Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 2069–2074

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Association of serum Interleukin-10, omentin-1 and visfatin concentration with metabolic risk factors in obese children

Kulshrestha Himani [a], Gupta Vani [a,*], Supriya Mishra [a], Abbas Ali Mahdi [b], Awasthi Shally [c]

[a] Department of Physiology, King George's Medical University, Lucknow, India
[b] Department of Biochemistry, King George's Medical University, Lucknow, India
[c] Department of Paediatric, King George's Medical University, Lucknow, India

ARTICLE INFO

Article history:
Received 12 January 2019
Accepted 25 January 2019

1. Introduction

Childhood obesity is an array of epidemic health problems worldwide and is associated with numerous metabolic disorders such as Type 2 Diabetes Mellitus (DM), cardiovascular diseases, osteoarthritis, cancer, insulin resistance, dyslipidemia, hypertension and other life-threatening conditions. The frequency of diabetes mellitus is increasing and it is expected that it will affect 300 million people in 2025 [1] · In terms of estimates, 200 million school-age children are overweight and 40–50 million of them are obese [2]. The prevalence of overweight was estimated 12.64% and that of obesity was 3.39% in 2012 in a meta-analysis of Indian children [3,4]. The overall prevalence by the International Obesity Task Force (IOTF) classification was 18.2% and WHO standards was 23.9% in India [4].

In children, several competing definitions of metabolic syndrome (MS) are in use include that of the National Cholesterol Education Program (NCEP) Adult Treatment Panel Third (ATP III), International Diabetes Federation (IDF) [5].

The chronic inflammation and secretion of adipokines such as chemokines and cytokines from adipose tissue may play a critical role in the development of obesity-related metabolic dysfunction [6] in childhood obesity [7].

Pro-inflammatory hormones such as visfatin produced by adipose tissues have been implicated as participants in the development of metabolic risk factors, whereas anti-inflammatory adipokines such as adiponectin, Interleukin-10 (IL-10) and omentin are decreased in developing obesity [8].

IL-10 (an immunoregulatory protein) exhibits a protective role against atherogenesis. Recently, in an adult population, it was suggested that IL-10 may be involved in the inflammatory network of MS [9].

Omentin-1/intelectin-1 (a secretory protein), have very low concentration in human blood [10] & are highly expressed in human visceral fat tissues. The circulating omentin-1 levels are reduced in obese subjects [11].

Visfatin or pre-B-cell colony-enhancing factor or Nicotinamide Phosphoribosyl Transferase (NAMPT), is also a secretory cytokine, found in very low concentration in human plasma. It in vitro enhanced glucose uptake by adipocytes. It has been shown that plasma visfatin levels increase with progressive beta cell deterioration in type 2 diabetes [12]. Several lines of evidence suggest a potential role of visfatin in the pathophysiology of metabolic disorders including obesity and its associated disease [13].

As on date, many aspects of biology of circulating IL-10, Omentin-1 and Visfatin including its biological effects on obesity and impact on development of metabolic syndrome are remain controversial and unanswered at least in children. The current study tested the susceptibility of association of these adipokines with metabolic risk factors (MRFs) in obese children.

2. Material and methods

2.1. Subjects

The study was planned as a cross-sectional field survey that will measure the prevalence of obesity in the schools of Lucknow district. For the sampling of schools, the list of schools was download from website www.schools.org.in. These schools were categorized by zone-wise clusters of blocks of Lucknow district. Lucknow is composed of 7 zones. The schools of Lucknow district were also divided into 3 major categories middle (5–10 years), secondary (5–12 years) & upper secondary (5–17 years). See http://www.lucknow.gov.in/school education. The study children have been

* Corresponding author.
E-mail address: vaniphysiology@gmail.com (G. Vani).

https://doi.org/10.1016/j.dsx.2019.01.052
1871-4021/

taken from schools of different demographic area of different zones (east, west north, south) of Lucknow district by conducting obesity awareness program in selected schools between Oct 2013 to Sep 2017.

