Table (1) Sex differences in the clinical, anthropometric parameters and laboratory investigations among total children

Parameters		Male (N= 45)		Female (N= 66)		(z)	p
		Mean	±Sd	Mean	±Sd		
Age (Years)		8.74	1.60	8.78	1.73	−0.226	0.821
Blood Pressure	SBP (mmHg)	102.15	18.88	103.11	11.36	−0.387	0.699
	DBP (mmHg)	63.44	12.10	63.56	7.68	−0.974	0.330
Anthropometry	Weight (Kg)	46.30	18.36	45.96	20.57	−0.003	0.998
	Height (Cm)	133.91	14.48	133.14	18.05	−0.051	0.959
	BMI (kg/m^2)	24.70	6.36	24.40	7.27	−0.063	0.950
	WC (Cm)	79.24	16.66	78.83	18.66	−0.123	0.902
	HC (Cm)	87.13	17.11	87.92	22.26	−0.183	0.855
Lab.	FBG (mg/dl)	88.14	15.24	94.00	17.34	− 1.882	0.060
	Insulin (uIU/mL)	8.58	9.12	8.34	10.66	−0.932	0.351
	Homa- Ir	2.53	6.02	1.98	2.60	−0.409	0.682
Lipid Profile	Cholesterol (mg/dl)	165.82	36.48	166.62	26.05	−0.828	0.408
	TG (mg/dl)	88.51	29.11	86.00	27.40	− 1.320	0.187
	HDL (mg/dl)	50.27	25.11	48.58	13.69	−0.721	0.471
	LDL (mg/dl)	66.84	10.47	66.86	8.24	−0.172	0.864
	Visfatin (ng/ml)	2.98	3.04	2.77	2.70	0.375	0.708
	FGF-21 (pg/ml)	48.72	39.74	39.33	36.19	−0.083	0.943

N.B.: p<0.05= significant differences. SBP systolic blood pressure, DBP diastolic blood pressure, WC waist circumference, HC hip circumference, FBG fasting blood glucose, HOMA- IR (Homeostasis Model Assessment- Insulin Resistance), TG= triglycerides, HDL (high- density lipoprotein, LDL= low- density lipoprotein. FGF-21 fibroblast growth factor 21

Table (2) Spearman's Correlation between Visfatin and FGF-21 with clinical, anthropometric parameters and laboratory investigations among total sample

Parameters	Visfatin ng/ml		FGF-21 pg/ml	
	r	P- Value	r	P- Value
Age (Years)	−0.006	0.953	0.093	0.336
SBP (mmHg)	0.115	0.233	0.237	0.013
DBP (mmHg)	0.136	0.155	0.239	0.012*
Weight (Kg)	0.103	0.286	0.298	0.002**
Height (Cm)	0.039	0.682	0.198	0.039*
BMI (kg/m2)	0.101	0.293	0.280	0.003**
WC (Cm)	0.133	0.167	0.355	0.000**
HC (Cm)	0.069	0.477	0.282	0.003**
FBG (mg/dl)	−0.069	0.478	0.133	0.168
Insulin (uIU/mL)	0.049	0.615	0.181	0.062
Homa- Ir	0.041	0.676	0.189	0.051
Cholesterol (mg/dl)	−0.011	0.911	−0.007	0.944
TG (mg/dl)	0.048	0.617	0.186	0.052
HDL (mg/dl)	0.177	0.064	0.101	0.296
LDL (mg/dl)	0.096	0.319	0.054	0.580
Visfatin (ng/ml)	-	-	0.585	0.000**
FGF-21 (pg/ml)	0.585	0.000**	-	-

N. B.: p<0.01= highly significant differences, p<0.05= Significant differences. SBP systolic blood pressure, DBP diastolic blood pressure, WC waist circumference, HC hip circumference, FBG fasting blood glucose, HOMA- IR (Homeostasis Model Assessment- Insulin Resistance), TG= triglycerides, HDL (high- density lipoprotein, LDL= low- density lipoprotein. FGF-21 fibroblast growth factor 21

Table (3) Partial Correlation to exclude effect of age between Visfatin and FGF-21 with clinical and anthropometric parameters among total sample

