

Original Research Article

CORRELATION BETWEEN POLYCYSTIC OVARY SYNDROME AND DRY EYE DISEASE

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ABSTRACT

Background: Hyperandrogenism and insulin resistance are seen in polycystic ovary syndrome (PCOS) which are also known risk factors for dry eyes. Dry eye is a potential comorbidity present in patients with PCOS. **Aim:** To find correlation between dry eye disease (DED) and PCOS.

Materials and Methods: A total of 50 women with polycystic ovary syndrome (PCOS) and 50 healthy controls were included in the study. They were then subjected to a complete ophthalmic evaluation which included tear film break-up time, Schirmer's test and Ocular Surface Disease Index (OSDI) questionnaire scoring.

Results: Correlation between DED and PCOS was found to be statistically significant in both TBUT and OSDI score while Schirmer's test was found to be statistically insignificant.

Conclusion: PCOS has a positive correlation with DED and hence regular eye check-ups are advisable for patients with PCOS.

Keywords: Polycystic ovary syndrome, dry eye disease, TBUT, OSDI, Schirmer's test.

INTRODUCTION

PCOS, known as Polycystic ovary syndrome, is identified as a prevalent endocrine disorder affecting 4.8-8% of women in their reproductive years.^[1]

This syndrome is characterized by a diverse range of endocrine dysfunctions, leading to disruptions in hormonal, reproductive, and metabolic processes. In addition to its classification as a gynecological disease, PCOS is linked with various metabolic and endocrine irregularities, such as insulin resistance (IR), obesity, and a susceptibility to developing type 2 diabetes.^[2,3,4] The manifestation of IR in individuals with PCOS is further connected to androgen production and reduced levels of sex hormone-binding globulin, thereby playing a crucial role in the development of hyperandrogenism.

Numerous studies have elucidated a potential association between dry eye syndrome and metabolic disorders such as diabetes mellitus.^[5,6] These studies suggest that insulin resistance (IR), prolonged hyperglycemia, oxidative stress, and

hyperandrogenism may exert a significant influence on the pathogenesis of dry eye syndrome.^[7,8,9]

Sex hormones have been known for influencing anatomical and functional structures of the ocular surface including changes in tear film.^[10] Only few studies have explored the connection between dry eye syndrome and PCOS. Thus, the rationale and the primary objective for this study were to determine the correlation between DED and PCOS.

MATERIALS AND METHODS

It was a case-control study conducted in 100 participants in the age group of 16-44 years, out of which 50 diagnosed cases of PCOS taken as case group and 50 healthy, normally menstruating women were taken as control group.

Exclusion criteria included smokers, alcoholics, contact lens users, patients with corneal opacities, prior history of dry eye disease, patients taking oral contraceptives, patients using topical drops for long time, any history of previous intraocular surgery.

The study was conducted in the Department of Ophthalmology, Sharda Hospital after ethical clearance was taken from the Institutional Ethical Committee. Written informed consent was obtained from all patients. The diagnosis of PCOS was confirmed on the basis of the diagnostic criteria of the Rotterdam European Society of Human Reproduction/American Society for Reproductive Medicine.^[11] Free testosterone and serum insulin levels were recorded on the third day of menstruation.

An ocular surface disease index (OSDI) validated questionnaire scoring was done in all subjects to assess symptoms of dry eye.^[12] Following which a complete ophthalmic evaluation was conducted which included Schirmer's Test and Tear Film Breakup Time (TBUT). In Schirmer's test, a 35x5 mm Whatman filter No. 41 paper strip was placed in the inferior conjunctival fornix at the junction of its lateral 1/3rd and medial 2/3rd to measure the quantity of tears produced over a period of 5 minutes. A test result of more than 15mm was considered to be normal while less suggested dry eyes. Five minutes after Schirmer's test, TBUT test was performed. In this the subject was instructed to look upwards and a sodium fluorescein strip was smoothly touched to the inferior fornix conjunctiva and then removed. Patients were directed to blink three times and then to look straight ahead without blinking. The tear film was observed under the cobalt-blue filtered light of a slit-lamp

biomicroscope, and the interval in seconds between the last blink and the appearance of the first dry spot was recorded as the TBUT. A TBUT of more than 10 secs was considered normal and less was taken as dry eyes.

Data was analyzed using latest Microsoft Excel worksheet and SPSS version 22. Percentages was compared using the chi-square test. The data was described as mean \pm standard deviation, median, and percentage, according to the type of variable. Pearson correlation analysis was performed to analyze correlations and $p < 0.05$ was taken as statistically significant.

