Archives of Razi Institute, Vol. 77, No. 2 (2022) 703-707

DOI: 10.22092/ARI.2022.356954.1945

Original Article

Serum Level of Inhibin B and Kisspeptin, as well as Their Correlation with Biochemical Factors in Obese Adult Patients

Ibrahim, S. A[1]*, Adnan, A. A[1], Gahzi, S. T[1]

1. Basic Science Department, College of Nursing, University of Baghdad, Baghdad, Iraq

Received 5 December 2021; Accepted 16 January 2022
Corresponding Author: jalal.2t@yahoo.com

Abstract

Obesity is one of the most important global health problems causing serious health risks and early death in human. It is also associated with disturbance of homeostasis of hormones and immunological biochemical factors inside the human body. This study aimed to evaluate the serum level of inhibin B and kisspeptin among Iraqi obese adult people and other biochemical parameters correlated with obesity. Inhibin B and levels of kisspeptin were evaluated in the samples of serum from 40 Iraqi obese adult patients and 30 healthy non-obese individuals. A significant decrease (P<0.0001) was observed in the kisspeptin level in both males and females, compared to the control group. Moreover, inhibin B decreased significantly in obese females only (P<0.001), while there was no differences between males and the control group in this regard. Finally, body mass index, serum glutamic pyruvic transaminase (SGPT), and leptin showed negative correlation with kisspeptin (0.01, 0.5, and 0.01), respectively. However, a positive association was observed with the level of Ca in the serum. On the other hand, inhibin B confirmed a positive correlation with SGPT. The present study revealed a significant increase in inhibin B and kisspeptin, with SGPT and Ca in the serum of obese patients, which could lead to complications and health problems among these patients.

Keywords: Biochemical factors, Inhibin B, Kisspeptin, Obesity

1. Introduction

Obesity is a medical condition represented by extreme adipose tissue which affects physical health and causes serious problems for both males and females throughout their life. Clinical observations assessed body mass index (BMI), as the ratio of body weight divided by height (kilograms/ meters) (1, 2). Inhibin is a hormone produced in humans by the granulosa cells of reproductive organs (3, 4).

It is very important to preserve different tissue functions that appear to be the markers for infertility, as well as gestational and gynaecological diseases (5). Inhibin B in particular is evaluated as a marker of spermatogenesis, while in women, it regulates menstruation, ovarian folliculogenesis, and steroidogenesis (6). Therefore, it is considered a follicle-stimulating hormone (FSH) physiological signal feedback and a serum Sertoli cell function marker to predict the quality of semen and male infertility factor (7). Kisspeptin (metastin) is another important hormone that is made in the hypothalamus and controls the releasing of several other hormones. Studies showed an association between the degree of obesity and the enzyme by increasing the expression of this factor (8). Kisspeptin signaling is related to the body weight and energy metabolism as an important player in glucose homeostasis regulation, feeding behavior, and composition of body; in addition (9). Considering the importance of inhibin B and kisspeptin in body metabolism, energy balance, and obesity, this

study aimed to evaluate their relationship with BMI and biochemical factors by measuring these factors.

2. Materials and Methods

2.1. Sampling

The study was carried out at Al-kindy Medical College (Obesity Research and Treatment Unit), Baghdad, Iraq. In total, 43 obese (18 females and 25 males) people were selected within the age range of 16-63 years.

2.2. Hormonal and Metabolic Measurements

A clinical examination, biochemical laboratory examination (fasting blood sugar, blood urea, serum creatinine, lipid profile, serum glutamic-oxaloacetic transaminase, serum glutamic pyruvic transaminase, serum calcium, and uric acid), and diagnosis were conducted for each patient by the consultant medical staff. To compare the results, 30 healthy adults (15 males and 15 females) with approximate age were examined as the control group.

5 milliliters of blood samples were obtained from the venous blood of each participant; afterward, blood sera were collected by centrifuging (at 3000 rpm for 5 min) and stored at -20˚C until preparation for the experiment. The sera were assessed for inhibin B, kisspeptin, and leptin by an ELISA kit (Elabscience®, USA). The instructions of the manufacturer were followed to assess the variables.

2.3. Statistical Analysis

The results were assessed in a data sheet of SPSS software (version 20). The significant differences (mean±SD) were assessed by Kruskal-Wallis, Mann-Whitney, and Independent-Samples T-test. Furthermore, the correlation among inhibin B, kisspeptin, leptin, and other biochemical parameters were estimated by Person's correlation. A *P*-value of <0.05 was considered statistically significant.

