Relation between RBP4,Resistin levels and insulin resistance in obese children

[1]Medhat Hassan Shehata, [2]Hamed Ahmed Elkayat, [3]Adel Naguib Hanna, Zakaria Ahmed El-Khayat[4], Iman Hussin Kamel[5] , and Alyaa Hossny Kamhawy

[1] Professor of Pediatrics, Institute of Postgraduate Childhood Studies, Ain Shams University, [2] Professor of Pediatrics, Faculty of Medicine Ain Shams University, [3] Research Professor of child health, National Research Centre, [4]Research Professor Biochemistry, National Research Centre, [5]Assistant Research Professor of Child Health, National Research Centre

Abstract

Background: Obesity is a leading cause of morbidity and mortality worldwide and is known to arise from an imbalance between energy intake and expenditure,. Hence research into childhood obesity is of paramount importance in preventing obesity- related mortality and morbidity in adults.

Objectives: The Aim of the study is Detection of the level of the serum RBP4 and resistin level in obese children, and Evaluation of serum RBP4 and resistin as an indicator of insulin resistance by exploring the possible correlation between serum resistin level, anthropometric measurements and insulin resistance in obese non diabetic children.

Methodology: This study is a case- control study included 88 children divided as forty five obese children and young adolescents attending nutrition Clinic, Children's Hospital, Ain shams University From january 2013 to November 2013, Forty three healthy children and young adolescents age and sex matched were included as control subjects. Assessment of BMI was done using categories reported by the World Health Organization (WHO) Child Growth Charts Standards for age and sex (2007).

Results: There was positive correlation between fasting serum RBP4 and anthropometric and clinical data (weight SDS, BMI SDS, waist/hip ratio, systolic, and diastolic blood pressure), laboratory data (Fasting serum insulin, HOMA- IR, total cholesterol, LDL- c), body composition data (body fat percent, fat mass and fat free mass), There were significant negative correlations between resistin and weight, BMI, cholesterol, triglycerides, LDL and TBF%, insulin& HOMA- IR, SBP, DBP, BMR in case group. There were significant positive correlations between resistin and HDL and TBW% in the case group.

Conclusion: RBP4 is positivity correlated to serum insulin level, HOMA/IR, and lipid profile, so RBP4 can be used as a marker for insulin resistance and obesity, Studies with large sample size and high power are needed to explain the link between resistin and obesity associated insulin resistance especially in children.

Keywords: Childhood obesity, Insulin resistance, RBP4 Resistin

العلاقة بين البروتين الرابط للريتينول ٤ والرزيستين هرمون فى حالات السمنة فى الاطفال

المقدمة: فى الأونة الاخيرة يعد مرض السمنة عند الاطفال مشكلة متزايدة على مستوى العالم حيث تمثل عامل خطورة للاصابة بامراض القلب والاوعية الدموية فى الكبر. ويعتبر الاطفال البدناء اكثر عرضة لكى يصبحوا كبار بدناء فى المستقبل. لذلك يعتبر البحث فى مجال السمنة فى الاطفال فى غاية الاهمية لمنع الامراض المصاحبة لها والوفاة المبكرة التى قد تحدث كنتيجة لهذة الامراض.

الهدف: الهدف من هذا البحث هو تقييم مؤشرات السمنة، ودراسة مستوى الريزيزتين والبروتين الرابط للريتينول ٤ بالدم وإمكانية استخدامهم كمؤشر لعدم الاستجابة للأنسولين فى الأطفال المصابين بالسمنة.

المنهجية: وقد أجريت هذه الرساله على ٨٨ طفل مقسمين كالاتى ٤٥ طفل مصابين بالسمنه من المترددين على عيادة التغذية بمستشفى الأطفال الجامعى كلية الطب جامعة عين شمس ومقارنتهم بنتائج ٤٣ طفل أصحاء أجريت عليهم نفس الدراسه ولا يعانون من السمنه ومتقاربين مع المجموعه الاولى فى العمر والنوع.