The final number of schools sampled was determined to consider representation of the geographical area as well as the socioeconomic status of the childhood population. The children & adolescents studying in the government or government-aided schools were categorized as to the lower & lower middle socioeconomic status on the basis of Kuppu-swami scale, because education in these schools is either at minimal cost or free. In spite of this, the cost of education in private or management run schools is high and children in these schools were categorized as to the middle and upper socioeconomic groups according to Kuppu Swami Scale. In private schools during the sampling, a gold "standard" (class or grade) was considered as the primary sampling unit for each school selected. From each school, 3rd to 10th standards were selected, depending on the class strength. All students in the selected class or grade were included in the study.

The specific object of sample collection was to collect the anthropometric data of school going children of age group of 5–17 years according to CDC growth chart for weight, height, BMI for boys & girls separately. Sample collection were considered from different socioeconomic status (upper middle class, middle class, lower middle class, lower class). The children's family of Lucknow's east schools was found of upper middle & middle class standard. They belong to the single type family of businessman, government sector service man etc. Their family educational background was of graduate or above and in northern Lucknow schools, the children family economic status was poor. Children were belonging of middle class, lower middle class and lower-class family. The family occupation most of them was of private sector service, labor class etc. The educational background of their family was high schools, primary class, middle class or illiterate. Mostly their family type was joint or extended. A randomly selection of 220 obese children were included in this case-control cohort study. These subjects were 82 males and 138 females of age group 5–11 years (pre-pubertal) and 12–17 years (pubertal). Exclusion criteria were defined as having the history of any condition that affects inflammatory markers such as cardiovascular diseases, thyroid diseases, malignancies, current smoking, known case of diabetes mellitus who were on oral or insulin therapy, known case of hypertension who were on anti-hypertensive therapy, heart failure, acute or chronic infections/inflammatory disease, hepatic or renal diseases, alcohol or drug abuse. All informed consent forms were sent home with the children on the previous day to obtain their parent's signatures and only children who brought back the signed consent form were screened on the day of the camp during enrollment. Information about the level of physical activity was recorded using a study performa including level of daily activities such as time for watching TV, using computers, playing video games, outdoor activities and studying, adaptation of sedentary life style. Pattern of nutrition, diet and age at onset of obesity were also assessed. This study was conducted under the ethical principles of the declaration of Helsinki. The study had the approval of the institutional ethics committee of King George Medical University Lucknow, India. The 100 children on the age and gender adjusted body mass index (BMI) ≥85th percentile was enrolled as obese without metabolic syndrome (control group) and the 120 children also having BMI ≥85 percentile to reflect overweight/obese with metabolic syndrome [BMI in percentile according to center for disease control and prevention (CDC) BMI growth chart] were enrolled as subjects according to National Cholesterol Education Program (NCEP-ATP III) [14]. The subjects were divided into study and control groups on the basis of International diabetes federation (IDF) guideline [31]. The subjects were recruited under homogeneous condition in both groups. "There is no conflict of interest to disclose" in the study.

2.2. Anthropometric measurements

Weight and height were measured to the nearest 0.1 kg and 0.5 cm respectively. The height was measured in a conventional stadiometer. Weight was assessed with children wearing minimal clothing using an electronic scale, previously calibrated. All subjects were evaluated by BMI calculated as weight (in kilograms) divided by height (in meters squared). But according to IDF guideline for children (Table 1), BMI in percentile is the determining factor of obesity in children, which was determined by using online BMI-for-age CDC software with the Lambda, Mu, Sigma (LMS) [15,32].

According to the Centres for Disease Control and Prevention (CDC) growth charts, adolescents with an 85th to <94th percentile of body mass index for age and gender were classified as overweight. Those with ≥95th percentile was classified as obese respectively.

