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Univerzitet Crne Gore
Odbor za doktorske studije

Poštovani,

U skladu sa članom 41 i 55 Pravila doktorskih studija, i tačkom 3.8. Vodiča za doktorske studije, u prilogu akta dostavljamo obrazac D2 uz Prijedlog odluke Vijeća o imenovanju Komisije za ocjenu doktorske disertacije dr med Marine Jakšić Kavarić, pod nazivom "Inflamacija, oksidativni stres i metabolički sindrom kod predgojazne i gojazne djece", sa pratećom dokumentacijom.

MEDICINSKI FAKULTET
D E K A N

Prof. dr Miodrag Radunović

ISPUNJENOST USLOVA DOKTORANDA

OPŠTI PODACI O DOKTORANDU			
Titula, ime, ime roditelja, prezime	Dr Marina (Željko) Jakšić		
Fakultet	Medicinski		
Studijski program	Medicina		
Broj indeksa	25/10		
NAZIV DOKTORSKE DISERTACIJE			
Na službenom jeziku	Inflamacija, oksidativni stres i metabolički sindrom kod predgojazne i gojazne djece u Crnoj Gori		
Na engleskom jeziku	Inflammation, oxidative stress and metabolic syndrome in pre-obese and obese children in Montenegro		
Naučna oblast	Patološka fiziologija i laboratorijska medicina		
MENTOR/MENTORI			
Prvi mentor	Prof. dr Milica Martinović	Medicinski fakultet Podgorica, Univerzitet Crne Gore	Patološka fiziologija i laboratorijska medicina
KOMISIJA ZA PREGLED I OCJENU DOKTORSKE DISERTACIJE			
Prof.dr Nela Rašeta Simović, redovni profesor		Medicinski fakultet Univerziteta u Banjoj Luci	Patološka fiziologija
Prof. dr Milica Martinović, redovni profesor		Medicinski fakultet Podgorica, Univerzitet Crne Gore	Patološka fiziologija i laboratorijska medicina
Doc. dr Snežana Pantović, docent		Medicinski fakultet Podgorica, Univerzitet Crne Gore	Medicinska biohemija

Datum značajni za ocjenu doktorske disertacije	
Sjednica Senata na kojoj je data saglasnost na ocjenu temu i kandidata	24.12.2019. godine
Dostavljanja doktorske disertacije organizacionoj jedinici i saglasanost mentora	23.04.2021. godine
Sjednica Vijeća organizacione jedinice na kojoj je dat predlog za imenovanje komisija za pregled i ocjenu doktorske disertacije	27-28.04.2021.godine

ISPUNJENOST USLOVA DOKTORANDA
U skladu sa članom 38 pravila doktorskih studija kandidat je cjelokupna ili dio sopstvenih istraživanja vezanih za doktorsku disertaciju publikovao u časopisu sa

(SCI/SCIE)/(SSCI/A&HCI) liste kao prvi autor.

Spisak radova doktoranda iz oblasti doktorskih studija koje je publikovao u časopisima sa (upisati odgovarajuću listu)

1. Jaksic Marina, Martinovic Milica, Gligorovic-Barhanovic Najdana, Vujacic Aleksandar, Djurovic Dijana, Nedovic-Vukovic Mirjana. **Association between inflammation, oxidative stress, vitamin D, copper and zinc with pre-obesity and obesity in school children from the city of Podgorica, Montenegro. Journal of Pediatric Endocrinology and Metabolism 2019 Sep 25;32(9):951-957. doi: 10.1515/jpem-2019-0086. PMID: 31444965.**
https://pubmed.ncbi.nlm.nih.gov/31444965/

2. Jaksic Marina, Martinovic Milica, Gligorovic-Barhanovic Najdana, Antunovic Tanja and Nedovic-Vukovic Mirjana."**Relationship between insulin-like growth factor-1, insulin resistance and metabolic profile with pre-obesity and obesity in children". Journal of Pediatric Endocrinology and Metabolism 2021; 34(3):301-309. https://doi.org/10.1515/jpem-2020-0447**

3. **Martinovic Milica, Belojevic Goran, Jaksic Marina, Kavaric Nebojsa, Klisic Aleksandra. Cardiometabolic risk among Montenegrin urban children in relation to obesity and gender. Accepted for publication 12-07-2018. Acta Clinica Croatica, Ahead of print**

Za radove pod rednim brojem 1 i 2 odštampani primjerici rada dati su uz ovaj obrazac, a za rad pod rednim brojem 3 priložen je dokaz o prihvatanju rada za publikovanje.

Obrazloženje mentora o korišćenju doktorske disertacije u publikovanim radovima

Dio istraživačkog materijala koji proističe iz doktorske disertacije, publikovan je u vidu dva rada i to 2019. i 2021. godine u renomiranom medunarodnom biomedicinskom časopisu "Journal of Pediatric Endocrinology and Metabolism" (indeksiran u SCI, SCIE, impakt faktor 1.27). U prvom radu publikovan je dio rezultata koji je potvrdio povezanost inflamacije, oksidativnog stresa, metaboličkog sindroma, kao i nekih specifičnih markera poput vitamina D, oligoelemenata bakra i cinka sa predgojaznošću i gojaznošću u dječijem uzrastu. U drugom radu prikazan je dio rezultata disertacije koji je proučavao povezanost specifičnog markera, insulinu-sličnog faktora rasta-1 sa metaboličkim profilom i insulinskom rezistencijom kog predgojazne i gojazne djece, gdje je ta povezanost uočena i naučno elaborirana. Takode, dio rezultata našeg istraživanja koji se odnosi na procjenu kardiometaboličkog rizika kod predgojazne i gojazne djece statističkom metodom računanja Z skora prihvaćen je za objavljivanje u biomedicinskom časopisu Acta Clinica Croatica (SCIE, impakt faktor 0.53)(dokaz u prilogu). Mišljenje nezavisnih, usko specijalizovanih, recenzentskih komisija gore navedenih biomedicinskih časopisa, koje su ocijenile naše istraživanje kao izuzetno značajno za pedijatrijsku populaciju, još jedna su potvrda sveukupnog doprinosa rezultata disertacije boljem razumijevanju patofiziološkog supstrata predgojaznosti/gojaznosti i bolesti udruženih sa njima.

Datum i ovjera (pečat i potpis odgovorne osobe)

U Podgorici, 28.04.2021.godine

MP

DEKAN
Prof.dr Miodrag Radunović

Prilog dokumenta sadrži:

1. Potvrdu o predaji doktorske disertacije organizacionoj jedinici
2. Odluku o imenovanju komisije za pregled i ocjenu doktorske disertacije
3. Kopiju rada publikovanog u časopisu sa odgovarajuće liste
4. Biografiju i bibliografiju kandidata
5. Biografiju i bibliografiju članova komisije za pregled i ocjenu doktorske disertacije sa potvrdom o izboru u odgovarajuće akademsko zvanje i potvrdom da barem jedan član komisije nije u radnom odnosu na Univerzitetu Crne Gore

UNIVERZITET CRNE GORE

MEDICINSKI FAKLTET

Broj:582/2

Podgorica23.04.2021 .godine

P O T V R D A

Potvrđuje se da je dr med Marina Jakšić predala 7 primjeraka doktorske disertacije, pod nazivom **„ Inflamacija, oksidativni stres i metabolički sindrom kod predgojazne i gojazna djece u Crnoj Gori"** dana 23.04.2021.godine i ista je zavedena pod brojem:582.

Potvrda se izdaje u svrhu pregleda i ocjene doktorske disrtacije.

ŠEF STUDENTSKE SLUŽBE

Sonja Vukićević

Sonja Vukičević,diplomirani pravnik

UNIVERZITET CRNE GORE
MEDICINSKI FAKULTET
Broj: 588/9
Podgorica, 28.04.2021. godine

Na osnovu člana 64 stav 1 tačka 9 Statuta Univerziteta Crne Gore, (Bilten UCG br.337/2015 i br 147/2018), člana 41 i 55 Pravila doktorskih studija, inicijalnog predloga Komisije za doktorske studije Medicinskog fakulteta broj: 582/3 od 26.04.2021. godine i tačke 3.8 Vodiča za doktorske studije Univerziteta Crne Gore, Vijeće Medicinskog fakulteta na elektronskoj sjednici održanoj 27-28.04.2021. godine, donijelo je

O D L U K U

I

Kandidat dr med Marina Jakšić Kavarić, ispunjava formalne uslove za ocjenu doktorske disertacije: **„Inflamacija, oksidativni stres i metabolički sindrom kod predgojazne i gojazne djece u Crnoj Gori".**

II

Predlaže se Komisija za ocjenu doktorske disertacije dr med Marine Jakšić Kavarić, pod navedenim nazivom: **„Inflamacija, oksidativni stres i metabolički sindrom kod predgojazne i gojazne djece u Crnoj Gori"** u sastavu:

1. **Prof. dr Nela Rašeta Simović**, redovni profesor Medicinskog fakulteta Univerziteta u Banjoj Luci, naučna oblast: patološka fiziologija;
2. **Prof. dr Milica Martinović**, redovni profesor Medicinskog fakulteta Univerziteta Crne Gore, naučna oblast: patološka fiziologija;
3. **Doc. dr Snežana Pantović**, docent Medicinskog fakulteta Univerzieta Crne Gore, naučna oblast: medicinska biohemija;

III

Komisija za ocjenu doktorske disertacije je dužna da Vijeću Medicinskog fakulteta, podnese izvještaj koji sadrži ocjenu doktorske disertacije.

Obrazloženje

Dr med Marina Jakšić Kavarić je predala doktorsku disertaciju pod nazivom: **„Inflamacija, oksidativni stres i metabolički sindrom kod predgojazne i gojazne djece u Crnoj Gori"** dana 23.04.2021. godine.
Vijeće Medicinskog fakulteta je utvrdilo da kandidat ispunjava uslove iz člana 38 Pravila doktorskih studija, da kandidat dr med Marina Jakšić Kavarić ima, kao prvi autor dva rada sa rezultatima iz teze objavljen u časopisu sa SCI/**SCIE** liste, kao i jedan rad u svojstvu koautora prihvaćen za publikovanje od strane časopisa sa SCIE liste. Samim tim su se stekli uslovi da se imenuje Komisija za ocjenu pomenute doktorske disertacije. Na osnovu svega navedenog, odlučeno je kao u dispozitivu ove Odluke.

VIJEĆE MEDICINSKOG FAKULTETA
PREDSJEDAVAJUĆI,

Prof. dr Miodrag Radunović, dekan

Marina Jaksic*, Milica Martinovic, Najdana Gligorovic-Barhanovic, Aleksandar Vujacic, Dijana Djurovic and Mirjana Nedovic-Vukovic

Association between inflammation, oxidative stress, vitamin D, copper and zinc with pre-obesity and obesity in school children from the city of Podgorica, Montenegro

https://doi.org/10.1515/jpem-2019-0086
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Abstract

Background: Childhood obesity is a serious health condition with increasing rates worldwide. The aim of this study was to investigate the association between inflammation, oxidative stress, vitamin D, copper and zinc in pre-obese and obese children compared to controls.
Methods: The study involved 202 children aged 7–15 years (63.9% boys), randomly chosen from 10 elementary schools in Podgorica, Montenegro. Participants were divided into three groups according to their nutritional status (International Obesity Task Force [IOTF] criteria): normal-weight (42.1%), pre-obese (40.6%) and obese (17.3%). Serum biochemical analyses were performed (C-reactive protein [CRP], retinol-binding protein [RBP], total antioxidant status [TAS], total vitamin D [VD], copper and zinc).
Results: Serum TAS and CRP concentrations were higher in pre-obese and obese children compared to controls ($p < 0.001$). Serum VD concentrations were lower in pre-obese and obese children compared to their normal-weight peers ($p = 0.027$ and $p = 0.054$, respectively). Copper, zinc and RBP concentrations did not differ significantly among the groups ($p > 0.05$). In pre-obese and obese children, a positive correlation was found between CRP and copper ($r = 0.305$, $p = 0.011$ and $r = 0.440$, $p = 0.013$, respectively), and TAS and RBP ($r = 0.528$, $p < 0.001$ and $r = 0.434$, $p = 0.015$, respectively). Standard regression analyses showed that CRP and TAS increase ($p < 0.001$) whereas VD decreases ($p = 0.011$) with the body mass index (BMI).
Conclusions: We show that pre-obesity and obesity in childhood are positively associated with oxidative stress and inflammation, and inversely associated with VD status. Copper and zinc concentrations were not associated with excess fat in children.

Keywords: inflammation; obesity; oligoelements; oxidative stress; vitamin D.

Introduction

Obesity is defined as an abnormal or excessive fat accumulation that presents a risk to health [1]. It is estimated that 20% of the world's adult population will be obese by 2030 [2]. A recent national study of childhood obesity in Montenegro showed that pre-obesity/obesity may be expected in one out of four Montenegrin school children; the prevalence has increased by 35% in the last 10 years [3]. Excess adipose tissue in children and adults is often accompanied by low-grade inflammation and oxidative stress [4]. Numerous studies have demonstrated an association between the body mass index (BMI) and large waist circumference (WC) with high concentrations of inflammation markers such as C-reactive protein (CRP) [5, 6] and proinflammatory adipokines such as retinol-binding protein (RBP) [7]. Inflammatory markers have been shown to stimulate vascular atherosclerotic lesions and may also affect metabolism by negatively influencing insulin sensitivity causing insulin resistance [6]. Furthermore, hypertrophic fat tissue generates reactive oxygen species which are an underlying cause of oxidative stress and additional proinflammatory cytokine release [8]. According to some authors, obesity is associated with reduced serum vitamin D concentrations. The possible explanation for this association might be increased storage and sequestration of vitamin D in enlarged adipose tissue [4, 9]. Vitamin D deficiency may contribute to the pathogenesis of obesity, metabolic syndrome (MS) and type 2 diabetes. Several *in vitro* studies have shown that vitamin D exerts an anti-inflammatory action on human adipocytes

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by decreasing inflammatory cytokine expression [10]. The anti-inflammatory and anti-oxidative effects of vitamin D have been described in numerous studies [11, 12]. Copper and zinc protect against inflammation and oxidative stress, and the deficiency of these oligoelements might play an important role in the development of cardiometabolic complications of obesity [13]. Studies have also shown that an adequate adipose tissue zinc status is required for normal leptin synthesis and appetite regulation [14]. It is also involved in insulin storage and secretion, which implicates the role of this microelement deficiency in the development of type-2 diabetes mellitus [15]. Copper, similar to zinc, is a component of antioxidant enzymes such as Cu/Zn superoxide dismutase, which protects the body against the action of free radicals [16], but in certain conditions, copper can act as a pro-oxidant, which makes its biological role and significance more complex [17]. Some investigations suggest that copper deficiency may be associated with atherogenic dyslipidemia and hepatic steatosis. Furthermore, in rodent models, copper restriction leads to hypertension, elevated triglycerides and total cholesterol [18].