Parameters	Visfatin Ng/Ml		FGF-21 pg/ml	
	r	P- Value	r	P- Value
SBP (mmHg)	0.171	0.080	0.247	0.011
DBP (mmHg)	0.169	0.083	0.187	0.055
Weight (Kg)	0.008	0.936	0.113	0.250
Height (Cm)	−0.009	0.930	0.143	0.144
BMI (Kg/m^2)	0.015	0.880	0.112	0.251
WC (Cm)	0.017	0.867	0.114	0.243
HC (Cm)	0.049	0.615	0.134	0.169
FBG (mg/dl)	−0.027	0.787	0.071	0.473
Insulin (uIU/mL)	−0.051	0.602	−0.069	0.481
Homa- Ir	−0.063	0.524	−0.065	0.508
Cholesterol (mg/dl)	0.084	0.389	0.044	0.653
TG (mg/dl)	0.097	0.323	0.124	0.204
HDL (mg/dl)	0.106	0.281	0.028	0.776
LDL (mg/dl)	−0.037	0.710	−0.050	0.608
Visfatin (ng/ml)	-	-	0.765	0.000**
FGF-21 (pg/ml)	0.765	0.000**	-	-

N.B.: p< 0.01= highly significant differences, p< 0.05= Significant differences. SBP systolic blood pressure, DBP diastolic blood pressure, WC waist circumference, HC hip circumference, FBG fasting blood glucose, HOMA- IR (Homeostasis Model Assessment- Insulin Resistance), TG= triglycerides, HDL (high-density lipoprotein, LDL= low-density lipoprotein. FGF-21 fibroblast growth factor 21

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metabolic syndrome (MS).

Conclusion:

Fibroblast growth factor-21 and Visfatin had highly significant positive correlations with each other among the Egyptian children, which persist after exclusion of age effect. Both FGF-21 and Visfatin had insignificant correlations with the metabolic disturbance risk factors (FBG, insulin, HOMAR and lipid profile). FGF-21 only had significant positive correlations with blood pressure and the obesity markers, but Age had an effect on these relations.

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c. Serum Visfatin and FGF-21 were measured by enzyme linked immunosorbent assay kit (ELISA) based on the principle of competitive enzyme immunoassay.

Statistical Analysis:

Collected data were complied, coded; verified and analysis was performed using the computer program SPSS (Statistical package for social science) version 18. Normality of data was tested using the Kolmogorov- Smirnov test. Most of the variables; such as the data of BMI, WC and laboratory investigations; particularly Visfatin and FGF-21; were not normally distributed. So, the data was analyzed using non parametric tests.

Descriptive statistics (mean± standard deviation) were calculated for the anthropometric parameters and laboratory investigations. In order to find out whether there are group differences, Mann- Whitney test was carried out to compare between 2 groups for the parametric data (quantitative). Spearman´s correlation was used to assess the association between either Visfatin or FGF21 with all the studied variables. Standards of probability were set to P< 0.01; which considered highly significant; and P< 0.05; which considered statistically significant; in all analyses.

Results:

This study included 111 children: 45 males with mean age 8.74± 1.60 years and 66 females with mean age 8.78± 1.73 years. There were insignificant sex differences in all the studied variables: age, clinical, anthropometric parameters and laboratory investigations table (1). So the analysis was completed as one sample; without sex differentiation.

Spearman's correlation analysis between FGF-21 and Visfatin in one side and all the studied variables on the other side among total sample were presented in table (2). Visfatin and FGF-21 had highly significant positive correlations with each other. Serum FGF-21 had highly significant positive correlations with weight, BMI, WC and HC, and significant positive correlations with SBP, DBP and height. On the other side, serum Visfatin had insignificant correlations with blood pressure and all the anthropometric parameters under study. Both FGF-21 and Visfatin had insignificant correlations with the laboratory investigations (FBG, insulin, HOMA- IR and lipid profile)

Partial Correlations; to exclude effect of age; between FGF-21 and Visfatin in one side and the studied variables on the other side among total sample were presented in table (3). The significant positive correlation between serum Visfatin and FGF-21 still presents after exclusion of age effect. Insignificant correlations were found between either FGF-21 and Visfatin and all of the studied parameters.

