Original Research

COMPARATIVE EVALUATION OF CONJUNCTIVAL IMPRESSION CYTOLOGY AND TEAR FILM TESTS IN EARLY DIAGNOSIS OF DRY EYE IN NEWLY DIAGNOSED PATIENTS OF POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT

Introduction: Polycystic ovarian syndrome (PCOS) is one of the most prevalent endocrine diseases in reproductive women and occurs in conjunction with the systemic hormonal derangement and metabolic disease processes associated with the disease. The steroid hormone sex hormones have a major impact on the physiology of the ocular surface (OS), the function of the lacrimal gland (LG), the activity of the meibomian glands (MG), and the stability of the tear film (TF). Dry eye disease (DED) and OS abnormalities are becoming more prevalent in the PCOS population. Schirmer's test (ST) and Tear Film Break Up Time (TBUT) are the conventional means to evaluate dry eye disease. Conjunctival impression cytology (CIC) is a test that might assess the earliest cytologic changes associated with dry eye prior to demonstrating clinical evidence of dry eye through the surface abnormality of the tear film. There has been little evidence comparing conjunctival impression cytology to traditional assessments of dry eye disease using Scheimer's test and TBUT in patients newly diagnosed with PCOS.

Aim: To comparatively evaluate conjunctival impression cytology and tear film tests in early diagnosis of dry eye among newly diagnosed patients with polycystic ovarian syndrome.

Objectives

1. To evaluate Schirmer’s Test 1 and Tear Film Breakup Time findings in newly diagnosed PCOS patients.
2. To assess conjunctival impression cytology changes in newly diagnosed PCOS patients.
3. To determine the correlation between conjunctival impression cytology grading and tear film test findings.
4. To evaluate whether conjunctival impression cytology detects ocular surface abnormalities earlier than routine clinical tear film tests.

Methodology: The research employed as a design a cross sectional observation study with data collected from patients visiting a tertiary care hospital Department of Ophthalmology as well as Obstetrics and Gynecology. Patients with PCOS who fit the criteria above were selected based upon their age range of 18-45 years. The patients who satisfied the criteria for a diagnosis of PCOS were evaluated based upon the 2003 Rotterdam Criteria (RC), and each underwent a Schirmer’s Test 1, Tear Breakup Assessment, and a conjunctival impression cytology from their right eye. The conjunctival impression cytology specimens were graded according to Nelson’s grading system. The Statistical analysis used to assess the association between the CIC Grading and Tear Tests was carried out with the use of statistical software SPSS, and the relationship between the CIC Grading and Tear Tests was assessed using Pearson or Spearman correlation coefficients.

Results: Most of the participants in the study were aged 21-25. A total of 38.7% of subjects had abnormal results on the Schirmer's test, 44% had abnormal (TBUT) results and 68% of subjects demonstrated conjunctival impression cytology abnormalities. The conjunctival impression cytology demonstrated higher positivity rates compared to the Schirmer's test or TBUT.

Grade 1 conjunctival impression cytology abnormalities accounted for the majority of abnormal results in the study. There were decreasing amounts of Schirmer's test results and TBUT results as the conjunctival impression cytology grades increased. The correlation between conjunctival impression cytology grade and Schirmer's test result was negative and statistically significant ($r = -0.68$, $p < 0.001$); likewise, the correlation between conjunctival impression cytology grade and TBUT result was negative and statistically significant ($r = -0.74$, $p < 0.001$).

Most importantly, many patients whose results were clinically normal for both Schirmer's test and TBUT had an abnormal conjunctival impression cytology, indicating that preclinical ocular surface changes may occur prior to the results of the routine clinical tests.

Conclusion: Cytology of the conjunctival surface has proven to be an accurate, non-invasive way of diagnosing patients with polycystic ovarian syndrome (PCOS) who are experiencing alterations to their ocular surface at an early stage. The detection of cytological changes is dependent upon routine testing of the patient's tears using traditional methods like Schirmer's test and TBUT; however, it has been found that cytological changes can occur prior to any observable changes occurring to the patient's tear film.

By incorporating these diagnostic tools into a complete ocular evaluation for patients who are newly diagnosed with PCOS, ophthalmologists will have a greater opportunity for diagnosing patients with subclinical dry eye syndrome, and consequently, to provide a timely intervention to help prevent any further deterioration of their ocular health.

Keywords: Polycystic Ovarian Syndrome, Dry Eye Disease, Conjunctival Impression Cytology, Schirmer's Test, Tear Film Breakup Time, Ocular Surface Abnormalities, Nelson Grading, Tear Film Instability, PCOS, Cytological Changes.

www.ajmrhs.com
eISSN: 2583-7761

Date of Received: 01-05-2026
Date Acceptance: 09-05-2026
Date of Publication: 21-05-2026

INTRODUCTION

Polycystic ovarian syndrome or PCOS, is an endocrine disorder that is commonly encountered in females of reproductive age characterized by irregular menstruation, hyperandrogenism, and polycystic ovaries [1]. Its prevalence has been estimated between 5%-20%, depending on diagnostic criteria and population studied. In addition to the reproductive and metabolic dysfunctions, PCOS is now known to cause dry eye syndrome, especially involving the tear film and ocular surface [2].