The objectives of this study were to:

- evaluate the difference in serum concentrations of biomarkers of inflammation and antioxidant defense in pre-obese and obese children, compared to their normal-weight peers;
- examine the correlation between the biomarkers of inflammation and antioxidant defense in pre-obese and obese children; and
- examine the relationship between children's BMI and the biomarkers of inflammation and antioxidant defense.

Materials and methods

The data used in this study were collected as a part of the national survey of school children obesity in Montenegro (2013–2015) entitled the "Research on Obesity and Poverty of Children in Montenegro – Clinical, Pathophysiological, Biochemical and Preventive Aspects". Details of data collection have been explained elsewhere [3]. The study was approved by the Ethics Committee of the Faculty of Medicine, University of Montenegro (Decision No. 3399, dated 24 December 2013).

The sample consisted of 202 children aged 7–15 years, 129 boys (63.9%) and 73 (36.1%) girls, randomly chosen from 10 elementary schools from Podgorica, Montenegro, within a representative national sample of children [3]. Informed consent was obtained from all children and their parents. The survey response rate was 100% (202 survey invitation letters delivered).

Anthropometric measurements were obtained for the 202 randomly selected children. Children were weighed on a digital scale accurate to 0.1 kg (SECA, model SE 808, Hamburg, Germany). A stadiometer was used for body height measurements accurate to 0.5 cm (GIMA, code 27328, Gessate, Milan, Italy). BMI was calculated by using the formula: body weight in kilograms divided by the squared height in meters. WC was measured midway between the lowest border of the rib cage and the upper border of the iliac crest, at the end of normal expiration, using an un-stretched tape-meter, and the measurements were recorded to the nearest 0.1 cm. The waist-to-height ratio (WtHR) was calculated by dividing WC by height in cm. An Omron HEM 907 XL (Kyoto, Japan) oscillometric monitor was used for the measurement of blood pressure. The measurement was performed at school in the afternoon, in a quiet room, in a sitting position, after a rest of 5 min. Three measurements with a 1-min interval were performed using an appropriately sized cuff. Mean values of the systolic blood pressure (SBP) and diastolic blood pressure (DBP) were calculated. Prehypertension in children is defined as an average SBP and/or DBP that is in at least the 90th percentile, but less than the 95th percentile, for sex, age and height. Hypertension in children is defined as an average SBP and/or DBP that is greater than or equal to the 95th percentile for sex, age and height [19]. We formed three groups of children according to their nutritional status: (1) normal-weight (n = 85/42.1%); (2) pre-obese (82/40.6%); and (3) obese (n = 35/17.3%).

Nutritional status was assessed according to the International Obesity Task Force (IOTF) criteria. IOTF provides BMI cut-points by age and sex for thinness, overweight and obesity for children and adolescents aged 2–18. The cut-points correspond to an adult BMI of 16.5 (thinness grade 1), BMI of 17 (thinness grade 2), BMI of 18.5 (thinness grade 3), BMI of 25 (pre-obese) or BMI of 30 (obesity) [20].

Pre-obese/obese children were diagnosed as having MS when they had any three or more of the five following criteria: WtHR ≥0.5, fasting glycemia ≥5.5 mmol/L, triglycerides ≥1.7 mmol/L, high-density lipoprotein cholesterol (HDL-c) <0.90 mmol/L and presence of hypertension. WtHR values of 0.5 and higher point to central obesity which is associated with an increased risk of MS in children [21, 22].

Biochemical analyses

Blood samples were taken in the morning at the departments within primary health care centers. Laboratory analyses were performed at the Center for Laboratory Diagnostics (Clinical Center of Montenegro and Primary Health Care Center in Podgorica). Serum CRP (mg/L) was measured using the spectrophotometric device Roche Cobas 6000 (Mannheim, Germany). For a general overview of the antioxidants in children's serum, we used an automated total antioxidant status (TAS) test (Randox, London, UK). The spectrophotometric measurement of TAS was performed using an Architect c4000 (Abbott, Chicago, IL, USA). An automated total vitamin D (VD) immunoassay was used for the determination of both vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol) in children's serum. Vitamin D (nmol/L) was measured using immunochemistry (Roche Cobas 6000, Mannheim, Germany). Serum RBP (g/L) was measured using turbidimetry (Dade Behring BN II Nephelometer, Siemens, Marburg, Germany). Serum copper and zinc (μmol/L) were determined by inductively coupled plasma-optical emission spectrometry (ICP-OES) (Spectro Arcos, Kleve, Germany).

Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corporation, Armonk, NY, USA). The Shapiro-Wilk test was used for testing the normality of variable distribution. Analysis of variance (ANOVA) and the Kruskal-Wallis

test were used for the assessment of differences between the three investigated groups. The results are presented as means and standard deviations (SD) for normally distributed variables or medians and interquartile ranges for non-normally distributed variables. We used the least significant difference (LSD) and the Mann-Whitney test for post-hoc testing. Depending on variable distribution, Pearson's or Spearman's correlation coefficients (r) were calculated to evaluate the correlations between oxidative and inflammatory biochemical parameters. The chi-square (χ^2) test was used for categorical variables. Standard linear regression was used for the assessment of oxidative and inflammatory parameters depending on the BMI values. A p-value <0.05 was considered as statistically significant.

Results

The three groups of studied children were similar in age but significantly different concerning the anthropometrics ($p<0.01$). The characteristics of the studied children are shown in Table 1.

Serum TAS and CRP concentrations were significantly higher in pre-obese and obese children compared to controls ($p<0.001$). Serum vitamin D concentration was lower in pre-obese and obese children compared to normal-weight children ($p=0.027$ and $p=0.054$, respectively). However, the difference in vitamin D concentration between obese and normal-weight children was only borderline significant ($p=0.054$). Serum copper, zinc and RBP concentrations did not differ significantly among the groups ($p>0.05$) (Table 2).

In pre-obese children, a weak positive correlation was found between CRP and copper ($r=0.305$, $p=0.011$), and a moderate positive correlation was found between TAS and RBP ($r=0.528$, $p<0.001$) (Table 3).

In obese children, a moderate positive correlation was found between copper and CRP ($r=0.440$, $p=0.013$), and TAS and RBP ($r=0.434$, $p=0.015$), while a moderate negative correlation was found between copper and RBP ($r=-0.423$, $p=0.02$) (Table 4).

Standard linear regression was used to evaluate the prediction of the value of inflammatory and antioxidative defense markers, depending on children's BMI. Serum levels of CRP and TAS increased ($p<0.001$), VD decreased ($p=0.011$) and RBP slightly changed ($p=0.001$) with increasing BMI. BMI explains the 9.4% variability of CRP, but if adjusted with copper, this percent increased to 17.6%. BMI also explains the 3.7% and 24.2% variability of vitamin D and antioxidant status without adjustment, respectively. The adjusted model with TAS and triglycerides explains almost 30% the variability of the antioxidant status. Serum values of copper and zinc do not depend on BMI (Table 5).

Table 1: Characteristics of the studied children.

	Normal-weight (n=85)	Pre-obese (n=82)	Obese (n=35)	p-Value
Age, years[a]	10.82±1.62	11.05±1.45	10.83±1.67	0.607
Body weight, kg[b,c]	30.15 [25.65–53.22]	42.60 [35.00–51.50]	50.00 [42.30–62.50]	<0.001
Body height, cm[a]	137.68±10.38	143.62±11.59[d]	144.89±11.59[d]	<0.001
BMI, kg/m^2[b,c]	16.3 [14.97–17.10]	20.70 [19.50–22.80]	24.10 [22.50–27.60]	<0.001
WC, cm[b,c]	57.25 [54.00–61.00]	69.00 [64.00–76.00]	78.00 [69.00–86.00]	<0.001

[a]Data are presented as mean value and standard deviation; [b]Data are presented as median value and interquartile ranges; [c]$p<0.001$. There was difference between all groups (Mann-Whitney U test); [d]$p<0.001$ vs. normal weight (LSD post-hoc test). BMI, body mass index; LSD, least significant difference; WC, waist circumference.

Table 2: Biochemical parameters in normal-weight, pre-obese and obese children.

	Normal-weight (n=85)	Pre-obese (n=82)	Obese (n=35)	p-Value
TAS[a,c]	1.50±0.14	1.60±0.12	1.70±0.11	<0.001
CRP[b,c]	0.30 [0.16–0.42]	0.59 [0.26–1.43]	1.03 [0.46–3.07]	<0.001
VD[b]	77.20 [67.70–95.10]	70.10 [56.00–86.60][d]	69.65 [59.30–85.87]	0.046
RBP[b]	0.026 [0.020–0.029]	0.026 [0.022–0.031]	0.028 [0.025–0.031]	0.157
Copper[a]	18.19±3.17	18.83±2.96	18.16±3.27	0.367
Zinc[b]	13.00 [12.10–14.35]	13.05 [11.42–14.42]	13.30 [11.90–13.80]	0.651

[a]Data are presented as mean value and standard deviation; [b]Data are presented as median value and interquartile ranges; [c]$p<0.001$. There was difference between all groups (LSD post-hoc test for TAS and Mann-Whitney for CRP); [d]$p=0.027$ vs. normal weight. CRP, C-reactive protein; LSD, least significant difference; RBP, retinol-binding protein; TAS, total antioxidant status; VD, total vitamin D.

Table 3: Correlation between inflammatory and antioxidative defense markers in pre-obese children.

Pre-obese	CRP		VD		RBP	
	r	p-Value	r	p-Value	r	p-Value
TAS	0.110	0.344	0.200	0.086	0.528	0.000
Copper	0.305	0.011	0.102	0.412	−0.216	0.104
Zinc	−0.065	0.598	−0.165	0.182	0.047	0.726

CRP, C-reactive protein; RBP, retinol-binding protein; TAS, total antioxidant status; VD, total vitamin D.

Table 4: Correlation between inflammatory and antioxidative defense markers in obese children.

Obese	CRP		VD		RBP	
	r	p	r	p	r	p
TAS	0.112	0.541	−0.172	0.347	0.434	0.015
Copper	0.440	0.013	0.133	0.477	−0.423	0.020
Zinc	0.186	0.316	−0.101	0.588	−0.011	0.954

CRP, C-reactive protein; RBP, retinol-binding protein; TAS, total antioxidant status; VD, total vitamin D.

Hyperglycemia was found more in obese children than in controls (p = 0.007). HDL-c did not significantly differ between the three groups (p = 0.216). The concentration of triglycerides was higher in the pre-obese (14.6%) and obese (8.6%) groups compared to normal-weight children (0.0%). There was no significant difference in triglyceride concentrations between the pre-obese and obese group of children. Hypertension was more present in obese children (54.3%) compared to controls (25.9%, p = 0.003) and the pre-obese group (31.1%, p = 0.020). There was no difference in the presence of hypertension between normal-weight and pre-obese children (p = 0.477). MS was present in 11.4% of obese, 9.8% of pre-obese and 0% of normal-weight children (p < 0.001) (Table 6).

Discussion

This study evaluated the inflammation and the antioxidative defense-related biomarkers, as the response induced by oxidative stress, in pre-obese and obese children in Montenegro. In our report, the value of the serum pro-inflammatory marker CRP was higher in obese and pre-obese children compared to their normal-weight peers. A similar elevation of inflammatory markers in obese children was found by Luciardi et al. [23] indicating that the excess fat is strongly associated with low-grade inflammation in white adipose tissue, caused by lipid accumulation in adipocytes, which stimulates the liver to produce systemic proinflammatory markers such as CRP [24]. Additionally, in pre-obese and obese children, CRP was positively related to copper. A significant elevation of serum copper followed by the increase in inflammatory markers and serum zinc decrease were also found in obese children in an Egyptian study, but the exact mechanism of these actions is still unknown [25]. In our report, serum TAS was higher in pre-obese and obese children in comparison to controls. A number of authors found lower total antioxidant capacity in obese prepubescent children [26, 27]. Some studies showed that TAS was raised in visceral obesity showing a positive relation with a number of

Table 5: Unadjusted and adjusted regression coefficients for BMI impact on inflammatory and antioxidative defense markers.

	Adjusted model[a]	Effect of BMI – linear standard regression		
		β [95% CI]	r^2	p-Value
CRP	Unadjusted, n = 196	0.162 [0.090–0.230]	0.094	<0.001
	Copper, n = 176	0.167 [0.096–0.238]	0.176	<0.001
VD	Unadjusted, n = 172	−1.119 [−1.984 to −0.255]	0.037	0.011
TAS	Unadjusted, n = 147	0.018 [0.014–0.023]	0.242	<0.001
	RBP, n = 147	0.011 [0.007–0.015]	0.363	<0.001
RBP	Unadjusted, n = 183	0.000 [0.000–0.001]	0.070	<0.001
	TAS, n = 145	0.000 [0.000–0.001]	0.237	
	Triglycerides, n = 147	0.000 [0.000–0.001]	0.161	
	TAS + triglycerides, n = 145	0.000 [0.000–0.001]	0.294	
Copper	Unadjusted, n = 176	−0.017 [−0.136–0.101]		0.771
Zinc	Unadjusted, n = 176	−0.048 [−0.126–0.029]		0.221

[a]Model was adjusted only for variables which showed correlation coefficient above 0.3 and did not correlate with BMI above 0.7. β, regression coefficient; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; n, number of observations units included in regression; RBP, retinol-binding protein; TAS, total antioxidant status; VD, total vitamin D.

Table 6: Metabolic syndrome criteria in normal-weight, pre-obese and obese children.