Discussion:

The current sample found insignificant sex differences in all the studied variables: age, clinical, anthropometric parameters and laboratory investigations. So the analysis was completed as one sample; without sex differentiation.

In agreement with the current results, Kim et.al. (2018) and Kozioł-Kozakowska et.al. (2020) found insignificant sex difference in the anthropometric parameters and obesity- related biomarkers among children and adolescents. Reddy et.al. (2020) found insignificant sex difference in the lipid profile among children. Insignificant sex difference in the serum Visfatin level was reported previously by Ismaiel et.al. (2021); among obese children with fatty liver disease; Tahir et.al. (2021); in Iraqi obese adolescence (with and without metabolic syndrome) and Jurdana et.al. (2013); among obese adults. While the insignificant sex difference in the level of serum FGF-21, comes in agreement with that concluded in previous studies conducted on both children and adolescents (Baek et.al., 2017; Akduman et.al., 2022).

In contrary to current results, Da Silva et.al. (2020) found that adolescent males had significant higher body weight than females. Asif et.al. (2021) reported that body height, weight and WC were higher in boys than girls with mean age of 8.87 years. Song et.al. (2020) found significant sex difference in the lipid profile (triglycerides, cholesterol, LDL and HDL) where adolescent's females had higher values than males; it may be due to the difference in age group and effect of puberty.

In the current study, assessment of serum FGF-21, Visfatin and their relation to each other and the rest of studied variables among the total sample, revealed that both Visfatin and FGF-21 had highly significant positive correlations with each other; serum FGF-21 had highly significant positive correlations with most of the anthropometric measurements under study (weight, BMI, WC and HC), and significant positive correlations with DBP and height. While serum Visfatin had insignificant correlations with blood pressure and all the anthropometric parameters under study. Both FGF-21 and Visfatin had insignificant correlations with the laboratory investigations (FBG, insulin, HOMA and lipid profile)

In agreement with the current results, Socha- Banasiak et.al (2020) reported that FGF-21 levels correlated with both the adiposity markers and blood pressure. Baek et.al. (2017) also found that serum FGF21 levels were remarkably increased in obese children. Li et.al. (2017) found that FGF21 levels were negatively correlated with insulin, HOMA- IR and leptin levels after adjusting for age, gender, puberty and lifestyle factors. Elkabany et.al. (2020) also found higher Visfatin levels among patients with dyslipidemia.

In contrary, Alnowihi et.al. (2020) found positive correlations were observed between Visfatin levels and waist and hip circumferences, BMI, diastolic BP, systolic BP (SBP) insulin, HOMA- IR, and LDL- C levels (P< 0.001- P< 0.05). Negative correlations were observed between Visfatin levels and HDL- C. Socha- Banasiak et.al (2020) found that increased FGF-21 concentrations in children and adolescents with

Introduction:

Fibroblast growth factor- 21 (FGF-21); a novel protein, has been identified to play an important role in liver and adipose tissue metabolism. FGF-21 is a member of the FGF family representing a group of peptides that regulate diverse biological functions, including cell differentiation, cell growth, and angiogenesis (Cuevas- Ramos et.al., 2019). Reinehr et.al. (2012) found that increased FGF-21 serum levels had shown not only to be associated with childhood obesity, but also with disturbed metabolic parameter such dyslipidemia and insulin resistance.

Visfatin is an adipokine that is predominantly expressed in visceral fat tissue and/or adipose tissue macrophages (Balistreri et.al., 2010). Adipose tissue was found to be actively secreting many adipokines as leptin, adiponectin, resistin and Visfatin. Much is known about leptin, adiponectin, resistin etc but very little is known about Visfatin as it is discovered recently and also has been found to be widely expressed and is associated with variety of functions in different cell types (Harrison's principles of internal medicine, 20th ed., Biology of Obesity).

This study aimed to assess the relation between plasma FGF-21 and Visfatin with each other, and their relations with the metabolic disturbances risk factors in Egyptian children.

Subjects:

A case- control cross sectional study was done, included 111 children (45 males and 66 females); with age ranged between 6 up to 10 years to avoid the effect of puberty (prepubertal). It was conducted in "Management of Visceral Obesity and Growth Disturbances clinic", in "Medical Excellence Research Centre MERC", National Research Centre (NRC), Giza, Egypt.

