CHILDHOOD OBESITY AND ITS IMPACT ON BLOOD PRESSURE

PhD THESIS

Andrea Emese Jakab, MD

Consultant: Csaba Bereczki, MD, PhD

Clinical Medical Sciences Doctoral School

Program Director: Prof. Lajos Kemény, MD, PhD, DSA

SZEGED



Department of Pediatrics and Pediatric Health Center, Faculty of Medicine

Albert Szent-Györgyi Health Center

University of Szeged

2019

PUBLICATIONS DIRECTLY RELATED TO SUBJECT OF THE THESIS

I. Andrea Emese Jakab, Miklós Illyés, Attila Cziráki, Erzsébet Valéria Hidvégi, Csaba Bereczki. Prevalence of Overweight and Obesity in Hungarian Children and Adolescents. *Annals of Nutrition and Metabolism.* 2018; 72:259-264. (IF: 2,424)

II. Andrea Emese Jakab, Erzsébet Valéria Hidvégi, Miklós Illyés, Attila Cziráki, Tibor Kalmár, Zoltán Maróti, Csaba Bereczki. Prevalence of Hypertension in Overweight and Obese Hungarian Children and Adolescents. *Orvosi Hetilap.* 2020; 161:151-160. (IF: 0,564)

III. Andrea Emese Jakab, Miklós Illyés, Attila Cziráki, Csaba Bereczki, Erzsébet Valéria Hidvégi. Prevalence of Overweight and Obesity in a Population Aged between 3-18 Years in Szolnok. *Gyermekgyógyászat.* 2018; 68:107-112.

ABSTRACTS DIRECTLY RELATED TO SUBJECT OF THE THESIS

I. Erzsébet Valéria Hidvégi, **Andrea Emese Jakab**, Miklós Illyós, Attila Cziráki. Childhood Obesity: Does it Have any Effect on Young Arteries? ARTERY18, 18–20 October 2018, Guimarães, Portugal. *Artery Research*. 2018; 24:75.

II. Andrea Emese Jakab, Erzsébet Valéria Hidvégi, Miklós Illyés, Attila Cziráki, Csaba Bereczki. Non-Invasive Assessment of Arterial Function in Overweight and Obese Children and Adolescents. 51st Annual Meeting of the Association for European Paediatric and Congenital Cardiology. 29 March - 01 April 2017, Lyon, France. *Cardiology in The Young.* 2017; 27:Suppl.2 p.12.

III. Erzsébet Valéria Hidvégi, **Andrea Emese Jakab**, Miklós Illyés, Attila Cziráki, Csaba Bereczki. Non-invasive Assessment of Arterial Function Parameters in Overweight and Obese Children and Adolescents. Annual Meeting of the Hungarian Society of Cardiology. 05-07 May 2016, Balatonfüred, Hungary. *Cardiologia Hungarica* 2016; 46:53-54.

IV. Andrea Emese Jakab, Erzsébet Valéria Hidvégi, Miklós Illyés, Attila Cziráki, Csaba Bereczki. Prevalence of Overweight and Obesity in a Population Aged between 3-18 Years in Szolnok. Annual Meeting of the Hungarian Society of Peadiatrics. 22-24 September 2016, Szeged, Hungary. *Gyermekgyógyászat.* 2016; 67:298.

PUBLICATION ON OTHER TOPIC:

I. Anette Wecker-Gussmann, Doris Ehringer-Schetitska, Vesna Herceg-Cavrak, Erzsébet Valéria Hidvégi, **Andrea Emese Jakab**, Andreas Petropoulos, Ero Jokinen, Peter Fritsch, Renate Oberhoffer. Prevention of Delayed Diagnosis in Congenital Heart Disease. *Cardiology in the Young*. 2019; 29:730-731.

