocytokines. It is proposed that chemerin is involved in the liver — adipose tissue — skeletal muscles system axis. Some data are also available showing that chemerin plays a role in the metabolism of carbohydrates and fats [13]. Hu et al. documented in their study in type 2 diabetic rats that creatinine clearance and serum creatinine remained significantly associated with serum chemerin [14]. Pfau et al. detected high circulating chemerin concentration in adult patients on haemodialysis, independently of age and gender [15].

Omentin is the adipocytokine secreted by the stroma cells of adipose tissue, not by adipocytes themselves, with the increased concentration in visceral adipose tissue [16]. Chen et al., in studies on rats, found that omentin has vasodilatory properties via the activation of synthesis of endothelial nitric oxide [17]. They concluded that omentin might play a role in blood pressure regulation, acting directly on blood vessel relaxation. Prats-Puig et al., in their study, were the first ones to show that circulating omentin-1 was associated with BP in childhood, which was independent of age, gender, and fat mass content [18].

Hida et al. [19] in 2005 identified a new adipocytokine: visceral adipose tissue-derived serpin, which was given the name vaspin. It is believed that the increase in expression of vaspin in the adipose tissue may be a compensatory mechanism that occurs in response to increasing obesity and insulin resistance [20]. The ability to block NADPH oxidase activity by vaspin, which was confirmed by Phalitakul et al., supports the hypothesis that vaspin may act as a protective factor against atherosclerosis [21]. The relationship between the vaspin concentration and renal dysfunction is not fully understood. Raised vaspin concentrations in patients with CKD may result from diminished elimination and persistent inflammatory condition. Seeger et al. showed higher vaspin levels in women with CKD on haemodialysis and in healthy female controls, independently of age [20].

The next adipocytokine that accounts for a factor of CKD progression is resistin. In adult patients with CKD it was found that resistin has a proinflammatory effect and can enhance cardio-vascular abnormalities resulting from persistent inflammation [22]. Stępień et al. observed a negative correlation between serum resistin and eGFR, both in CKD and non-CKD patients, in their study of obese adult patients [23]. Nehus et al. examined serum resistin levels in children with chronic kidney disease and documented a negative correlation with GFR and a positive correlation with urine protein-to-creatinine ratio. They also found positive association of pubertal status with serum resistin levels [1].

In the present study we evaluated simultaneously six different adipocytokines: adiponectin, apelin, chemerin, omentin, resistin and vaspin in children with CKD stage 5. To date, there are no available studies in children on such adipocytokine combinations, which includes both adipocytokines of a protective role in CKD (apelin, adiponectin, omentin, vaspin) and of a promoting role in CKD (resistin, chemerin).

Material and methods

The study group consisted of 28 children and young adults with CKD stage 5 and 20 healthy children. Gender, mean age, anthropometric data, blood pressure values,

and laboratory test results are shown in Table I. In all children, Cole index, body mass index (BMI) (body weight [kg)]/height [m^2]), and percentiles for BMI and body surface area (BSA) were calculated. The examined children and healthy controls were in Tanner stage 3–5, similarly in both groups.

The main causes of CKD were: tubulointerstitial nephritis (TIN) together with congenital defects of the urinary tract and/or recurrent infections (12 children — 42.9%) and polycystic kidney disease (5 children — 17.9%). Other causes were chronic glomerulonephritis (4 children — 14.3%), TIN accompanying myelomeningocele (3 children — 10.7%), nephronophthisis (2 children — 7.1%), hypo-dysplasia of the kidneys (1 child — 3.6%), and neurofibromatosis (1 child — 3.6%). During the study and for the preceding month, children were in stable clinical condition without features of acute infection. All the children remained on pharmacotherapy of CKD (diuretics, renoprotection with ACE inhibitor, carbohydrate supplementation, antihypertensive agents, ferric and folate formulas). Twenty-seven children received erythropoietin.

Ten children were treated by haemodialysis. Dialysis was performed using Fresenius 2008 C and A (Fresenius Medical Care AG, Bad Homburg, Germany) machines. Bicarbonate buffered dialysis fluid was applied. Water for haemodialysis was prepared by reverse osmosis and bacteriologically tested according to European standards. The mean time of session was 4 hours (3.5–5.0 hours). The velocity of dialysate flow was 500 ml per minute, and blood flow was 130180 mL per minute. Low molecular weight heparin was used for anticoagulation during haemodialysis sessions.

