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Evaluation of Serum Levels of C-peptide, Cortisol, and Some Biochemical Parameters in Children with Obesity

ABSTRACT

Background:-Obesity has become a leading health concern; this condition is a chronic, multifactorial complex in which a child's weight ≥ 20% of the ideal weight for a given height.

Aim of the study:- Is to find out the liability of obese children to the diabetes mellitus.

Objectives of the study:- To measure the serum levels of C-peptide, Cortisol, and some biochemical parameters in children with obesity and comparing them with lean or normal weight children in some primary schools in Kirkuk city.

Methods:- This study was carried on 152 children divided into two groups :-

1. Obese children (n 100 from both gender). 2. Lean or normal weight children (n 52 from both gender). For all of them studied serum C-peptide, Cortisol, Biochemical parameters (serum Leptin, Adiponectin, Malondialdehyde,

Results: This study showed that mean BMI, serum c-peptide , leptin, malondialdehyde, were significantly ($P<0.05$) higher in obese group than in lean or normal weight group, and serum adiponectin, was significantly lower in obese group than in normal weight group. **Conclusion:-**This present study identified high prevalence of obesity among primary school children, increased BMI in obese children, increased circulating levels of leptin as a biological marker for obesity, increased circulating c-peptide level as a marker of insulinoma, increased oxidative stress in obese children, and finally decreased adiponectin level in obese children.

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Introduction:

Childhood obesity is a condition where excess body fat negatively affects child's health or wellbeing. The last decades have been characterized by a global growing obesity epidemic, starting already in childhood. Obesity prevalence has been increasing among children and adolescents as it has in adults[1]. Childhood obesity is emerging as a serious health problem in developed and developing countries worldwide. Excessive caloric intake, insufficient physical activity and sleep deprivation are major lifestyle factors involved in the development of obesity [2] . The amount of body fat is difficult to measure directly and is usually determined from an indirect measure-the body mass index (BMI) which has been shown to correlate with the amount of fat in most individual. Body mass index BMI is acceptable for determining obesity for children two years of age and older. The normal range for BMI in children vary with age and sex[3] .C-peptide is a polypeptide originating from proinsulin after its cleavage in the B-cell. C-peptide is a 31 amino acid peptide that bridges the insulin A and B chains in the proinsulin molecule. It is secreted equimolarly with the other cleavage product, insulin, into the portal circulation. C-peptide has a half-life of about 30 minute, it is metabolized in the proximal renal tubule and is about 5-10% is excreted in the urine, it can be measured either in serum, plasma, or in urine [4]. Cortisol, known more formally as hydrocortisone, is a steroid hormone, more specifically a glucocorticoid, produced by the zona fasciculata of the adrenal cortex. It is released in response to stress and a low level of blood glucocorticoids. Its primary function are to increase blood sugar through gluconeogenesis; suppress the immune system; and aid in fat, protein and carbohydrate metabolism. Cortisol stimulates gluconeogenesis (formation, in the liver, of glucose from certain amino acids, glycerol, lactate and/or propionate) and it activates anti-stress and anti-inflammatory pathways,

however cortisol facilitates the activation of glycogen phosphorylase, which is essential for the effects of epinephrine on glycogenolysis [5] .Leptin (also termed OB protein), is a protein discovered in 1994 by Friedman and Colleagues with the identification of mutant (OB) gene that underlies obesity in ob/0b mice. Leptin, (from the Greek word leptos, meaning thin) is a peptide hormone, has 146 amino acid residues, the molecular weight of leptin is around (16 KDa) with crystal structure reveals a four-helix bundle. In human, it is well established that plasma leptin level are directly proportional to percentage body fat level. Leptin has also been reported to have profound effects on carbohydrate and lipid metabolism that may, at least in part, be independent of its centrally mediated effects on energy balance. Adiponectin is abundant protein which in humans is encoded by the *ADIPOQ* gene , its belong to a family of so-called adipokines, and is important regulator of lipid and glucose metabolism. Adiponectin is secreted into the blood stream where it accounts for approximately 0.01% of all plasma protein at around 5-10 µg/ml [6]. Malondialdehyde (MDA) is one of many low molecular weight end-products of lipid hydroperoxide decomposition and is the most often measured as an index of lipid peroxidation . Reactive oxygen species degrade polyunsaturated lipids forming Malondialdehyde. This compound is a reactive aldehyde and is one of the many reactive electrophile species that cause toxic stress in cells and form covalent protein adducts referred to as advanced lipoxidation end-products (ALE) .The production of this aldehyde is used as a biomarker to measure the level of oxidative stress in an organism[7].