ABSTRACTS ON OTHER TOPIC:

I. Erzsébet Valéria Hidvégi, **Andrea Emese Jakab**, Attila Cziráki, Miklós Illyés. Updated and Revised Reference Values of Aortic Pulse Wave Velocity in Children and Adolescents Aged 3-18 Years. 53rd Annual Meeting of the Association for European Paediatric and Congenital Cardiology (AEPC) 15-18 May, 2019, Seville, Spain. *Cardiology in the Young*. 2019; 29:Suppl.1 p.143.

II. Andrea Emese Jakab, Robert Dalla Pozza, Doris Ehringer-Schietitska, Peter Fritsch, Renate Oberhoffer, Andreas Petropoulos. Assessment of Pulse Oximetry Screening Trends in AEPC. 52nd Annual Meeting of the Association for European Paediatric and Congenital Cardiology (AEPC). 9–12 May 2018, Athens, Greece. *Cardiology in the Young.* 2018; 28:Suppl.1 p.175.

III. Andreas Petropoulos, Peter Fritsch, Doris Ehringer-Schietitska, Vesna Herceg-Cavrak, **Andrea Emese Jakab**, Erzsébet Valéria Hidvégi, Renate Oberhoffer. Adapting Pulse Oximetry Measurements for Early Detection of Critical Congenital Heart Disease in Early Neonatal Period. 50th Annual Meeting of the Association for European Paediatric and Congenital Cardiology (AEPC). 1–4 June 2016, Rome, Italy. *Cardiology in the Young*. 2016; 26:Suppl.2 p.12.

Introduction

Childhood Obesity

According to the World Health Organisation (WHO), overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health. The increasing number of overweight and obese children and adolescents has become a serious and alarming phenomenon worldwide. Obese children are more prone to have early atherosclerosis, hypertension, diabetes mellitus, insulin resistance, metabolic syndrome, dyslipidaemia, etc.

Obesity Related Hypertension

Overweight and obesity are main contributing factors to develop hypertension not only in adulthood but in childhood, as well. Recent study has found that the odds for hypertension are 1.5 times higher in children with overweight, while in obese patients these odds are 1.8 - 3.5 - 5.7 times higher for primary hypertension compared to their normal weight pupils. Consequently, the higher is the frequency of children and adolescents with overweight or obesity, the higher is the portion of this population suffering from hypertension.

Aims

1. To determine the prevalence of overweight and obesity in a healthy population aged 3–18 years in Szolnok city and the surrounding area.

- A. To discover if there is any difference in age and sex distribution regarding the prevalence of overweight and obesity.
- B. To observe if there have been any changes in the prevalence and in the trends of overweight and obesity from the data measured previously in Hungary.

2. To assess the prevalence of overweight and obesity associated hypertension in children and adolescents aged 3-18 years in Szolnok city and the surrounding area.

- A. To observe if there is any difference in age and sex distribution in this population.
- B. To establish if there is any relationship between body mass index (BMI) categories and frequency of hypertension.
- C. To compare our data with international findings on overweight and obesity associated hypertension.

Materials and Methods

Subjects

In order to assess the prevalence of overweight (OW), obese (O) and normal weighted (N) children and adolescents in the first analysis 6.824 subjects (3.673 boys) aged 3–18 years were recruited from elementary, primary and high schools in Szolnok town (Hungary) between 2012 and 2016. For the second study 8.624 subjects (4.719 boys) aged 3–18 years were enrolled between 2005 and 2018 to estimate the prevalence of hypertension in subjects with elevated BMI. All the subjects were Caucasian without any chronic diseases, and they were not on any regular medications. Informed consent for the measurements was asked for from the parents of the subjects. The protocol was reviewed and approved by the local Institutional Ethics Committee of the University of Pécs, Pécs, Hungary.

Methods

Height and weight measurements were performed in accordance with the Hungarian professional rules. The subjects were categorised by their BMI into N, OW, O groups regarding their age and sex, as well.

