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Relation Of Adiponectin And Leptin Hormones In Obese Adolescent Females During Puberty

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Abstract

The current study was carried out to estimate adipose tissue hormones during puberty in obese girls and compare it with control group, in addition to its relationship with the total antioxidants capacity (TAC).

The study included 50 females aged 11-15 years from primary and secondary schools located in Nineveh governorate. The study contain 2 groups depending on the body mass index (BMI): The first group included the control group BMI equal to (20.4±0.44) kg/m^2 with pubertal age (13.58± 0.16) years and the second group was the obese females group and overweight females BMI equal to (30.14±0.51) kg/m^2 with pubertal age (11.38± 0.19) years After obtaining the approval of the parents, this number of females was joined to the study and blood was drawn and serum separated from it for the purpose of conducting the tests under study.

The results observed that the group$_2$ showed a significant increase the BMI, TNF-α and Leptin and Vaspin hormones with a significant decrease in the Pubertal age and Adiponectin hormone compared to the group$_1$, in addition to a significant decrease in the TAC of in the second group compared with the control group.

Keyword: Vaspin hormone, Puberty, Adiponectin hormone, Leptin hormone, Obesity

INTRODUCTION

The prevalence and recurrence of obesity in children and adolescents portends a great alarm to health in general (Reinehr and Roth, 2019); (Nieuwenhuis et al., 2020). Too much accumulation of white adipose tissue (WAT) is referred to as “obesity” and can always be indicated by an important indicator called BMI with a value greater than 30 (Guglielmi and Sbraccia, 2018). There are many functions that can be attributed to adipose tissue, including thermogenesis, the generation and storage of energy, and the most important of these functions is the synthesis and secretion of important compounds called adipokines, these include hormones, cytokines, and peptides (Gulyaeva et al., 2019); (Khan and Joseph, 2014). Currently, Adipose tissue (AT) is one of the most important endocrine organs and is considered the largest in terms of size compared to its counterparts in the body. There are many important diseases that are associated with AT dysfunctionality, the most important of which are obesity, type 2 diabetes, dyslipidemia and non-alcoholic fatty liver. Hypertrophy, hyperplasia, AT inflammation, fibrosis and an altered secretion of adipokines, these are the mechanisms underlying adipose tissue dysfunction (Huhtaniemi Martini, 2019).

The word 'Puberty' is derived from the Latin pubescere, meaning 'to grow hairy.' For a mammal, puberty is the time of life when the sex glands be functional (Bogin, 2011). Puberty is defined as the period of time between childhood and adulthood represented by physiological and somatic changes related to the maturation of the internal and external genitalia, in addition to the emergence of secondary sexual characteristics (Sanfilippo and Jamieson, 2008). The physiological mechanisms between obesity and puberty onset stay unclear (Nieuwenhuis et al., 2020), although several findings have clarified associations between obesity and puberty (Reinehr and Roth, 2019); (Li et al., 2018). Hereafter, we review in detail

about some hormones specially adipokines and its role in the onset of puberty in obese females. Physiologically, when puberty begins, when changes occur in brain, and how this change plays a role in the secretion of sex hormones (Bogin, 2011).

As we mentioned before, energy storage is not only the sole function of adipose tissues, but it has many functions as an endocrine gland and secrets many biologically active compounds (bioactive mediators). These secretions is under the name of 'adipokines" (Kershaw and Flier, 2004), these adipokines play a vital role in participating in many physiological processes in the body, including metabolism, glucose balance and vascular homeostasis, in addition to the key role they play in determining the onset of puberty (Cousminer et al., 2014). Adipokines are an important connect between puberty with lifestyle and adioposity, due to these bioactive compounds (hormones) are produced in state of obesity and transformation of the body energy status to the brain. Really, severe anorexia nervosa patients or with leptin deficiency develop hypogonadism (Bohlen et al., 2016). Leptin, which was the first adipokine to be known and identified, has many function one of these plays a role by appetite control in the regulation of body fat volume and elevated metabolism. There is a positive correlation between the secretion of leptin hormone with fat tissue mass and the amount of food intake (Maffei et al., 1995). Adiponectin is a fat-derived hormone that ameliorates insulin sensitivity in muscle as well as the liver. There is a negatively correlation between the gene expression of Adiponectin and blood values with BMI (Lee and Shao, 2014). The physiological pathway represented by central adiponectin/leptin signaling is noted to be associated with energy metabolism (Kubota et al., 2007). Timing of sexual maturation related to well- known factors represented by obesity and nutritional state, so adipokines, especially adiponectin and leptin by affecting the hypothalamic pituitary gonadal axis HPG, which stimulate an early onset of puberty in obese girls as well as boys (Yoo et al., 2016).