For automated peritoneal dialysis — 18 children (APD) dialysis fluid and equipment of Baxter (Baxter International, Deerfield, Illinois, USA) and Fresenius (Fresenius Medical Care AG, Bad Homburg, Germany) was used in accordance with the applicable schedule and under adequate control.

Children included into the control group attended the outpatient paediatric clinic for non-immunological, non-inflammatory health problems and needed venous puncture.

The present study was approved by the Ethics Committee of the Medical University of Silesia in Katowice. Written informed consent was obtained from the children's parents.

Table I. *Characteristics of examined children*
Tabela I. *Charakterystyka badanych dzieci*

Characteristics	Children with CKD (n = 28)	Healthy Children (n = 20)
Age (years)	13.5 ± 5.5	10.9 ± 4.4
Sex (n)	F:16; M:12	F:12; M:8
Age at dialysis beginning (years)	11.5 ± 4.22	–
Height [cm]	137.5 ± 24.6	144.9 ± 21.7
[percentile]	7.5 ± 15.4 ‡	55.5 ± 30.0
Weight [kg]	36.5 ± 15.7	39.5 ± 13.0
[percentile]	17.5 ± 26.5 ‡	55.9 ± 26.8
BMI [kg/m^2]	18.1 ± 3.3	18.3 ± 2.1
[percentile]	40.9 ± 34.5	55.2 ± 31.2
Cole index	98.6 ± 17.9	104.0 ± 15.5
BSA [m^2]	1.17 ± 0.35	1.26 ± 0.3
Serum creatinine [μmol/L]	696.5 ± 276.0 ‡	50.11 ± 0.93
BUN [mmol/L]	17.6 ± 6.8‡	2.21 ± 0.4
Haemoglobin [g/dL]	10.3 ± 1.42‡	13.4 ± 1.3
Haematocrit (%)	30.2 ± 4.23‡	38.5 ± 4.2

BMI — body mass index; BSA — body surface area. Numeric data were shown as mean ± SD; ‡$P < 0.0001$ CKD *vs.* control

Laboratory assays

Blood samples for assays were collected in the fasting state between 08^{00} and 09^{30} h. After centrifugation at 1000 × g for 15 minutes at 4°C, the serum samples were frozen at –20°C until analysed. The absorbance measurements for all samples were performed using a Quant Universal Microplate Spectrophotometer (BioTek Instruments Inc., Winooski, VT) determined on the basis of the standard curve made for a series of dilutions of the standards available in the kit. Acquired data were analysed using KC Junior Software (v.1.31.5, Bio-Tek Instruments,Winooski, VT, USA).

— Serum apelin-12 concentration was determined using commercial human Apelin-12 enzyme immunoassay kit (Phoenix Pharmaceuticals Inc., Burlingame, CA) following the manufacturer's instructions.
— Serum **resistin** concentration was measured by enzyme-linked immunosorbent assay kit (Mediagnost, Reutlingen, Germany).
— Serum **adiponectin** concentration was measured by enzyme-linked immunosorbent assay kit (BioVendor, LLC, USA).
— Serum **omentin** concentration was determined using the immunoenzymatic method with the application of the Human Omentin-1 kit (BioVendor, Czech Republic).
— Serum concentrations of **chemerin** were determined using the immunoenzymatic method by the Human Chemerin kit (BioVendor, Czech Republic).
— Serum **vaspin** concentration was determined using the immunoenzymatic method by the Human Vaspin kit (BioVendor, Czech Republic).

Absolute values of each adipocytokine serum concentration were correlated with age, anthropometrical parameters (height, weight, BMI, Cole index), serum creatinine, BUN, haemoglobin concentration, haematocrit, dialysis treatment duration, CKD duration, and systolic and diastolic blood pressure (BP sys and BP dia) values.

In the statistical analysis we used the Mann-Whitney U-test. Correlations were analysed with Pearson's or Spearman tests, whichever was appropriate. The p values < 0.05 were considered significant.

