ORIGINAL ARTICLE

A COMPARATIVE STUDY OF LIPID PROFILE AND LEPTIN RESISTANCE IN CHILDREN WITH METABOLIC SYNDROME DEPENDING ON HYPERTENSION IN KYIV

DOI: 10.36740/WLek202110220

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ABSTRACT

The aim: To compare lipid metabolism and leptin levels among the children with and without hypertension to identify associated risk factors for the course of metabolic syndrome in children.

Materials and methods: This observational, cross-sectional study recruited children from the Rheumocardiology Department of Children's Clinical Hospital No 6 in Kyiv, with metabolic syndrome, identification of waist-to-height ratio, leptin level, homeostasis model assessment of insulin resistance and lipid profile. The main group included 41 children with metabolic syndrome and hypertension and the control group included 40 children with metabolic syndrome without hypertension. Statistical data analysis was performed using the MedStat 2.6.2. package.

Results: A total of 81 children aged 10 to 17 with metabolic syndrome were examined. The group of children with hypertension had significantly lower high-density lipoprotein cholesterol (0.85±0.04) than children without hypertension (0.94±0.03), with $p < 0.05$. Leptin resistance was detected in 65.2% of children with hypertension and 35.3% of children with normal blood pressure ($p < 0.01$).

Conclusions: Children with metabolic syndrome and hypertension had a significantly higher body mass index and waist circumference as opposed to children with normal blood pressure. In the lipid profile high-density lipoprotein cholesterol was significantly lower in hypertensive children. There was no reliable difference in other lipid profile indicators between the two groups, but there was an upward trend of them in group with hypertension. Leptin resistance is also significantly higher in hypertensive children.

KEY WORDS: hypertension, metabolic syndrome, lipid profile, leptin resistance, insulin resistance

Wiad Lek. 2021;74(10 p.II):2630-2633

INTRODUCTION

According to a WHO report, about 124 million children between the ages of 5 and 19 all over the world are obese. Overweight children may have cardiovascular pathologies, including hypertension, dyslipidemia and endocrine pathology associated with metabolic syndrome [1].

The pathogenesis of the metabolic syndrome is based on insulin resistance, an evolutionarily fixed mechanism of survival in starvation [2]. Normally, the satiety hormone leptin increases in response to an increase in insulin levels in plasma [3,4]. Constant activation of leptin receptors from adipose tissue leads to leptin resistance [5]. Recently, the hypothesis of the role of hypertriglyceridemia, which is the main dyslipidemia in metabolic syndrome, in violation of the transport of leptin through the blood–brain barrier, became increasingly widespread. It was firstly confirmed by the experimental studies of W.A. Banks et al. that have shown that mice with impaired triglyceride synthesis are protected from developing both diet-induced obesity and obesity-induced resistance of leptin [6]. Later studies have shown that triglycerides are able to change the function of receptors in the brain not only to leptin, but also to insulin, and to cause insulin resistance [7].

Although the role in the regulation of hunger is the main function of leptin, it also plays a role in other physiological processes in the body. A number of studies have shown that leptin correlates with the activity of angiotensin II and noradrenaline in plasma, which may indicate a pathogenetic connection in the development of hypertension due to activation of the sympathetic nervous system [8-11].

Unhealthy lifestyle in childhood with subsequent development of the obesity is associated with a high chance of premature death and disability in adulthood. Hypertension as one of the criteria complicates the course of the metabolic syndrome.

THE AIM

The aim of the study is to compare lipid metabolism and leptin levels among the children with and without hypertension to identify associated risk factors for the course of metabolic syndrome in children.

MATERIALS AND METHODS

A comprehensive examination of 81 children aged from 10 to 17 with metabolic syndrome was conducted at the Rheu-

Table I. Comparative characteristics of average values and median of biochemical parameters

Parameters	Value of the parameter in groups (M ± m)	
	MetS without HTN (n=40)	MetS with HTN (n=41)
Sex: Male Female	 28 12	 35 6
BMI, kg/m²	27.7±0.6	30.6±0.8*
WC, cm	88.9±0.3	94.4±1.2*
Fasting glucose, mmol / l	4.92±0.11	4.75±0.13
Leptin, ng/ml	15.16±4.8	24.6±5.2
TC, mmol/l	3.6±0.3	3.8±0.2
TG, mmol/l	0.9±0.3	1.2±0.2
HDL-C, mmol/l	0.94±0.03*	0.85±0.04*
LDL-C, mmol/l	2.3±0.2	2.5±0.1
VLDL-C, mmol/l	0.36±0.05	0.43±0.1
AC, IU	1.85±0.36	2.6±0.24

Note. * - the difference of parameters in the group of MetS with HTN is reliable compared to those in the group of MetS without HTN ($p < 0,05$)

