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Original Article

Polycystic Ovary Syndrome

Pak Armed Forces Med J 2020; 70 (6): 1870-73

# ASSOCIATION OF ANEMIA WITH SERUM SEX HORMONE BINDING GLOBULIN LEVELS IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME

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## ABSTRACT

***Objective***: To find association of anemia with serum sex hormone binding globulin levels in women with PCOS.

***Study Design:*** Cross sectional study.

***Place and Duration of Study:*** University of Health Sciences Lahore, from Jan 2018 to Jun 2018.

***Methodology***: The study was conducted after approval from Ethics review committee of University of Health Sciences, Lahore. The Data was assessed by IBM-SPSS version 22. Normality of different continuous variables was checked by Shapiro-wilk test. Frequency distributions of study participants were calculated. Significance of the associations was assessed by Mann Whitney-U test and *p*-value <0.05 was taken as statistically significant.

***Results***: Most of the participants of our study were married (53.3%) and 77.9% of these married women don't have children. 35 out of 60 were anemic (58.3%). The median ± interquartile ranges of age, BMI, SHBG and serum testosterone were 25 ± 9, 25.5 ± 9.75, 22.2 ± 13.08 and 0.24 ± 0.15 respectively. Mean Serum sex hormone binding globulin levels were found to be significantly associated with anemia (P=0.046) with mean ± SD of 16.30 ± 5.61 in anemic patients which was lower than the normal blood levels of SHBG (18-140 nmol/l). Anemia was non-significantly associated with the other factors like age, BMI and serum testosterone.

***Conclusions***: It was evident from this study that anemia is strongly associated with SHBG levels in PCOS. Further studies are required with larger sample size in future to rule out the underlying causes.

**Keywords**: Anemia, Polycystic ovary syndrome, Sex hormone binding globulin.



## INTRODUCTION

Polycystic ovary syndrome (PCOS) is a disease characterized by the accumulation of various cysts (fluid-filled sacs) in the ovaries with raised male hormone levels, long term anovulation (absent ovulation), and some other metabolic disturbances[1]. PCOS is of public health and clinical importance as it is quite common and affects one in five women of reproductive age[2]. It has also been reported that the prevalence rate of PCOS in Pakistan is 20.7%[3]. Sex hormone binding globulin (SHBG) is a protein which binds to both estradiol and testosterone[4]. Its amount can vary in women with PCOS. If levels of the SHBG are either low or high, the amount of active testosterone can change accordingly[5]. Therefore, it is very critical to measure SHBG in all subjects being evaluated for PCOS. Serum Testosterone is a steroid hormone formed by zonareticularis of adrenal cortex in women. It was seen in previous literature that in PCOS women these levels were recorded on higher side[6].

Anemia in women generally in the world and specifically in Pakistani women is quite prevalent as recent studies showed[8]. There are many factors which contribute to anemia in women including dietary deficiencies, menstrual issues, pregnancy related problems and many more[9]. Anemia itself is a dangerous disease which provides ground for many other problems as well. PCOS women usually have menstrual issues during the disease including amenorrhea and menorrhagia[10].

The association of anemia with different hormonal factors was calculated in the past[11], but its association with SHBG has not been recorded yet in Pakistan. As SHBG has a direct impact on

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*Received: 30 Jul 2018; revised received: 02 Feb 2019; accepted: 15 Feb 2019*

the circulating androgen levels in females[12], and it is also thought that it can affect the levels of hemoglobin as well. This study was aimed to find the association of anemia with SHBG levels in the patients with PCOS.

## METHODOLOGY

This cross sectional study was conducted at University of Health Sciences, Lahore, from January 2018 to June 2018 after approval from ethics review committee of UHS, Lahore. A validated questionnaire was filled by the patients after taking informed consent from them.

Sample size was calculated according to following formula:

$$\text{Sample size} = \frac{Z_{1-\alpha/2^2}\, p(1-p)}{d^2}$$

$Z_{1\text{-}a/2}$= is standard normal variate (at 5% type 1 error ($p$<0.05) it is 1.96. As in majority of studies

$p$-values are considered significant below 0.05 hence 1.96 is used in formula.

$p$=Expected proportion in population based on previous studies or pilot studies = 0.20 (7).

d = Absolute error or precision = 0.08.

Sample size=60.

Women aged between 20-40 years with diagnosed PCOS by AES criteria presenting to outdoor departments of different tertiary care hospitals of Lahore were included. Women aged >20 or >40 years and those with any other endocrinological disorder were excluded from the study.

Convenient sampling technique was used. Blood samples of the study participants were taken and serum was separated by centrifugation. Levels of Sex Hormone Binding Globulin were assessed by using ELISA.