Additionally, waist circumference (WC), systolic and diastolic blood pressure (BP) was also calculated. Waist circumference was measured at the midpoint between the lateral iliac crest and the lowest rib in cm during expiration, to the nearest 0.1 cm. Blood pressure was measured with an appropriate size cut-off with a standardized automated B.P. instrument for children in the right arm in the sitting position, the average of three readings was recorded for analysis. Elevated systolic or diastolic blood pressure was defined as values above the 90th percentile for age and gender [33].

2.3. Biochemical assay

The peripheral blood samples were collected following 10–12 h overnight fasting. Serum was separated, aliquoted and stored at −80 °C. All samples were analyzed by means of a single assay. GOD/POD method was used for the measurement of fasting serum glucose (Randox Laboratories Ltd., Antrim, UK). Serum lipid profile such as total cholesterol (TC), high density lipoprotein (HDL), triglyceride (TG)) was done by using enzymatic method (Randox Laboratories Ltd., Antrim, UK). LDL and VLDL were calculated by Friedewald formula [16].

VLDL = Triglyceride/5.

LDL-Cholesterol = Total Cholesterol- (HDL-C + VLDL).

2.4. Determination of serum IL-10, omentin-1 and visfatin levels

The serum concentration of IL-10, omentin and visfatin was measured with sandwich enzyme-linked immunosorbent assay (ELISA) kit (Biovendor Research and Diagnostic Products), according to the manufacturer's protocol. Serum samples were diluted with 1:3 with dilution buffer. The lowest level of human IL-10, omentin-1 and visfatin detectable by the assay was 0.99 pg/ml, 0.50 ng/ml, 0.027 ng/ml respectively. The storage temperature for these proteins was 2–8 °C. The inter-assay variability for IL10 was 4.8% and the intra-assay variability was 5.3%, for omentin-1 inter-assay variability 4.6% and intra-assay variability 3.7% and for visfatin inter-assay 6.3% and intra-assay variability was 2.3%. For this analysis, an aliquot of serum kept at −20 °C was thawed for the first time and processed.

2.5. Ethics

The study was performed in accordance with the ethical standard laid down by the Declaration of Helsinki and was approved by the Institutional Ethical Committee of King George's Medical

Table 1
IDF proposal for metabolic syndrome definition in children & adolescents.

Criteria	Age 6-<10 years	Age 10–16 years	>16 years
Adiposity definition	WC ≥ 90th percentile	WC ≥ 90th percentile	WC ≥ 90 cm (boys) or ≥ 80 cm (girls)
Glucose metabolism	Without cut-off definition for MS Diagnosis	Fasting blood glucose ≥ 100 mg/dl	Fasting blood glucose ≥ 100 mg/dl
Dyslipidaemia			
TG	Without cut-off definition for MS Diagnosis	≥150 mg/dl	≥150 mg/dl
HDL	Without cut-off definition for MS Diagnosis	≥40 mg/dl	≥40 (boys) or ≥ 50 mg/dl (girls)
Arterial hypertension	Without cut-off definition for MS Diagnosis	DBP ≥ 130 or SBP ≥ 85 mmHg	DBP ≥ 130 or SBP ≥ 85 mmHg

University UP, Lucknow and all children involved in study and their parents gave informed consent form prior to inclusion in the study. A structured performa was also filled to collect the information regarding medical, personal, family, dietary and menstrual history.

2.6. Statistical analysis

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS) version 21.0. Comparisons of continuous data between two independent groups were done by student's t-test assuming that (i) the study variable is a normal variate in the population and (ii) the variances in the two groups are homogeneous.

Paired *t*-test was applied to determine the mean difference between two groups were zero. χ [2] test were used to assess the relationship between variables in categorical data. Multiple logistic regression analysis was performed to test the IL-10, omentin-1 & visfatin as a dependent variable separately regressed over independent variables like metabolic risk factors (BMI-percentile, WC, SBP, fasting blood glucose, TG, HDL). All statistical tests were two tailed. The value $P > 0.05$ was considered to be significant.