Blood pressure (BP) was taken with an occlusive-oscillometric device (Arteriograph, Tensiomed Ltd., Hungary). If the systolic (SBP) and/or diastolic blood pressure (DBP) were found to be over 90th percentile according to age, sex and height the subject was referred to a detailed examination. Abdominal ultrasound was performed (especially focusing on the kidneys and the adrenal glands), followed by a blood test (including bloodwork, fasting glucose, ions, renal- and liver functions, lipids, thyroid stimulating hormone). The examination composed of 12-leads ECG, echocardiography (also to rule aortic coarctation and to assess left ventricular hypertrophy), and finally 24-hours ambulatory blood pressure monitoring (ABPM) (CardioTens 01, CardioTens 02, Meditech Ltd, Budapest, Hungary). The diagnosis of hypertension (HTN) was set up if the average SBP and/or DBP was equal or above the 95th percentile according to age, sex and height and secondary hypertension was excluded. "Elevated BP" subgroup (90th \leq BP<95th) was created for the appropriate result-comparison with the relevant literature.

Statistics

Data are reported as mean and SD for continuous data. For data comparison, Student's *t*-test was carried out after checking that the assumption of normality was met. Significance levels were set at the 5% level using the student t-test. To ensure data comparison between sexes,

chi-squared test was carried out. Fisher's exact test was applied to compare the prevalence with the previous Hungarian data. Statistical analysis was performed with the SPSS 23.0 statistical package (SPSS Inc., Chicago, Illinois, USA).

Results

Prevalence of Overweight and Obesity

Table 1 contains the results of the prevalence of overweight and obesity. The prevalence of overweight was 13.4% (n=915), and 6.6% of obesity, which is 20% (n=1.363) of the studied population aged 3-18, in total.

| Table 1 | Prevalence | of | overweight | and obesity |
|---------|------------|----|------------|-------------|
| | | | | |

| | boys | | girls | | total | |
|--------------------|------|------|-------|------|-------|------|
| | n | % | n | % | n | % |
| normal BMI | 2881 | 78.4 | 2580 | 81.9 | 5461 | 80.0 |
| overweight | 518 | 14.1 | 397 | 12.6 | 915 | 13.4 |
| obese | 274 | 7.5 | 174 | 5.5 | 448 | 6.6 |
| overweight + obese | 792 | 21.6 | 571 | 18.1 | 1363 | 20.0 |
| | | | | | | |

BMI; body mass index

Table 1 demonstrates that the rate of overweight and obesity is higher in case of boys, than in girls, since the total prevalence of overweight and obesity was 21.6% (n=792) in boys and 18.1% (n=571) in girls. This difference was proven by statistical analysis (chi-square test, p<0.005). In order to ensure more informative data the age and weight distribution of the participants is indicated in percentage in Figure 1 and 2.