The data was assessed by IBM-SPSS-22. Normality of different continuous variables was checked by Shapiro-wilk test. Frequency distributions of study participants were calculated along with medians. Significance of the associations was assessed by Mann Whitney-U test and $p$-value>0.05 was taken as statistically significant.

## RESULTS

This results showed that most of the participants of our study were married (53.3%) and 77.9% of these married women don't have children. Thirty five out of 60 were anemic (58.3%). We also checked normality of continuous variables of our data by Shapiro-Wilk test where the $p$-values of all the continuous variables were found to be >0.05. Hence it signified that the distribution of the data was skewed. The median ± interquartile ranges of age, BMI, SHBG and serum testosterone were 25 ± 9, 25.5 ± 9.75, 22.2 ± 13.08 and 0.24 ± 0.15 respectively.

**Table-I: Frequency distributions of different characteristics in the women with PCOS (n=60).**

| Demographic Characteristics | Groups | Frequency n (%) |
|---|---|---|
| Marital Status | Married | 32 (53.3) |
| | Unmarried | 28 (46.7) |
| Having Child/Children | Yes | 7 (22.1) |
| | No | 25 (77.9) |
| Anemia | Yes | 35 (58.3) |
| | No | 25 (41.7) |

**Table-II: Normality of data by shapiro-wilk test along with medians ± interquartile ranges (n=60).**

| Variables | Median ± Interquartile Range | $p$-value* |
|---|---|---|
| Age (Years) | 25 ± 9 | 0.002 |
| Basal Metabolic Index | 25.5 ± 9.75 | 0.011 |
| Sex Hormone Binding Globulin (nmol/l) | 22.20 ± 13.08 | 0.003 |
| Serum Testosterone (pg/dl) | 0.24 ± 0.15 | 0.004 |

**According to Shapiro wilk test if p-value ≤0.05 than data is having skewed distribution.*

**Table-III: Association of anemia with serum sex hormone binding globulin and serum testosterone levels by Mann Whitney-U test (n=60).**

| Variables | Anemia | | $p$-value |
|---|---|---|---|
| | Yes | No | |
| SHBG | 16.30 ± 5.61 | 20.30 ± 8.34 | 0.046 |
| Serum Testosterone | 0.26 ± 0.16 | 0.20 ± 0.10 | 0.121 |
| Age | 27.57 ± 6.21 | 26.88 ± 6.19 | 0.765 |
| BMI | 26.34 ± 5.65 | 27.44 ± 6.68 | 1.000 |

We also checked for any association of anemia with the above mentioned variables. Mean

Serum sex hormone binding globulin levels were found to be significantly associated with anemia ($p$=0.046) with mean ± SD of 16.30 ± 5.61 in anemic patients which was lower than the normal blood levels of SHBG (18-140 nmol/l). Anemia was non-significantly associated with the other factors like age, BMI and serum testosterone table-I.

## DISCUSSION

Polycystic ovarian syndrome is becoming the disease of younger females now across the world generally and in Pakistan specially[13]. Though we took samples from women aged between 20 to 40 yet the median age of our study population was found to be 25 ± 9 which showed that the women affected by PCOS in our study also belonged to younger age group. In a previous study the mean age was 28 years[14]. As the previous literature review of PCOS showed that infertility is quite common in PCOS women due to menstrual irregularities[15], and it was also shown in our results as 77.9% of married women were having no children hence affected by primary infertility.

Prevalence of anemia is generally higher in Pakistan[16], but in PCOS patients it was not found much prevalent in the previous studies[17], as it is not the main feature of PCOS. In contrary our results showed high prevalence of anemic patients (58.3%) in women with PCOS. Though amenorrhea dominates among menstrual irregularities in PCOS[18], yet our study population was having higher ratios of anemia.

The mean levels of serum sex hormone binding globulin (SHBG) in all the patients were found to be within normal range (22.20 ± 13.08) but surprisingly it was found to be towards the lower side (16.30 ± 5.61) among anemic patients which was quite striking. The non-anemic were having higher levels of SHBG as compared with anemic. Anemia was also found to be highly significant associated with SHBG ($p$=0.046). SHBG do affect the free serum testosterone levels among PCOS in females and testosterone is a potent stimulator of erythropoietin which in turn causes increase production of red blood cells from bone marrow[19]. As the levels of testosterone were found to be within normal range in our study population so SHBG may be affecting the production of red blood cells directly. Another reason can be that SHBG is produced from liver[20], and liver has also role to play with red blood cells degradation along with spleen so decreased SHBG production from liver can also affect hemoglobin levels in blood. Extensive research is required further to know the pathology of such anemia.

## CONCLUSION

It was evident from our study that anemia is strongly associated with SHBG levels in PCOS. Further studies are required with larger sample size in future to rule out the underlying causes.

## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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