3. Results

Compared with obese without MS children & adolescents, obese with MS children & adolescents have all laboratory values (fasting plasma glucose, lipid profile TG & VLDL-C) significantly higher ($p < 0.01$) except LDL-C, HDL-C & total cholesterol (TC). Triglyceride (TG) is a better index in this group (Table 2). Serum levels of circulating IL-10 and omentin-1 were significantly lower ($p < 0.01$) but serum visfatin level was significantly higher ($p < 0.01$) in obese subjects with MS than without MS. In both groups, there were no significant difference in IL-10 & omentin-1 levels in boys & girls but level of visfatin was significantly higher ($p < 0.01$) in girls (15.23 ± 5.89) than boys (9.30 ± 4.51) in the obese with MS subjects (Table 3).

The level of IL-10 was insignificantly lower in pre-pubertal (Age 5–11 years) and pubertal (Age 12–17 years) children in the MS group. The level of omentin-1 was significantly lower ($p < 0.01$) in pubertal than pre-pubertal group of children with MS while the level of visfatin was significantly higher ($p < 0.01$) in prepubertal group than pubertal group with MS (Table 4).

It showed that IL-10 was significantly associated ($p < 0.01$) with three metabolic risk factors while omentin-1 and visfatin were significantly associated ($p < 0.01$) with two metabolic risk factors out of six in girls (best coefficient with TG ($R = 0.592$) rather than boys, so out of three adipokines, IL-10 may be an early diagnostic marker for assessment of metabolic syndrome in girls (Table 5).

It showed that IL-10 was significantly associated ($p < 0.01$) with four metabolic risk factors while omentin-1 was significantly associated ($p < 0.01$) with three and visfatin was significantly associated ($p < 0.01$) with two metabolic risk factors out of six in pubertal groups rather than prepubertal group [best associated with BMI-percentile ($R = 0.66$)], so out of three adipokines IL-10 may be a good marker for assessment of any cardiovascular risk factor in pubertal group of children (Table 6).

4. Discussion

Obesity plays a central role in the development of MS and

Table 2
Anthropometric and biochemical characteristics of study children of without MS (n = 100) and with MS (n = 120).

Characteristics	Without MS (n = 100) (45.45%)	With MS (n = 120) (54.55%)
Weight (Kg)	37.96 ± 9.54	44.98 ± 12.45**
Height (cm)	144.19 ± 13.87	133.54 ± 16.21**
BMI(Kg/m*m)	17.88 ± 1.34	24.85 ± 3.49**
BMI (Percentile)	54.75 ± 12.67	94.66 ± 4.08**
BMI z-score	0.14 ± 0.35	1.80 ± 0.58**
Age (Years)	11.23 ± 2.77	10.72 ± 2.97 (NS)
Systolic BP (mm Hg)	105.83 ± 9.53	114.88 ± 7.29**
Diastolic BP (mm Hg)	68.32 ± 7.14	77.16 ± 5.66**
Waist circumference(cm)	74.26 ± 7.81	78.59 ± 8.10**
Fasting glucose, mg/dl	107.42 ± 4.45	115.02 ± 12.51**
Blood Glucose (PP)	151.03 ± 15.40	145.96 ± 3.13**
Triglycerides (mg/dl)	103.09 ± 13.86	114.63 ± 9.86**
Total cholesterol (mg/dl)	184.80 ± 7.71	188.51 ± 24.88(NS)
LDL-cholesterol (mg/dl)	121.19 ± 7.99	122.83 ± 24.23(NS)
HDL-cholesterol (mg/dl)	42.59 ± 4.09	42.66 ± 6.12(NS)
VLDL-cholesterol(mg/dl)	20.6182 ± 2.77	23.0975 ± 0.72**
IL-10 Conc.(pg/ml)	17.78 ± 5.51	7.53 ± 1.32**
Omentin-1(ng/ml)	5.63 ± 0.24	2.29 ± 1.15**
Visfatin (ng/ml)	6.91 ± 1.99	12.96 ± 6.11**

MS = metabolic syndrome; BMI = body mass index, LDL = low-density lipoprotein; HDL = high-density lipoprotein; VLDL = very-low-density lipoprotein. (Data represented in mean ± SD, p»0.05 = not significant (NS), p < 0.00.05 = significant (*), p < 0.01 = highly significant (**)).