النتائج: وجدنا ارتفاع فى مستوى البروتين الرابط للريتينول ٤بالدم فى الاطفال المصابين بالسمنه. وتوجد علاقة أيجابئة بين دور البروتين الرابط للريتينول ٤ فى المجموعه المصابه بالسمنه ومؤشر معامل انحراف كثافة الجسم، ضغط الدم ونسبة السكر صائم بالدم، نسبة الدهون، كتله الدهون، معدل الحرق الداخلي، نسبة الكوليسترول العامه، نسبة البروتين الدهنى عالى الكثافه نسبة الانسولين صائم بالدم، قياس معامل مقاومة الجسم للإنسولين وقد تبين من هذه الدراسة ارتفاع معدل عدم الاستجابة للأنسولين بين الأطفال المصابين بالسمنة وأيضا ارتفاع مستوى الأنسولين بالدم فى هؤلاء الأطفال وقد تبين من هذه الدراسة أن نسبة الريزيزتين بالدم تتناسب عكسيا فى المجموعه المصابه بالسمنه ومؤشر معامل انحراف كثافة الجسم، ضغط الدم ونسبة الدهون، كتله الدهون، معدل الحرق الداخلي، نسبة الكوليسترول العامه، نسبة البروتين الدهنى عالى الكثافه نسبة الانسولين صائم بالدم، قياس معامل مقاومة الجسم للإنسولين، كما وجد انة هناك علاقة عكسية بين البروتين الرابط للريتينول ٤ بالدم والريزستين هرمون.

الخلاصة: يمكن ان يستخدم البروتين الرابط للريتينول ٤ بالدم مؤشر مبكر لحدوث مقاومة الانسولين فى الاطفال والمراهقين البدناء.

Introduction:

Obesity in children and adolescents is a multi- factorial disorder, developed as a result of genetic and environmental changes, along with lack of physical activity resulting in imbalance in energy homeostasis, and accumulation of excess energy as fat. It is increasing at an alarming rate even in developing countries. (Huang, McCrory, 2005)

In last years, white adipose tissue (WAT) has been considered as an endocrine organ because of its capacity to secrete hormones and cytokines. Thus, adipose tissue is not only known for its capacity to store the excess of dietary energy in the form of triglycerides, but also is now recognized as a fundamental participant in the control of energy metabolism by secreting many proteins called adipocytokines such as retinol binding protein 4 (RBP4), resistin, tumor necrosis factor a (TNF- a), interleukin 6 (IL- 6), leptin, vaspin, visfatin, omentin, chemerin, apelin, etc.. (Rasouli and Kern, 2008) (Va´zquez-Vela et al., 2008)

Resistin is an adipokine secreted from adipose tissue, which is likely involved in the development of obesity and insulin resistance via its interaction with other organs, as well as affecting adipose tissue function. The impact of resistin treatment on lipolysis and adiponectin secretion in human visceral adipose tissue is currently unknown (Chen et al., 2014) Several experimental and clinical studies have suggested an association between increased resistin levels and severe conditions associated with obesity such as cardiovascular disease and malignancies. (Codoñer- Franch and Alonso- Iglesias, 2015)

Retinol binding protein 4 (RBP4) is a recently identified adipokine suggested to link obesity with its comorbidities, especially insulin resistance, type 2 diabetes (T2D), and certain components of the metabolic syndrome. (Primoz et al., 2011)

Objectives:

The Aim of the study is:

1. Detection of the level of the serum RBP4 and resistin level in obese children.
2. Evaluation of serum RBP4 and resistin as an indicator of insulin resistance by exploring the possible correlation between serum resistin level, anthropometric measurements and insulin resistance in obese non diabetic children.

Patients And Methods:

This case- control study included 88 children, 45 obese children compared to 43 healthy control who were recruited from the outpatient clinic of the Nutrition clinic Ain shams university from January, 2013 to November, 2013. This includes full personal, past history for systemic diseases, drug administration (as corticosteroids), and symptoms covering various systems, and family history of chronic non- communicable diseases (obesity, diabetes, cardiovascular diseases and hypertension).

All anthropometric measurements have been obtained using standardized equipment, and following the recommendations of the International Biological program (Hiernaux and Tanner, 1969).

Assessment of BMI was done using categories reported by the World Health Organization (WHO) Child Growth Charts Standards for age and sex (2007). Obesity considered when BMI exceeds 95th percentile (Schwarz and Freemark, 2010).

Waist Circumference was measured using inelastic insertion tape to the nearest 0.1 cm, with the subject in a standing position; the tape was applied horizontally midway between the lowest rib margin and the iliac crest. Assessment of waist circumference was done using categories reported by Fernandez et al., 2004. Thorough medical general examination (head& neck, chest, heart, abdomen, upper& lower limbs) including measurement of blood pressure and comparing it to age specific blood pressure percentiles reported by NHANES, 2004.