MS criteria	Normal-weight (n=85)	Pre-obese (n=82)	Obese (n=35)	p-Value between all groups
Glycemia > 5.5	11 [12.9%]	20 [24.4%]	12 [34.3%][a]	0.023
HDL-c < 0.9	1 [1.2%]	5 [6.1%]	1 [2.9%]	0.216
Triglycerides	0 [0.0%]	12 [14.6%][b]	3 [8.6%][c]	0.001
Hypertension	21 [25.9%]	23 [31.1%]	19 [54.3%][d,e]	0.011
WtHR[f]	1 [1.2%]	29 [36.7%]	27 [77.1%]	<0.001
MS present[f]	0 [0.0%]	8 [9.8%]	4 [11.4%]	<0.001

[a]p = 0.007 vs. normal weight; [b]p < 0.001 vs. normal weight; [c]p = 0.006 vs. normal weight; [d]p = 0.003 vs. normal weight; [e]p = 0.020 vs. pre-obese; [f]There was difference between all groups. HDL-c, high-density lipoprotein cholesterol; MS, metabolic syndrome; WtHR, waist-to-height ratio.

metabolic risk factors [28]. This may be explained by the stronger activation of antioxidant mechanisms in order to balance oxidation in obese subjects [8]. In addition to this, a significant positive correlation was observed between TAS and RBP in pre-obese and obese subjects. The proinflammatory adipokine RBP has an impact on the development of β-cell dysfunction and insulin resistance, which are markedly associated with oxidative stress [29]. It may also be viewed as an independent marker of many adiposity-related co-morbidity risk factors in children, such as dyslipidemia, abdominal obesity or hypertension [30]. Still, in our study, values of RBP did not significantly differ among the investigated groups. We observed a decrease in VD in pre-obese and obese compared to normal-weight children, which is concordant with studies reporting a reverse association between vitamin D serum concentration and adiposity [9]. Some researchers found that low serum vitamin D was significantly associated with increased inflammatory markers in obese children [31]. However, the associations between serum vitamin D concentrations and biomarkers of inflammation were rarely reported in large-scale cross-sectional studies in school-aged children [11]. Our results are not an exception in that sense. Reports also suggest that vitamin D has both anti-inflammatory [32] and antioxidant activity [33, 34], but the recent review on vitamin D was controversial about the ability of vitamin D to prevent or reduce oxidative stress [35].

We found no statistically significant difference in the values of copper and zinc between normal-weight, pre-obese and obese children. In several studies which examined serum oligoelements in obese children, copper concentrations were higher in obese compared to normal-weight children, whereas serum zinc concentrations were lower compared to non-obese controls [13]. These findings indicate the antioxidant role of copper in fat-stimulated oxidative stress [36].

MS is among the most common comorbidities associated with obesity [37]. In our study, high prevalence of MS was recorded in pre-obese and obese children. Numerous other studies have been reporting the increase of the prevalence of MS worldwide, mainly due to the escalating global epidemic of obesity. It is important to mention that some of the underlying causes of obesity and MS may also include poor lifestyle choices such as low physical activity, sedentary behavior and poor dietary factors. As a final result, the risk of MS greatly increases during adulthood for those children exposed to cardiometabolic risk factors in their early lives [37].

Conclusions

We show that inflammation and accentuated antioxidative defense, as a result of increased oxidative stress, are positively associated with pre-obesity and obesity in childhood, representing a pathological basis of obesity-related diseases in children. Our study also determined an inverse association between vitamin D status and excess adiposity in children. Serum copper was associated with inflammation markers in both pre-obese and obese subjects. Zinc nutritional status in pre-obese and obese individuals was not altered. The worrying presence of MS, which is known to contribute to the onset of cardiovascular diseases even in childhood, was found in a significant number of pre-obese and obese children. Further investigations are needed to clarify the complex association between inflammation, oxidative stress and biomarkers such as copper, zinc and vitamin D in pre-obese/obese children. It is important to ensure the clinical and laboratory follow-up of pre-obese and obese children in order to prevent these subjects from developing cardiometabolic complications as a result of the long-term presence of excess adiposity.

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Relationship between insulin-like growth factor-1, insulin resistance and metabolic profile with pre-obesity and obesity in children

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Abstract

Objectives: Childhood obesity is a serious medical condition with alarmingly high rates worldwide. There is controversy regarding the relationship between insulin-like growth factor-1 (IGF-1) and pediatric obesity. We investigated the relationship between IGF-1, insulin resistance and metabolic profile with childhood pre-obesity/obesity.

Methods: The study involved 201 children aged 7–15 years, divided in three groups according to their nutritional status (International Obesity Task Force criteria): normal-weight (n=84), pre-obese (n=82), obese (n=35). Laboratory IGF-1, insulin, fasting blood glucose (FBG), lipid profile, alanine-aminotransferase (ALT), uric acid (UA), anthropometric and body composition parameters were analyzed. Body mass index and IGF-1 standard deviation score (SDS), waist-to-height ratio (WtHR) and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) score were calculated.

Results: Pre-obese/obese children had significantly higher IGF-1 SDS, FBG, insulin, HOMA-IR, UA, ALT, triglycerides, and lower high-density lipoprotein cholesterol (HDL-c); obese group had higher WtHR and low-density lipoprotein cholesterol (LDL-c) compared to controls ($p<0.05$). In obese group, IGF-1 SDS was positively correlated with fat free/muscle mass, total body water ($p<0.05$) and negatively correlated with LDL-c ($p<0.05$). In pre-obese/obese HOMA-IR and insulin were positively correlated with age, total body fat (TBF) ($p<0.05$) and negatively correlated with HDL-c (pre-obese) ($p<0.05$). Multivariate ordinal logistic regression analyses showed that IGF-1 SDS (OR=1.94; 95% CI: 1.21–3.11), TBF (OR=1.37; 95%CI: 1.21–1.54) were predictors of nutritional status ($p<0.001$). FBG (OR=42.39; 95%CI: 2.31–77.2) and UA (OR=1.03; 95%CI: 1.01–1.05) were predictors of IR ($p<0.001$).

Conclusions: IGF-1 SDS and TBF were predictors of nutritional status. Further studies are required to clarify the role of IGF-1 in pathophysiology of obesity and its comorbidities.

Keywords: childhood obesity; insulin-like growth factor-1; insulin resistance; metabolic profile.

Introduction

Obesity is recognized as a chronic non-communicable disease with global rise and serious health consequences in both children and adults. A wide spectrum of obesity-induced metabolic disorders contributes to increased cardiovascular, cancer and other health risks in untreated obese patients [1–3]. Abnormal insulin-like growth hormone-1 (IGF-1) levels have been suggested to play a significant role in obesity [4]. It is hypothesized that obesity-mediated alterations in the growth hormone (GH)/IGF-1 axis in childhood may play a causative role in the pathogenesis of many of the obesity-related comorbidities [5]. Despite the intense scientific efforts toward better understanding the pathophysiology of obesity, there was little related research on the relationship between metabolic obesity profile, insulin resistance and IGF-1 serum concentration in children. Therefore, the identification of obesity-related serum biomarkers is one of the crucial interests in the clarification of the pathophysiology of obesity and obesity-associated cardiometabolic complications [6]. In this regard, some authors even propose IGF-1 as a potential marker for the over-nutritional state in children, although the results of studies on this topic are very heterogeneous [3, 4].

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Although it is best known for its growth-promoting effects, a number of growth-unrelated actions have been recently linked to IGF-1 [4]. IGF-1 is a peptide hormone with a structural homology with insulin, causing the hypoglycemic response in healthy individuals as well as the uptake of free fatty acids into adipocytes and other tissues [7, 8]. Current evidence show that IGF-1 serum concentration might be altered in obesity and also related to impaired metabolic profile including dysregulated lipid and glucose homeostasis and insulin resistance. However, the exact association of these obesity-caused metabolic alterations and IGF-1 concentrations remains insufficiently clear [4].

Obesity is strongly linked with insulin resistance, which is defined as the decreased tissue response to insulin-mediated cellular action [9]. Among physiological conditions, puberty may also be responsible for insulin resistance itself [10]. In order to assess insulin resistance in pre-obese and obese children, the calculation of Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) is usually recommended, although there are no studies defining cut–off levels for HOMA–IR in children yet [11].

Some reports show that IGF-1 levels increase with adiposity, which could be attributed to hyperinsulinemia in obese subjects, since insulin promotes the hepatic synthesis and biological activity of IGF-1 through its lowering effects on IGF-binding proteins [12]. IGF-1 may contribute to the development of obesity due to its role in cell proliferation and apoptosis inhibition, which is also suggested as a link between obesity and cancerogenesis by some authors [2, 13]. It is also hypothesized that high IGF-1 concentrations in infancy could be associated with later obesity [14], but due to complex interactions between diet, growth and IGF axis in infancy and childhood, the exact mechanism of these interactions remains unclear. Contrary to this evidence, numerous reports found that a number of traditional cardiovascular disease risk factors including obesity, dyslipidemia, insulin resistance, elevated C-reactive protein and hypertension have been associated with low serum IGF-1 levels, though mostly in adults [15–17]. Multiple studies show that central or abdominal obesity is an independent marker of obesity-related cardiometabolic diseases. Waist measurement corrected for height (WtHR) is recommended as a surrogate marker of central obesity more than waist circumference measurement alone [13]. The serum activity of alanine aminotransferase (ALT) is another well recognized insulin resistance and cardiometabolic risk biomarker, which may predict the later development of type 2 diabetes [3, 18]. A number of evidence suggest that high uric acid (UA) concentration might be positively associated with many obesity-related diseases such as metabolic syndrome, type 2 diabetes, insulin resistance, dyslipidemia and cardiovascular diseases [19–21].

Methods

The study was approved by Ethics Committee of the Faculty of Medicine, University of Montenegro (Decision No. 3399, 24th of December, 2013).

The study included 115 pre-obese and obese school children aged 7–15 years, and 84 normal-weight subjects. The sample was randomly chosen from 10 elementary schools from the Capital of Montenegro, Podgorica, within a representative national sample of children [22]. Informed consent was obtained from all individuals included in this study. We formed three groups of children according to their nutritional status: 1. Normal weight (n=84/41.8%); 2. Pre-obese (n=82/40.8%); 3. Obese (n=35/17.4%). We assessed the children's nutritional status using the anthropometric criteria of the International Obesity Task Force (IOTF) [23]. Anthropometric measurements were performed in schools. Body height was measured using the stadiometer (Gima 27,328, Gessate, Milan, Italy) with an accuracy of 0.1 cm. Body weight was measured on barefoot children in light clothes using the digital scale (SECA, model SE 808, Hamburg, Germany) with an accuracy of 0.1 kg. Body mass index (BMI) was calculated by dividing body weight in kilograms by the squared height in meters. SDS BMI was calculated according to the LMS system according to the formula ((BMI/M)^L-1)/(L*S) using length/height for age for boys and girls available on the World Health Organization website https://www.who.int/childgrowth/standards/height_for_age/en/. SDS IGF-1 was calculated using a calculator available at https://www.esoterix.com/endocrinology-services/endocrinology-tools/calculator-igf1. Waist circumference was measured by a measuring track on a midway between the lower edge of the rib cage and the upper edge of the iliac bone, with an accuracy of 0.1 cm. Waist to height ratio (WtHR) was calculated by dividing waist circumference with height in cm. WtHR values of 0.5 and higher point to central obesity, which is associated with an increased risk of cardiometabolic complications in children [24]. Pubertal stage according to the definition of Marshall and Tanner was determined by well-trained physicians. Pubertal developmental stage of boys and girls was categorized into two groups: prepubertal (Tanner stage I) and pubertal (Tanner stage II; II, IV and V) [25].

Body composition (total body fat-TBF [kg], muscle mass-MM [kg], fat free mass-FFM [kg] total body water-TBW [kg]) were assessed by using the bioelectric impedance device Tanita BC – 418, Tokyo, Japan.

Biochemical tests were performed on blood samples collected from the antecubital vein after overnight fasting (>10 h). Serum samples were kept at –80 °C until analyzed. IGF-1 (ng/mL) and fasting insulin (mU/L) concentrations were determined by immunometric assay (Roche Cobas 6000, Mannheim, Germany) with intra- and inter-assay coefficient of variations for IGF-1 less than 8%. HOMA-IR was calculated according to the formula: glucose (mmol/L) × fasting insulin (mU/L)/22.5. Insulin resistance was defined as HOMA-IR ≥ 3.4 [26]. Measurements of fasting blood glucose (FBG) (mmol/L), uric acid (μmol/L), ALT activity (U/L) and lipid profile expressed in mmol/L triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) were

tested by biochemical autoanalyzer (Roche Cobas 6000, Mannheim, Germany). The performance of all the assays was monitored using internal quality control.

Statistical analyses

IBM SPSS Statistics for Windows, Version 22.0 was used for statistical analyses. First we tested normality of variable's distribution using several tests. The Shapiro–Wilk test was decisive. Kruskall Wallis and Mann Whitney were used for the assessment of differences between investigated groups. Depending on variable distribution, Pearson's or Spearmen correlation coefficients (r) were calculated to evaluate correlations between laboratory parameters. Ordinal logistic regression was used to evaluate the predictive factors for nutritional status. Binary logistic regression was used to evaluate the prediction of insulin resistance depending on investigated parameters. p-Value <0.05 was considered as statistically significant.

The major goal of this study was to examine the association between IGF-1, metabolic profile and insulin resistance with pre-obesity and obesity in children aged 7–15 years.

Results

In our sample, both pre-obese and obese children had significantly higher IGF-1 SDS, insulin, HOMA-IR, fasting blood glucose, uric acid, triglycerides, ALT levels and all body composition parameters, while obese group had higher WtHR and LDL-c compared to their normal weight peers (p<0.05). HDL-c was significantly lower in pre-obese and obese compared to controls (p<0.05). Total cholesterol concentrations did not differ significantly among the groups (p=0.210) (Table 1).

BMI SDS, fasting blood glucose, insulin, uric acid, ALT, and all body composition parameters were significantly higher in children with insulin resistance (HOMA-IR≥3.4, n=24), while HDL-c was significantly lower than in children without insulin resistance (HOMA-IR<3.4, n=79) (p<0.05). Almost all investigated children with insulin resistance (95.8%) were in some of the stages of puberty (Table 2).

Girls had more total body fat than boys (p=0.010), however boys had more elevated ALT levels than girls (p=0.036). Other gender-based differences in metabolic profile of the investigated children were not found (Table 3).