3. Results

The comparisons between the experimental and control groups showed a significant difference in the mean serum levels of inhibin B, kisspeptin, leptin, and other biochemical parameters. According to the data in figure 1, kisspeptin level decreased significantly in both obese males and females, compared to the control group ($P \leq 0.0001$).

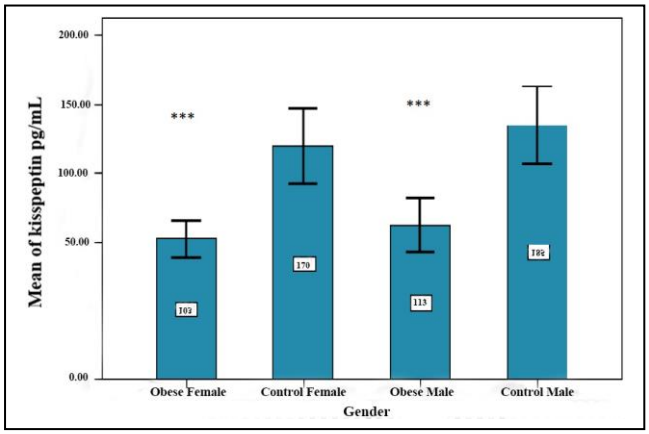

Figure 1. Kisspeptin mean levels in obese males and females, compared to the control group

On the other hand, inhibin B showed a significant decrease in obese females, compared to the control group ($P \leq 0.0001$); however, no significant difference was observed in the obese men, compared to the control group (Figure 2).

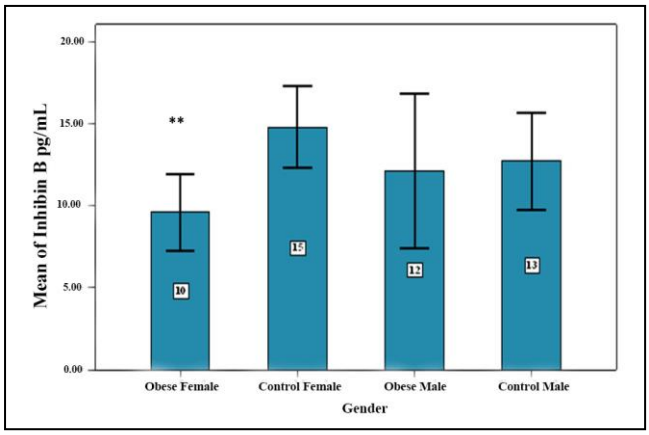

Figure 2. Inhibin B mean level in obese males and females, compared to the control group

Correlation of kisspeptin with BMI, SGPT, and leptin showed a negative relationship among these factors. Kisspeptin correlated positively with the level of Ca in serum, and inhibin B has a positive correlation with SGPT (Table 1).

Table 1. Relationship among kisspeptin, inhibin, leptin, and some biochemical factors in serum

Biomarkers	Kisspeptin (pg/mL)	Inhibin (pg/mL)
BM1 (kg/m^2)	-.573(**)	-.063
FBS (mg/dL)	.144	.141
B. UREA (mg/dL)	.139	.126
S. CREAT (mg/dL)	.148	.105
S. CHOLES (mg/dL)	-.223	-.213
S. TRIG (mg/dL)	-.178	-.067
S. VLDL (mg/dL)	-.184	-.065
S. HDL (mg/dL)	-.150	-.082
S. LDL (mg/dL)	-.039	-.187
S. GOT (u/L)	-.242	.225
S. GPT (u/L)	-.304(*)	.364(**)
S. Ca (mg/dL)	.309(*)	-.078
S. uricACID (mg/dL)	.247	-.031
Leptin	-.366(**)	.153

** Correlation is of significance at the level of 0.01 (2-tailed).
* Correlation is of significance at the level of 0.05 (2-tailed).