Blood samples were withdrawn from patients and controls after overnight fasting (>12 hours). Fasting venous blood samples were collected in heparinized centrifuge tubes. Plasma was separated by centrifugation (3000 rpm, 15 min). Separated plasma aliquots were removed and stored frozen at- 32 C until further analyses were carried out, following testes were performed: Fasting serum glucose, fasting serum insulin, serum retinol, RBP4 level, Cholesterol, Triglysrides, Hdl- cholesterol, LDL- cholesterol

Insulin resistance was estimated by using the Homeostasis Model Assessment (HOMA), which calculated according to the known formula, Insulin resistance being defined as a HOMA index > 3.16) The greater the HOMA value the greater the level of insulin resistance (Keskin et al., 2005).

Statistical Analysis:

Data management and analysis were performed using Statistical Package for Social Sciences (SPSS) vs.21.

Numerical data were summarized using means and standard deviations or medians and ranges. Categorical data were summarized as percentages. Comparisons between groups for normally distributed numeric variables were done using the Student's t- test while for non normally distributed numeric variables were done by Mann- Whitney test. Chisquare test or Fisher's exact test were used to compare between the groups with respect to categorical data. To measure the strength of association between numeric variables, Spearman's correlation coefficients were computed. All p- values are two- sided. P-values< 0.05 were considered significant.

Ethical Considerations:

The study protocol was reviewed and approved by the Research Ethical Committee at the National Research Center and the Ethical committee of Scientific Research at theInstitute of Postgraduate Childhood Studies, Ain Shams University and Hwritten informed consent was taken from all children's parents before enrollment in the study and after full explanation of the objectives of the study and their role in it.

Results:

Comparing studied sample as regard their anthropometric measurements, as shown in table (1), mean weight was 85.1± 19.1Kg in cases and 44.0± 12.8Kg in control, mean BMI was 33.9± 4.7in cases and 19.5± 2.9 in control while mean waist circumference was 102.3± 14.3 cm in cases and 69.2± 9.4cm in control.

There was significant difference in weight, BMI, Waist circumference, Hip circumference and waist hip ratio where p< 0.001*, while there was no significant difference as regard height measurement between cases and controls.

Table (1) Comparison of anthropometric data in obese children and control

Parameter	Measures	Cases (N= 45)	Control (N= 43)	Test Value	P
Weight (Kg)	Mean± SD	85.1± 19.1	44.0± 12.8	t=11.807	< 0.001*
	Range	56.8- 169.1	19.0- 80.0		
Weight (sds)	Med (IQR)	2.7 (2.1- 3.0)	3.3 (3.1- 3.4)	Z=- 7.951	< 0.001*
	Range	0.7- 5.2	2.8- 4.2		

Parameter	Measures	Cases (N= 45)	Control (N= 43)	Test Value	P
Height (Cm)	Mean± SD	156.2± 9.8	156.7± 11.2	t=0.242	0.810
	Range	132.0- 172.0	130.0- 173.0		
Height (sds)	Med (IQR)	- 0.6 (- 1.4- 0.1)	2.6 (2.5- 2.8)	Z=- 1.277	0.202
	Range	- 2.6- 1.3	2.0- 3.2		
BMI	Mean± SD	33.9± 4.7	19.5± 2.9	t=17.082	< 0.001*
	Range	28.0- 49.1	15.3- 24.8		
BMI (sds)	Med (IQR)	3.0 (2.6- 3.3)	0.1 (- 1.0- 1.1)	Z=- 8.068	< 0.001*
	Range	2.0- 4.2	- 1.7- 2.0		
Wc (Cm)	Mean± SD	102.3± 14.3	69.2± 9.4	t=12.746	< 0.001*
	Range	80.0- 155.0	54.0- 86.0		
Hc (Cm)	Mean± SD	117.1± 13.9	86.3± 10.8	t=11.572	< 0.001*
	Range	97.0- 185.6	68.0- 105.0		
WH Ratio	Mean± SD	0.87± 0.07	0.80± 0.06	t=5.180	< 0.001*
	Range	0.72- 1.09	0.66- 0.94		

Med (IQR): Median (1st –3rd interquartile range), *Significan, †BMI= Body Mass Index
t#: Independent t- test, χ2&: Chi square test, *Significant at p< 0.001

