Short Communication

Effect of Obesity on Androgen Receptor and Androgen Levels in the Serum of Women with Infertility in Babylon, Iraq

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Abstract

Background: Infertility is the inability to get pregnant after engaging in unprotected sexual activity for at least a year. Obesity and overweight are terms used to describe abnormal or excessive weight growth that is harmful to one's health. **Objectives:** The aim of this study was to measure the androgen receptor (AR), total and free testosterone, and dehydroepiandrosterone sulfates (DHEA-S) levels in the serum of Iraqi women who were having trouble getting pregnant and study the change of these parameters in the case of obesity and infertility. **Materials and Methods:** The case–control group was made up of 45 additional, presumably healthy women, whereas the sick group was made up of 45 obese infertile women. A study was carried out in the Babylon teaching hospital for maternity and children in Hilla city and private clinics from July to January 2022. An enzyme-linked immunosorbent assay (ELISA) was used to evaluate the serum concentrations of DHEA-S, total testosterone, and free testosterone (ELISA). SPSS software was used to conduct the statistical analysis. **Results:** A considerable drop in total testosterone and AR levels, infertile women exhibited significantly greater serum levels of free testosterone and DHEA-S than the control group ($P > 0.05$). **Conclusion:** Infertile women had considerably lower serum levels of total testosterone and ARs and significantly higher serum levels of free testosterone and DHEA-S. On the basis of the results of this investigation, obesity participates in the pathogenesis of infertility.

Keywords: Androgen, DHEA-S, obesity, SHBG, testosterone

Introduction

Infertility is the inability to get pregnant after engaging in unprotected sexual activity for at least a year. Numerous factors can contribute to infertility, and some of which can be managed by medical treatment. Drug use, advanced age, obesity, as well as problems with the hypothalamus, pituitary, thyroid, adrenal, and ovaries, can all have a severe impact on fertility. Obesity and overweight are terms used to describe abnormal or excessive weight growth that is harmful to one's health[1-3]

Once a man or woman has engaged in an uninterrupted, unprotected, sexual activity for a period of 12 months and is still unable to conceive, that condition is known as infertility. Having trouble getting pregnant is the main symptom.[4] Male infertility accounts for 20%–30% of cases of infertility, and female infertility accounts for 20%–35%. The most common reason for female infertility is ovulatory problems, which are typically characterized by erratic or nonexistent menstrual cycles. Defects in the semen are the most common cause of male infertility, and male fecundity is proxied by the semen's quality.[5]

Primary infertility refers to when a couple is unable to conceive. Secondary infertility occurs when a woman is unable to conceive after having a previous child. Infertility can sometimes be caused by an illness in either a man or a woman even though there is not always a clear underlying cause. In order for a woman to become pregnant, her uterus, fallopian tubes, and ovaries must be healthy. Fertility and an ova are likely influenced by hyperandrogenism in addition to an ovulation. Androgens are frequently associated with infertility, and historically, it was thought that they were bad for ovarian function.[6]

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Varied forms of obesity carry significantly different risks for the emergence of complex disorders. Our comprehension of the mechanisms by which metabolic and cardiovascular risk factors and diseases may be connected to obesity has considerably enhanced as a result of our growing awareness of the different variations between excess fat that is located in diverse physiological locations. Because of the expanding scientific interest, we now understand more about the key metabolic and hormonal mechanisms underlying the pathophysiology of obesity.[3]

Whereas testosterone (T) is the primary androgen in mature men, estrogen is created in women by converting androgen precursors, even though their T concentration is typically 15 times lower. Men primarily manufacture T in testicular Leydig cells, but women biosynthesize precursors into T in the adrenal cortex and ovaries, which is ultimately produced in the peripheral nervous system.[7] By means of several enzymatic processes, T is biosynthesized in tissues that are steroidogenic.

The traditional metabolic pathway can convert T into the stronger androgen, dihydro-testosterone, but there are other metabolic pathways that exist as well. The hormone-receptor complex is moved from the cell's cytoplasm to the nucleus, where it attaches to a specific region in the promoter of the target gene and starts the transcription of the gene, in accordance with the usual method of androgen action. Testosterone levels may be impacted by several variables, including age, physical activity, food, and weight.[8] The normal effect of testosterone on the target organ is mediated by the androgen receptor (AR), which also controls nuclear receptor gene transcription and directly interacts with membrane proteins or signaling molecules to speed the action.[9]

Materials and Methods

A study was carried out in the Babylon teaching hospital for maternity and children in Hilla city and private clinics from July to January 2022. The study included 90 women, with age ranging from 18 to 44 years, who were split into two groups. The first group included of 45 infertile women. The second group included 45 women, who have children, look to be in good health, and serve as the control group. Women who smoke, have chronic conditions such as diabetes or high blood pressure, or who use illicit drugs were excluded from both groups. All females (patients and controls) have a body mass index (BMI) that is used to determine their amount of obesity.

Inclusion and exclusion criteria

Inclusion criteria include obese infertile women, reproductive age ranging from 18 to 44 years, and normal weight. Exclusion criteria include hirsutism, acne, hypertension, thyroid disease, polycystic ovary syndrome (PCOS), and patients who had taken any hormonal medicine.