4. Discussion

Obesity is a global epidemic that is considered one of the risk factors for multiple metabolic disorders that can also affect impaired fertility in females and males (1, 2). The level of leptin, inhibin B, kisspeptin, and other biochemical parameters in obese penitents have been investigated in this study, and the correlation of these parameter was evaluated. Serum kisspeptin (Kiss-1) level decreased significantly in both obese males and females. This may be due to this fact that kisspeptin has ascended as a vital gonadotropin-releasing hormone stimulator (GnRH), facilitating the energy metabolism effect (10, 11). Many experimental studies detected that system of Kiss-1 is so susceptible to the alterations in the balance of energy and responding to the leptin stimulatory effect. The negative balance of energy and its related metabolic disorders repressed the hypothalamic Kiss-1 gene expression. An increasing in production and expression of Kiss-1 gene among obese patients relied on the obesity degree and duration. Therefore, it is well expected that disrupted homeostasis of energy condition, as a metabolite, interferes with Kiss-1 gene expression and modifies hypothalamic-pituitary-gonad sensitivity of axis to the stimulation of leptin (12, 13).

Consistent with a significant decrease of inhibin B in women, an association was observed with premature ovarian failure (14). However, others hypothesized that the syndrome of polycystic ovary and inhibin B levels are correlated inversely with BMI (15). It shows that BMI may inhibit the secretion of inhibin B, as well as the activity of granulosa cells, the production of B-blocking follicles, and possibly the follicle health in obese patients (16).The non-significant decrease of inhibin B in obese males is consistent with the results of a study by Globerman, Shen-Orr (17). This may be due to hypogonadotropic and relative hypogonadism (also low FSH).

Study on the correlation of kisspeptin with biochemical factors and enzymes showed a negative association with BMI, SGPT, and leptin. Kisspeptin correlated positively with the level of Ca in serum. Rance (13) in 2009 showed Kiss-1 expression in adipose tissues of both humans and rodents, which indicated that kisspeptin may play a role in regulating body weight. Few studies have examined kisspeptin signaling in relation to body weight and energy metabolism. Malnutrition and low body weight have been reported to be associated with low kisspeptin expression in hypothalamus (8). The elevation of liver enzymes is a common finding in obese patients without symptoms. Since obesity is linked to the increase in the estrogen hormone in women, it affects sexual activity, thereby impairing the secretion of both hypothalamus and the pituitary glands, which leads to a weakening of the secretion of the hormone kisspeptin (18). The most significant factor affecting the circulating levels of leptin is body fat mass, and leptin reflects the adipose tissue proportion at the steady eating cycle conditions (19).

Binding of kisspeptin into its receptors increases intracellular calcium which explains the positive relationship between them (20). In obese patients, the production of inflammatory cytokines is induced, which stimulates bone absorption by osteoclasts that may lead to the high level of serum calcium (21). Furthermore, the results showed a positive correlation

between inhibin B and SGPT, which interferes with the studies that indicated liver enzymes are a common finding in obese patients without symptoms and previous history of liver disease. This led to testosterone conversion to estradiol via the aromatase enzyme detected in elevated adipose tissue in such men and maintenance of fertility (22, 23).

Authors' Contribution

Study concept and design: S. A. I.
Acquisition of data: S. A. I.
Analysis and interpretation of data: S. A. I.
Drafting of the manuscript: A. A. A.
Critical revision of the manuscript for important intellectual content: A. A. A.
Statistical analysis: S. T. G.
Administrative, technical, and material support: S. T. G.