Table 3
IL-10, Omentin-1 and Visfatin level in with MS (n = 120) and without MS (n = 100) children according to sex.

Characters	Without MS (n = 100)		With MS (n = 120)	
	Boys (n = 36)	Girls (n = 64)	Boys (n = 46)	Girls (n = 74)
IL-10 (pg/ml)	6.78 ± 1.13	7.96 ± 1.22 (NS)	18.69 ± 7.38	17.22 ± 3.86 (NS)
Omentin-1(ng/ml)	5.35 ± .081	5.80 ± .111 (NS)	1.60 ± .946	2.71 ± 1.05 (NS)
Visfatin (ng/ml)	4.78 ± .919	8.11 ± 1.31 (NS)	9.30 ± 4.51	15.23 ± 5.89**

(Data represented in mean ± SD, p»0.05 = not significant (NS), p < 0.00.05 = significant (*), p < 0.01 = highly significant (**)).

Table 4
IL-10, Omentin-1 and Visfatin levels in with MS (n = 120) and without MS (n = 100) children according to pubertal status.

Characters	Without MS (n = 100)		With MS (n = 120)	
	5–11 years (Prepubertal group) (n = 49)	12–17 years (Pubertal group) (n = 51)	5–11 years (Prepubertal group) (n = 55)	12–17 years (Pubertal group) (n = 65)
IL-10(pg/ml)	18.58 ± 5.43	16.85 ± 5.49 (NS)	7.26 ± 1.32	7.79 ± 1.26 (NS)
Omentin-1(ng/ml)	5.60 ± .237	5.67 ± .241(NS)	2.60 ± 1.071	1.92 ± 1.13**
Visfatin (ng/ml)	6.59 ± 1.93	7.22 ± 2.02 (NS)	14.22 ± 5.95	11.46 ± 6.00**

(Data represented in mean ± SD, p»0.05 = not significant (NS), p < 0.00.05 = significant (*), p < 0.01 = highly significant (**)).

Table 5
Gender based logistic regression analysis between the proteins and metabolic risk factors in obese with MS children (n = 120).

Metabolic risk parameters	IL-10		Omentin-1		Visfatin	
	Boys (n = 46)	Girls(n = 74)	Boys (n = 46)	Girls (n = 74)	Boys (n = 46)	Girls (n = 74)
BMI (percentile)	0.39	0.31**	0.549	0.283*	0.328	0.263**
Waist Circumference(cm)	−0.04**	−0.66*	−0.336**	−0.487	0.248	−0.478*
Triglyceride (mg/dl)	0.49*	0.59**	0.272	0.550**	0.346**	0.540
HDL (mg/dl)	0.35**	0.52**	0.549	0.480**	0.474*	0.457
Systolic Blood Pressure(mmHg)	0.29	0.19	0.358	0.249	0.397	0.265**
Fasting blood glucose (mg/dl)	0.47	0.45	0.531*	0.393	0.749	0.937

Association is *significant at the level 0.05, ** highly significant at the 0.01 level (2-tailed).

Table 6
Puberty based logistic regression analysis between the proteins and metabolic risk factors in obese with MS children (n = 120).