Aim of the study:- Is to find out the liability of obese children to diabetes mellitus.

Materials and methods:-

The following biochemical tests were done for 152 study subjects (100 obese children and 52 non obese or control children of primary schools in Kirkuk City from December 2012 to the end of April 2013. Serum C-peptide,

Cortisol ,Leptin, Adiponectin and Malondialdehyde were done for all of them.

Statistical analysis:-

To compare the significance of the difference in the mean values of any two groups chosen, student t-test was applied; $P<0.05$ was considered statistically significant.

Result:-

A total obese group were 100 children (36 girls and 64 boys), and total lean or normal weight group were 52 children (23 girls and 29 boys), table (1).

Table (1) : Variation of Obesity in Children Aged 8 -12 Years Old With Lean Group:

Age (Year)	Obese children group			Lean children group		
	Female n	Male n	Total	Female n	Male n	Total
8	5	4	9	2	2	4
9	6	8	14	3	4	7
10	7	11	18	4	5	9
11	8	15	23	6	6	12
12	10	26	36	8	12	20
Total	36	64	100	23	29	52

Obesity phenomena seen in significant ($P<0.001$) difference in ages 11-12 years, BMI mean ± SD (28.39 ± 3.31)than 8 <10 years BMI mean ± SD (24.50 ± 1.96), table (2).

Table (2) : Elevation of Obesity Phenomena in Age (11-12) Years More Than in (8 – <11) Years Old in Both Gender:

Age (year).	BMI ($kg/m^{2)}$ mean ±SD	*P value*
8- <11	24.50 ± 1.96	<0.001
11-12	28.39 ± 3.31	

There was a significant (p<0.00) difference in BMI, mean ± SD in obese children was (F 27.07 ± 3.86), (M 27.74 ± 3.22) compared with lean children mean ± SD (F 18.44 ± 3.24) , (M 18.57 ± 2.56) , table (3).

Table (3) : Variation of BMI in Obese From That in Lean or Normal Weight Group :

Variable Kg/m^2	Female (F) mean ± SD		*P Value*	Male (M) mean ± SD		*P value*
	Obese	Lean		Obese	Lean	
BMI	27.07± 3.86	18.44 ± 3.24	<0.001	27.74 ± 3.22	18.57 ± 2.56	<0.001

There was a significant (P<0.001) difference in MDA test in obese and lean group, mean ± SD in obese group (F 13.23 ± 2.85, M 11.58 ± 4.99), and mean ± SD in lean group (F 4.56 ± 1.45, M 4.81 ± 2.13).

There was a significant (P<0.001) difference in C-peptide test in both group, mean ± SD in obese group (F 4.41 ± 2.15, M 3.08 ± 1.52), and mean ± SD in lean group (F 2.052 ± 0.555, M 1.634 ± 0.516).

There was a non significant (FP=0.79, MP=0.25) difference in serum cortisol test in both group, mean ± SD in obese group (F 12.39 ± 4.15, M 12.07 ±3.42), and mean ± SD in lean group (F 12.11 ± 3.86, M 12.99 ± 3.59).

There was a significant (P<0.001) difference in serum leptin test in both group, mean ± SD in obese group (F 34.0 ± 15.8, M 28.3 ± 10.4), and mean ± SD in lean group (F 5.98 ± 1.92, M 4.055 ± 0.811).

There was a significant (P<0.001) difference in serum adiponectin test in both group, mean ± SD in obese group (F 1.238 ± 0.197, M 1.281 ± 0.180), and mean ± SD in lean group (F 2.00 ±0.367, M 2.17 ± 0.376), table (4).