Ethical Consent:

Ethical approval was obtained from both the Ethics Committee of "Faculty of Postgraduate Childhood Studies" and that of the "National Research Centre" (Approval No 17125). Informed written consents were obtained from one of the parents after explanation of the aim of the study and its possible benefits for identifying the impact of obesity on health. This was confirmed orally and by the personally dated signature from one of the parents.

Methods:

Each child was subjected to the following: full history was taken, clinical examination including blood pressure, anthropometric measurements and laboratory investigations.

1. Full History Taking: Including:
    a. Personal History: Name, age (date of birth), sex and address.
    b. Present History: Onset (acute or gradual), course (i.e. the progress) and duration of gaining weight, previous diet regimens, medical attention and medications received.
    c. Past History: Birth weight, neonatal complications, type of feeding (breast feeding, artificial or mixed), and weaning age.
    d. Family History: Family history of (positive consanguinity, obesity, type 2 diabetes, cardiac disease& hypertension).
2. General Clinical Examination: Including cardiac, chest and abdominal examination; to exclude presence of any chronic or genetic disorders; with special emphasis on endocrinal diseases; that would affect the normal growth of the children.
3. Blood Pressure Measurement: Both systolic and diastolic blood pressures were measured in the sitting position using a standardized mercury sphygmomanometer with an age appropriate blood pressure cuff that cover at least two thirds of the left upper arm length and did not encroach on the antecubital space. Three successive blood pressure readings were taken, and if the error was acceptable the mean was recorded (Lee et.al., 2020).
4. Anthropometric Assessment:
    a. Anthropometric measurements; body weight, height, waist and hip circumferences; were performed using standardized equipment's following the recommendations of the International Biological Program (Hiernaux and Tanner, 1969).
    b. Weight was measured using a digital SECA scale balance (Model 707 standing scale). Children were weighed wearing light clothes; with no shoes; while standing on the scale with their weight equally placed on both feet. Weight was measured and recorded to the nearest 0.1kg. Height was measured using a wall mounted Holtain Stadiometer. Each child was asked to remove his clothes, except for light underwear and stand with their feet fairly close together then asked to breathe normally. Height was measured three times and the average was recorded to the nearest 0.1cm. Waist circumference (WC) was measured at a level midway between the lower rib margin and iliac crest using simple non-stretchable plastic measuring tape all around the body in horizontal position. The reading of the measuring tape was taken at the end of normal expiration to prevent subjects from contracting their abdominal muscles or from holding their breath. The measuring tape was held firmly, ensuring its horizontal position but loosened enough to allow the observer to place one finger between the tape and the subject's body. The readings were approximated to the nearest 0.1cm. Hip circumference (HC) was measured using flexible non- stretchable plastic tape, which was held horizontally around the maximum extension of the buttocks, the reading was approximated to the nearest 0.1cm. BMI was calculated using the formula: BMI= Weight (Kg) /[Height (m^2)] (Krebs et.al., 2007).
5. Laboratory Investigations:
    a. A 5ml sample of venous blood was obtained from each child between 09:00am and 11:00am after 12 hours of fasting. After clotting, the blood samples were centrifuged and the serum was separated and kept at –80°C for batch assessment. Professional staff performed the venipuncture for assessment of fasting blood glucose (FBG), insulin, lipid profile, Visfatin and FGF21.
    b. FBG was assessed using GOD- POD enzymatic colorimetric

Assessment of Fibroblast Growth Factor- 21 and Visfatin as Potential Predictors for Insulin Resistance in Obese Children

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Summary

Objective: To assess the relation between plasma Visfatin and fibroblast growth factor- 21 (FGF21) with each other, and their relations with the metabolic disturbances risk factors in Egyptian children.

Methods: The study included 111 children; with age ranged between 6 up to 10 years to avoid the effect of puberty (prepubertal): 45 males (with mean age 8.74± 1.60 years) and 66 females (with mean age 8.78± 1.73 years). Full History taking, general clinical examination, blood pressure measurement, anthropometric measurements (body weight, height, BMI, waist and hip circumferences) and biochemical parameters (fasting blood glucose, insulin, lipid profile, Visfatin and FGF- 21) were measured, and calculation of HOMA- IR was done.