Results

The mean age, absolute height, weight, BMI, BMI percentiles, Cole index, and BSA did not differ in comparison between children with CKD and healthy controls. Children with CKD had lower height and weight expressed in percentiles than healthy controls. The mean concentration of serum creatinine and BUN were significantly higher and the mean level of haemoglobin and Hct were lower in children with CKD, as compared to healthy children (Table I). In children with CKD the BP sys value was 112.4 ± 16.6 mm Hg and BP dia was 67.8 ± 13.9 mm Hg. The concentration of serum cholesterol and triglycerides was 4.79 ± 1.17 mmol/L and 1.98 ± 1.4 mmol/L, respectively. In Table II the mean values of serum levels of adipocytokines in children with CKD and healthy children are shown. The concentration of apelin, omentin, and resistin was significantly higher and the concentration of vaspin, adiponectin, chemerin was significantly lower than in the control group. After adjusting to BMI value the same results of serum adipocytokine concentration were obtained in a comparison between children with CKD and healthy children. The application of adipocytokine/Cole index ratio gave the same results (data not shown). After adjusting to BSA value the concentration of vaspin, adiponectin, and chemerin did not differ between children with CKD and the control group.

In Table III the mean values of serum levels of adipocytokines in children with CKD regarding to gender and the type of renal replacement therapy are presented. There was only one significant difference in resistin concentration between boys and girls. The higher value of this adipocytokine we found in girls. There was no difference after adjustment of the adipocytokine values to BMI or BSA.

In Table IV we analysed the correlations between total adipocytokine serum levels and anthropometric, biochemical parameters listed in Table I (and, additionally, blood pressure values in the CKD group) in the examined children.

Table II. *Mean values of adipocytokine serum levels in children with chronic kidney disease and healthy children*

Tabela II. *Średnie stężenie adipocytokin w surowicy krwi u dzieci z przewlekłą chorobą nerek i u dzieci zdrowych*

Mean Adipocytokine Serum Levels	Children with CKD (n = 28)	Healthy Children (n = 20)
Apelin [pg/mL]		
All subjects	99.0 ± 8.0	82.1 ± 11.2*
Apelin/BMI	5.6 ± 1.1	4.5 ± 0.7*
Apelin/BSA	94.4 ± 36.3	69.2 ± 19.2#
Vaspin [ng/mL]		
All subjects	1.83 ± 0.26	2.3 ± 0.21*
Vaspin/BMI	0.10 ± 0.02	0.13 ± 0.02*
Vaspin/BSA	1.78 ± 0.83	2.0 ± 0.5
Adiponectin [ng/mL]		
All subjects	11.9 ± 1.4	15.2 ± 2.2*
Adiponectin/BMI	0.68 ± 0.16	1.8 ± 0.13*
Adiponectin/BSA	11.6 ± 5.4	12.7 ± 3.1
Omentin [ng/mL]		
All subjects	46.2 ± 3.7	31.7 ± 3.0*
Omentin/BMI	2.6 ± 0.5	1.8 ± 0.3*
Omentin/BSA	44.3 ± 17.6	26.8 ± 7.5*
Chemerin [ng/mL]		
All subjects	127.8 ± 16.4	184.0 ± 15.2*
Chemerin/BMI	7.3 ± 1.8	10.1 ± 1.0*
Chemerin/BSA	125.8 ± 65.3	154.7 ± 38.6
Resistin [ng/L]		
All Subjects	14.4 ± 1.4	5.5 ± 0.9*
Resistin/BMI	0.8 ± 0.2	0.3 ± 0.1*
Resistin/BSA	14.0 ± 6.1	4.7 ± 1.45*

Data are shown as mean ± standard deviation. *$P < 0.0001$ CKD *vs.* control, #$P < 0.006$ CKD *vs.* control

Significant correlations were not found regarding vaspin and omentin levels. In children with CKD the apelin concentration positively correlated with age, and the chemerin level showed negative correlation with height, weight, and BSA. In healthy children we documented a positive correlation of adiponectin level with height percentile, chemerin level with weight percentile and BMI, BMI percentile, Cole index, and negative correlation of resistin concentration with serum Hb concentration.

In analysis of the correlation between serum total adipocytokine levels in children with CKD we found a negative relationship in the following pairs: omentin–apelin and omentin–vaspin, and positive in: adiponectin–chemerin and adiponectin–resistin. After adjusting to BMI, positive correlations were noted between all examined adipocytokines (Table V).