In pre-obese children, HOMA-IR and insulin were positively correlated with age (r=0.421, p<0.05; r=0.428, p<0.05), FBG (r=0.469, p<0.05; r=0.387, p<0.05), total body fat (r=0.462, p<0.05; r=0.419, p<0.05), and negatively correlated with HDL-c (r=−0.313, p<0.05; r=−0.328, p<0.05). Insulin but not HOMA-IR was positively correlated with uric acid (r=0.327, p<0.05) in pre-obese children.

Total cholesterol was positively correlated with LDL-c (r=0.831, p<0.05), HDL-c (r=0.259, p<0.0.5), FBG (r=0.286, p<0.05) and ALT (r=0.230, p<0.05). HDL-c was inversely

Table 1: Sample characteristics and metabolic profile of the children stratified by nutritional status.

	Normal weight, 84 [41.8%]		Pre-obese, 82 [40.8%]		Obese, 35 [17.4%]		p-Value
	n	Median [IR[a]]	n	Median [IR]	n	Median [IR]	
Age, years	84	10.5 [10–12]	82	11 [10–12]	35	10 [9–12]	0.536
BMI[b], kg/m^2	81	16.3 [15.0–17.1]	79	20.7 [19.5–22.8]	35	23.9 [22.5–27.5]	0.000
SDS BMI[b]	81	−0.11 [−0.67 to 0.28]	79	1.84 [1.46–2.27]	35	2.75 [2.49–2.94]	0.000
WtHR	82	0.44 [0.4–0.5]	77	0.46 [0.4–0.5]	35	0.5 [0.4–0.5][c]	0.033
FBG, mmol/L	84	5.1 [4.8–5.4][d]	82	5.3 [5.1–5.5]	35	5.3 [5.1–5.7]	0.001
TC, mmol/L	84	4.1 [3.7–4.6]	82	4.2 [3.8–5.0]	35	4.5 [4.0–5.2]	0.210
HDL-c, mmol/L	84	1.6 [1.4–1.8][d]	82	1.4 [1.1–1.7]	35	1.3 [1.1–1.8]	0.000
LDL-c, mmol/L	84	2.3 [2.0–2.8]	82	2.5 [2.1–2.9]	35	2.9 [2.2–3.4][c]	0.008
TG, mmol/L	84	0.6 [0.5–0.8][d]	82	0.9 [0.6–1.2]	35	0.7 [0.6–1.2]	0.000
ALT[b], U/L	80	12.5 [11–15]	82	14 [12–18]	35	18 [13–23]	0.000
IGF-1, ng/mL	33	177.4 [121.9–239.2][d]	42	233.2 [165.7–301.8]	28	227.45 [160.1–426.3]	0.035
SDS IGF-1	33	−0.17 [−0.85 to 0.44][d]	42	0.29 [−0.21 to 0.83]	28	0.40 [−0.39 to 1.75]	0.016
Insulin, mU/L	33	6.7 [4.7–9.8][d]	42	10.3 [8.2–14.6]	28	11.3 [7.8–18.4]	0.000
UA[b], µmol/L	33	191 [160.5–223.5]	42	228.5 [196.0–262.7]	28	266.5 [235–318.75]	0.000
HOMA-IR	33	1.5 [1.1–2.3][d]	42	2.4 [1.9–3.5]	28	2.8 [1.8–4.4]	0.000
TBF[b], kg	83	5.1 [3.8–7.7]	82	13.4 [10.4–17.75]	35	17.2 [12.9–23.7]	0.000
FFM[b], kg	83	29.7 [25.6–34.5]	82	37.9 [32.9–43.0]	35	42.2 [36.3–48.9]	0.000
MM[b], kg	83	28.6 [24.3–33.1]	82	35.9 [31.2–40.8]	35	40 [34.4–46.4]	0.000
TBW[b], kg	83	22.1 [18.7–25.6]	82	27.7 [24.1–31.5]	35	30.9 [26.6–35.8]	0.000
Without pubertal development		34 [40.5%]		25 [30.5%]		14 [40.0%]	0.362
With pubertal development		50 [59.5%]		57 [69.5%]		21 [60.0%]	

[a]Interquartile range; [b]There was difference between all groups; [c]vs. normal-weight; [d]vs. pre-obese and obese.

Table 2: Metabolic profile between insulin resistant and non-insulin resistant children.

	Insulin resistance				p-Value
	HOMA-IR< 3.4, n=79 [76.7%]		HOMA-IR≥3.4, n=24 [23.3%]		
	n	Median [IR[a]] or frequency	n	Median [IR] or frequency	
BMI, kg/m^2	79	18.9 [16.8–21.4]	24	23.5 [20.4–27.7]	0.000
SDS BMI	79	1.41 [0.10–2.21]	24	2.31 [1.61–2.71]	0.001
WtHR	79	0.4 [0.4–0.5]	24	0.5 [0.4–0.5]	0.069
FBG, mmol/L	79	5.2 [4.9–5.5]	24	5.5 [5.2–5.8]	0.002
TC, mmol/L	79	4.2 [4–5]	24	4.1 [3.4–4.74	0.070
HDL-c, mmol/L	79	1.6 [1.4–1.9]	24	1.2 [1.1–1.7]	0.003
LDL-c, mmol/L	79	2.6 [2.2–3.1]	24	2.5 [1.8–2.8]	0.243
TG, mmol/L	79	0.6 [0.5–0.9]	24	0.8 [0.6–1.0]	0.335
ALT, U/L	77	13 [10–17]	24	17 [11.5–22.7]	0.018
IGF-1, ng/mL	78	184.9 [143.9–248.2]	24	363.2 [226.1–462.9]	0.000
SDS IGF-1	78	0.15 [–0.49 to 0.63]	24	0.85 [–0.24 to 1.74]	0.050
Insulin, mU/L	78	8.1 [6.3–10.2]	24	18.2 [15.5–22.5]	0.000
UA, µmol/L	78	210.5 [180–243.2]	24	305 [253–322]	0.000
TBF, kg	78	9.2 [5.5–13.4]	24	18.6 [13.8–21.4]	0.000
FFM, kg	78	33.1 [29.6–41.4]	24	44.2 [37.9–53.2]	0.000
MM, kg	78	31.5 [28.2–39.3]	24	42 [35.9–50.5]	0.000
TBW, kg	78	24.4 [21.8–30.3]	24	32.4 [27.7–38.9]	0.000
Without pubertal development		39 [49.4%]		1 [4.2%]	0.000
With pubertal development		40 [50.6%]		23 [95.8%]	

[a]Interquartile range.

Table 3: Metabolic profile of the children stratified by gender.

Variables	n	Male Mean ± SD[a] or Median [IR[b]]	n	Female Mean ± SD[a] or Median [IR[b]]	p-Value
Age, years	129	11 [10–12]	72	11 [10–13]	0.268
BMI, kg/m2	125	19.6 ± 3.87	70	19.9 ± 3.86	0.677
SDS BMI	125	1.51 ± 1.26	70	1.26 ± 1.41	0.287
WtHR	124	0.5 [0.4–0.5]	68	0.4 [0.4–0.5]	0.304
FBG, mmol/L	129	5.28 ± 0.39	72	5.17 ± 0.73	0.174
TC, mmol/L	129	4.32 ± 0.84	72	4.33 ± 0.93	0.940
HDL-c, mmol/L	129	1.53 ± 0.40	72	1.47 ± 0.40	0.310
LDL-c, mmol/L	129	2.55 ± 0.73	72	2.55 ± 0.77	0.982
TG, mmol/L	129	0.7 [0.5–0.9]	72	0.7 [0.5–1.1]	0.462
ALT, U/L	125	14 [12–18]	72	13 [11–16]	0.036
IGF-1, ng/mL	71	2.4 [2.0–3.1]	32	2.4 [2.0–2.7]	0.243
SDS IGF-1	71	0.29 [–0.45 to 1.08]	32	0.20 [–0.53 to 0.98]	0.079
Insulin, mU/L	71	190.3 [144.8–273.5]	32	221.6 [174.3–335.7]	0.303
UA, µmol/L	71	9 [6.7–14.3]	32	10.4 [7.4–13.6]	0.637
HOMA-IR	71	2.08 [1.4–3.3]	32	2.4 [1.7–3.0]	0.308
TBF, kg	128	9 [5.1–14.7]	72	12 [8.6–16.9]	0.010
FFM, kg	128	33.8 [29.5–42.2]	72	36.8 [28.8–40.8]	0.922
MM, kg	128	32.2 [27.9–40.0]	72	34.9 [27.3–38.7]	0.909
TBW, kg	128	24.9 [21.6–30.9]	72	26.9 [20.5–29.9]	0.810

[a]Standard deviation; [b]Interquartile range.

correlated with total body fat (r=– 0.348, p<0.05) and WtHR (r=–0.380, p<0.05). Uric acid was positively correlated with ALT (r=0.328, p<0.05) (Table 4).

In obese children, IGF-1 SDS was significantly positively correlated with fat free mass (r=0.460, p<0.05), muscle mass (r=0.460, p<0.05), total body water (r=0.459, p<0.05) and negatively correlated with LDL-c (r=–0.360, p<0.05). HOMA-IR and insulin were positively correlated with age (r=0.718 p<0.05; r=0.721, p<0.05), total body fat (r=0.484, p<0.05; r=0.472, p<0.05), and uric acid (r=0.558, p<0.05; r=0.561, p<0.05). A positive correlation was also observed between total cholesterol and LDL-c (r=0.899, p<0.05), uric acid and WtHR (r=0.459, p<0.05), uric acid and total body fat (r=0.576, p<0.05) (Table 5):

Multivariate ordinal logistic regression analyses showed that IGF-1 SDS and total body fat were predictors of nutritional status (Cox & Snell R Square=58.3%, Nagelkerke R Square=65.9%, p<0.001) (Table 6).

The multivariate model with insulin resistance as a dependent variable showed that predictors of insulin resistance probability in children were fasting blood glucose and uric acid (Cox & Snell R Square=0.504, Nagelkerke R Square=0.760, p<0.001) (Table 7):

Discussion

Our results showed that IGF-1 SDS were significantly higher in pre-obese and obese compared to normal weight children. Additionally, in our study IGF-1 SDS and total body fat were predictors of nutritional status, which is concordant with some findings [5]. In a recent research, Ricco et al. [27] reported significantly higher IGF-1 mitochondrial ribonucleic acid receptor (mRNA) expression in obese children than in controls. A possible explanation for higher IGF-1 concentration in obese children is that individuals in overnourished states have high endogenous insulin levels, high hepatic growth hormone receptors and lower IGF binding proteins and therefore increased IGF-1 levels [2, 12]. In contrast, some studies showed that obese subjects had significantly lower IGF-1 than those in the control group [28, 29]. In a retrospective study including 574 obese children, Inzaghi et al. [1] found that IGF-1 concentrations were not different among obese subjects with metabolic syndrome components nor related to body composition parameters. The parameters in the prediction of insulin resistance in our sample of children were fasting blood glucose and uric acid. Additionally, an unfavorable metabolic profile was noticed among insulin-resistant participants compared to the non-insulin resistant group in our study. Despite some worldwide research suggesting either a positive or negative association between IGF, insulin resistance and diabetes mellitus [7, 30], our results did not support any relationship between IGF-1 and insulin resistance in childhood. These controversial worldwide results clearly indicate the need for further research on this topic.

Among our participants, obese children had significantly higher fasting blood glucose, uric acid, presence of central obesity, and ALT compared to the normal-weight group. Obese children also exhibited less favorable lipid profiles characterized by higher triglyceride and LDL-c levels, and lower concentrations of HDL-c compared with their normal-weight peers. Besides, in pre-obese subjects, ALT levels were positively correlated with total cholesterol and LDL-c. Similar results were obtained for pre-obese children, suggesting that any excessive body fat accumulation might trigger dyslipidemia or increased ALT which are both recognized as independent cardiometabolic risk factors, even in childhood [18]. These results clearly show the presence of cardiometabolic risk components in obese children.

In our study, a negative correlation was observed between IGF-1 SDS and LDL-c among obese participants. Concordantly to these results, Berryman et al. [31] demonstrated a marked effect of growth hormone therapy, which stimulates the liver and other tissues to produce IGF-1, on body composition and lipid improvement in patients with central obesity. Unlike our results, El-Maghraby et al. [32] reported highly significant correlation between the low concentration of IGF-1, ALT and total cholesterol in patients with nonalcoholic fatty liver disease and metabolic syndrome. Although we did not show any correlation between IGF-1 SDS and HDL-c, some studies [1, 3] reported a positive correlation between these two biomarkers in obese children. This evidence suggests that IGF-1 may have some favorable effects on serum lipids in obese subjects, however, further research is needed to confirm this hypothesis.

We showed that uric acid was positively correlated with insulin and ALT in the group of pre-obese children, and also positively correlated with insulin, total body fat, and central obesity in the group of obese children. As was the case with our results, some studies also reported a positive association between uric acid and insulin resistance in obese children. It is assumed that obesity-related hyperinsulinemia may enhance renal urate reabsorption and thus cause hyperuricemia [20, 21]. In contrast to our findings, some researches [3, 33] demonstrated an inverse relationship between IGF-1 and uric acid levels in obese

Table 4: Correlation between anthropometric, biochemical and body composition parameters in pre-obese children.

	Age	SDS BMI	WtHR	FBG	TC	HDL-c	LDL-c	TG	ALT	SDS IGF-1	Insulin	UA	HOMA	TBF	FFM	MM	TBW
Age	1.000																
SDS BMI	−0.100	1.000															
WtHR	0.063	0.221	1.000														
FBG	0.125	0.017	−0.044	1.000													
TC	−0.251[a]	−0.079	−0.151	0.286[a]	1.000												
HDL-c	−0.245[a]	−0.255[a]	−0.380[a]	−0.021	0.259[a]	1.000											
LDL-c	−0.193	−0.170	0.020	−0.048	0.831[a]	0.026	1										
TG	0.130	0.130	0.230[a]	−0.112	−0.087	−0.144	−0.073	1.000									
ALT	−0.073	0.238[a]	−0.087	−0.141	0.230[a]	−0.072	0.220[a]	0.182	1.000								
SDS IGF1	−0.074	0.205	0.205	−0.099	−0.115	−0.203	−0.058	0.042	0.212	1.000							
Insulin	0.428[a]	−0.050	0.042	0.387[a]	−0.290	−0.328[a]	−0.249	0.010	0.008	0.251	1.000						
UA	0.325[a]	0.068	0.148	−0.112	−0.087	−0.144	−0.073	0.213	0.328[a]	0.209	0.327[a]	1.000					
HOMA	0.421[a]	−0.068	0.073	0.469[a]	−0.304	−0.313[a]	−0.288	0.045	−0.036	0.226	0.989[a]	0.274	1.000				
TBF	0.382[a]	0.396[a]	0.116	0.155	−0.085	−0.348[a]	0.005	0.220[a]	0.035	−0.115	0.419[a]	0.062	0.462[a]	1.000			
FFM	0.842[a]	0.059	0.107	0.062	−0.269[a]	−0.299[a]	−0.223[a]	0.201	0.017	0.045	0.360[a]	0.342[a]	0.348[a]	0.470[a]	1.000		
MM	0.843[a]	0.059	0.106	0.062	−0.270[a]	−0.301[a]	−0.224[a]	0.200	0.017	0.044	0.361[a]	0.342[a]	0.348[a]	0.471[a]	1.000[a]	1.000	
TBW	0.842[a]	0.059	0.106	0.062	−0.268[a]	−0.298[a]	−0.222[a]	0.202	0.018	0.045	0.358[a]	0.343[a]	0.345[a]	0.469[a]	1.000[a]	1.000[a]	1.000

[a]Correlation is significant.