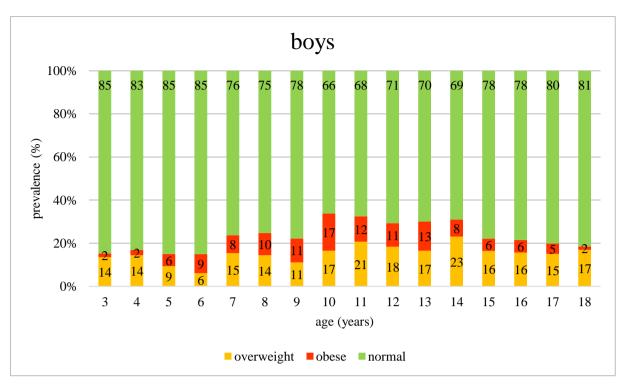


Figure 1 Age-related distribution of BMI categories for boys

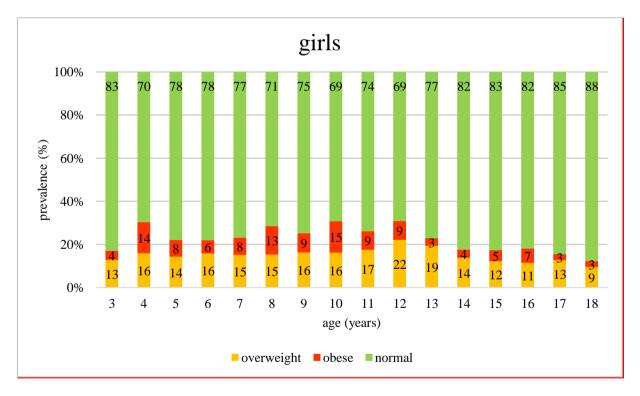


Figure 2 Age-related distribution of BMI categories for girls

Prevalence of Overweight and Obesity Associated Hypertension

Figure 3 provides the summary of the distribution of normal BP, elevated BP and hypertension percentages in different weight categories. From this graph we can see that in boys hypertension was identified in 1.3% - 12.7% - 32.2% of the subjects in N, OW and O

groups, respectively (3/A). In girls, hypertension was diagnosed in 0.2% - 2.4% - 17.1% of the individuals, in N, OW and O groups, respectively (3/B). Both in OW and O boys the prevalence of HTN was significantly higher compared to girls (p<0.0001). In both genders, the frequency of HTN was 8.3% in OW patients, and 26.7% in O patients (3/C). The rate of elevated BP was 0.6% - 17.3% and 7.2% in N, OW and O boys, respectively. In N girls this rate was 0.1%, surprisingly there was no patient with elevated BP in OW or O girls. Considering the whole investigated population, elevated BP was identified in 0.4% of N, 9.8% of OW and 4.6% in O patients.

normal weighted overweight obese А 0.6% 1.3% 12.7% 32.2% 17.3% 60.6% 70.0% 98.1% 7.2% В 0.1% 0.2% 2.4% 17.1% 82.9% 97.6% 99.7% С 0.4% 0.8% 8.3% 9.8% 26.7% 4.6% 68.7% 81.9% 98.8% elevated BP **HTN** normal BP

Figure 3 Prevalence of normal BP, elevated BP and HTN in N, OW and O boys (A), girls (B) and in the total population (C);
BP; blood pressure, HTN; hypertension, N; normal weight, OW; overweight, O; obese

6

Discussion

Prevalence of Overweight and Obesity

The prevalence of overweight and obesity is constantly increasing in children, adolescents, and adults. Between 1975 and 2016 the global mean BMI raised from 16.8 kg/m² to 18.5 kg/m² in boys, and from 17.2 kg/m² to 18.6 kg/m² in girls. The Hungarian mean BMI increased from 18.8 kg/m² to 20.0 kg/m² in boys, and from 18.2 kg/m² to 19.9 kg/m² in girls.

Our research lasted for 3 years, and the 3-18-year-old population was basically assessed simultaneously. Due to such circumstances, our findings may give an accurate picture of the condition of a well-balanced, young generation with significant number (n=6.824) of participants. Figure 4 represents our findings compared with the data previously measured in Hungary (IDEFICS Hungarian and *Antal* and her co-workers).

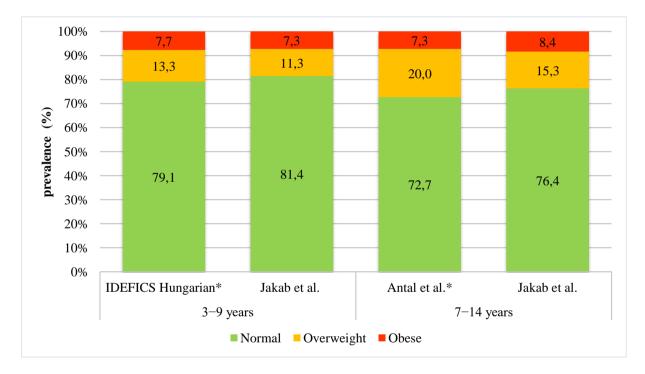


Figure 4 Comparison of normal weight, overweight and obesity prevalence between European data, latest Hungarian data and results from this study

To ensure the comparability of the data, our data have been determined in accordance with the age groups applied in the previous studies (3–9 years, 7–14 years). A slight decrease is observed in the prevalence of overweight, since the p-value of is relatively close to the level of significance. In contrast, a significant decrease is presented in the older age group (7–14 years), in both sexes, with respect to overweight: the total prevalence has decreased from 20% to 15.3% (p<0.005), while in this age group the prevalence of normal BMI increased from 72.7% to 76.4% (p<0.001), and no difference is presented in the case of obesity (p=0.2).