Table III. *Mean values of adipocytokine serum levels in children with chronic kidney disease according to gender and the type of renal replacement therapy*

Tabela III. *Średnie stężenie adipocytokin w surowicy krwi u dzieci z przewlekłą chorobą nerek w zależności od płci i od rodzaju leczenia nerkozastępczego*

Mean Adipocytokine Serum Levels	Children with CKD			
	Boys	Girls	Haemodialysis	Peritoneal Dialysis
Apelin [pg/mL]				
All subjects	99.4 ± 10.1	98.6 ± 6.4	98.7 ± 6.5	100.3 ± 7.6
Apelin/BMI	5.6 ± 1.1	5.7 ± 1.2	5.2 ± 0.8	5.9 ± 1.1
Apelin/BSA	92.2 ± 41.9	96.1 ± 32.8	77.3 ± 19.4	104.6 ± 42.6
Vaspin [ng/mL]				
All subjects	1.85 ± 0.2	1.8 ± 0.3	1.9 ± 0.2	1.8 ± 0.3
Vaspin/BMI	0.09 ± 0.01	0.10 ± 0.03	0.10 ± 0.02	0.11 ± 0.03
Vaspin/BSA	1.7 ± 0.9	1.8 ± 0.8	1.5 ± 0.3	1.9 ± 1.0
Adiponectin [ng/mL]				
All subjects	11.9 ± 1.4	12.2 ± 1.3	12.0 ± 2.0	12.0 ± 1.0
Adiponectin/BMI	0.68 ± 0.16	0.7 ± 0.2	0.64 ± 0.15	0.7 ± 0.2
Adiponectin/BSA	11.6 ± 5.4	11.6 ± 5.4	9.4 ± 2.5	12.9 ± 6.4
Omentin [ng/mL]				
All subjects	46.2 ± 3.7	46.2 ± 3.7	45.8 ± 3.3	46.1 ± 3.9
Omentin/BMI	2.5 ± 0.4	2.7 ± 0.6	2.4 ± 0.3	2.7 ± 0.6
Omentin/BSA	43.2 ± 20.5	45.0 ± 15.8	35.6 ± 5.3	48.4 ± 20.6
Chemerin [ng/mL]				
All subjects	127.8 ± 16.4	128.5 ± 17.8	127.9 ± 16.0	127.2 ± 17.4
Chemerin/BMI	7.3 ± 1.8	7.5 ± 1.9	6.8 ± 1.4	7.6 ± 2.0
Chemerin/BSA	125.8 ± 86.5	125.9 ± 46.8	100.9 ± 26.6	138.5 ± 78.5
Resistin [ng/L]				
All Subjects	13.7 ± 1.6*	14.9 ± 0.9	14.4 ± 2.1	14.6 ± 1.5
Resistin/BMI	0.8 ± 0.2	0.9 ± 0.2	0.76 ± 0.13	0.9 ± 0.2
Resistin/BSA	12.9 ± 6.8	14.7 ± 5.6	11.3 ± 2.1	15.5 ± 7.3

Data are shown as mean ± standard deviation. *$P < 0.01$ boys *vs.* girls

Discussion

Adipose tissue could have a harmful or beneficial influence depending on its content in the body. In CKD various adipocytokines could play a role enhancing endothelial dysfunction, oxidative stress, inflammation, atherosclerosis, kidney sympathetic activity, blood pressure, and anaemia [24, 25]. Alam et al. revealed that elevated adiponectin concentration is linked to higher risk for death in adult CKD patients after kidney transplantation [26]. However, they did not document the higher rate of allograft failure in these patients. Niemczyk et al. reported that adipocytokine levels in CKD are in most cases elevated, which is associated with their impaired excretion [20]. Contrary to the study by Kamariski et al. [2], we have shown lower adiponectin levels and adiponectin levels adjusted to BMI or Cole index in children with CKD, independently of renal replacement therapy PD or HD. There was also no correlation of adiponectin level with anthropometrical parameters in this group, but we demonstrated positive correlation with height percentile in healthy controls. Adiponectin deficiency is an independent risk factor for endothelial dysfunction, arterial hypertension, coronary heart disease, and other cardiovascular complications [28]. So our observation on low adiponectin level in children with CKD could confirm that the protective influence of this adipocytokine was lost despite the existing positive correlation of adiponectin with chemerin and resistin, which promote atherosclerosis. As adiponectin in the Kamariski et al. study was directly correlated with age, the higher levels of this adipocy-