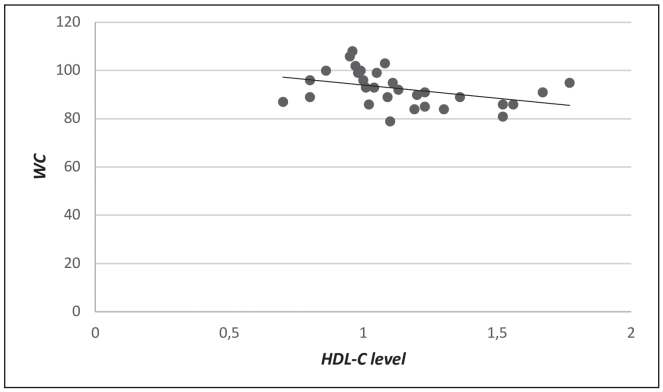

Fig. 1. Correlation field in coordinates: HDL-C level (X axis) and WC (Y axis). Correlation relation, Ro <0 (Ro = -0,529), at significance level p <0,01 is revealed.

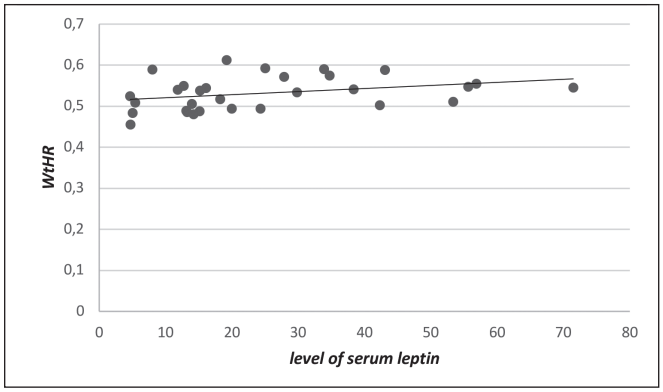

Fig. 2. Correlation field in coordinates: level of serum leptin (X axis) and WtHR index (Y axis). The correlation relation, Ro> 0 (Ro = 0.436), at the significance level p = 0.02 is revealed

mocardiology Department of Children's Clinical Hospital No.6 in Kyiv. The diagnosis "metabolic syndrome" (MetS) was established according to IDF 2007 criteria, which includes abdominal obesity and 2 or more of the following indicators; triglyceride level ≥ 1.7 mmol / l, high-density lipoprotein cholesterol <1.03 mmol / l, blood pressure ≥ 130 / 85 mmHg, fasting plasma glucose ≥ 5.6 mmol / l [12]. Exclusion criteria are as follows patients with other conditions and nosologies, associated with genetic syndromes and obesity associated with treatment.

According to the ambulatory blood pressure monitoring diagnosis of hypertension (HTN), children were divided into two groups: the main group included 41 children with HTN, the control group included 40 children without HTN. 24-h ambulatory blood pressure monitoring was performed using ABM-04 («Meditech», Hungary). Blood pressure was measured every 15 minutes over the day (6:00-22:00) and every 30 minutes at night (22:00-6:00) [13,14]. All children were checked a body mass index (BMI), waist circumference (WC), and the WtHR (Waist-to-height ratio) of ≥0.5 recommended by meta-analysis 2018 [15]. BMI was calculated as the ration of weight (kg) to height (m²) and was assessed according to WHO growth charts. Abdominal obesity was established by measuring the WC ≥90 percentile for age and sex-specific WC based on WHO reference in adolescents [16]. The fasting plasma glucose was measured. Serum leptin was measured using the LDN immunoassay (Germany). Leptin Resistance was calculated using the formula leptin/BMI > 0.7 [17]. Lipid profile included the determination of total cholesterol (TC), triglycerides (TG), high-density lipoproteins (HDL-C), low-density lipoproteins (LDL-C), very low density lipoproteins (VLDL-C), atherogenic coefficient (AC) by enzymatic colorimetric method of analyzer and test system Cobas 6000, Roche Diagnostics (Switzerland). Statistical data analysis were performed using the MedStat 2.6.2. package.

RESULTS

There was a predominance of boys – 77,8% (n=63) over girls – 22,2 % (n=18) among children with metabolic syndrome. Median age of boys was 14±0.46, girls 14±0.74 (p=0.724). It was found that 50.6% of children (n = 41) with metabolic syndrome had hypertension. The BMI (30.6 ± 0.8) and WC (94.4 ± 1.2) were significantly higher in the group of children with MetS with HTN, as opposed to the group of children without HTN (27.7 ± 0.6 and 88.9 ± 0.3 respectively). (Table I).