Table 5: Correlation between anthropometric, biochemical and body composition parameters in obese children.

	Age	SDS BMI	WtHR	FBG	TC	HDL-c	LDL-c	TG	ALT	SDS IGF-1	Insulin	UA	HOMA	TBF	FFM	MM	TBW
Age	1.000																
SDS BMI	−0.331	1.000															
WtHR	0.178	0.029	1.000														
FBG	0.219	−0.082	−0.003	1.000													
TC	−0.212	−0.191	−0.080	−0.117	1.000												
HDL-c	−0.078	−0.330	0.187	−0.095	0.297	1.000											
LDL-c	−0.304	−0.010	−0.137	−0.082	0.917[a]	−0.051	1.000										
TG	0.057	−0.170	−0.113	0.056	−0.069	−0.322	0.311	1.000									
ALT	0.022	0.117	−0.151	0.039	0.245	−0.006	0.219	−0.006	1.000								
SDS IGF1	0.207	−0.117	−0.146	0.284	−0.270	0.101	−0.360[a]	−0.055	0.096	1.000							
Insulin	0.721[a]	−0.036	0.232	0.184	−0.098	−0.212	−0.089	0.035	0.276	0.201	1.000						
UA	0.404[a]	0.093	0.459[a]	0.056	−0.069	−0.322	0.041	0.121	0.256	0.008	0.561[a]	1.000					
HOMA	0.718[a]	−0.008	0.213	0.260	−0.096	−0.218	−0.090	0.018	0.301	0.233	0.992[a]	0.558[a]	1.000				
TBF	0.446[a]	0.097	0.335[a]	0.031	−0.131	−0.098	−0.144	0.053	0.240	−0.222	0.472[a]	0.576[a]	0.484[a]	1.000			
FFM	0.804[a]	−0.251	0.152	0.335[a]	−0.303	0.030	−0.434[a]	−0.020	0.023	0.460[a]	0.564[a]	0.407[a]	0.601[a]	0.510[a]	1.000		
MM	0.806	−0.252	0.155	0.332	−0.306	0.027	−0.436[a]	−0.020	0.022	0.460[a]	0.568[a]	0.414[a]	0.604[a]	0.514[a]	1.000[a]	1.000	
TBW	0.805[a]	−0.250	0.150	0.329	−0.321	0.030	−0.450[a]	−0.045	0.016	0.459[a]	0.568[a]	0.414[a]	0.604[a]	0.519[a]	0.998[a]	0.998[a]	1.000

[a]Correlation is significant.

Table 6: Predictive parameters for nutritional status of children, results of ordinal logistic regression.

Variable	Univariate ordinal logistic regression		Multivariate ordinal logistic regression	
	OR[a] [95%CI[b]]	p-Value	OR [95%CI]	p-Value
Age, years	1.04 [0.88–1.22]	0.676		
WtHR	464.21 [5.68–38]	0.006		
FBG, mmol/L	2.28 [1.24–4.19]	0.008		
TC, mmol/L	1.18 [0.88–1.59]	0.266		
HDL-c, mmol/L	0.24 [0.125–0.49]	0.000		
LDL-c, mmol/L	1.58 [1.11–2.24]	0.011		
TG, mmol/L	2.98 [1.66–5.34]	0.000		
ALT, U/L	1.06 [1.02–1.10]	0.002		
SDS IGF-1	1.66 [1.19–2.33]	0.003	1.94 [1.21–3.11]	0.006
Insulin, mU/L	1.10 [1.04–1.18]	0.002		
UA, µmol/L	1.02 [1.01–1.03]	0.000		
HOMA-IR	1.47 [1.13–1.90]	0.003		
TBF, kg	1.31 [1.24–1.40]	0.000	1.37 [1.21–1.54]	0.000
Gender	1.11 [0.65–1.91]	0.703		
Puberty	0.85 [0.49–1.45]	0.550		

[a]Odds ratio; [b]Confidence interval.

Table 7: Predictive parameters for insulin resistance, results of logistic regression.

Variables	Univariate logistic regression		Multivariate logistic regression	
	OR[a] [95%CI[b]]	p-Value	OR [95% CI]	p-Value
Age, years	2.15 [1.47–3.13]	0.000		
SDS BMI	2.12 [1.3–3.46]	0.002		
WtHR	9.02 [0.61–13.35]	0.068		
FBG, mmol/L	9.54 [2.31–39.48]	0.002	42.39 [2.32–77.2]	0.011
TC, mmol/L	0.48 [0.25–0.93]	0.030		
HDL-c, mmol/L	0.12 [0.03–0.55]	0.006		
LDL-c, mmol/L	0.62 [0.31–1.26]	0.191		
TG, mmol/L	1.45 [0.61–3.47]	0.404		
ALT, U/L	1.08 [1.01–1.16]	0.019		
SDS IGF-1	1.43 [0.95–2.16]	0.088		
Insulin, mU/L	4.29 [0.01–14.44]	0.254		
UA, µmol/L	1.03 [1.02–1.04]	0.000	1.03 [1.01–1.05]	0.007
TBF, kg	1.19 [1.1–1.3]	0.000		
Gender	1.12 [0.41–3.05]	0.818		
Puberty	0.04 [0.01–0.34]	0.003		

[a]Odds ratio; [b]Confidence interval.

patients. Despite the studies conducted, the exact mechanism of potential interaction between IGF-1 and uric acid remains insufficiently clear [33].

However, our study has some limitations. The here presented results could have been influenced by the combined effects of other IGF axis components that were not investigated in this study. The pubertal status of children, based on the five-point rating scale according to Tanner, has been presented in the paper in a simplified form, by showing only two categories of children (with and without puberty), due to our wish to emphasize growth and puberty unrelated actions of IGF-1, although being fully aware of the intertwining of these processes.

Conclusion

In our study, pre-obesity and obesity were associated with higher IGF-1 SDS values in children. Moreover, we found that IGF-1 SDS values and total body fat were predictors of

nutritional status in children, while fasting blood glucose and uric acid were predictors of insulin resistance in children. Our results support previous evidence which associate IGF-1 and pathophysiology of obesity. More thorough examination of the complex relationship between IGF-1, obesity pathways and obesity-associated cardiometabolic complications would have marked scientific and clinical significance. Further studies are highly required to evaluate application of IGF-1 as a biomarker in clinical practice regarding specificity of pediatric age.

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Original Scientific Paper

CARDIOMETABOLIC RISK AMONG MONTENEGRIN URBAN CHILDREN IN RELATION TO OBESITY AND GENDER

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SUMMARY – Considering previously reported discrepant results in the literature, we aimed to investigate the impact of gender and overweight/obesity on cardiometabolic risk (CMR) among Montenegrin urban children. The cross-sectional study included random sample of 201 schoolchildren aged 7-12 years (64% of boys) from Podgorica. Children's nutritional status was determined according to the International Obesity Task Force criteria. CMR was assessed using a sum of z values of the following five indicators: glucose, total cholesterol, inverted value of high-density lipoprotein cholesterol, triglycerides, and hypertension. Higher CMR was found among both overweight and obese boys compared to normal weight boys ($p<0.001$). The effect size of the difference in CMR between overweight and obese girls and normal weight counterparts was less prominent ($p<0.05$). Logistic regression analysis revealed that body mass index was independent predictor of high CMR [odds ratio (OR)=1.06; 95% confidence interval (CI)=1.02-1.10); p=0.002]. On the contrary, we found no impact of socioeconomic status, physical activity or sedentary time on CMR in the examined cohort of schoolchildren. In conclusion, both overweight and obesity even among young population are related to higher CMR and this effect is more prominent among boys as compared to girls.

Key words: *Cardiometabolic risk; Childhood obesity; Hypertension; Metabolic syndrome*

Introduction

Obesity is a global public health problem[1] with an ever-increasing prevalence both among children and adults over the past decade[2]. This is also a public health concern in Montenegro since the prevalence of childhood overweight and obesity (OOb) is reported to be 22.9% and 5.3%, respectively[3].

Obesity is a risk factor for many disorders such as metabolic syndrome, type 2 diabetes mellitus, cardiovascular disease, cancer, psychosocial and neurocognitive distress[4-6]. Childhood and adulthood obesity are related and there is evidence that even 80% of obese children continue to be obese later in life, which is often accompanied with an increased cardiometabolic risk (CMR)[7]. Therefore, of utmost public health interest is to deeply investigate the underlying mechanisms of increased CMR among young population[8].

Although previous studies confirmed the relationship between childhood obesity and CMR[9-13], it is still unclear whether this relationship also exists in overweight children, since some studies did not find difference in CMR between overweight and normal weight children[14]. Additionally, controversial results were shown with regard to gender, reporting no difference between

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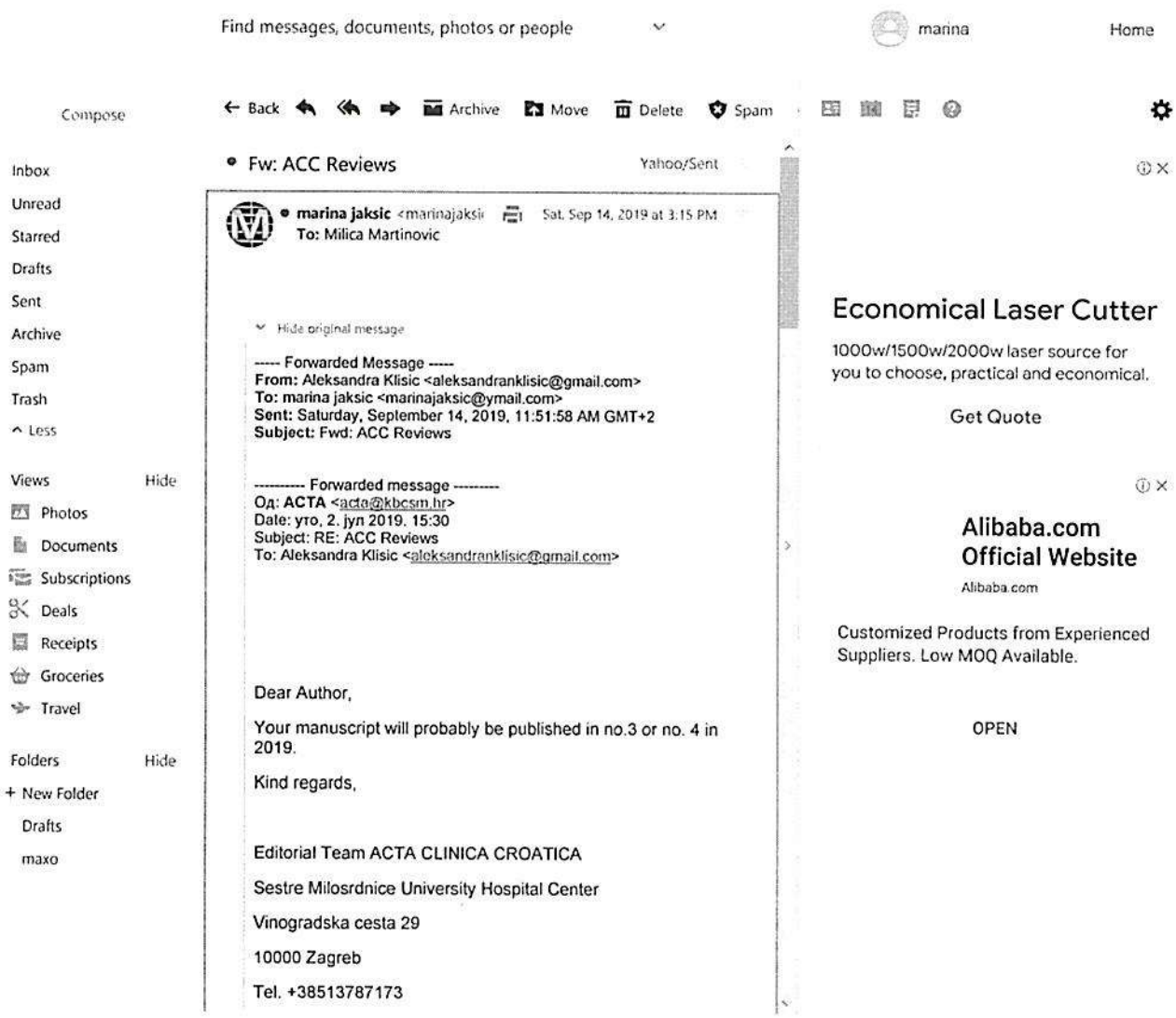
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BIOGRAFIJA

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Medicinski fakultet u Podgorici, Univerziteta Crne Gore upisala je 2004. godine i diplomirala 2010. godine, stekavši zvanje doktora medicine. Od 2011. godine do danas, zaposlena je na Medicinskom fakultetu u Podgorici kao stručni saradnik na predmetu Patološka fiziologija i laboratorijska medicina. Od 2012. godine bila je zaposlena u Centru za kliničko-laboratorijsku dijagnostiku Kliničkog centra Crne Gore (KCCG), kao klinički ljekar za biohemiju, a od 2017. godine obavlja poslove ljekara na specijalizaciji iz oblasti kliničke biohemije za potrebe Instituta za bolesti djece KCCG.

