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Correlation Between Shbg And Pregnancy Outcome In Pcos Women Undergoing Icsi Cycle

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Abstract

Background: Sex hormone-binding globulin (SHBG) is a glycoprotein which regulates bioavailability of sex steroid hormones. Interest in SHBG has escalated in recent years because of its inverse association with polycystic ovary syndrome (PCOS), obesity, insulin resistance, metabolic syndrome, and diabetes type II.

Aim of the study: To determine if there is a correlation between SHBG and pregnancy out come in PCOS women undergoing ICSI cycle .

Patients, Materials and Methods: Sixty infertile Iraqi women with PCOS and non-PCOS criteria from the Higher Institute for Infertility Diagnosis and Assisted Reproductive Technologies clinic were nominated. The women included in the study ranged in age from 20 to 45 years. SHBG levels are measured in serum (on pick-up and transfer days) and follicular fluid. All mature ova from both groups were injected with intracytoplasmic sperm. The outcomes of biochemical pregnancy were recorded, and the relationship between SHBG and pregnancy outcomes was established.

Results: Concentrations of SHBG were found to be significantly higher in infertile women with PCOS (serum and follicular fluid at oocyte retrieval and serum on the day of embryo transfer) than in infertile women without PCOS. In terms of pregnancy outcomes, elevated SHBG levels are an excellent predictor of pregnancy outcomes. More than 17.9 SHBG at pick-up day have a 100 percent prediction of a positive pregnancy outcome.

Conclusions: This study concluded that, levels of SHBG in PCOs was higher than non PCOs female. The elevation of SHBG have an excellent prediction of pregnancy outcome in PCOS women.

Keywords: Infertility, Sex-hormone binding globulin, Polycystic ovarian syndrome, pregnancy outcome ,ICSI.

Introduction

(Polycystic ovary syndrome) PCOS is a major cause of female anovulation and hyperandrogenism (1). In the long run, PCOS has been shown to cause a variety of systemic problems, including cardiovascular events, type 2 diabetes mellitus, metabolic syndrome, and infertility (2, 3). Female patients in their adolescence and childbearing years are the most commonly affected, with a 6 to 10% prevalence (4).

The Rotterdam consensus workshop, held in 2003, recommended that PCOS be diagnosed with at least two of the three features listed below: amenorrhea or oligomenorrhea ii. Hyperandrogenism as evidenced by clinical or laboratory tests. iii. Polycystic ovaries (defined as 12 or more follicles in at least one ovary measuring 2-9 mm in diameter or an ovarian volume greater than 10m3) (3).

(Sex hormone binding globulin) SHBG is a protein that binds to both testosterone and estradiol. Its amount varies greatly between patients, and whether the SHBG is low or high, so does the amount of active (bioavailable) testosterone. As a result, measuring SHBG in all polycystic ovarian syndrome patients is critical (5).

A decrease in plasma sex hormone-binding globulin (SHBG), a transport carrier that binds estrogen and androgens and regulates their biological activities, is commonly used as an indicator of hyperandrogenism in women with PCOS (6). Low serum SHBG levels are regarded as a biomarker of abnormal metabolism and have been linked to insulin resistance (IR), compensatory hyperinsulinemia, and abnormal glucose and lipid metabolism in PCOS patients (6). The SHBG gene polymorphism has been linked to an increased risk of PCOS. Because SHBG is involved in the onset and progression of PCOS (7). Understanding the molecular mechanism of SHBG in PCOS development and providing new ideas for treating female infertility are aided by understanding its role in PCOS.

SHBG may be thought of as a link between metabolic and reproductive pathways, and thus changes in hepatic SHBG production may be to blame for infertility issues in affected women (8). Women with PCOS have lower levels of SHBG, which is a glycoprotein produced in the liver that binds to the majority of sex steroids. SHBG synthesis is inhibited by insulin, as well as androgens, corticoids, progestins, and growth hormone (9). As a result, the current study will investigate the relationship between SHBG levels in PCOS women enrolled in IVF/ICSI cycles and pregnancy outcome.

Subjects, Materials and Methods

Sixty infertile females who were enrolled in assisted reproductive technology programs through undergoing ICSI cycles at the High Institute for Infertility Diagnosis and Assisted Reproductive Technologies/Al-Nahrain University, Baghdad /Iraq, during the period from November 2020 to May 2021. The couples were subjected to the basic fertility work-up of the fertility clinic, which involves case history, physical examination, ovulation detection, assessment of the tubal and uterine cavity.Seminal fluid analysis as recorded as recommended by WHO 1999 (10) and 2010 (11). While the measurement of sex-hormone binding globulin SHBG in serum and follicular fluid by ELISA kit (Shanghai Biological/China).