Vaspin or (Visceral Adipose Tissue Derived Serpin) is a novel Adipocytokine that regulate glucose and lipid metabolism (Li et al., 2008), also known as Serpin A_{12} (Huhtaniemi and Martini, 2016) in human, Vaspin is a protein, contains 415 amino acids, and the main expression site is in visceral adipose tissue (Hida et al., 2005). Interestingly, there are other tissues to Vaspin expression, including the pancreatic islets, hypothalamus, skin and stomach. In 2005, it was first discovered that visceral white adipose tissues are the site of highly expressed of Vaspin. A study in children more observed Vaspin values elevate with age and pubertal stage in girls, whereas there is a lack of change in Vaspin with development in boys (Huhtaniemi and Martini, 2016).

MATERIAL and METHODS

A total of 50 females between 11- 15 years old were collected from primary and secondary schools in Nineveh governorate from the period 15/10/2019 to 1/2/2020. The diagnosis was dependent on the measurement of BMI (was calculated for all females by dividing the body weight in kg by the square of height in meters) (Fan et al., 2017) and they divided into 2 groups:

Group$_1$: Control, include 25 females have normal weight with BMI (20.4± 0.44) and do not have chronic disease.

Group$_2$: The obese and overweight females, include (25) females with high abnormal levels in BMI (30.14±0.51).

Data have been taken from the females, which contain personal information, symptoms and disease they may have. Blood samples have been collected for measuring Leptin, Adiponectin, Vaspin hormones, Total antioxidant capacity (TAC) and TNF-α.

Collecting samples: (5) ml of veinous blood had been collect, put in a tightly gel tube, left at room temperature for 20 minutes, then separated by a centrifuge at a speed of 5000 rpm for a period of 10 minutes to obtain the serum.

Hormonal tests: The concentration of the hormones Leptin, Adiponectin, Vaspin concentration were determined by using a prepared analysis kit manufactured by the US Company MyBiosource, using the Enzyme Linked Immune Sorbent Assay (ELISA). This test was based on an enzyme system bound with a biotin double antibody.

Biochemical test: The concentration of the TAC and TNF-α in the serum was estimated, using a prepared analysis kit provided by the US Company MyBioSource, using ELISA technology, and the principle of action is based on an enzymatic double-antibody sandwich system.

Statistical analysis

One-way ANOVA analysis of variance using the General Linear Model, (SAS software) was used in the statistical analysis (SAS, 2004). To separate the means when significant differences exist Duncan used. Means and standard deviations were calculated for all parameter. Difference were considered significant at $P \leq 0.01$.

RESULTS

In the table below, the results showed a significant increase at ($P \leq 0.01$) in Leptin with (6.23±0.14) pg/ml and Vaspin (620± 50) pg/ml in group$_2$ in obese pubertal females compared with control group (4.23± 0.11) pg/ml and (495± 20) pg/ml respectively. In contrast showed a significant decrease at ($P \leq 0.01$) in Adiponectin hormone (4.88± 0.12) mg/L and TAC (53.32± 0.15) ng/ml in group $_2$ obese pubertal females in compared with control group. BMI in group$_2$ was (30.14±0.51) while in group$_1$ (20.4±0.44), the table showed the pubertal age in group$_2$ is (11.38±0.19) compared to control group (13.58± 0.16) at ($P \leq 0.01$).

Table (1)the result of Hormonal and Biochemical tests

Groups / Parameters	**Group$_1$ (no.=25)**	**Group $_2$ (no.=25)**
BMI (kg/ m^2)	**20.4± 0.44 b**	**30.14± 0.51 a**
Pubertal age (years)	**13.58± 0.16 a**	**11.38± 0.19 b**
Leptin (pg/mL)	**4.23± 0.11 b**	**6.23± 0.14 a**
Adiponectin (mg/L)	**7.58± 0.17 a**	**4.88± 0.12 b**
Vaspin (pg/mL)	**495± 20 b**	**620± 50 a**
TAC (ng/mL)	**75.28± 1.4 a**	**53.32± 0.15 b**
TNF-α (pg/mL)	**6.16± 1.06 b**	**7.82± 2.8 a**

The no. followed by different letters means there is significant difference.