Table (4): Levels of Variables in obese and lean group:

Variable	Female mean ± SD		P Value	Male mean ± SD		P Value
	Obese	Lean		Obese	Lean	
MDA mmol/l	13.23 ± 2.85	4.56 ± 1.45	<0.001	11.58 ± 4.99	4.81 ± 2.13	<0.001
C-peptide ng/ml	4.41 ± 2.15	2.052 ± 0.555	<0.001	3.08 ± 1.52	1.634 ± 0.516	<0.001
Cortisol µg/dl	12.39 ± 4.15	12.11 ± 3.86	0.79	12.07 ± 3.42	12.99 ± 3.59	0.25
Leptin ng/ml	34.0 ± 15.8	5.98 ± 1.92	<0.001	28.3 ± 10.4	4.055 ± 0.811	<0.001
Adiponectin ng/ml	1.238 ± 0.197	2.00 ± 0.367	<0.001	1.281 ± 0.180	2.170 ± 0.376	<0.001

Discussion:

Childhood obesity has become one of the most serious public health challenges of the 21st century Overweight or obesity is the most important risk factor for the development of Type 2 Diabetes Mellitus T2DM. The results of this study support this contention by demonstrating the emergence of a highly increasing prevalence of overweight and obesity among school children. It is in line with the global trends; in the USA, the problem more than tripled in the past thirty years. This reported also notes that in Saudi Arabia one in every six children aged 6 to 18 years old is obese. The prevalence of obesity in children age group 6-12 years has been increased 6.5 – 17% [8].

A review of data on childhood obesity for Saudi Arabia shows interesting variations. The examination of the relationship of overweight and

obesity with age showed a positive trend, progressively increasing with age after the children joined the school. These finding could be due to the exposure of children to an external environment where their diet habits changed or they were exposed to more fatty diets. This finding is in agreement with AL-Mohaimeed *et al* in Saudi Arabia which indeed found obesity in early years of school children [9].

In this study found significant prevalence of obesity was familiar in male than female, this found in agreement with Davallow *et al* in Qatar which found the prevalence of obesity in male more than that in female[10], but disagreed with Garasky *et al* which found that female more exposure to obesity[11]. Also it found that children with age group 11-12 years old more exposure to the obesity than age group 8-10 years old, this founding is in agreement with Al-Isa *et al* which found association of obesity among Kuwaiti school children aged 6-12 years in both gender [12] . Body Mass Index in children is differ from that of adult, and also differ according to age and gender. BMI is higher in lean female than in lean male , also it is 2-3 time higher in obese female than in obese male, in this study it was statistically significant. This is in agreement with Chris M, Erdal Tekin that found the variation of BMI in their study [13].

Regarding to the lipid peroxidation test, serum malondialdehyde was elevated in obese children in both gender compared with lean children in this present study, there is strong positive relation between obesity and MDA test, and it is statistically significant. This finding is in agreement with Selvakumar *et al* that demonstrated an elevated serum level of MDA in Indian obese children [14].

Present study suggests that fasting serum C-peptide levels were a better predictor of cardiovascular and overall death than fasting serum insulin and its derived measures of insulin resistance in a nationwide sample of non diabetic adults between 40 and 74 years of age. In this study demonstrated elevated levels of serum c-peptide in obese children in both gender compared with

lean children, and it was statistically significant. This study is in agreement with Srinivasa *et al* in India which also found elevated levels of c-peptide in obese children compared with lean children [15] .

Cortisol is the primary glucocorticoid secreted by the adrenal cortex and an important regulatory hormone for blood glucose homeostasis. Morning serum cortisol samples was obtained in this study, and found normal serum cortisol levels in obese and lean children in both gender. This is statistically insignificant , this finding disagreed with Edavan *et al* in United State which found low serum cortisol levels in obese children compared with lean children [16] , and also disagreed with Prodam *et al* in Italy that demonstrated high cortisol levels in obese children compared with that of lean children [17].

Leptin secretion per gram of adipose tissue is twice greater in obese as compared to slim people. In this present study found elevated serum levels of leptin in obese children in both gender compared with lean children, and obese females have higher leptin levels than obese males, and this is statistically significant . This finding is in agreement with Henedina *et al* in Portugal which also demonstrated this finding [18].

It has been reported that increased body adiposity in childhood is an important risk factor for hypoadiponectinmia in adulthood. Adiponectin level that decreases in obesity and related diseases pathology, might be a valuable biomarker for identifying non-overweight children at risk for later metabolic issues. In this study found decrease serum adiponectin level in obese children in both gender compared with lean children, this finding agreed with Arslan *et al* in Turkey which also found decreased adiponectin levels in obese children compared with lean children [19]

Conclution:-

This present study identified high prevalence of obesity among primary school children, increased BMI in obese children, increased circulating levels of leptin as a biological marker for obesity, increased circulating c-peptide

level as a marker of insulinoma, increased oxidative stress in obese children, and finally decreased adiponectin level in obese children.

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