RESULTS

The study group comprised 50 women with PCOS in the case group (group 1), and the control group (group 2) comprised 50 normal, healthy women. The mean age was 23.22 \pm 3.12 years and 22.47 \pm 3.66 years in group 1 and 2 respectively. Free testosterone and serum insulin levels were significantly higher in Group 1 and was statistically found to be significant ($p < 0.05$). [Table 1] Schirmer's test results were similar between groups ($p > 0.05$), but OSDI questionnaire score and TBUT test results were significantly affected in Group 1 and was statistically found to be significant ($p < 0.05$). [Table 2]

Table 1: Comparison of free testosterone and serum insulin levels between case and control groups

Parameter	Group 1 (n=50)	Group 2 (n=50)	P value
Free Testosterone (pg/ml)	7.97 \pm 1.07	3.22 \pm 0.50	0.004*
Serum Insulin (μ U/mL)	11.8 \pm 4.6	6.5 \pm 1.51	0.002*

Data are presented as mean \pm standard deviation for each of group (* $p < 0.05$ is considered statistically significant).

Table 2: Comparison of dry eye test parameters between case and control groups

Test	Group 1 (n=50)	Group 2 (n=50)	P value
Schirmer's Test (mm)	26.13 \pm 7.09	28.79 \pm 7.55	0.51
TBUT (secs)	9.2 \pm 2.07	12.57 \pm 3.15	0.002*
OSDI Score	19.29 \pm 4.38	11.23 \pm 2.47	<0.001*

Abbreviations: TBUT: tear break-up time; OSDI: ocular surface disease index. Data are presented as mean \pm standard deviation for each of group (* $p < 0.05$ is considered statistically significant).

DISCUSSION

The impact of insulin resistance and hyperandrogenism on the eyes, leading to ocular surface changes which can result in dry eyes, has recently gained significant attention in the area of reproductive endocrinology. Both of these conditions are widely prevalent in PCOS with almost 75-90% of them having hyperandrogenism and 35-80% having insulin resistance.^[13,14] A prevalence of DED, reaching up to 54.3%, is seen in patients with insulin resistance.^[14]

PCOS is a complex disorder presenting with hyperandrogenism, chronic anovulation, and various metabolic complications, including insulin

resistance and hyperinsulinemia. Our current study evaluated the correlation of DED and PCOS. An expert meeting in 2003 in Rotterdam recommended that PCOS can be defined when at least two of the following features were present oligo or anovulation, clinical or hyperandrogenism or polycystic ovaries.^[15] Adali reported that BMI, hirsutism score, LH/FSH ratio, serum testosterone levels and insulin resistance in greater in PCOS patients than in healthy individuals.^[16] Similarly in our study serum insulin and testosterone levels were found to be significantly higher in PCOS patients.

A composite assessment involving OSDI, TBUT, and Schirmer test has been identified as the most

effective diagnostic approach for dry eye, offering a sensitivity of 100%, specificity of 95%, and an accuracy of 99.3%.^[17] Consequently, these three tests were implemented in our study.

The Schirmer's test did not yield statistically significant differences but patients with PCOS showed notably lower TBUT values and higher OSDI questionnaire score which was found to be statistically significant. While the Schirmer test serves as a valuable tool for identifying lacrimal hyposecretion, it should be considered merely a preliminary screening method, with reported sensitivity levels ranging as low as 30-60%.^[17] Various studies have struggled to establish a direct correlation among different diagnostic tests. A recent study involving 491 participants did not reveal any significant distinctions between individuals with and without dry eyes concerning Schirmer test outcomes or epithelial damage.^[17] In a separate study, tear function assessments in symptomatic patients indicated that most individuals (94%) had normal results on the Schirmer I test, while TBUT values were notably diminished, aligning with current research findings.^[18]

Research has pointed to the influence of sex hormones on meibomian gland functions, androgens in particular are known to modulate meibomian gland secretion affecting the lipid layer of tear film as well as lacrimal gland function influencing the aqueous tear film layer alongside the regulation of mucin gene expressions.^[19] Studies have indicated a potential negative relationship between TBUT values and free testosterone levels.^[20,21] Few previous studies have explored the interplay between PCOS and ocular health, recent findings have linked higher corneal thickness in PCOS patients to elevated IGF-1 levels, potentially leading to conditions like glaucoma.^[22] Similar various other research have also associated hyperandrogenism in PCOS patients with reduced tear volume.^[23] Nevertheless, these studies have yet to show the broader connection between DED and PCOS.^[24] Hence, we have conducted our study to show the correlation between DED and PCOS

It is worth noting that a portion of PCOS patients may experience dry eye to some extent without exhibiting subjective symptoms (evaluated through the OSDI questionnaire) as seen in patients with normal OSDI score but decreased TBUT and Schirmer's test. Signs of dry eye can be identified through alternative sensitive examinations in a considerable proportion of these individuals. The limitation of our study was that we could not study the long-term manifestations on ocular surface and affect on dry eye disease due to PCOS in our study and could be a topic of research for future investigations.

CONCLUSION

Dry eye disease is often overlooked in context of PCOS and only limited studies have been done correlating dry eye disease in PCOS patients. Our study shows that there is a positive correlation between DED and PCOS and hence, PCOS patients should undergo regular ophthalmic examination so that early diagnosis of DED can be established for its early and timely management.

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