Postdiplomske studije na Medicinskom fakultetu u Podgorici upisala je 2010. godine i odbranila polazna istraživanja (ekvivalent magistarskim studijama) 2015. godine pod nazivom „Istraživanje stanja uhranjenosti (gojaznost i pothranjenost) kod djece školskog uzrasta u Podgorici – klinički, patofiziološki i epidemiološki aspekti".

Kao student osnovnih studija bila je primalac stipendije Opštine Bar kao i stipendije Republike Crne Gore u periodu od 2004.-2010. godine. Dobitnica je „ZAMTES" nagrade, koju najboljim studentima Univerziteta Crne Gore dodjeljuje Zavod za međunarodnu naučnu, prosvjetno-kulturnu i tehničku saradnju, Vlade Crne Gore, 2009. godine.

U okviru Centralno-evropskog programa za univerzitetsku razmjenu (CEEPUS), u svojstvu doktoranda, bila je na studijskom boravku na Transilvanija Univerzitetu u Brašovu, Rumunija, oktobra 2011. godine kao i na Medicinskom Univerzitetu u Varšavi, Poljska, jula 2013. godine.

U periodu od 2012-2015. godine učestvovala je u naučno-istraživačkom crnogorskom projektu pod nazivom „Istraživanje gojaznosti i siromaštva kod djece Crne Gore - klinički, patofiziološki, biohemijski i preventivni aspekti".

U periodu od 2015-2016 godine učestvovala je u bilateralnom, naučno-istraživačkom, crnogorsko-hrvatskom projektu pod nazivom „Komparativna studija o uticaju siromaštva na pothranjenost, prehrambene i životne navike školske djece gradova Podgorice i Osijeka".

Autor je ili koautor više naučnih radova objavljenih u časopisima koji se nalaze u međunarodnim i domaćim bazama podataka.

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Република Српска
УНИВЕРЗИТЕТ У БАЊОЈ ЛУЦИ
Сенат Универзитета

Број: 02/04-3.1879-29/17
Дана, 29.06.2017. године

На основу члана 77., 83. и 94. Закона о високом образовању („Службени гласник Републике Српске", број: 73/10, 104/11, 84/12, 108/13, 44/15 и 90/16) и члана 33. Статута Универзитета у Бањој Луци, Сенат Универзитета на 12. сједници од 29.06.2017. године, д о н о с и

О Д Л У К У

1. **Др Нела Рашета** бира се у звање редовног професора за ужу научну област Патолошка физиологија, на неодређено вријеме.

2. Ова Одлука ступа на снагу даном доношења.

О б р а з л о ж е њ е

Универзитет у Бањој Луци на приједлог Наставно-научног вијећа Медицинског факултета расписао је дана 08.03.2017. године Конкурс за избор наставника за ужу научну област Патолошка физиологија.

На расписан Конкурс пријавио се један кандидат и то: др Нела Рашета.

Наставно-научно вијеће Медицинског факултета на сједници одржаној 14.03.2017. године образовало је Комисију за писање извјештаја за избор наставника у одређено звање. Комисија је припремила писмени извјештај, предложила да се изврши избор као у диспозитиву ове Одлуке и исти доставила Наставно-научном вијећу Медицинског факултета на разматрање и одлучивање.

Наставно-научно вијеће Медицинског факултета у Бањој Луци на сједници одржаној 20.06.2017. године констатовало је да др Нела Рашета испуњава у цијелости услове и утврдило приједлог да се др Нела Рашета бира у звање редовног професора за ужу научну област Патолошка физиологија, на неодређено вријеме и исти доставило Сенату Универзитета у Бањој Луци ради даљег поступка.

Сенат Универзитета је на 12. сједници одржаној 29.06.2017. године, утврдио да је утврђени приједлог из претходног става у складу са одредбама Закона о високом образовању.

Сагласно члану 77. Закона о високом образовању, одлучено је као у диспозитиву ове Одлуке.

ПРАВНА ПОУКА: Против ове Одлуке може се поднијети захтјев за преиспитивање Сенату Универзитета у Бањој Луци у року од 15 дана од дана пријема исте.

ПРЕДСЈЕДАВАЈУЋИ СЕНАТА
Р Е К Т О Р
Проф. др Милан Матаруга

Достављено:
1. Именованој,
2. Медицинском факултету,
3. Руководиоцу службе за стручне послове,
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2. Dr med. Zorislava Bajić. **Uticaj aerobne fizičke aktivnosti na metabolizam kosti i tjelesnu kompoziciju,** magistarski rad - komentor (odbranjen septembar 2011.)
3. Dr med. Tatjana Milivojac. **Uticaj manjka vitamina D na promjene nivoa kalcija i paratireoidnog hormona u postmenopauzalnoj osteoporozi,** magistarski rad - mentor (odbranjen decembar 2011)
4. Mr sc. med. Tatjana Milivojac. **Uticaj glukokortikoidne terapije na N-MID osteocalcin, β-CrossLaps i kost vezane minerale u serumu i pljuvački djece sa imunološkom tombocitopeničnom purpurom,** doktorska disertacija - mentor (2017)
5. Mr sc. med. Alma Prtina. **Uticaj vitamina D na vrijednosti interleukina 6 i interleukina 10 kod bolesnika sa psorijazom,** doktorska disertacija – mentor (2018)
6. Dr med. Andreja Figurek. **Uloga fibroblastnog faktora rasta 23 u ranoj dijagnostici poremećaja metabolizma minerala i koštane mase u hroničnoj bubrežnoj bolesti,** doktorska disertacija – komentor (odbranjen mart 2018)

Komisije za odbranu magistarskih i doktorskih radova:

1. Dr med. Alma Prtina. **Učestalost metaboličkog sindroma kod zdravstvenih radnika grada Banja Luka**, magistarski rad odbranjen decembar 2010.
2. Dr med. Milorad Vujnić. **Ispitivanje prisustva i značaja metaboličkog sindroma kod bolesnika sa miotoničnim distrofijama**, doktorska disertacija odbranjena septembar 2016 Medicinski fakultet Univerzitet u Beogradu.
3. Mr sc. med. Faruk Nišić. **Uticaj vrijednosti vaskularnih endotelijalnih faktora rasta u staklastom tijelu na komplikacije pars plana vitrektomije kod proliferativne dijabetičke retinopatije,** doktorska disertacija odbranjena oktobar 2017.

Mentorstvo 18 specijalizanata Medicinske i Kliničke biohemije i dvadesetak završnih radova studenata Medicinskog fakulteta Univerziteta u Banjoj Luci

Naučni odbori:

1. **Prvi kongres doktora medicine.** Teslić, 10-13. maj 2007. Naučno-stručni skup sa međunarodnim učešćem
2. **Studenti u susret nauci.** Banja Luka 2009. 2. Naučno-stručni skup studenata sa međunarodnim učešćem
3. **Studenti u susret nauci.** Banja Luka 2010. 3. Naučno-stručni skup studenata sa međunarodnim učešćem
4. **Konges medicinskih biohemičara Bosne i Hercegovine sa međunarodnim učešćem.** Sarajevo 2010.
5. **Studenti u susretnauci.** Banja Luka 2011. 4. Naučno-stručni skup studenata sa međunarodnim učešćem
6. **Studenti u susretnauci.** Banja Luka 2012. 5. Naučno-stručni skup studenata sa međunarodnim učešćem
7. **23rd Meeting of the Balkan Clinical Laboratory Federation.** Sarajevo, 2015.
8. **2nd National Congress of the Association of Medical Biochemists in Bosnia and Herzegovina.** Sarajevo, 2015.

Član uređivačkog odbora:

1. **SciptaMedica.** Časopis Društva doktora medicine Republike Srpske i Medicinskog fakulteta Univerziteta Banja Luka

Član Etičkog odbora Medicinski fakultet Banja Luka

Udruženja:

1. Komora i Društvo Doktora medicine Republike Srpske
2. Udruženje medicinskih biohemičara Republike Srpske, predsjednik
3. Udruženje za osteoporozu Republike Srpske, predsjedništvo
4. Udruženje biohemičara i molekularnih biologa Bosne i Hercegovine, predsjedništvo
5. Udruženje reumatologa Srbije, sekcija za osetoporozu, član
6. European Federation of Clinical Chemistry and Laboratory Medicine, member

Projekti:

1. **Inflamacija i antioksidativni sistem.** Tematski projekt Ministarstva nauke i tehnologije Republike Srpske 2008 god. - **koordinator**
2. **Metabolička aktivnost kosti kod prolongirane fizičke aktivnosti.** Projekt Ministarstva nauke i tehnologije Republike Srpske 2008. god – **koordinator**
3. **Inflamacija, oksidativni stres i antioksidativni sistem u intenzivnoj fizičkoj aktivnosti.** Projekt Ministarstva nauke i tehnologije Republike Srpske 2009 god. – **učesnik** (koordinator je Doc. Dr Nenad Ponorac)
4. **Uticaj aerobne fizičke aktivnosti na markere oksidativnog stresa, antioksidativni kapacitet i tjelesnu kompoziciju.** Projekt Ministarstva nauke i tehnologije Republike Srpske 2010 god. – **učesnik** (koordinator je Doc. Dr Nenad Ponorac)
5. **Procjena kvaliteta glikoregulacije i prisustvo vaskularnih komplikacija u osoba sa šećernom bolešću u Republici Srpskoj.** Projekat Ministarstva zdravlja i socijane zaštite Republike Srpske 2015 god. – instruktor
6. **Osteoprotektivni efekti fizičke aktivnosti kod starijih žena: Prevencija osteoporotičnih fraktura.** Projekt Ministarstva nauke i tehnologije Republike Srpske, 2018. godina. Rukovodilac projekta

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Na osnovu člana 75 stav 2 Zakona o visokom obrazovanju (Sl.list RCG, br. 60/03 i Sl.list CG, br. 45/10 i 47/11) i člana 18 stav 1 tačka 3 Statuta Univerziteta Crne Gore, Senat Univerziteta Crne Gore, na sjednici održanoj 19.12.2013. godine, donio je

ODLUKU
O IZBORU U ZVANJE

Dr sci med. MILICA MARTINOVIĆ bira se u akademsko zvanje **redovni profesor** Univerziteta Crne Gore za predmet: Patološka fiziologija i labaratorijska medicina, na Medicinskom fakultetu.

REKTOR

Prof.dr Predrag Miranović

BIOGRAFIJA

Rodjena 29.X 1960. g. U Nikšiću , Crna Gora. Osnovnu školu i gimnaziju završila u Nikšiću. Diplomirala na Medicinskom fakultetu Univerziteta u Beogradu 1983.g. Specijalizaciju iz pedijatrije završila 1992.g, položivši sa odličnom ocjenom specijalistički ispit, na Institutu za zdravstvenu zaštitu majke i deteta Medicinskog fakulteta Univerziteta u Beogradu. Magistarski rad pod nazivom „ Komparativna studija etiopatogenetskih i kliničkih parametara bronhijalne astme sa efektima terapije u kontinentalnom i priobalnom dijelu Crne Gore" odbranila 1997.g. na Medicinskom fakultetu Univerziteta u Nišu, Srbija. Zvanje doktora medicinskih nauka stekla na Medicinskom fakultetu Univerziteta u Nišu, odbranivši doktorsku disertaciju pod nazivom „ Uloga i značaj primjene inhalacionih glikokortikoida u prevenciji dječije astme".

Od 1999. Zaposlena na Medicinskom fakultetu Univerziteta Crne Gore, na predmetu Patološka fiziologija i laboratorijska medicina. U zvanje docenta izabrana 2003.g., vanredni profesor 2008., a u zvanje redovni profesor 2013.g.

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3. Milica Martinovic, Goran Belojevic, Marina Jaksic, Nebojsa Kavaric, Aleksandra Klisic CARDIOMETABOLIC RISK AMONG MONTENEGRIN URBAN CHILDREN IN RELATION TO OVERWEIGHT AND OBESITY Acta clinica Croatica,prihvaćen za objavljivanje
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Radovi objavljeni u časopisima koji se ne nalaze u međunarodnim bazama podataka

14. Milica Martinović, Sigurnosni profil inhalacionih kortikosteroida (beclomethason dipropionat)primijenjenih u konvencionalnim i u visokim dozama u prevenciji dječje astme, ACTA MEDIKA MEDIANAE, ISSNYU 0365-4478, Vol.47, No.1,2008.

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PROJEKTI

1. Rukovodilac crnogorskog nacionalnog naučno-istraživačkog projekta " Istraživanje siromaštva i gojaznosti kod školske djece u Crnoj Gori- klinički, patofiziološki, biohemijski i preventivni aspekti", 2013-2015.

2. Koordinator za Medicinski fakultet u Podgorici CEEPUS projekta: » Developing a network for monitoring the impact of environmental and nutritional factors on fertility and neonatal health«, Network Coordinator assoc.prof Marius Moga, Transilvania University of Brashov, Romania, 2007- 2013

3. Rukovodilac crnogorskog tima u bilateralnom crnogorsko-hrvatskom projektu : „ Komparativna studija o uticaju siromaštva na pothranjenost i gojaznost, dijetetske navike i životni stil kod skolske djece Podgorice i Osijeka" Član istraživačkog tima

4. CRNOGORSKO-SRPSKI BILATERALNI PROJEKAT: „Značaj praćenja odnosa mokraćnwe kisjeline i oksidativnog stresa u definisanju kardiovaskularnog rizika metabolički zdrave i metabolički bolesne djece sa viškom tjelesne mase" (The importance of monitoring the interrelation between uris acid and oxidative stress in defining cardiovascular risk at metabolically healthy and sick children with excess body weight"), član istraživačkog tima

5. Competency based Curriculum Reform in Nursing and Caring in Western Balkan Universities 544169-TEMPUS-1-2013-1-BE-TEMPUS-JPCR, rukovodilac prof.dr Bogdan Ašanin, član istraživačkog tima

6. Član istraživačkog tima u projektu Ministarstva nauke CG- „Balneološki efekti peloida, mineralne vode, ljekovitog i aromatičnog bilja na inflamatorni odgovor kod reumatoidnih i kardiovaskularnih bolesti", rukovodilac doc.dr Snežana Pantović

7. Član istraživačkog tima u projektu Ministarstva nauke CG- „Procjena jodnog statusa, razvoj i standardizacija preventivnog programa u Crnoj Gori", rukovodilac prof.dr Mira Samardžić

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Datum / Date 16.05.2016

Na osnovu člana 72 stav 2 Zakona o visokom obrazovanju (Službeni list Crne Gore br. 44/14 i 47/15) i člana 32 stav 1 tačka 9 Statuta Univerziteta Crne Gore, Senat Univerziteta Crne Gore na sjednici održanoj 16.maja 2016.godine, donio je

O D L U K U
O IZBORU U ZVANJE

Dr SNEŽANA PANTOVIĆ bira se u akademsko zvanje **docenta Univerziteta Crne Gore** za predmete: Medicinska biohemija i hemija na osnovnom akademskom studijskom programu Medicina, Opšta i oralna biohemija na osnovnom akademskom studijskom programu Stomatologija i Medicinska biohemija na osnovnom akademskom studijskom programu Farmacija **na Medicinskom fakultetu,** na period od pet godina.