Ethics

This study was approved by the Ethics Committee of the Obesity Research and Treatment Unit, Al-kindy Medical College, Baghdad, Iraq. It should be mentioned that all participants provided informed consent.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Chambers TJ, Richard RA. The impact of obesity on male fertility. Hormones. 2015;14(4):563-8.
2. Du Plessis SS, Cabler S, McAlister DA, Sabanegh E, Agarwal A. The effect of obesity on sperm disorders and male infertility. Nat Rev Urol. 2010;7(3):153-61.
3. Bilezikjian LM, Blount AL, Donaldson CJ, Vale WW. Pituitary actions of ligands of the TGF-beta family: activins and inhibins. Reproduction. 2006;132(2):207-15.
4. Hayes FJ, Hall JE, Boeplle PA, Crowley WFJ. Differential Control of Gonadotropin Secretion in the Human: Endocrine Role of Inhibin. J Clin Endocrinol Metab. 1998;83: 1835-41.
5. Reis FMD, Rezende CP. Clinical usefulness of inhibin assays in Gynecology and Obstetrics. J Revista Brasileira de Ginecologia e Obstetrícia. 2009;31:621-5.
6. Makanji Y, Zhu J, Mishra R, Holmquist C, Wong WP, Schwartz NB, et al. Inhibin at 90: from discovery to clinical application, a historical review. Endocr Rev. 2014;35(5):747-94.
7. Laniyan D, Charles-Davies M, Fasanmade A, Olaniyi J, Oyewole O, Owolabi M, et al. Inhibin B Levels in Relation to Obesity Measures and Lipids in Males with Different Numbers of Metabolic Syndrome Components. J Sci Res Rep. 2016;10(5):1-2.
8. Hestiantoro A, Astuti BPK, Muharam R, Pratama G, Witjaksono F, Wiweko B. Dysregulation of Kisspeptin and Leptin, as Anorexigenic Agents, Plays Role in the Development of Obesity in Postmenopausal Women. Int J Endocrinol. 2019;2019:1347208.
9. Wolfe A, Hussain MA. The Emerging Role(s) for Kisspeptin in Metabolism in Mammals. Front Endocrinol. 2018;9:184.
10. De Bond JA, Smith JT. Kisspeptin and energy balance in reproduction. Reproduction. 2014;147(3):R53-63.
11. Turki S, Asmehan A, al-naqeeb A, Mohammed Z, Hameed W. Evaluation of Serum Leptin, Interlukein-6 and some Biochemical Parameters in Iraq obese Adult Patients. Medico-Legal Update. 2021;20:996-1002.
12. Quennell JH, Howell CS, Roa J, Augustine RA, Grattan DR, Anderson GM. Leptin deficiency and diet-induced obesity reduce hypothalamic kisspeptin expression in mice. Endocrinology. 2011;152(4):1541-50.
13. Rance NE. Menopause and the human hypothalamus: evidence for the role of kisspeptin/neurokinin B neurons in the regulation of estrogen negative feedback. Peptides. 2009;30(1):111-22.
14. Sharief M, Alharoon D, Mohammed H. Inhibin B as a Marker for Detection of Ovarian Activity in Premature Ovarian Failure. J Women's Health. 2018;07.
15. Hassan H, Ghazi S. Study of a hormonal assay in PCOS patients with type 2 DM and their correlation with inhibin B. Med-Leg Update.2020; 20(3): 575–580
16. Cortet-Rudelli C, Pigny P, Decanter C, Leroy M, Maunoury-Lefebvre C, Thomas-Desrousseaux P, et al. Obesity and serum luteinizing hormone level have an independent and opposite effect on the serum inhibin B level in patients with polycystic ovary syndrome. Fertil Steril. 2002;77(2):281-7.

17. Globerman H, Shen-Orr Z, Karnieli E, Aloni Y, Charuzi I. Inhibin B in men with severe obesity and after weight reduction following gastroplasty. Endocr Res. 2005;31(1):17-26.
18. Harter CJL, Kavanagh GS, Smith JT. The role of kisspeptin neurons in reproduction and metabolism. J Endocrinol. 2018;238(3): 173-83.
19. Crujeiras AB, Carreira MC, Cabia B, Andrade S, Amil M, Casanueva FF. Leptin resistance in obesity: An epigenetic landscape. Life Sci. 2015;140:57-63.
20. Babwah AV, Pampillo M, Min L, Kaiser UB, Bhattacharya M. Single-cell analyses reveal that KISS1R-expressing cells undergo sustained kisspeptin-induced signaling that is dependent upon an influx of extracellular Ca2+. Endocrinology. 2012;153(12):5875-87.
21. Dalfardi O, Jahandideh D, Ranjbar Omrani GH. The Correlation of Serum Calcium Level and Obesity; Is There Any Explanation? Galen Med J. 2013;2(1):26-31.
22. Fabian UA, Charles-Davies MA, Fasanmade AA, Olaniyi JA, Oyewole OE, Owolabi MO, et al. Male Sexual Dysfunction, Leptin, Pituitary and Gonadal Hormones in Nigerian Males with Metabolic Syndrome and Type 2 Diabetes Mellitus.J Reprod Infertil. 2016;17(1):17-25.
23. Okoli S, Charles-Davies M, Onifade A, Adekola S. Hypogonadism in Males Exposed to Mixed Chemicals in a Mechanic Village in Bodija, Ibadan. J Sci Res Rep. 2015;8(7):1-9.