Table IV. *Analysis of correlation between total adipocytokine serum levels and anthropometric, biochemical parameters and blood pressure values in children with chronic kidney disease (Spearman)*

Tabela IV. *Analiza korelacji pomiędzy całkowitym stężeniem adipocytokin w surowicy krwi a parametrami antropometrycznymi, biochemicznymi i wartością ciśnienia tętniczego u dzieci z przewlekłą chorobą nerek*

	CKD	Control
Apelin	Age r = 0.4139, p < 0.03	No correlation
Vaspin	No correlation	No correlation
Adiponectin	No correlation	Height percentile r = 0.4779, p < 0.04
Omentin	No correlation	No correlation
Chemerin	Height r = –0.4394, p < 0.02	BMI r = 0.5365, p < 0.02
	Weight r = –0.4676, p < 0.02	BMI percentile r = 0.5015, p < 0.03
	BSA r = –0.4656, p < 0.01	Weight percentile r = 0.4804, p < 0.04
	Cole index	r = 0.5213, p < 0.02
Resistin	No correlation	Hb r = –0.5324, p < 0.02

tokine in adults may result also from advanced age, and not only GFR decline [2]. Kaynar et al. found that adiponectin and resistin levels were significantly positively correlated with the presence of protein-energy wasting in adult patients with CKD [29]. Elshamaa et al. found higher levels of adiponectin in HD children as compared to children on conservative therapy of CKD. They also documented that genetic variations in the adiponectin gene seemed to have an impact on circulating adiponectin levels in these children groups (single-nucleotide polymorphisms at position 276) [3]. Unfortunately we did not have the opportunity to perform genetic evaluation in our study group.

Apelin according to Mafra et al., it is also an osteoblastic factor, which is protective to bone in adult patients on haemodialysis, and its action is mediated by G-protein-coupled receptor with a theoretically opposite effect to PTH receptor [30]. In children we detected higher levels of apelin irrespectively to dialysis method, with a positive correlation with age. This adipocytokine may promote growth, increasing its concentration with age. Additionally, its higher concentration could be the result of progression of endothelial dysfunction/inflammation in CKD patients, as reported by Małyszko et al. [31]. It is also a valuable finding because the examined children with CKD had no superimposed co-morbidity as adult patients.

In recent investigations, high chemerin levels have also been shown to correlate with better survival in patients on haemodialysis (HD), and were a predictor of regional adiposity in HD patients [17]. Yamamoto et al. reported that, in incident patients on dialysis, elevated chemerin concentration is associated with better survival, despite its significant positive association with markers of inflammation and dyslipidaemia [32].

To our knowledge, this is the first study on the serum chemerin concentrations in children suffering from CKD. Our study demonstrated significantly lower serum levels of chemerin in children with CKD in comparison to the concentrations of this hormone in healthy children, also after adjustment for BMI, but not after adjustment to BSA. We have not shown any positive correlation of chemerin level and BMI in children with CKD. The negative correlation of chemerin concentration and weight in this group supports the hypothesis that low levels of the hormone might result from the loss of the body mass, caused by nutritional restrictions or poor appetite in children with CKD or low-grade inflammatory processes.

Possibly the increased production and/or release of adipose tissue hormones, such as omentin into the blood, enhancing insulin sensitivity, is one of the mechanisms of the adaptation to the state of malnutrition. Similar relationships have been demonstrated in girls with anorexia nervosa [Ziora — unpublished data]. Shang et al. believe that the concentration of serum omentin may be a potential biomarker for the development and progression of atherosclerosis in the coronary arteries in people with metabolic syndrome [33]. Omentin circulating in the blood can be considered as a useful biomarker of vascular endothelium function and proper synthesis of nitric oxide [34]. Higher levels of omentin in children with CKD, regardless of treatment modality, point to its beneficial effect in protecting arteries. Alcelik et al. found also elevated levels of omentin in adult patients with CKD on haemodialysis [35].