UNIVERZITET CRNE GORE 1974

REKTOR

Ljudmila Vojvodić

BIOGRAFIJA

Rođena sam 21. oktobra 1970. godine, u Marbachu, SR Njemačka. Medicinski fakultet Univerziteta u Banjaluci upisala sam 1991. godine, gdje sam diplomirala jula 1997. godine, u roku, kao redovan student, sa prosječnom ocjenom 8.75. Tokom studiranja bila sam demonstrator na predmetima anatomija i mikrobiologija, a kasnije kao aktivni učesnik na nekoliko kongresa studenata medicine i stomatologije na kojima sam izlagala svoje studentske radove.

Magistarske studije iz naučne oblasti Biohemija upisala sam školske 2003/2004. godine na Medicinskom fakultetu u Nišu i položila sve ispite predviđene nastavnim planom i programom sa prosječnom ocjenom 10 (deset). Magistarsku tezu pod nazivom »Lp(a) lipoproteini, adhezione molekule i citokini: Uloga i interakcija u restenozi nakon transluminalne angioplastike krvnih sudova« odbranila sam 18. septembra 2007. godine na Medicinskom fakultetu u Podgorici.

Specijalistički ispit iz specijalističke oblasti Transfuziologija položila sam ocjenom vrlo dobar 2005. godine.

Doktorsku disertaciju pod nazivom „Biohemijski pokazatelji faktora rizika u razvoju stenoze prije i poslije PCI'' odbranila sam 26. februara 2015. godine na Medicinskom fakultetu u Podgorici, Univerziteta Crne Gore.

U prethodnom periodu, bila sam saradnik na brojnim projektima finansiranim od strane Ministarstva nauke Crne Gore i međunarodnih institucija. Rukovodila sam naučno-istraživačkim projektom „Balneološki značaj peloida, mineralne vode, ljekovitog i aromatičnog bilja na inflamatorni odgovor kod reumatoidnih i kardiovaskularnih bolesti" (BEPMARK) koji je finansiralo Ministarstvo nauke Crne Gore a bila sam i član istraživačkog tima u bilateralnom projektu sa NR Kinom pod nazivom „Identifikacija antimikrobnih peptida i njihovih funkcionalnih tipova korišćenjem celularnih automata". Aktivni sam istraživač u nacionalnom naučno-istraživačkom projektu „Nove metode za stratifikaciju rizika za progresiju kancera i Alchajmerove bolesti kod pacijenata u Crnoj Gori". Rukovodilac sam projektnih aktivnosti ispred Medicinskog fakulteta Univerziteta Crne Gore u realizaciji projekta „Centar izvrsnosti za biomedicinska istraživanja - CEBIMER''.

Član sam Ljekarske komore Crne Gore; Evropskog tima za laboratorijska istraživanja sa sjedištem u Parizu; tima za komunikaciju u okviru COST –a; tima za COMET – metodologija za humani monitoring u okviru COST; Evropskog udruženja za aterosklerozu (EAS) kao i ekspertske grupe koja se bavila proučavanjem evolutivnog modela proteina baziranog na modelu ćelijskih automata. Bila sam članica više naučnih odbora za kongrese sa međunarodnim učešćem organizovane u Crnoj Gori.

Od strane Univerziteta Crne Gore objavljen je udžbenik „Osnovi biohemije za studente Visoke medicinske škole" čiji sam autor, a autor sam i „Priručnika za laboratorijsku dijagnostiku" koji je prihvaćen od strane Vijeća Medicinskog fakulteta. Mentor sam i komentor studentima doktorskih studija, a članica sam većeg broja komisija za odbrane završnih, specijalističkih i master radova na Medicinskom fakultetu i drugim organizacionim jedinicama UCG.

PODACI O RADNIM MJESTIMA I IZBORIMA U ZVANJA

Profesionalni angažman započela sam 1. oktobra 1997. godine u JZU Dom Zdravlja Mojkovac, gdje sam radila godinu dana. Od oktobra 1998. godine i naredne četiri godine, radila sam na Medicinskom fakultetu, Univerziteta Crne Gore – studijski program Medicina u Podgorici kao saradnik u nastavi na predmetu Medicinska biohemija i hemija.

Od aprila 2002. godine svoj radni odnos započinjem u JZU Klinički centar Crne Gore u Centru za transfuziju krvi, gdje radim narednih sedam godina.

Od septembra 2009. godine sam zaposlena na Medicinskom fakultetu, Univerziteta Crne Gore, kao saradnik u nastavi na predmetima Medicinska biohemija i hemija – studijski program Medicina, Opšta i oralna biohemija – studijski program Stomatologija i Medicinska biohemija – studijski program Farmacija.

Odlukom Senata Univerziteta Crne Gore od 16.05.2016. godine (broj 03-1332) izabrana sam u zvanje docenta Medicinskog fakulteta za predmete Medicinska biohemija i hemija na osnovnom akademskom studijskom programu Medicina, Opšta i oralna biohemija na osnovnom akademskom studijskom programu Stomatologija i Medicinska biohemija na osnovnom akademskom studijskom programu Farmacija. Osim na pomenutim predmetima, nastavu sam izvodila i na izbornom predmetu Laboratorijska dijagnostika poremećaja metabolizma (osnovni akademski studijski program Farmacija) i na predmetu Oksidativni stres u humanoj patologiji (osnovni akademski studijski program Farmacija), kao i na predmetu Osnovi biohemije (primijenjeni studijski program Visoka medicinska škola).

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Radna biografija

Lični podaci

Prezime(na) / Ime(na)	**PANTOVIĆ SNEŽANA**		
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Državljanstvo	Crnogorsko		
Datum rođenja	21.10.1970.		
Pol	ŽENSKI		

Željeno zaposlenje / zanimanje **DOCENT**

Radno iskustvo

Datumi	**2015 -**
Zanimanje ili radno mjesto	Docent na UCG, Medicinski fakultet, Predmet Medicinska biohemija
Glavni poslovi i odgovornosti	Odgovorna za realizaciju nastave na predmetima: Medicinska biohemija i hemija – studijski program Medicina; Medicinska biohemija – studijski program Farmacija; Opšta i oralna biohemija – studijski program Stomatologija Laboratorijska dijagnostika poremećaja metabolizma –studijski program Farmacija; Osnovi biohemije – Visoka medicinska škola Berane
Ime i adresa poslodavca	Univerzitet Crne Gore Medicinski fakultet, Podgorica
Vrsta djelatnosti ili sektor	Visoko obrazovanje
Datumi	**2004 - 2008**
Zanimanje ili radno mjesto	Specijalista transfuzione medicine, KC Crne Gore
Glavni poslovi i odgovornosti	Rad na poslovima prikupljanja i testiranja ljudske krvi kao lijeka humanog porijekla, njene obrade i prerade, skladištenja, distribucije i izdavanja, odnosno primjene za potrebe alogene ili autologne transfuzije. Rad na pružanju specijalističkih usluga iz domena transfuzione medicine u cilju dijagnostike, prevencije i terapije za potrebe bolničkih i ambulatnih pacijenata.
Ime i adresa poslodavca	KC Crne Gore Centar za transfuziju krvi, Podgorica, Crna Gora
Vrsta djelatnosti ili sektor	Zdravstvena
Datumi	**2001 - 2004**
Zanimanje ili radno mjesto	Klinički ljekar, KC Crne Gore
Glavni poslovi i odgovornosti	Rad u laboratoriji Centra za laboratorijsku dijagnostiku, KC Crne Gore i Rad u Centru za transfuziju, KC Crne Gore
Ime i adresa poslodavca	KC Crne Gore

Vrsta djelatnosti ili sektor	Zdravstveni
Datumi	**1998 – 2015**
Zanimanje ili radno mjesto	Asistent UCG
Glavni poslovi i odgovornosti	Izvođenje vježbi na predmetu Medicinska biohemija studijskih programa Medicinskog fakulteta
Ime i adresa poslodavca	Univerzitet Crne Gore
Vrsta djelatnosti ili sektor	Visoko obrazovanje

Obrazovanje i osposobljavanje

Datumi	**2015**
Naziv dodijeljene kvalifikacije	Doktor medicinskih nauka
Glavni predmeti / stečene profesionalne vještine	Praćenje i analiza markera inflamatornog odgovora i parametara oksidacionog stresa, od značaja u razvoju restenoze nakon PCI u cilju bolje interpretacije patogeneze restenoze i brže i efikasnije prevencije iste, kod pacijenata sa kardiovaskularnom patologijom.
Ime i vrsta organizacije obrazovne institucije	Medicinski fakultet, UCG
Nivo prema nacionalnoj ili međunarodnoj klasifikaciji	Nivo VIII
Datumi	**2007**
Naziv dodijeljene kvalifikacije	Magistar medicinskih nauka
Glavni predmeti / stečene profesionalne vještine	Determinacija ključnog vremenskog perioda za inicijaciju angiogeneze nakon PCI, analizom markera inflamacije i faktora rasta od značaja u signalnim putevima etiopatogeneze razvoja ateroskleroze kod KVB.
Ime i vrsta organizacije obrazovne institucije	Medicinski fakultet, UCG
Nivo prema nacionalnoj ili međunarodnoj klasifikaciji	Nivo VII
Datumi	**2005**
Naziv dodijeljene kvalifikacije	Specijalista transfuzione medicine
Glavni predmeti / stečene profesionalne vještine	Obezbijeđenja krvi kao lijeka i djelatnosti kliničke i urgentne transfuzije odnosno, pružanja usluga pacijentima.
Ime i vrsta organizacije obrazovne institucije	Medicinski fakultet, Univerzitet u Beogradu
Nivo prema nacionalnoj ili međunarodnoj klasifikaciji	Nivo VII
Datumi	**1997**
Naziv dodijeljene kvalifikacije	Doktor medicine
Glavni predmeti / stečene profesionalne vještine	Ljekar opšte prakse
Ime i vrsta organizacije obrazovne institucije	Medicinski fakultet u Banjaluci, Univerzitet u Banjaluci
Nivo prema nacionalnoj ili međunarodnoj klasifikaciji	Nivo VI

Lične vještine i kompetencije

Maternji jezik(ci)	**Crnogoski**

Drugi jezik(ci) **engleski, njemački**

Samoprocjena	Razumijevanje				Govor				Pisanje	
Evropski nivo (*)	Slušanje		Čitanje		Govorna interakcija		Govorna produkcija			
Engleski jezik	C2	Iskusni korisnik	C2	Iskusni korisnik	C2	Iskusni korisnik	C2	Iskusni korisnik	C2	Iskusni korisnik
Njemački jezik	A1	Samostalni korisnik	A1	Samostalni korisnik	A1	Samostalni korisnik	A1	samostalni korisnik	A1	samostalni korisnik

(*) Zajednički evropski referentni okvir za jezike

Društvene vještine i kompetencije Dobra sposobnost komunikacije, dijaloga kao i prilagođavanja u multikulturnim sredinama, dokazano kroz pisane preporuke od strane mentora i profesora tokom obavljanja profesionalne i naučne karijere.

Organizacione vještine i kompetencije Stručno kreativna i organizaciona sposobnost, koja se ogleda kroz pisanje naučnih radova i publikacija, radom i elaboracijom više nacionalnih istraživačkih i bilateralnih projekata, kao i aktivnim učešćem na kongresima i konferecijama ili seminarima kroz predavanja kao predavača po pozivu.

- Član Savjeta za regionalnu saradnju (PCC) ispred MN
- Član Evropskog tima za laboratorijska istraživanja sa sjedistem u Parizu;
- Član tima menadžement za komunikaciju u okviru COST –a;
- Član tima za COMET – metodologija za humani monitoring u okviru COST;
- Član uredništva u časopisu SCIREA Yournal of Medicine;
- Član Evrpskog udruženja za aterosklerozu (EAS);
- Član ekspertske grupe koja se bavila proučavanjem evolutivnog modela proteina baziranog na modelu ćelijskih automata
- rukovodilac tima za nabavku medicinske opreme COSV za Crnu Goru

Računarske vještine i kompetencije Rada na računaru, sa znanjem rada u Wordu 10, Exellu; i drugim alatima Microsoft Office, Corela, open-sorce programa za tekstualne, numeričke i web dokumente; pretraživanje baza podataka (PubMed, KOBSON, EBSCO, COBIS, IOP);

Vozačka dozvola B kategorija

Dodaci

IZABRANE PUBLIKACIJE:

I.Banjari, M.Martinović, G.Belojević, B.Ašanin, N.D.Kovačević, D.Kenjerić, M.Miškulin, **S.Pantović,** S.Pušeljić, D.Sokolić, V.Buljan, V.Bilić-Kirin, M.Jakšić. Poverty and other correlates of obesity and underweight among 7-year-olds from Croatia and Montenegro. Public Health 2020;182:64-69.

Marcin Wysokowski, Tomasz Machałowski, Iaroslav Petrenko, Christian Schimpf, David Rafaja, Roberta Galli, Jerzy Zietek, **Snežana Pantovic**, Alona Voronkina, Valentine Kovalchuk, Viatcheslav N. Ivanenko, Bert W. Hoeksema, Cristina Diaz, Yuliya Khrunyk, Allison L. Stelling, Marco Giovine, Teofil Jesionowski and Hermann Ehrlich. 3D Chitin Scafolds of Marine Demosponge Origin for Biomimetic Mollusk Hemolymph-Associated Biomineralization Ex-Vivo. Mar. Drugs 2020, 18, 123; doi:10.3390/md18020123.