Table (2) Comparison of the laboratory parameters of cases and controls

Parameter	Measures	Cases (N= 45)	Control (N= 43)	t	P
Cholesterol (Mg/Dl)	Mean± SD	249.4± 88.7	183.5± 54.0	2.641	0.010*
	Range	105.9- 503.5	58.6- 288.2		
Triglycerides (Mg/Dl)	Mean± SD	243.8± 34.7	64.4± 37.9	23.185	< 0.001
	Range	196.0- 325.0	13.5- 158.6		
Ldl (Mg/Dl)	Mean± SD	173.6± 89.6	156.1± 66.2	1.036	0.303
	Range	13.2- 426.8	47.1- 300.6		
Hdl (Mg/Dl)	Mean± SD	27.1± 8.5	36.5± 9.7	4.864	< 0.001*
	Range	11.7- 53.5	22.7- 56.1		
Sgot (Iu/L)	Mean± SD	11.8± 4.7	11.4± 3.8	0.491	0.625
	Range	4.0- 24.0	4.0- 19.0		
Sgpt (Iu/L)	Mean± SD	5.3± 2.2	5.5± 2.0	0.491	0.625
	Range	4.0- 14.0	3.0- 10.0		
Glucose (Mg/Dl)	Mean± SD	81.5± 8.0	81.6± 9.0	0.026	0.979
	Range	70.0- 100.0	70.0- 110.0		
Insulin (µiu/Ml)	Mean± SD	16.4± 7.5	9.0± 4.5	5.611	< 0.001*
	Range	3.5- 40.6	1.1- 21.5		
Homa- Ir	Mean± SD	5.9± 2.7	3.3± 1.7	5.524	< 0.001*
	Range	11.0- 14.4	0.4- 7.6		
Resistin (Ng/Ml)	Mean± SD	5.8± 2.3	8.1± 2.0	0.969	< 0.001*
	Range	1.0- 10.8	4.7- 13.5		
Retinol (µmol/L)	Mean± SD	49.1± 13.4	33.7± 16.9	4.760	< 0.001*
	Range	22.9- 76.5	10.0- 69.7		
Rbp4 (µmol/L)	Mean± SD	54.1± 17.5	39.6± 11.3	4.597	< 0.001*
	Range	22.0- 92.6	11.7- 59.8		

t: t- value of Independent t- test, *Significan

Table (2) show that: Cholesterol, Triglycerides were siginificantly higher in case group than in control group. HDL was siginificantly lower in case group than in control group. No significant difference between the two groups regarding LDL- c. also Serum insulin and insulin resistence was siginificantly higher in case group than in control group. No significant difference between study groups regarding serum SGOT, SGPT and glucose.

Table (3) Comparison between study groups regarding resistin and RBP4

Parameter	Measures	Cases (N= 45)	Control (N= 43)	P- Value
Resistin	Mean± SD	7.6± 3	8.1± 2.0	0.335
(Ng/Ml)	Range	1.3- 14.1	4.7- 13.5	
Rbp4	Mean± SD	54.1± 17.5	39.6± 11.3	< 0.001*
(µmol/L)	Range	22.0- 92.6	11.7- 59.8	

#Independent t- test, *Significant

Table (3) show that: RBP4 were siginificantly higher in case group than in control group. No significant difference in Resistin level in both groups

Table (4) Comparison between study groups regarding blood pressure

Parameter	Measures	Cases (N= 45)	Control (N= 43)	P- Value
Sbp (Mmhg)	Mean± SD	115.7± 9.4	107.8± 6.8	0.009*
	Range	100.0- 130.0	90.0- 120.0	
Dbp (Mmhg)	Mean± SD	73.8± 6.5	68.6± 5.2	0.005*
	Range	60.0- 90.0	60.0- 75.0	

#Independent t- test, *Significant

Table 4 shows that: SBP and DBP were siginificantly higher in case group than in control group.