Prevalence of Overweight and Obesity Associated Hypertension

Much of the available literature on OW and O associated HTN deals with the question of the frequency in children and adolescents. Analysing the current literature, we found two relevant articles: the first article (Chinese) suggested the prevalence of HTN is 13.9% in OW patients (OR: 1.67) and 21.6% in O patients (OR: 2.17). In the second publication (American), obese children were further classified into 3 different subgroups based on BMI expressed as a percentage above the 95th BMI percentile according to age and sex. In this study, the frequency of elevated BP was 23.6% among OW patients, and 29.4% among O patients. Furthermore, prevalence of HTN was 10.8% in OW subjects, whereas it was 19% in O patients (OR: 1.8-3.5-5.7).

In our study this rate was 8.3% in OW and 26.7% in O patients. Our findings show a great accordance with the above mentioned results, however, minor discrepancies may stem from the following methodical difference: on one hand, in the first (Chinese) study local reference values were used to categorize subjects based on their BP, on the other hand, in the second (American) study the reference values of BP published in 2004 and revised in 2012 were applied. In the study conducted by us European BP cut-off values were adopted to create subgroups.

OW, O and associated HTN is a major public health problem, since the rising frequency of OW and O consequently increases the incidence of HTN in these patients. Nowadays, it is suggested to follow-up closely patients with OW, O in order to monitor possible comorbidities, and supporting them in a body weight reducing lifestyle, finally, if needed treating them appropriately. However, the final goal should be proper primary prevention targeting these abnormal conditions.

Summary

A summary of the main findings and of the principal issues which have arisen in this thesis are the followings:

1. We have found the prevalence of overweight and obesity is 13.4% and obesity is 6.6% measured between 2012 and 2016 in Szolnok, in Hungary.

2. Overweight and obesity are more common in boys, than in girls (p<0.005).

3. Compared to the previous Hungarian data, we have identified a mild decrease in the youngest age group (3-9 years) in both sexes, in respect of overweight (2006-2012 vs. 2012-2016). We have established, that the prevalence of overweight significantly decreased, while the prevalence of normal BMI significantly increased in the older age group (7-14 years) (2005-2006 vs. 2012-2016).

4. Prevalence of overweight and obesity associated hypertension was 8.3%, and 26.7% respectively.

5. Increased BMI associated HTN was more common in boys. In OW boys the peak was between the ages of 11 and 13 years, and in OW girls between 16 to 17. In O groups, HTN was most common in boys aged 14-18 years, while 13-15 years in girls.

6. Overweight raises the risk for hypertension (odds ratio: 1.1) not as much, as obesity, where the odds ratio is 3.6.

7. Regarding the prevalence of overweight and obesity associated hypertension, our findings show a great accordance with the great, international, relevant and contemporary population studies.

Acknowledgements

First, I would like to say thank you to Prof. Dr. Lajos Kemény, DSA the program director of Clinical Medical Sciences Doctoral School to enable me to study in this doctoral program.

I also would like to express my appreciation to my consultant, Dr. Csaba Bereczki, PhD who always supported and encouraged me during my PhD studies.

I am thankful to Zoltán Maróti PhD and Tibor Kalmár PhD for their constant help in every aspect of the writing of this thesis and my publications. I am very grateful for their guidance.

I would like to thank Dr. Miklós Illyés, PhD and Prof. Dr. Attila Cziráki, PhD for sharing their knowledge with me.

I wish to thank Gábor Érsek for his help in the field of statistics and data analyzing and I also want to thank Judit Kelemen and Csilla Keresztes, PhD for being the lecturer of my publications.

I am very thankful to my colleagues, friends and family, especially to my mother who helped me all the way with her scientific experience, supported with her enthusiasm, I cannot express my appreciation enough for her investment in this thesis.