Metabolic risk parameters	IL-10		Omentin-1		Visfatin	
	5–11 years (Prepubertal group) (n = 55)	12–17 years (Pubertal group) (n = 65)	5–11 years (Prepubertal group) (n = 55)	12–17 years (Pubertal group) (n = 65)	5–11 years (Prepubertal group) (n = 55)	12–17 years (Pubertal group) (n = 65)
BMI (percentile)	0.35	0.66**	0.58	0.632*	0.532	0.658**
Waist Circumference(cm)	−0.02**	−0.04**	−0.36**	−0.228**	0.378	−0.188*
Triglyceride (mg/dl)	0.68*	0.47**	0.29	0.439**	0.234**	0.407
HDL (mg/dl)	0.48**	0.09**	0.59	0.328**	0.591*	0.370
Systolic Blood Pressure(mmHg)	0.37	0.29	0.49	0.133	0.498	0.165**
Fasting blood glucose (mg/dl)	0.54	0.56*	0.69	0.487	0.721	0.478

Association is *significant at the level 0.05, ** highly significant at the 0.01 level (2-tailed).

development of adult's morbidity [17] due to intake of high calorific diet & have low physical activity [18] in children. A recent research has demonstrated that the dysregulation of numerous neuroendocrine peptides & cytokines secreted from adipose tissues play a role in the development of the MS [19].

It has been demonstrated in obesity that the serum IL-10 levels were associated with MS more clearly and independently than the other inflammatory factors. Therefore, it is possible that decreased plasma concentrations of IL-10 play a significant role in the development of the MS in childhood obesity [21].

Our results are in agreement with previous studies linking low IL-10 production with type 2 diabetes in an elderly population and low IL-10 levels with metabolic syndrome within the subgroups of lean and obese women [22]. In our study, we have found low level of serum IL-10 concentration in obese with MS on contrary without MS children. In contradictory of our study, Esposito et al. reported that circulating levels of IL-10 are elevated in obese women and that low levels of IL-10 are associated with the MS [23]. Recent studies have demonstrated associations between lower serum IL-10 concentration and clinical events with MS [24]. It is possible that children with a reduced capacity of producing IL-10 in adult age presented a progressive decrease of serum IL-10 concentration and an increased risk for developing metabolic risk factors.

We demonstrated significant association between triacyl glyceride, BMI & IL-10 ($p < 0.01$) in obese with MS children, no any difference was found in the mean value of IL-10 concentration at pubertal stage (age 12–17 years) & non-significantly lower concentration of IL-10 was observed in girls in comparison to boys. Manigrasso et al. described no correlation of IL-10 with BMI and triacylglycerol in both boys and girls children [25]. Our data provide the first evidence linking low level of IL-10 concentration with MS in Indian obese children specially in girls.

This study was undertaken to better understand the role of plasma omentin-1 in MS in obese children. As, we have found inverse relation of this secretory protein in obese with MS groups (Table 2) & a significant association ($p < 0.01$) of omentin-1 with WC, TG & HDL (Tables 5 and 6). The de Souza Batistaet al, study also support our results, as they measured plasma levels of omentin in lean, overweight and obese subjects [26] and found plasma omentin were significantly higher ($p < 0.01$) among the lean subject and the level was inversely associated with BMI, waist circumference & other responsible factors for MS. Thus, from our study obesity is considered as a state of chronic low-grade inflammation.

In our study, we have found significant elevated ($p < 0.01$) visfatin level in obese with MS children specially in girls than boys compared to obese without MS children (Tables 2 and 3), which supported by Krzyzanowska et al., 2006 study, as they reported that visfatin significantly elevated ($p < 0.01$) in women with gestational diabetes which is a classic example of metabolic risk factors [28]. As in another study, Sandeep et al., in 2006 reported in Asian Indians diabetic subjects that elevated serum visfatin levels in obese subjects sounds acceptable because visceral fat is the source of Visfatin [30].

This present study had a number of limitations. First, our analyses are based on single measurements of blood IL-10, omentin-1 and visfatin level, which may not reflect the relationship over time, it would be measure serial changes of plasma IL-10, omentin-1 and visfatin levels in obese with MS subjects to further clarify the role of these three secretory proteins in the development of metabolic risk factors. Secondly, the lack of comparable study of obese children with non-obese children of same age group, due to limitation of time. Therefore, a further study is needed with large sample size to confirm our results.