The lipid profile was characterized by an increase in LDL-C in 80.2% of children (n = 65) and a decrease in HDL-C in 38.3% (n = 31), hypertriglyceridemia in 23.5% (n = 19), increased TC in 8.6% (n = 7) and VLDL-C only in 4.9% of all children (n = 4).

The group of children with HTN has significantly lower HDL-C <1.03 mmol/l (0.85±0.04) than children without

HTN (0.94±0.03), with p<0.05. There was no reliable difference in other lipid profile indicators between the two groups (p >0.05). Characteristics of the groups are presented in the table I.

The correlation was also found between WC and HDL-C level with r = -0,529 (p <0,01) (Fig.1)

At the same time, with changes in the lipid profile, an increase in the adipose tissue hormone leptin was found in 86.4% of children (n = 70). Although there is no significant difference between the medians of both groups, there is a tendency to an increase in leptin in the group with hypertension.

Statistically, we found that the higher the BMI, the greater the WC (r = 0.375) and WtHR (r = 0.584). In the group with hypertension, WtHR was in 63% and in the other group – 57.5%. WtHR ≥ 0.5 is defined in 67% of children with hyperleptinemia from both groups . It was confirmed in our study, that WtHR is closely correlated with serum leptin levels (r = 0.436). (Fig.2)

Leptin resistance was significantly more common in the group of children with HTN – 65.2% (n = 27), as opposed to children without HTN – 35.3% (n = 15) (p < 0.01).

DISCUSSION

Analysing the Mets IDF criteria [12] in the children participating in the study, it should be noted that all children were obese, just over half of the children had HTN, 38.3% had low levels of "protective" HDL-C and 23.5% had high levels of TG. Although LDL-C is not included in the Mets criteria, high levels of this parameter were found in 80.2% of children in both groups. WtHR≥ 0.5 was found in 61% of children, which according to the 2018 meta-analysis indicates a high cardiometabolic risk [15]. We also recommended this anthropometric tool for mass screening of obese children. The results obtained indicate a high prevalence of abdominal obesity and the possible inclusion of the WtHR parameter in one of the additional criteria for Mets in the next IDF review.

Analysis of patient groups with and without hypertension showed that 'bad' LDL-C levels in hypertensive children were significantly higher.

It was found that 80.4% of children had high levels of leptin, and 51.8% of children had leptin resistance, which may be due to the acquired non-sensitivity of tissues to the "satiety hormone", including at the level of blood-brain barrier, and/or genetic mutations of the defect in the leptin receptor. The correlation between the level of leptin and WtHR was also found, which proves the role of this laboratory indicator in the development of abdominal obesity. Such relationship has been found in children and adults in recent studies [18, 19]. According to our results, leptin resistance has been reliably identified more frequently in hypertensive patients (65.2%), which proves the aforementioned pathogenetic mechanism of the action of leptin in the activation of the sympathetic nervous system[8-11].

These results indicate a burden of HTN in the development of obesity and Mets.

This study did not examine how the development of Mets will be affected, but identified key parameters for future studies.

CONCLUSIONS

1. In the lipid profile of the two groups, the changes were mainly due to an increase in LDL-C and a decrease in "protective" HDL-C. It was found that HDL-C was significantly lower in hypertensive children. There was no reliable difference in other lipid profile indicators between the two groups, but there was an upward trend of them in group Mets and HTN.
2. Elevated WHtR was found in more than half of children with Mets, which indicates a high cardiometabolic risk. Children with hypertension had a significantly higher BMI and WC as opposed to children with normal blood pressure. In the analysis of correlated links, it was found that WHtR is associated with serum leptin levels and WC with HDL-C level.
3. Hyperleptinemia was found in the majority of children and more than half of the children with Mets lost tissue sensitivity to leptin. Leptin resistance is significantly higher in the group of children with hypertension, in contrast to children without hypertension.
4. Although patients were selected according to defined criteria of Mets, we have shown that children with and without HTN have significantly different indicators of cardiometabolic risk factors such as increased WC, WHtR, dislipidemia, hyperleptinemia with consequent development of leptin resistance. Children at high cardiometabolic risk require regular check-ups and lipid monitoring to prevent complications of the metabolic syndrome such strokes and heart attacks.

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The laboratory research of patients was carried out thanks to grant support that was provided by O.O. Bogomolets National Medical University. This scientific work is part of the research work No. 0118U000151 of the Department of Pediatrics 4.
The study was approved by the local ethics committees of the respecting Departments. Each patient's parents were informed on the purpose and methods of the research and reserved the right to respond anonymously.
We would like to thank the head of Cardiology Department of Children's Clinical Hospital № 6 Kukhta Nataliia for allowing to exam the children.

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Conflict of interest:
The Authors declare no conflict of interest.

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Received: 17.06.2021
Accepted: 17.09.2021

A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article