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Snezana Pantovic, Vjeroslava Slavic, Milovan Roganovic. Heat shock protein 27 and glycogen phosphorylase isoenzyme BB as markers of myocardial stunning in male water polo players. Biomedical Research 2018; 29 (15): 3069-3073.

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KNJIGE:

Snežana Pantović. Osnovi biohemije za studente Visoke medicinske škole. UCG, Podgorica, 2019.
Snežana Pantović, Ivan Dožić. Priručnik za laboratorijsku dijagnostiku. Medicinski fakultet – UCG, Podgorica, 2017.

RECENZIRANJE RADOVA KOJI SE NALAZE U MEĐUNARODNIM BAZAMA PODATAKA:

Journal of Sports Medicine and Therapy. Manuscript No: JSMT0023. ISSN: 2573-1726
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MENTORSTVA

1. Mentor pri izradi doktorske disertacije, **kandidatu Milovanu Roganoviću** (u proceduri za odobravanje).
2. Komentor pri izradi doktorske disertacije, **kandidatkinji Mileni Petrović.**
3. Mentor većeg broja završnih radova svršenih studenata studijskog programa Farmacija i Medicinana Medicinskom fakultetu UCG.

PROJEKTI:

1. Centar izvrsnosti za biomedicinska istraživanja (CEBIMER), 2020 – 2023.
2. Bilateralni projekat (Crna Gora – NR Kina): Identifikacija antimikrobnih peptida i njihovih funkcionalnih tipova korišćenjem celularnih automata, 2019-2020.
3. Nacionalni naučno-istraživački projekat: Balneološki efekti peloida, mineralne vode, ljekovitog i aromatičnog bilja na inflamatorni odgovor kod reumatoidnih i kardiovaskularnih bolesti; 2018-2020
4. Bilateralni projekat (Crna Gora-Republika Srbija): Ispitivanje hemipreventivnog potencijala ljekovitih i aromatičnih biljaka iz ruralnih regiona Crne Gore, 2016-2018.
5. EUREKA: "Comprehensive processing of plant extracts for high value added products", 2016-2018.
6. Bilateralni projekat (Crna Gora-Hrvatska): Komparativna studija o uticaju siromaštva na pothranjenost i gojaznost, ishrane i načina života u školskim gradovima Podgorice i Osijeka, 2015-2017.
7. Nacionalni projekat: "Studija gojaznosti i siromaštva među djecom u Crnoj Gori - klinički, patofiziološki, biohemijski i preventivni aspekti", 2013-2016.
8. Bilateralni projekat (Crna Gora – NR Kina): Studyng Protein Evolution Model Based on cellular Automata, 2012-2014.
9. Nacionalni projekat: "IVUS u dijagnozi razvoja restenoze u koronarnim krvnim sudovima i praćenje patobiokemijskih parametara u patobiomehanizmu, u dobi DES-a kod crnogorskog stanovništva", 2008-2011.
10. Međunarodni projekat: " ECHO/TPS/210/2001/07045, COSV, 2001-2002.

Naučni boravci:

1. Montenegrin-Chinese science and technology cooperation in the period **2019-2021;** Studyng protein evolution model based on cellular automata in Jingdenzhen ceramic institute, Jingdezhen city, The Peoples Republic of China.
2. Postdiplomsko obrazovanje iz eferentne terapije (Transfuzija), Medicinski univerzitet I.P.Pavlov, san Petersburg, Rusija **2018 – 2019;**
3. NIH/Forgaty: Research ethics education in the Balkans and black sea region- Ichan School of medicine at Mount Sinai **2013-2015.**
4. School of medicine – University of Belgrade; Cours of real time PCR-I,II,III parts in **Belgrade 2012.**
5. Montenegrin-Chinese science and technology cooperation in the period **2012-2015;** Studyng protein evolution model based on cellular automata in Jingdenzhen ceramic institute, Jingdezhen city, The Peoples Republic of China.
6. International Academic Summer School – Adressing Nutritional, Environmental and Behavioral Risk on Publik Health in the Central and East European Area, in the frame of CEEPUS CII-RO-0313 project: „Developing a network for monitoring the impact of enviromental and nutritional factors on fertility and neonatal health. **July 2010, Brasov.**

7. Standardizacija VCT programa u Srbiji i Crnoj Gori, pod pokroviteljstvom CAFOD. **Maj 2008, Novi Sad.**

Predavanja po pozivu:

- Pantovic S. (2019) Does the Montenegrian healing mud is a powerful tool in the balneological treatment of inflammatory rheumathoid diseases. 13th Mediterranean Congress of Physical and Rehabilitation medicine, Marrakech, Marocco.
- Pantovic S. (2019) Biochemical parameters and adverse drug reactions. Montenegrin international Medical summit, Podgorica, Montenegro
- Pantovic S. (2019) Stres jezikom hormona. PRONA, Ivanova Korita, Crna Gora
- Pantovic S. Bigović M. Balneologija – multidisciplinarnost na djelu. PRONA, Ivanova Korita, Crna Gora.
- Pantović S. (2017) Slobodni radikali u nama i oko nas, Fondacija za promovisanje nauke (PRONA), Ivanova Korita, Lovćen, Crna Gora.
- Pantović S (2015) Markers of inlammation and antioxidate enzyme activities in restenosis following PCI, 23 rd Meeting of the Balcan clinical laboratory federation, Sarajevo, Bosnia and Hercegovina.
- Pantović S. (2014) Maternal serum free-β-chorionic gonadotrophin and pregnancy-associated plasma protein-A in relation to co-variables at 10-13 weeks of gestation. 22nd International Congress of Clinical Chemistry and Laboratory Medicine, Istanbul, Turkey.
- Pantovic S. (2013) The predicitive value of circulating levels of lipid and inflammatory markers in restenosis following PCI. 21st meeting of Balkan Clinical Laboratory Federation, Budva, Montenegro.
- Pantovic S. (2011) Risk factors in development of restenosis after PCI in the population of Montenegro. Postgraduate seminar and cordination meeting „ South East European Network-Metabolic Syndrome of the DAAD Program, Banjaluka, Republic of Srpska.
- Pantovic S. (2009) How to preserve health for a lifetime. Festival of Science-Researchers' Night. Podgorica, Montenegro, September.

Vijeću Medicinskog fakulteta

Na osnovu Odluke Vijeća Medicinskog fakulteta o formiranju Komisije za doktorske studije, broj:1457 od 16.06.2015.godine, a u skladu sa tačkom 3.8 Vodiča za doktorske studije UCG - Centra za doktorske studije, nakon razmatranja ispunjavanja formalnih uslova za ocjenu doktorske disertacije i poštujući princip kompetentnosti, Komisija za doktorske studije dostavlja Vijeću Medicinskog fakulteta

INICIJALNI PRIJEDLOG
Sastava Komisije za ocjenu doktorske disertacije

I. DOKTORAND**: Dr med Marina Jakšić Kavarić**

Naziv doktorske disertacije: "**Inflamacija, oksidativni stres i metabolički sindrom kod predgojazne i gojazne djece u Crnoj Gori"**

II. U skladu sa članom 38 Pravila doktorskih studija, doktorand dr med Marina Jakšić Kavarić ispunjava uslove za ocjenu doktorske disertacije.

III. Komisija za ocjenu doktorske disertacije:

- **Prof. dr Nela Rašeta Simović**, redovni profesor Medicinskog fakulteta Univerziteta u Banjoj Luci - predsjednik

- **Prof. dr Milica Martinović**, redovni profesor Medicinskog fakulteta Univerziteta Crne Gore – mentor

- **Doc. dr Snežana Pantović**, docent Medicinskog fakulteta Univerzieta Crne Gore - član

KOMISIJA ZA DOKTORSKE STUDIJE

Prof. dr Filip Vukmirović

UNIVERZITET CRNE GORE

Vijeću Medicinskog fakulteta

Komisiji za doktorske studije

23.04.2021

med 582

PREDMET: Zahtjev za ocjenu doktorske disertacije

Poštovani,

U skladu sa Pravilima studiranja na doktorskim studijama Univerziteta Crne Gore, ovim putem podnosim zahtjev za ocjenom doktorske disertacije pod nazivom "Inflamacija, oksidativni stres i metabolički sindrom kod predgojazne i gojazne djece u Crnoj Gori".

Završetkom doktorske disertacije, objavom dva rada u časopisima sa SCI/SCIE liste, kao i prihvatanja jednog rada za publikaciju od strane časopisa sa SCIE liste, a od kojih svi sadrže dio istraživanja sprovedenih u okviru rada na izradi doktorske disertacije, ispunila sam uslove za predaju disertacije na pregled i ocjenu, predviđene Pravilima doktorskih studija Univerziteta Crne Gore.

Ovim putem se obraćam Komisiji za doktorske studije Medicinskog fakulteta, sa molbom da inicira predlog Komisije za ocjenu gore navedene doktorske disertacije. Uz Zahtjev, u prilogu dostavljam sljedeće:

- Pismenu saglasnost mentora da rad zadovoljava kriterijume doktorske disertacije
- Sedam primjeraka doktorske disertacije
- Fotokopiju dva rada objavljena u časopisu sa SCI/SCIE liste tematski vezanih za doktorsku disertaciju
- Štampani e-mail kao potvrdu o prihvaćenosti trećeg po redu rada za publikaciju u časopisu sa SCIE liste, tematski vezanog za doktorsku disertaciju
- Biografiju i bibliografiju
- CD sa cjelokupnim sadržajem doktorske disertacije u PDF formatu
- Potpisanu izjavu o autorstvu (prilog 1 iz Uputstva o oblikovanju doktorske disertacije)

S poštovanjem,

U Podgorici, 19.04.2021.

Dr Marina Jakšić-Kavarić

Marina Jakšić

93.04.2021

med 582/1

UNIVERZITET CRNE GORE

MEDICINSKI FAKULTET

Na osnovu odluke Senata Univerziteta Crne Gore br. 3419 od 20.12.2012. godine, imenovana sam za mentora za izradu doktorske disertacije kandidata dr Marine Jakšić-Kavarić. U fazi predaje doktorske disertacije na pregled i ocjenu, u skladu sa Pravilima doktorskih studija Univerziteta Crne Gore dajem:

SAGLASNOST

Saglasna sam da kandidat dr Marina Jakšić-Kavarić može predati doktorsku disertaciju pod nazivom "Inflamacija, oksidativni stres i metabolički sindrom kod predgojazne i gojazne djece u Crnoj Gori" na pregled i ocjenu.

U Podgorici, 19.04.2021. godine

Mentor:

Prof dr. Milica Martinović

Prilog 1.

Izjava o autorstvu

Potpisani-a dr Marina Jakšić
Broj indeksa/upisa 25/10

Izjavljujem

da je doktorska disertacija pod naslovom

Inflamacija, oksidativni stres i metabolički sindrom kod predgojazne i gojazne djece u Crnoj Gori

- rezultat sopstvenog istraživačkog rada,
- da predložena disertacija ni u cjelini ni u djelovima nije bila predložena za dobijanje bilo koje diplome prema studijskim programima drugih ustanova visokog obrazovanja,
- da su rezultati korektno navedeni, i
- da nijesam povrijedio/la autorska i druga prava intelektualne svojine koja pripadaju trećim licima.

U Podgorici, 19.04.2021.

Potpis doktoranda

Marina Jakšić

UNIVERZITET CRNE GORE

MEDICINSKI FAKULTET

Broj: 598

Podgorica 28.04. 2021 godine.

Uvidom u službenu evidenciju ,izdaje se

POTVRDA

Prof dr Nela Rašeta Simović,redovni profesor Medicinskog fakulteta Univerziteta u Banjoj Luci, nije u radnom odnosu na Medicinskom fakultetu Univerziteta Crne Gore.

Potvrda se izdaje kao prilog obrascu D2 za kandidata dr med Marinu Jakšić , i u druge svrhe se ne može koristiti.

UNIVERZITET CRNE GORE MEDICINSKI FAKULTET UCG 4

ŠEF STUDENTSKE SLUUŽBE

Sonja Vukićević

Sonja Vukićević,diplomirani pravnik

UNIVERZITET CRNE GORE
MEDICINSKI FAKULTET
MEDICINA
Broj dosijea: **25/2010**

Na osnovu člana 165 stava 1 Zakona o opštem upravnom postupku ("Službeni list RCG", broj 60/03.), člana 115 stava 2 Zakona o visokom obrazovanju ("Službeni list CG", broj 44/14.) i službene evidencije, a po zahtjevu studenta Jakšić Željko Marina, izdaje se

UVJERENJE O POLOŽENIM ISPITIMA

Student **Jakšić Željko Marina**, rođena **28-10-1985** godine u mjestu **Zadar**, Republika **Hrvatska**, upisana je studijske **2010/2011** godine, u **I** godinu studija, kao student koji se **samofinansira** na **doktorske akademske studije**, studijski program **MEDICINA**, koji realizuje **MEDICINSKI FAKULTET** - Podgorica Univerziteta Crne Gore u trajanju od **3 (tri)** godine sa obimom **180** ECTS kredita.

Student je položio ispite iz sljedećih predmeta:

Redni broj	Semestar	Naziv predmeta	Ocjena	Uspjeh	Broj ECTS kredita
1.	1	BIOSTATISTIKA	"A"	(odličan)	10.00
2.	1	MEDICINSKA INFORMATIKA	"A"	(odličan)	10.00
3.	1	METODOLOGIJA NAUČNOG ISTRAŽIVANJA	"A"	(odličan)	10.00
4.	2	OSNOVI ĆELIJSKE BIOLOGIJE	"B"	(vrlodobar)	10.00
5.	2	OSNOVI IMUNOLOGIJE	"A"	(odličan)	10.00
6.	2	POČETNA ISTRAŽIVANJA	"A"	(odličan)	10.00

Zaključno sa rednim brojem **6.**

Ostvareni uspjeh u toku dosadašnjih studija je:
- srednja ocjena položenih ispita **"A" (9.83)**
- ukupan broj osvojenih ECTS kredita **60.00** ili **100.00%**
- indeks uspjeha **9.83.**

Uvjerenje se izdaje na osnovu službene evidencije, a u svrhu ostvarivanja prava na: (dječji dodatak, porodičnu penziju, invalidski dodatak, zdravstvenu legitimaciju, povlašćenu vožnju za gradski saobraćaj, studentski dom, studentski kredit, stipendiju, regulisanje vojne obaveze i slično).

Broj:
Podgorica, 28.04.2021 godine

M. P.

SEKRETARKA