Table (5) Comparison between study groups regarding body composition

Parameter	Measures	Cases (N= 45)	Control (N= 43)	P- Value
Tbw%	Mean± SD	42.8± 4.6	60.2± 8.8	< 0.001*
	Range	35.4- 52.0	24.8- 69.5	
Tbf%	Mean± SD	41.4± 5.1	16.7± 9.4	< 0.001*
	Range	28.8- 47.3	5.0- 38.8	
Fat Mass (Kg)	Mean± SD	33.0± 8.6	8.2± 5.7	< 0.001*
	Range	16.9- 49.4	1.2- 23.0	
Ffm (Kg)	Mean± SD	50.6± 9.3	37.3± 6.3	< 0.001*
	Range	36.5- 73.4	23.1- 50.6	
TBW (Kg)	Mean± SD	36.6± 6.7	26.8± 5.1	< 0.001*
	Range	26.7- 53.2	12.4- 37.0	

#Independent t- test, *Significant

Table (5) shows a comparison between case and control group regarding their body composition data shows statistically significant increase in their body fat%, fat mass, fat free mass

Table (6) Correlation between resistin, and RBP4 in study groups

	Cases		Control	
	r	P- Value	r	P- Value
	Resistin			
RBP4	- 0.686	0.023*	- 0.555	0.021*

Table (6) show that: There were significant negative correlations between resistin and RBP4 in the study groups.

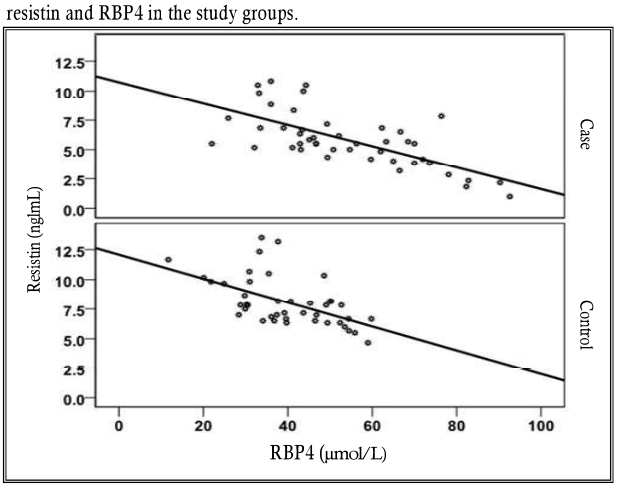

Figure (1) Correlation between resistin and RBP4 in study groups

Table (7) Comparison between males and females regarding Resistin, and RBP4 among case group

Case Group		Male (N= 15)	Female (N= 30)	P- Value
Resistin (Ng/Ml)	Mean± SD	5.0± 1.5	6.2± 2.6	0.110
	Range	2.3- 7.8	1.0- 10.8	
Rbp4 (µmol/L)	Mean± SD	58.2± 15.1	52.0± 18.4	0.268
	Range	39.0- 82.8	22.0- 92.6	

Table (7) shows that there is no significant difference between males and females regarding Resistin, and RBP4 among case group.

Table (8) Correlation between resistin and other variables in study groups

	Cases		Control	
	r	P- Value	r	P- Value
Age	- 0.121	0.261	0.099	0.529
Tanner^	- 0.086	0.424	0.139	0.373
Wtsds^	- 0.650	0.062	- 0.261	0.092
Htsds^	- 0.318	0.051	- 0.290	0.059
Bmisds^	- 0.705	0.091	- 0.658	0.421
WH Ratio	- 0.425	0.086	- 0.134	0.392
Cholesterol	- 0.665	0.004*	- 0.557	0.054
Triglycer	- 0.627	0.040*	- 0.551	0.031
LDL	- 0.620	0.003*	- 0.573	0.041
HDL	0.743	0.021*	0.627	0.051
SGOT	- 0.091	0.401	- 0.181	0.245
SGPT	0.000	0.999	- 0.193	0.215
Glucose	- 0.016	0.881	- 0.002	0.991
Insulin	- 0.516	0.034*	- 0.125	0.423
Homa- Ir	- 0.497	0.011*	- 0.116	0.460
Tbw%	0.669	< 0.001*	0.532	< 0.001*
Tbf%	- 0.672	< 0.001*	- 0.600	< 0.001*
BMR	- 0.498	< 0.001*	- 0.085	0.586
SBP	- 0.275	0.009*	0.073	0.643
DBP	- 0.251	0.018*	- 0.021	0.892

r: Pearson correlation, ^Spearman correlation, *Significant

Table (8) and figure (2) show that: There were significant negative correlations between resistin and weight sds, BMI sds, cholesterol, triglycerides, LDL and TBF%, insulin& HOMA- IR, SBP, DBP, BMR in obese group. There were significant positive correlations between resistin and HDL and TBW% in the obese group.