Results: Examining the sex differences in all the studied variables: age, clinical, anthropometric parameters and laboratory investigations were insignificant. So, the analysis was completed as one sample; without sex differentiation. Spearman's correlation analysis revealed that FGF- 21 and Visfatin had highly significant positive correlations with each other. Serum FGF- 21 only had highly significant positive correlations with weight, BMI, WC and HC, and significant positive correlations with SBP, DBP and height. Both FGF- 21 and Visfatin had insignificant correlations with the laboratory investigations (FBG, insulin, HOMA- IR and lipid profile). Partial Correlations; to exclude effect of age; found that the significant positive correlation between serum Visfatin and FGF- 21 still present, while correlations between either FGF- 21 and Visfatin and all of the studied parameters became insignificant..

Conclusion: Among the Egyptian children, there were significant positive correlation between serum FGF- 21 and Visfatin. However, neither of them had significant correlations with the metabolic disturbances risk factors.

Keywords: Visfatin, FGF21, blood pressure, anthropometry, lipid profile, Egyptian children.

تقييم عامل نمو الخلايا الليفية-٢١ وفيسفاتين كمؤشرات محتملة لمقاومة الأنسولين في الأطفال المصابين بالسمنة

الهدف: تقييم العلاقة بين فيسفاتين وعامل نمو الخلايا الليفية-٢١ مع بعضهما البعض وعلاقتهما بعوامل خطر الاضطرابات، الأيضية لدى الأطفال المصريين.

الطرق: اشتملت الدراسة على ١١١ طفلا. تتراوح أعمارهم بين ٦ إلى ١٠ سنوات لتجنب تأثير البلوغ (ما قبل البلوغ)، ٤٥ ذكرا (بمتوسط عمر ٨,٧٤± ١,٦٠ عاما) و٦٦ أنثى (بمتوسط عمر ٨,٧٨± ١,٧٣ عاما). أخذ التاريخ الكامل، والفحص السريري العام، وقياس ضغط الدم، والقياسات البشرية (وزن الجسم، والطول، ومؤشر كتلة الجسم، ومحيط الخصر الارداف) والمعايير البيوكيميائية (جلوكوز الدم، والأنسولين، الدهون، فيسفاتين وعامل نمو الخلايا الليفية-٢١).

النتائج: لم يكن يوجد فروق بين الجنسين في جميع المتغيرات المدروسة: العمر، والمعايير السريرية، والقياسات البشرية، والفحوصات المخبرية. لذلك، تم الانتهاء من التحليل كعينة واحدة؛ بدون تمايز بين الجنسين. كشف تحليل الارتباط لسبيرمان أن فيسفاتين وعامل نمو الخلايا الليفية-٢١ كان لهما ارتباطات إيجابية مهمة للغاية مع بعضهما البعض. كان لدى عامل نمو الخلايا الليفية-٢١ ارتباطات إيجابية ذات دلالة إحصائية مع الوزن، ومؤشر كتلة الجسم، ودورة المياه، ومحيط الارداف، وارتباطات إيجابية معنوية مع ضغط الدم الانبساطي والانقباضي والطول. كان لكل من عامل نمو الخلايا الليفية-٢١ ارتباطات غير مهمة مع التحقيقات المعملية (مستوى السكر، والأنسولين، ومعامل مقاومة الانسولين، الدهون). الارتباطات الجزئية لاستبعاد تأثير العمر؛ وجد أن الارتباط الإيجابي المعنوي بين فيسفاتين وعامل نمو الخلايا الليفية-٢١ لا يزال موجودا.

الخلاصة: بين الأطفال المصريين، كان هناك ارتباط إيجابي معنوي بين فيسفاتين وعامل نمو الخلايا الليفية-٢١ ومع ذلك، لم يكن لأي منهما ارتباطات كبيرة مع عوامل خطر الاضطرابات الأيضية.

الكلمات المفتاحية: فيسفاتين وعامل نمو الخلايا الليفية-٢١، ضغط الدم، قياس الأنثروبومترية، تحليل الدهون، الأطفال المصريون.

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