The values is means ± standard deviation SD

DISUCSSION

In our results there is a significant increase in Leptin and Vaspin hormones level, BMI and TNF-α in obese pubertal females, also a significant reduce in pubertal age and Adiponectin hormone.

Obese Girls reach puberty earlier than the normal weight girls (De Leonibus et al., 2014); (Li and Liu, 2018). An Interpretation of the early entry of obese girls into pubertyagreement with our study and it is might be related to the production of adipokines (Venancio et al., 2017).

Adipokines are have essential link between onset puberty with obesity and nutritional state, because Adipokines are produced in obesity and transfer the body energy to the brain. Really, patients with severe anorexia nervosa or with deficiency of leptin develop hypogonadism (Bohlen et al., 2016).

Leptin play an important role in puberty as its serum value elevates with higher values of body adipose tissues and as it can modify both the Hypothalamus-Pituitary- Adrenal axes and Hypothalamus- Pituitary- Gonadal axis. These axes are functionally integrated during puberty (Cizza et al., 2001).

Other studies showed that the increase in the level of leptin with age was in relation with reduce in the soluble leptin receptor level, and age related changes leptin levels and its receptor preceded pubertal increase in sexual hormones (Meier and Gressner, 2004).

Obesity is linked with many changes in the glands secretions of endocrine system, consisting abnormal hormone levels, which can be related to alterations in pattern of their production and/or metabolism, changed hormone transport and/or action at the level of target tissues. In last years, a big incentive in both basic and clinical research has, on one hand, produced a great deal of knowledge on the pathophysiology of obesity, and, on the other, led to the discovery of new hormones, such as Adiponectin and leptin (Bray and York, 1997); (Sarhat, 2015) (Al-Hadidy and Dawood, 2021). As previous studies have reported, leptin values were higher in obese persons than in normal-weight persons (Considine et al., 1996).

The proposition that leptin have a decisive role in pubertal development and that there is a critical value being essential for the beginning of puberty, a causal association between leptin and pubertal development is not can always be proven. Some of the patients delayed maturation or may became infertile especially those with acquired or congenital generalized lipo-dystrophy, whereas the others was fertile and have normal development of reproductive system and normal development of puberty seems that the very low leptin values do not prevent puberty and fertility (Farooq et al., 2013).

Yu et al. (1997) associated leptin level as well as the hormones of pituitary, having a strong effect on the pituitary gland especially the anterior lobe in vitro, motivating follicle stimulating hormone and Luteinizing hormone (Yu et al., 1997), these hormones is the key of female puberty and development the reproductive system (Guyton and Hall, 2010).

Activate the HPG axes to accelerate puberty and keep sexual functions accomplished by the stimulation the receptors of leptin in the hypothalamus gland (Caprio et al., 2001). In addition, the stimulation of the receptors of leptin and adiponectin in pituitary gland have activating effect on GnRH production (Psilopanagioti et al., 2009)[34]. Furthermore, higher Leptin values have adverse effect on ovarian steroid formation (steroidogenesis) (Caprio et al., 2001).

Lately, some studies have concentrated on the role of the associations between leptin, Kisspeptin, and the HPG axis as a metabolic control initiation and progression of puberty (Bohlen et al., 2016). In gonadarche, leptin can accelerate the production of Kisspeptin, and subsequently stimulation of the HPG axis, which eventually increases the estrogen expression in the ovaries (Michalakis et al., 2013). In return, estrogen activates Ob gene expression in WAT, resulting inthe synthesis and production of Leptin (Machinal-Quelin et al., 2002). Therefore, high values of leptin stimulate onset of puberty in girls by

production of Kisspeptin, and estrogen promotes also leptin production. In addition, adiponectin can affect the H-P-G axis because of the adiponectin receptors expression inthe gonads, hypothalamus as well as pituitary gland (Dobrzyn et al., 2018). In detail, adiponectin is an organizer of puberty onset as it inhibits the production of Kisspeptin and GnRH in the hypothalamus and the secretion of GH and LH in the pituitary gland, and thereby depressing the beginning of puberty (Mathew et al., 2018). Persons with obesity often have low values of Adiponectin (Dobrzyn et al., 2018)، which the gene expression of it and BMI is in negatively correlation (Lee and Shao, 2014). This agreement with our study. Moreover, adiponectin had negative relationship with progression of girl's puberty. These results suggested that decreased reproductive status was correlated with very high total adiponectin levels (Sitticharoon et al., 2017).