5. Conclusion

In our knowledge this is the first time that the present study clearly indicates that lower circulating IL-10, omentin-1 concentration together with higher serum visfatin concentration are associated with an increase of numerous metabolic risk factors in children. Because all three adipokines are continue variables & are subjects to wide variability so for diagnosis purpose, these characteristics have uncertainty of reliability, thus determination of these adipokines are associated with metabolic risk factors in obese children. These may be good markers for epidemiological studies. As our study reported that IL-10 was associated with more than two metabolic risk factors in girls of pubertal age rather than prepubertal or boys than omentin-1 and visfatin. So, suggesting that IL-10 is the best adipokines out of three, which may serve as early biomarkers for assessment of metabolic risk factors in children.

Conflicts of interest

All the authors declare no conflict of interest with regard to this study.

Acknowledgments

We would like to thanks to Moraceae Pharmaceutical Pvt Ltd. for financial support.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.01.052.

References

[1] World Health Organization. reportScreening for type 2 diabetes: report of a world health organization and international diabetes federation meeting.
[2] Magrone T, Jirillo E. Childhood obesity: immune response and nutritional approaches. Front Immunol 2015 Feb 24;6:76.
[3] Midha T, Nath B, Kumari R, Rao YK, Pandey U. Childhood obesity in India: a meta-analysis. Indian J Pediatr 2012 Jul 1;79(7):945–8.
[4] Khadilkar VV, Khadilkar AV, Cole TJ, Chiplonkar SA, Pandit D. Overweight and obesity prevalence and body mass index trends in Indian children. Int J Pediatr Obes 2011 Jun 1;6(sup3):e216–24.
[5] Zimmet P, Alberti KG, Kaufman F, Tajima N, Silink M, Arslanian S, Wong G, Bennett P, Shaw J, Caprio S, IDF Consensus Group. The metabolic syndrome in children and adolescents–an IDF consensus report. Pediatr Diabetes 2007 Oct;8(5):299–306.
[6] Wang Y, Lobstein TI. Worldwide trends in childhood overweight and obesity. Int J Pediatr Obes 2006 Jan 1;1(1):11–25.
[7] Bremer AA, Mietus-Snyder M, Lustig RH. Toward a unifying hypothesis of metabolic syndrome. Pediatrics 2012 Mar 1;129(3):557–70.
[8] Knights AJ, Funnell AP, Pearson RC, Crossley M, Bell-Anderson KS. Adipokines and insulin action: a sensitive issue. Adipocyte 2014 Apr 8;3(2):88–96.
[9] Calcaterra Valeria, De Amici Mara, Klersy Catherine, et al. Adiponectin, IL-10 and metabolic syndrome in obese children and adolescents. Acta Biomed 2009;80:117–23.
[10] Yang RZ, Lee MJ, Hu H, Pray J, Wu HB, Hansen BC, Shuldiner AR, Fried SK, McLenithan JC, Gong DW. Identification of omentin as a novel depot-specific adipokine in human adipose tissue: possible role in modulating insulin action. Am J Physiol Endocrinol Metab 2006 Jun;290(6):E1253–61.
[11] Pan HY, Guo L, Li Q. Changes of serum omentin-1 levels in normal subjects and in patients with impaired glucose regulation and with newly diagnosed and untreated type 2 diabetes. Diabetes Res Clin Pract 2010 Apr 1;88(1):29–33.
[12] Chen MP, Chung FM, Chang DM, Tsai JC, Huang HF, Shin SJ, Lee YJ. Elevated plasma level of visfatin/pre-B cell colony-enhancing factor in patients with type 2 diabetes mellitus. J Clin Endocrinol Metab 2006 Jan 1;91(1):295–9.