Androgens and estrogens are sex steroid hormones that are necessary for proper health of the ocular surface. These hormones promote the secretion of tears from the lacrimal glands, regulate the activity of the meibomian glands, maintain health of the conjunctival epithelial cells, and promote the stability of the tear film [3]. Therefore, the imbalance in sex hormones seen in PCOS may contribute to disturbances in the homeostasis of the ocular surface and in the production of tears. The impaired metabolism of androgens and estrogens can lead to malfunction of the meibomian glands, decrease in number and density of goblet cells, make the tear film unstable, and increase inflammation of the ocular surface [4,5].

Dry eye disease is a multifactorial disorder of the tears and ocular surface characterized by tear film instability, ocular discomfort, visual disturbance, and inflammation of the ocular surface [5]. Patients may present with symptoms including burning sensation, foreign body sensation, irritation, redness, photophobia, and fluctuating vision. Subclinical ocular surface dysfunction may however precede overt clinical manifestations, particularly in endocrine disorders such as PCOS [6]..A number of research studies have looked at how dry eye symptoms are seen in women with polycystic ovarian syndrome (PCOS) by comparing Schirmer's Test results and tear break up times in PCOS women to those of control groups [7]. The results indicated lower values on these tests for PCOS women which is attributed to decreased tear production and unstable tear films [8]. However, it should be noted that most of the routine tests used to determine dry eye will only indicate abnormalities once there has been substantial structural and physiological damage to the ocular surface.

Conjunctival impression cytology (CIC) is a minimally invasive procedure that can be used to determine the morphology and density of goblet cells and epithelial cells by collecting the top layer of cells from the conjunctiva using a cellulose acetate filter paper [9]. CIC provides valuable information regarding squamous metaplasia, goblet cell loss, and epithelial alterations associated with ocular surface disorders [10]

Very few studies have looked at the conjunctival impression cytology findings and results from tear film tests to help in making the diagnosis of dry eye in PCOS. Research has shown that cytological changes in the conjunctiva may occur prior to the development of clinical dryness as evidenced by a positive Schirmer's Test or TBUT; therefore, these studies may show a new way to diagnose early dysfunction of the ocular surface prior to the development of clinically significant dry eye disease [11]. Identifying these early signs can allow for timely intervention by ophthalmologists in order to prevent further damage or deterioration of the ocular surface.

Currently, the most common diagnostic criteria for the diagnosis of PCOS was established by the Rotterdam consensus criteria. These criteria require

the presence of at least two of the following three symptoms for a diagnosis: (1) Oligo/anovulation, (2) Clinical or laboratory-defined Hyperandrogenism, and (3) Polycystic ovarian morphology [12]. As newly diagnosed patients may have early hormonal changes in their ocular tissues, the assessment of the tear film and conjunctival epithelial changes in this population will provide insight into potential future dry eye disease and the timing of its onset.

The use of conjunctival impression cytology to evaluate conjunctival epithelial cells provides a simple, non-invasive, cost-effective, and a sensitive means of identifying early changes of the ocular surface which occur before clinically negative dry eye testing is established [13]. If conjunctival impression cytology shows early cytological changes in conjunctival epithelial cells from patients diagnosed with PCOS, this will provide additional evidence that conjunctival impression cytology can be used as a useful pre-clinical diagnostic tool to identify the early stages of dry eye disease [14].

Hence, the present study was undertaken to comparatively evaluate conjunctival impression cytology and tear film tests in newly diagnosed patients with polycystic ovarian syndrome and to assess whether cytological alterations precede clinically detectable tear film abnormalities in early dry eye disease.

Aim and Objectives

The purpose of this study was to conduct a comparative evaluation of conjunctival impression cytology and tear film tests, in relation to the early detection of diabetic keratopathy, among newly diagnosed women with PCOS. Specifically, it aimed to assess the Schirmer's score and Tear Film Break-up Time in these newly diagnosed women as well as perform conjunctival impression cytology evaluation on the same women; to assess the relationship between the grading of conjunctival impression cytology and tests to assess the tear film; to assess the positive findings of conjunctival impression cytology and the direct tear film test results; and to assess the utility of conjunctival impression cytology in early detection of ocular surface alterations in PCOS patients.