Seeger et al. found that circulating vaspin is negatively correlated with GFR but they did not document the difference between vaspin levels of patients on HD and healthy controls [20]. The connection between circulating levels of vaspin and components of the renal function in children has not been determined yet. In our study we found lower levels of total vaspin in children with CKD, as compared to the healthy group, without any difference between children on HD or PD. The difference was also seen after adjusting the vaspin level to BMI, but not after adjusting to BSA. There was no correlation with anthropometric or biochemical parameters. Inoue et al. examined adult haemodialysis patients and also found lower vaspin levels in this group. Vaspin protects vascular endothelial cells from apoptosis induced by free fatty acids, which may suggest the beneficial antiatherosclerotic effect of this adipocytokine [36].

Table V. *Correlation coefficients (p) between adipocytokines in children with chronic kidney disease (Spearman) (n = 28)*
Tabela V. *Współczynniki korelacji pomiędzy adipocytokinami u dzieci z przewlekłą chorobą nerek*

	Apelin	Vaspin	Adiponectin	Omentin	Chemerin	Resistin
Apelin		0.1831	0.1415	–0.3860	–0.2890	–0.1900
P value		p = 0.351	p = 0.473	p = 0.042	p = 0.136	0.333
Vaspin	0.7511		0.0332	–0.4980	–0.2825	–0.0780
P value	p < 0.0001		p = 0.867	p = 0.007	p = 0.145	p = 0.693
Adiponectin	0.8171	0.6685		0.0756	0.4390	0.4211
P value	p < 0.0001	p = 0.0130		p = 0.702	p = 0.019	p = 0.026
Omentin	0.7599	0.4628	0.8104		0.1460	0.1943
P value	p < 0.0001	p = 0.0017	p < 0.0001		p = 0.458	p = 0.322
Chemerin	0.7183	0.4953	0.8371	0.8316		0.1361
P value	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001		p = 0.490
Resistin	0.7862	0.6312	0.8740	0.8502	0.7962	
P value	p < 0.0001	p = 0.0120	p < 0.0001	p < 0.0001	p < 0.0001	

In the upper-right part of the table correlation coefficients for directly measured adipocytokines levels are presented. In the lower-left part of the table adipocytokines levels are correlated after adjustment for BMI

Mills et al. examined resistin levels in patients with CKD and found that higher resistin concentration was independently associated with lower eGFR and higher urinary albumin excretion [6]. Also, in children with CKD we confirmed higher absolute resistin level and level adjusted to BMI, and a negative correlation with haemoglobin concentration was revealed, which underlines the relationship of this adipocytokine with the severity of CKD. Similar conclusions were drawn by Maggio et al., who found that normal resistin levels result from both adequate nutritional state and controlled inflammatory state in children with CKD [4].

Our study has limitations that should be considered. The examined group was rather small as the paediatric population of children with CKD in stage 5 is not numerous, which reduced the power of the study. The causes of CKD showed also wide variability; however, children had no currently active immunological disease. All the children with CKD received various pharmacological treatments and remained on a low phosphate, low/normal protein diet, which could have an influence on serum adipocytokine concentration. A serious difficulty in our study was to establish the control group. Children with CKD are usually physically poorly developed with delayed puberty in comparison to their healthy counterparts. So we decided to perform additional relative adjustments of obtained serum adipocytokine values to BMI, BSA, and Cole index, which were similar in both groups of children. We did not collect data on body composition (*e.g.* based on bio-impedance), which could have provided a better tool for adipocytokine concentration adjustment before comparisons than basic anthropometric parameters. The attempt to determine if changed levels of adipocytokines are a causative factor in CKD progression or just reflect the modification in their own metabolism, is also of limited value if based on cross-sectional study. This study also has several strengths, including the standardised methods of obtaining clinical and laboratory data and the unique simultaneous evaluation of six different adipocytokines. The time of CKD duration in children is usually shorter than in adult patients. In our studied group of children there were no age-related comorbidities such as diabetes or coronary artery ischaemic disease.

Conslusions

Our results show that serum adipocytokines are associated with renal impairment in CKD. Longitudinal studies carried out in larger paediatric cohorts would be helpful in investigation if adipocytokines play a harmful role in the development of CKD, and would enable further understanding of risk factors for CKD progression or its complications (*e.g.* cardiovascular disease).

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