[13] Belo VA, Luizon MR, Lacchini R, Miranda JA, Lanna CM, Souza-Costa DC, Tanus-Santos JE. The effects of NAMPT haplotypes and metabolic risk factors on circulating visfatin/NAMPT levels in childhood obesity. Int J Obes 2015 Jan;39(1):130.
[14] Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994. Arch Pediatr Adolesc Med 2003 Aug 1;157(8):821–7.
[15] Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ 2000 May 6;320(7244):1240.
[16] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972 Jun 1;18(6):499–502.
[17] Isomaa BO, Almgren P, Tuomi T, Forsén B, Lahti K, Nissén M, Taskinen MR, Groop L. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care 2001 Apr 1;24(4):683–9.
[18] Kelishadi R. Childhood overweight, obesity, and the metabolic syndrome in developing countries. Epidemiol Rev 2007 Jan 1;29(1):62–76.
[19] Matsuzawa Y, Funahashi T, Nakamura T. Molecular mechanism of vascular disease in metabolic syndrome X. J Diabetes Complicat 2002;1(16):17–8.
[21] Ryo M, Nakamura T, Kihara S, Kumada M, Shibazaki S, Takahashi M, Nagai M, Matsuzawa Y, Funahashi T. Adiponectin as a biomarker of the metabolic syndrome. Circ J 2004;68(11):975–81.
[22] Nishida M, Moriyama T, Sugita Y, Yamauchi-Takihara K. Interleukin-10 associates with adiponectin predominantly in subjects with metabolic syndrome. Circ J 2007;71(8):1234–8.
[23] Esposito K, Pontillo A, Giugliano F, Giugliano G, Marfella R, Nicoletti G, Giugliano D. Association of low interleukin-10 levels with the metabolic syndrome in obese women. J Clin Endocrinol Metab 2003 Mar 1;88(3):1055–8.
[24] van Exel E, Gussekloo J, de Craen AJ, Frölich M, Bootsma-van der Wiel A, Westendorp RG. Low production capacity of interleukin-10 associates with the metabolic syndrome and type 2 diabetes: the Leiden 85-Plus Study. Diabetes 2002 Apr 1;51(4):1088–92.
[25] Martos-Moreno GÁ, Barrios V, Argente J. Normative data for adiponectin, resistin, interleukin 6, and leptin/receptor ratio in a healthy Spanish pediatric population: relationship with sex steroids. Eur J Endocrinol 2006 Sep 1;155(3):429–34.
[26] de Souza Batista CM, Yang RZ, Lee MJ, Glynn NM, Yu DZ, Pray J, Ndubuizu K, Patil S, Schwartz A, Kligman M, Fried SK. Omentin plasma levels and gene expression are decreased in obesity. Diabetes 2007 Jun 1;56(6):1655–61.
[28] Krzyzanowska K, Krugluger W, Mittermayer F, Rahman R, Haider D, Shnawa N, Schernthaner G. Increased visfatin concentrations in women with gestational diabetes mellitus. Clin Sci 2006 May 1;110(5):605–9.
[30] Sandeep S, Velmurugan K, Deepa R, Mohan V. Serum visfatin in relation to visceral fat, obesity, and type 2 diabetes mellitus in Asian Indians. Metabolism 2007 Apr 1;56(4):565–70.
[31] Mancini MC. Metabolic syndrome in children and adolescents-criteria for

diagnosis. Diabetol Metab Syndrome 2009 Dec;1(1):20.
[32] Ogden CL, Kuczmarski RJ, Flegal KM, Mei Z, Guo S, Wei R, Grummer-Strawn LM, Curtin LR, Roche AF, Johnson CL. Centers for disease control and prevention 2000 growth charts for the United States: improvements to the 1977 national center for health statistics version. Pediatrics 2002 Jan 1;109(1):45–60.
[33] National Heart Lung, Blood Institute. Update on the 1987 Task Force report on high blood pressure in children and adlescents: a work group report from the national high blood pressure education program. Pediatrics 1996;98: 649–57.