In addition, patients with obesity often develop a chronic state of inflammatory, this may be specified by increased value of inflammatory cytokines like TNF-α and IL-6, and as is known, IL-6 can inhibit the expression of adiponectin (Zwick et al., 2018). Thereby, a decreased value of total adiponectin and/or increased values of inflammatory cytokines in patients with obesity can stimulate the onset of puberty (Budak et al., 2006). Thus, specifically leptin, adiponectin, and inflammatory cytokines secreted by WAT could be key players during an early beginning of puberty in obese girls (Alotaibi, 2019); (Mathew et al., 2018), and this is in agreement with our study.

Our findings observed a significant elevate in Vaspin level in obese puberty females ($group_2$). This increased level can be explained by diet induced obesity as Vaspin is mainly expressed in visceral adipose tissue (Weiner et al., 2017). Regarding Vaspin, there was a significantly higher circulating level in obese PCOS rats compared with controls, while, metformin treatment produced a significant decrease in these levels. Furthermore, there was positively relationship with significant between Vaspin and body mass index (Ashour et al., 2021), and have a vital function in reproduction. In previous published data, described the dependence on oestrous phase Vaspin expression of porcine ovarian structures, ovarian follicles (Kurowska et al., 2019a), and corpus luteum (Kurowska et al., 2020a). Obesity was associated with increased serum Vaspin (Cho et al., 2009). Vaspin values is positively correlated with triglycerides as well as BMI in pubertal obese children (Suleymanoglu et al., 2009).

Another studies showed that in both plasma and perirenal white fat tissue, the amount of Vaspin was increased in Meishan pigs. Moreover, the expression of Vaspin is strongly dependent on hormones, which are connected to ovarian follicle growth and development, ovulation, CL formation and regression, and levels of gonadotropins and steroid hormones such as estradiol, testosterone, insulin and prostaglandins E and $F_2\alpha$ (Kurowska et al., 2020); (Kurowska et al., 2019a). Furthermore, Vaspin regulates ovarian physiology by a direct stimulatory effect on phosphorylation of multiple kinases MAP3/1, protein kinase A (PKA), Janus kinase (STAT3) and PRKAA1(Kurowska et al., 2020a); (Kurowska et al., 2020b); steroidogenesis (Kurowska et al., 2020b) proliferation, and inhibition of apoptosis in ovarian follicle cells (Kurowska et al., 2019b).

In porcine cells, Vaspin enhances steroidogenesis by increasing level of estradiol, as well as enzymes participating in its synthesis via 78-kDa glucose-regulated protein (GRP78) receptors and the PKA signaling pathway (Kurowska et al., 2020c).

Vaspin is believed to be one of the putative adipocytokines that have an important function in obesity-related metabolic disease (Wada, 2008).The potential role of Vaspin in obesity of human and glucose metabolism is still unclear despite recent studies (Ko¨rner et al., 2011). In humans, the expression of Vaspin in terms of mRNA was founded in subcutaneous fat tissue and human visceral (Kloting et al., 2006). Recent studies in addition detect that circulating Vaspin values and gene expression of Vaspin in human fat tissue were positively correlated with diseases related to obesity (Tan et al., 2008).

There is many of proven evidence from previous studies showing the close relationship between Vaspin and obesity, which was looking to determine the level of Vaspin after gastric surgery that is performed to reduce body weight, noticed a decrease in the level of BMI and Leptin is associated with a decrease in Vaspin level (Figen et al., 2020). There is a study from several studies that indicated an increase in the level of the Vaspin in obese children and adolescents, and its level decreased after relying on a program to modify the short-term dietary lifestyle (Suleymanoglu et al., 2009). Finally, some studies conducted on humans showed the association of Vaspin with obesity and body mass index (Wada, 2008) though the association was more subtle or absent (Seeger et al., 2008).

CONCLUSION

From our study, we can conclude that there is a positive relationship between obesity and hormones (Leptin and Vaspin) in pubertal females. Adiponectin hormone and TAC in negative relationship with obesity in pubertal females.

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Author contribution statement

AA and SO contributed to the experimental design. AA and SO performed the experiment. AA wrote the manuscript.

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