The infertile females in this study were subjected to antagonist ovarian stimulation protocols. The type of stimulation protocol used in previous IVF/ICSI trials, as well as the female's age, markers of ovarian reserve (such as antral follicle counts (AFC), Antimullerian hormone (AMH) levels, and/or early Follicle stimulating hormone (FSH), Luteinizing hormone (LH), and Estradiol levels), were considered.

All 60 infertile women had normal ovarian reserve based on their serum AMH levels. Polycystic ovarian syndrome was diagnosed in 40 women using the Rotterdam criteria (oligo-and/or anovulation, hyperandrogenism signs, and polycystic ovary morphology on ultrasound examination), as mentioned in (12) study.

Blood samples were drawn from each infertile woman via venipuncture on the day of oocyte retrieval and the day of embryo transfer. They were then centrifuged at 1000 g for 15 minutes. The serum was extracted and stored at -20°C or -80°C. To avoid contamination of the blood and flushing medium, the follicular fluid (FF) was obtained from the first retrieved follicle. Before being analyzed, it was frozen at -20°C for about 20 minutes. The enzyme-linked immunosorbent assay was used to measure SHBG serum and follicular fluid levels.

Statistical Analysis: The statistical analysis of this prospective study performed with the statistical package for social sciences (SPSS) 21.0 software and Microsoft Excel 2013. Numerical data were described as mean and standard deviation. While, categorical data were described as count and percentage. Chi-square test or Fisher exact test was used to describe the association between variables. The lower level of accepted statistical significant difference is equal or bellow to 0.05. The accuracy of diagnostic test was tested by calculation of Sensitivity, specificity, positive and negative predictive values (13).

Results

Whole number of 60 infertile women were chosen in this comparative study, 20 patients without polycystic ovary syndrome (Non-PCOS group) and 40 patients were diagnosed with polycystic ovary syndrome (PCOS group).

Comparison of the age and duration of infertility distribution of the studied women

This study involved measurement of SHBG in PCOS and non-PCOS females. However, there was no statistical significant difference (p=0.659) in the mean age of PCOS (30.35±4.84) and non PCOS groups (31.30±6.70). Both groups have the same duration of infertility (p=0.573) in which the duration in PCOS group was (8.40±4.64) and in non- PCOS was (7.20±6.79). No statistically significant difference (p=0.339) in the mean of body mass index was recorded between PCOS (26.78±5.16) and non- PCOS (28.67±4.65) group as shown in Table 1.

Table 1: mean age and duration infertility women classified into PCOS and non- PCOS groups

Demographic features	Study groups	N	Mean± SD	P value
Age (year)	PCOS	40	30.35±4.84	0.659^{NS}
	Non PCOS	20	31.30±6.70	
Duration (year)	PCOS	40	8.40±4.64	0.573^{NS}
	Non PCOS	20	7.20±6.79	
BMI	PCOS	40	26.78±5.16	0.339^{NS}

	Non PCOS	20	28.67±4.65	

N= number of cases, SD= standard deviation, PCOS= polycystic ovary syndrome ,BMI=body mass index

Comparison between type of infertility and pregnancy status

Regarding the type of infertility, PCOS group have (85%) primary infertility and only (15%) were secondary infertility while non- PCOS group have (70%) were primary infertility and (30%) was secondary infertility (p=0.334).Regarding outcome of pregnancy, (45%) in PCOS group and only two pregnant (20%) in non- PCOS group (p=0.246).

Table 2: Type of infertility and pregnancy status in PCOS and Non-PCOS groups.

Parameters		Study groups				P value
		PCOS		Non PCOS		
		N. patients	%	N. patients	%	
Infertility	Primary	34	85.0%	14	70.0%	0.334 ^{NS}
	Secondary	6	15.0%	6	30.0%	
Pregnancy	Negative	22	55.0%	16	80.0%	0.246^{NS}
	Positive	18	45.0%	4	20.0%	

N= number of cases, PCOS= polycystic ovary syndrome

Comparison of SHBG concentrations among study groups

The results in table -3 showed that there was highly statistical significant difference (p<0.001) in the mean of serum SHBG at ova pick up in PCOS females (25.03) in comparison with non PCOS (11.88). Pregnant females of non PCOS group have statistically higher level than those non pregnant females in which 15.18 compared with 11.06 respectively. While PCOS group have no statistically difference between pregnant and none pregnant females (25.46 and 22.27) respectively.

When the SHBG concentration measured in the follicular fluid, there was high statistical significant difference (p<0.001) in the mean of follicular fluid SHBG in PCOS females (19.67) compared with non PCOS (6.11). Pregnant females of both groups have not reach the significant level than those of non-pregnant females in which 7.14 and 18.57 compared with 5.85 and 20.57 respectively.