Statistical analysis

Statistical analysis was carried out using the Statistical Package for Social Science Software version 25 (SPSS, IBM Company, Chicago, Illinois). The results of phenotypes data were expressed as mean ± standard deviation (SD). Student's *t*-test and the linear regression analysis were used for the evaluation of data. The output data expressed 95% confidence interval (CI) and *P* value. A *P* value less than 0.05 was considered to be statistically significant.

Ethical approval

The objectives and methodology of this study were explained to all participants in the current study to gain their verbal acceptance. The study protocol and the subject information and consent from were reviewed and approved by a local ethics committee according to the document number 429 in August 23, 2022 to obtain this approval.

Results

The results found that there was a considerable drop in the total testosterone and AR levels. Infertile women exhibited significantly greater serum levels of free testosterone and dehydroepiandrosterone sulfates (DHEA-S) than the control group ($P > 0.05$). Table 1 shows the biochemical characteristics of the control and infertile populations.

The correlation between the measured parameters sequence variables of the control and infertile populations are illustrated in Table 2.

Discussion

Particularly in those with central obesity, obese women typically have reduced serum levels of sex hormone-binding globulin (SHBG). Whereas insulin and androgens lower it, it can be increased by estrogens, iodothyronines, and growth hormones. Because of the decreased hepatic synthesis, the hyperinsulinemia state brought on by obesity may be the main factor for the SHBG levels to be lower.[10] Because of their greater propensity to be metabolically cleared, free circulating sex steroids are produced more frequently as a result. A state of relative functional hyperandrogenism results from enhanced clearance being met by an increase in the body's androgen production as a result. Like how hypoandrogenism causes ovarian dysfunction by causing granulosa cells and follicles to apoptosis and luteinize too early.[11] This agrees with other research that found that obese women had increased free testosterone compared with normal weight women, which showed a significant difference ($P < 0.05$) between patients and control. This elevation in free testosterone is caused by obesity.

On the other hand, androgen overproduction can result in weakened ovarian function and unbalanced follicle growth, resulting in irregular periods, oligo-ovulation, and polycystic ovaries. These results corroborate our findings that infertile women with greater T levels.[12] As

Table 1: Biochemical characteristics of the control and infertile populations

Variables	Group	No	Mean ± SD	95% CI for mean		Sig. value
				Min	Max	
FT pg/mL	Patients	45	3.12±0.88	1.20	4.81	$P < 0.05$
	Control	45	1.03±0.86	0.01	2.1	
T ng/mL	Patients	45	0.14±0.185	0.01	0.80	$P < 0.05$
	Control	45	0.41±0.12	0.21	0.57	
DHEA-S µg/dL	Patients	45	249.6±87.33	46.30	363.60	$P < 0.05$
	Control	45	169±61.63	20.70	252.10	
AR ng/mL	Patients	45	1.09±0.82	0.18	2.91	$P < 0.05$
	Control	45	2.11±0.73	0.31	2.98	
BMI kg/m^2	Patients	45	32.22±1.44	30.1	35.8	$P < 0.05$
	Control	45	22.0±1.47	18.9	24.8	

$P < 0.05$

Table 2: A correlation (*r*) between the measured parameters sequence variables against each other correlation (*r*)

Sequence	Variables against each other	Correlation (*r*)	Sig. value
1	BMI vs FT	0.378	$P < 0.05$
2	BMI vs T	–0.55	$P < 0.05$
3	BMI vs DHEA-S	0.295	$P < 0.05$
4	BMI vs AR	–0.340	$P < 0.05$

a result, sustaining normal ovarian function requires an ideal balance between androgenic effects, and androgens support the health of follicles.

To have androgenic effects, DHEA-S must be converted to testosterone because it is attached to albumin. As androstenedione is the primary precursor of testosterone and DHEA only contributes to 5%–13% of the circulating testosterone in females of reproductive age, the serum level of DHEA-S is greater.[13]

Numerous tissues in the female body have ARs, and as we learn more about the specific actions of androgens in various tissues and the roles they play in different pathophysiological circumstances, our understanding of how androgens function in different tissues is also expanding. The nuclear transcription factor known as the AR, a member of the nuclear receptor family for steroid hormones, mediates androgens such as testosterone and dihydro-testosterone.[14]

Because its widespread expression in multiple cells and tissues, the AR plays important roles in the development and maintenance of the reproductive, muscular-skeletal, cardiovascular, immune, neurological, and hemopoietic systems.[15]

Androgens can function through the AR in ways that include DNA binding to influence the transcription of their target genes or methods that do not involve DNA binding to start fast cellular processes such the phosphorylation of 2nd messenger signaling cascades. A variety of organs, including the central nervous system, liver, skeletal muscle, adipose, and b-cells, are affected by androgen status, with androgen excess in women producing metabolic dysfunction through inadequate or excessive AR activity, respectively.[16]

Table 1 shows that, in contrast to control group members, infertile women had considerably lower serum levels of total testosterone and ARs and significantly higher serum levels of free testosterone and DHEA-S. The current study observed a significant (P value < 0.05) positive correlation for BMI with free testosterone (FT) and DHEA-S, significant (P value < 0.05) negative correlation for BMI with T and AR.

Conclusion

Based on the results of this investigation, we can conclude that obesity and insulin resistance participate in the pathogenesis of infertility.

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Conflicts of interest

There are no conflicts of interest.

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