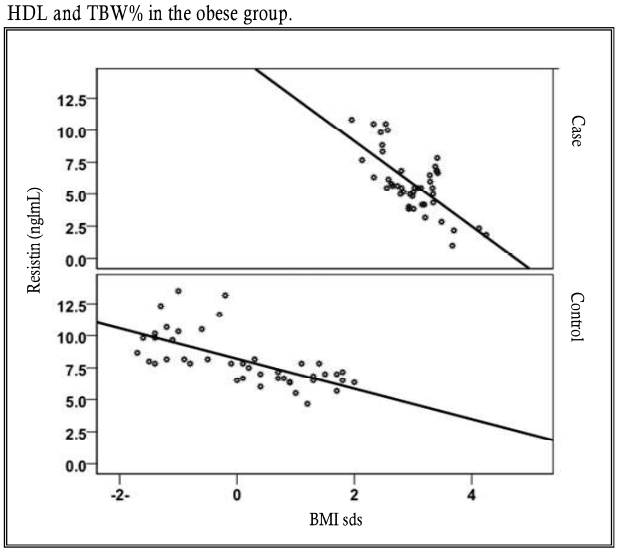

Figure (2) Correlation between resistin and BMI sds

Table (9) Correlation between RBP4 and other variables in study groups

	Cases		Control	
	r	P- Value	r	P- Value
Age	0.209	0.050	0.017	0.916
Tanner^	0.104	0.335	0.026	0.870
Wtsds^	0.508	< 0.001*	0.237	0.127
Htsds^	0.158	0.141	0.209	0.179
Bmisds^	0.551	< 0.001*	0.268	0.082
WHratio	0.380	< 0.001*	0.221	0.154
Cholesterol	0.608	< 0.001*	0.187	0.229
Triglyc.	0.572	< 0.001*	0.166	0.289
LDL	0.555	< 0.001*	0.187	< 0.001*
HDL	- 0.584	< 0.001*	- 0.280	0.069
SGOT	0.065	0.550	0.017	0.912
SGPT	0.019	0.859	0.181	0.246
Glucose	- 0.016	0.882	0.013	0.935
Insulin	0.559	< 0.001*	0.105	0.501
Homa- Ir	0.538	< 0.001*	0.114	0.466
Tbw%	- 0.569	< 0.001*	- 0.199	0.201
Tbf%	0.562	< 0.001*	0.225	0.148
BMR	0.502	< 0.001*	0.198	0.204
SBP	0.198	0.065	- 0.217	0.163
DBP	0.189	0.078	- 0.258	0.095

r: Pearson correlation, ^Spearman correlation, *Significant

Table (9) and figure (2) show that: There were significant positive correlations between RBP4 andWt sds BMI sds, WH ratio cholesterol, triglycerides, LDL and TBF%, insulin& HOMA- IR SBP, DBP in obesegroup. There were significant negative correlations between retinol and HDL and TBW% in obese group

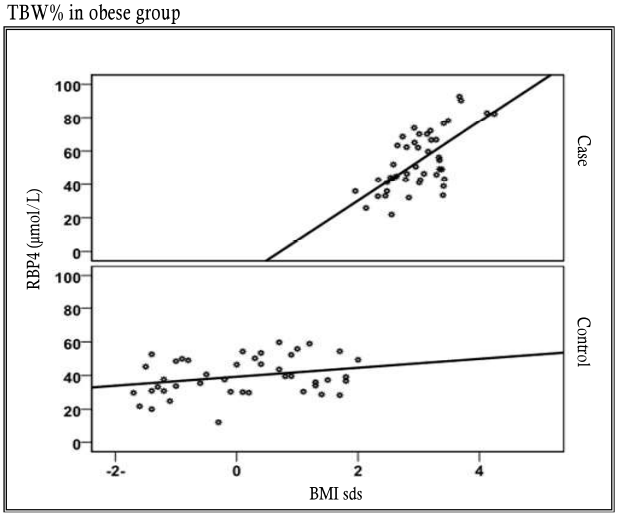

Figure (3) Correlation between RBP4 and BMI sds

Discussion:

In the present study Serum RBP4 levels of case group were significantly higher than those of control group, The means and corresponding ranges of plasma concentrations of RBP4 were: 54.1± 17.5 µmol/L in the case group versus in the control group were: 39.6± 11.3 µmol/L, in this study no statistical significant difference in RBP4 between both sexs, this agree with a study done by Young et al. (2011) on Sixty- one boys and forty- two girls between the ages of 6 and 18 yr were included in this study. There was no significant difference in serum RBP4 between male and female (54.94± 20.18 vs 49.67± 16.66 mg/L, P= 0.166).