Table 3-: SHBG concentration in pregnant and non pregnant women complaining from PCOS and non-PCOS

SHBG concentration µg/ml		Study groups				P value
		non PCOS no=20		PCOS no=40		
		Mean	SD	Mean	SD	
SHBG serum at ova pick up	Non pregnant	11.06	7.37	25.46	3.15	<0.001**
	Pregnant	15.18	0.06	22.27	6.44	0.016*
	Total	11.88	6.73	24.03	5.03	<0.001**
SHBG FF at ova pick up	Non pregnant	5.85	1.34	20.57	4.93	<0.001**
	Pregnant	7.14	3.01	18.57	5.13	<0.001**
	Total	6.11	1.64	19.67	4.99	<0.001**
SHBG ET	Non pregnant	9.35	3.8	21.77	2.07	<0.001**
	Pregnant	5.11	1.86	20.49	2.17	<0.001**
	Total	8.50	3.85	21.19	2.16	<0.001**

FF: follicular fluid .ET: embryo transfer.

Discussion

The age and duration of infertility distribution of the studied women Female age

In the current study, there was no significant difference in the mean age of patients (20-42 years) between PCOS and non-PCOS patients. This finding demonstrated that both groups were of comparable age, which is important in eliminating any variable that could influence pregnancy outcomes in IVF/ICSI cycles. Furthermore, this finding can be compared to recent findings by (14) who found that the likelihood of conceiving after completing a treatment cycle decreases with age, with a dramatic drop in women over 35. After the age of 35, both the total number of embryos and the total number of high-quality embryos plummet. These findings imply that the age-related decline in IVF success is most likely due to a gradually decreasing ovarian reserve, with oocyte number and quality declining over time (15). According to some, a female's age is one of the most important predictors of fertility. Fertility declines with age due to a reduction in the quantity and quality of oocytes, resulting in lower ICSI/IVF pregnancy success rates (16). However, as previously stated, the age of the women in the two groups was comparable in the current study and had no effect on the results.

Type of infertility and pregnancy status

The difference in pregnancy rate between PCOS patients and non-PCOS patients was not statistically significant in the current study (Table 2). This result corroborated the findings of (17). This, however,

contradicts the findings of (18), who discovered that a sufficient number of collected oocytes, fertilized oocytes, and transferred high-quality embryos were responsible for satisfactory pregnancy rates in ovulatory PCO and PCOS patients. Furthermore, there were 40 more PCOS patients in our study than controls (n=40) (20). Others, however, did not find a difference in the pregnancy rate. The clinical abortion rate for PCOS patients, on the other hand, was higher than the control group. According to the authors, only cytoplasmic maturation was influenced in PCOS patients, not nuclear maturation (19).

Female age has a significant impact on IVF success rates, which can be easily found online for individual clinics. Among the maternal risks of IVF are OHSS, ectopic pregnancy, placental abruption, hypertensive disorders of pregnancy, gestational diabetes, and cesarean delivery (17).

Comparison of SHBG concentrations among study groups

Tables -3 revealed a statistically significant difference ($p<0.001$) in the mean serum SHBG at pick up in PCOS females (25.03) compared to non PCOS females (11.88). This study discovered that PCOS women undergoing IVF/ICSI cycles had significantly higher serum and FF SHBG levels than non-PCOS women. PCOS women typically complain of hyperinsulinemia, which increases theca cell androgen production (20), and when combined with low levels of SHBG – a buffer to sequester free testosterone – can result in hyperandrogenemia (21). It has been proposed that SHBG is linked to PCOS due to its influence on sex hormones. SHBG appears to play an important role in metabolic health, according to new evidence. Low SHBG levels have been linked to an increased risk of developing hypertension and type 2 diabetes mellitus (T2DM) in the general population, all of which are associated with PCOS (22). Some studies, on the other hand, have discovered that estrogen raises SHBG levels while androgen decreases them (23, 24). As a result, an increase in SHBG in PCOS women may be due to an increase in estrogen levels. (In addition, women with PCOS who underwent IVF/ ICSI cycles produced more oocytes, which were often of poor quality, contributing to lower fertilization, cleavage, and implantation rates.) This finding contradicted the findings on fertilization rates presented in this study.

Non-PCOS pregnant women have statistically higher levels of SHBG than non-pregnant women (15.18 compared with 11.06 ,respectively). While there is no statistical difference in the PCOS group between pregnant and non-pregnant females (25.46 and 22.27), when SHBG concentrations in follicular fluid were measured, there was a high statistically significant difference ($p<0.001$) in the mean of follicular fluid SHBG in PCOS females (19.67) compared to non PCOS females (6.11). There is no statistically significant difference in levels between pregnant females and non-pregnant females in either group. It has been concluded that elevated SHBG levels in FF may reflect the functional state of ovarian stimulation, and that such elevations may influence pregnancy outcome via modulation of circulating estrogen and androgen balance during IVF/ICSI cycles with down-regulated COH levels (25).

Conclusions: This study concluded that SHBG levels in PCOs were higher than in non-PCO females. In PCOS women, elevated SHBG levels are an excellent predictor of pregnancy outcome.

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