In our study RBP4 positively correlated with BMI, WH ratio, TBW%, TBF%, BMR this agree with a study done by Chin- Jung et al. (2013) on a total of 1082 adolescents were enrolled and categorized based on their body mass index (521 boys and 561 girls) with a mean (range) age of 13.7 (13- 15) years were included in the final analyses. In this large adolescent population, we found that the RBP4 levels were positively correlated with most of the obesity indices, Also this agree with Lee et al. (2007) who reported a strong association between elevated serum RBP4 concentrations and components of the metabolic syndrome, including increased BMI and waist circumference

This agree with Several previous studies in adolescents suggested that RBP4 levels had an important effect on obesity indices, as measured by BMI, (Choi et al., 2011), (Goodman et al., 2009). WC, waist- to- hip ratio, and body

fat percentage/ fat mass (Santoro et al., 2009) Also this is consistant with a study done by Santanam et al. (2014) who found that RBP4 (p= 0.016) was significantly higher in obese children and were positively correlated with body mass index (p< 0.001), BMI- -SDS (Standard- -Deviation Score) (p< 0.001) and waist circumference (p= 0.03).

This disagree with other studies who suggested that in adults, RBP4 is associated with visceral fat amount rather than body weight or BMI. (Jia et al., 2007), also this disagree with studies in adults and adolescents by (Santoro et al., 2009)who found that RBP4 levels were better correlated with WC (a rough proxy for visceral fat) rather than BMI. Another prospective study suggested that baseline RBP4 levels predict subsequent increase in WC in a Korean adolescent population. (Choi et al., 2011). Also this disagree with Janke et al. (2006)who reported that serum RBP4 wasn't increased in overweight and not related to BMI.

Also our results disagree with another retrospective study by Goodman and others who observed that RBP4 did not predict further obesity change. (Goodman et al., 2009). In the study by Kim et al. (2011) the authors suggested that higher RBP4 concentration was a consequence rather than a cause of excess weight

In this study, there is a significant positive correlation between RBP4 and HOMA- IR(r= 0.538; p< 0.001), W\ H ratio(r= 0.380; p< 0.001) TG(r= 0.572; p< 0.001) systolic(r= 0.198; p= 0.065) and diastolic blood pressure(r= 0.189; p=0.0 78) and inversely correlated with HDL cholesterol(r=- 0.584; p< 0.001). This agree with the study done by Mehmet et al. (2013) in a study done on 148 nondiabetic pubertal obese subjects. who found that RBP4 concentrations were significantly directly correlated with HOMA- IR (r= 0.653; p< 0.001), followed by W\ H (r= 0.247; p< 0.001), TG level (r= 0.390; p< 0.001), diastolic blood pressure (r= 0.279; p< 0.001) and systolic blood pressure (r= 0.419; p< 0.001), and were inversely correlated with HDL cholesterol (r= - 0.275; p< 0.001). and this consistant with a study done by Ansar et al. (2015) in a case- control study on 73 obese and 90 non- obese participants were assessed RBP4 following an overnight fasting for RMR by means of indirect calorimetry. Circulating RBP4 level correlated positively with log insulin (r= 0.278, p= 0.04) in obese subjects. Our results agree with Choi et al. (2011) in a study done in obese Korean boys and also agree with Goodman et al. (2009) in a study done on overweight black adolescence who found that RBP4 positively correlates with HOMA- IR

Also this agree with a study done by Chin- Jung et al. (2013) who found that RBP4 levels were positively correlated with TG in which RBP4 was positively associated with BP, (An et al., 2009), (Choi et al., 2011) lipid profiles (Choi et al., 2011), (Kim et al., 2011).

This Agree with Bobbert et al. (2010) found that circulating RBP4 levels were correlated positively with cholesterol, triglyceride, body mass index and waist circumference. Also, Circulating RBP4 levels were positively associated with increase intima media thickness. So, they suggested that RBP4 might be a possible predictor of atherosclerosis.

Also, Haider et al. (2007) found an association of increased circulating RBP4 levels with insulin resistance, and the metabolic syndrome. They also found that improving insulin sensitivity by interventions such as exercise training, lifestyle modification, or gastric banding surgery reduced serum RBP4 levels.

Also this doesn, t agree with a cross sectional study by Thiruvengadam et al. (2015) in a tertiary care children's hospital where in 98 obese children were included and their metabolic parameters analysed with regards to insulin resistance and RBP4 levels. high RBP4 levels were observed in 69.6%. But there was no significant association between insulin resistance and RBP4 levels (p0.8) detecting that RBP4, the sole retinol transporter in blood, secreted from adipocytes and liver has been implicated in insulin resistance. The index study however, did not show a significant positive association.

On the other hand Broch et al. (2007) failed to establish an association of RBP4 levels with obesity, insulin resistance, type 2 diabetes or components of the metabolic syndrome.

However Kanaka- Gantenbein et al. (2008) found that no significant correlation between RBP4 concentration and the HOMA index, the fasting insulin concentration, or the fasting glucose concentration, suggesting that RBP4 may not be a good marker of insulin resistance at young ages.

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The means and corresponding ranges of plasma concentrations of resistin in the case group were: 7.6± 3ng/ml, respectively. Whereas the plasma concentrations of resistin in the control group were 8.1± 2.0 ng/ml, respectively. NO statistically significant difference was found in resistin levels between cases and controls. This agrees with Savage et al. (2001); Zou et al. (2007) who found that resistin level in obese children was not different from that of controls.

This diagree to De Courten et al. (2004) and Vendrell et al. (2004) and Youn et al. (2004) who found significant difference in resistin levels in obese subjects compared with control subjects. This also doesn, t agree with a study done in Egypt- Ain Shams University 2006 which found a statistically significant difference in serum resistin levels between obese children and non obese controls (Salem et al., 2006).

Also this doesn, t agree with a study done by Fatemehet al. (2014) who found that Serum levels of resistin were higher among both obese and normal-weight women with PCOS in comparison with the controls (2.36 and 1.58 ng/mL in normal- weight women with PCOS and controls, respectively; and 2.10 and 1.91 ng/mL in obese women with PCOS and controls, respectively).

In the present study, no statistical difference in serum resistin level between males and females in both cases and controls; this agrees with Schaffler et al. (2004), however, other studies reported that serum resistin levels were significantly higher in females as compared with males (Silha et al., 2003); (Yannakoulia at al., 2003).

In our study there is a significant negative correlation between resistin and IR(r= - 0.497, p=0.0 11), W\ H ratio(r= - 0.425, p=0.0 86) TG(r= - 0.627, p=0.0 40) systolic (r= - 0.275, p=0.0 09) and diastolic blood pressure(r= - 0.251, p=0.0 18) and directly correlated with HDL cholesterol(r= 0.743, p= 0.021). This agree with the study done by Mehmet et al. (2013) who found that resistin concentrations were significantly inversely correlated with HOMA- IR (r= - 0.679, p< 0.001 and r= - 0.644, p< 0.001, respectively), W\ H (r= - 0.274, p< 0.001 and r= - 0.347, p< 0.001, respectively), TG (r= - 0.368, p< 0.001 and r= - 0.456, p< 0.001, respectively), diastolic blood pressure (r= - 0.256, p< 0.001 and r= - 0.319, p< 0.001, respectively), systolic blood pressure (r= - 0.414, p< 0.001 and r= - 0.506, p< 0.001, respectively) and positively correlated with HDL cholesterol (r= 0.274, p< 0.001 and r= 0.338, p< 0.001, respectively).

In this study, significant correlation has been found between serum resistin

and each of fasting insulin and HOMA in obese children which agrees with the results of Koebnick et al. (2006). On the contrary, other studies performed by De Courten et al. (2004) and Barbora et al. (2004) found that serum resistin levels were not associated with insulin levels in their sample. However, (Gambino et al., 2005) found a correlation between serum resistin and fasting insulin only in normal subjects but not in obese subjects.

On the contrary Azuma et al., (2003) in a study done on Japanese population found that although cross- sectional analysis in obese subjects revealed no correlation between serums resistin and parameters related to adiposity or insulin resistance, longitudinal analysis revealed that the change in serum resistin was positively correlated with changes in BMI, body fat, fat mass, visceral fat area, and mean glucose and insulin.

Conclusion:

RBP4 is positivity correlated to serum insulin level, HOMA/IR, and lipid profile, so RBP4 can be used as a marker for insulin resistance and obesity..S tudies with large sample size and high power are needed to explain the link between resistin and obesity associated insulin resistance especially in children.

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