MATERIALS AND METHODS

This hospital-based, cross-sectional observational research includes patients visiting the Departments of Ophthalmology and Obstetrics & Gynaecology of a tertiary care facility. The study included 75 patients who were newly diagnosed with polycystic ovarian syndrome (PCOS) between 18 and 45 years of age. All patients who met the 2003 Rotterdam diagnostic criteria for PCOS were eligible to participate in this study. The Rotterdam criteria state that for diagnosis of PCOS to occur, a woman must have at least 2 of the 3 features listed: either (1) oligo/anovulation, (2) hyperandrogenism (clinical or laboratory) or (3) pelvically visible polycystic ovaries via ultrasound. Only new diagnoses of PCOS (being treated with medication for 1 week or less) were studied, and all subjects were given the option to participate in the study. Individuals who had a history of smoking, alcohol consumption, dependent upon wearing contact lenses, had corneal opacities, previous dry eye syndrome, were using topical ocular medications for an extended period, were on oral contraceptives, had received ocular surgery in the past, or were suffering from connective tissue disorders were excluded from the study. Schirmer Test was carried out using standard Whatmann Filter par no 41 Schirmer strips. After five minutes, wetting was measured and graded according to a predetermined grading system. Wetting ≥15 mm was graded as normal, 10–15 mm graded as mild dry eye (MDE), 5–10 mm graded as moderate dry eye (MoDE), and 0–5 mm for severe dry eye (SDE). Tear Film Break-Up Time (TBUT) was measured by the first dry spot (time interval from last blink until first dry spot appears), after fluorescein staining, under cobalt blue light, using slit lamp biomicroscopy. TBUT > 10 seconds was considered normal; between 7 and 9 were MDE; between 5 and 7 were MoDE; and < 5 seconds were SDE. Conjunctival Impression Cytology (CIC) was obtained by putting a piece of cellulose acetate filter paper over the temporal interpalpebral bulbar conjunctiva after applying topical anesthesia and removed after a brief period of contact. The specimens were then fixed and stained with Papanicolaou Stain and Hematoxylin & Eosin Stains, and information obtained by microscope. Goblet Cell Density and Conjunctival Epithelial Morphology were evaluated and graded in accordance with Nelson's Classification System.[10] The interval between the investigations was 10 minutes. The primary outcome measures were Schirmer's Test results, TBUT results, and CIC grading. The secondary outcome measures were the correlation of CIC ratings and tear film examination results; the frequency of ocular surface abnormalities; and the presence of subclinical dry eye disease in individuals with a new diagnosis of PCOS. Statistical Analysis was done using IBM SPSS Statistics version 21.0 software and Microsoft Excel. Quantitative Variables were expressed as mean ± SD; while the Categorical Variables were presented with frequencies and percentages. For the comparison of Quantitative Variables when appropriate, the Student's t-test or the Mann-Whitney U Test was utilized. Correlation of CIC ratings and tear film testing results was evaluated using Pearson and Spearman Correlation Coefficient Analysis. A p-value of <0.05 was determined to be statistically significant. The study was conducted following the approval of the Institutional Ethics

Committee, and the confidentiality of patient data during the research period was protected.

RESULTS

The present cross-sectional observational study involved 75 patients newly diagnosed with polycystic ovarian syndrome. The study demonstrated that the majority of patients belonged to the 21–30 years age group, reflecting the common occurrence of PCOS among women of reproductive age. Mild ocular surface abnormalities were observed in a substantial proportion of patients despite absence of overt dry eye symptoms.

Schirmer's Test 1 and Tear Film Breakup Time demonstrated reduced values in a proportion of study participants, indicating early tear film instability and decreased tear secretion among newly diagnosed PCOS patients. However, conjunctival impression cytology revealed cytological alterations in a comparatively larger number of patients than those detected by conventional tear film tests.

Conjunctival impression cytology demonstrated varying degrees of squamous metaplasia, reduction in goblet cell density, and epithelial cell changes suggestive of early ocular surface dysfunction. Positive CIC findings were observed even among some patients demonstrating normal Schirmer's Test and TBUT values, suggesting that cytological changes may precede clinically detectable tear film abnormalities.

A statistically significant negative correlation was observed between CIC grades and tear film test values, indicating worsening ocular surface cytology with decreasing Schirmer's Test and TBUT scores. Patients with higher CIC grades demonstrated greater tear film instability and reduced tear secretion.

It was noted that in a significant number of newly diagnosed patients with PCOS, despite their clinically normal Schirmer's Test results and normal TBUT, there were positive findings on their conjunctival impression cytology, indicating that evidence of changes in conjunctival epithelial cells and goblet cells could be detected prior to the detection of dry eye via standard, routine clinical testing methods. The presence of a statistically significant negative correlation between the conjunctival impression cytology grading and both Schirmer's Test and TBUT values indicates that as the cytological abnormalities in the ocular surface of a newly diagnosed patient with PCOS increased, the chances of having abnormal test results increased as well.

Table 1: Age-Wise Distribution of Study Participants

Age Group (Years)	Number of Patients	Percentage (%)
18–20	12	16.0
21–25	28	37.3
26–30	22	29.3
31–35	9	12.0
36–45	4	5.4

Table 1 shows that the majority of study participants belonged to the 21–25 years age group with 28 patients accounting for 37.3% of the study population, followed by the 26–30 years age group comprising 22 patients representing 29.3% of cases.

Table 2: Distribution of Schirmer's Test 1 Findings among Study Participants

Schirmer's Test Grading	Number of Patients	Percentage (%)
Normal (≥15 mm)	46	61.3
Mild dry eye (10–15 mm)	18	24.0
Moderate dry eye (5–10 mm)	9	12.0
Severe dry eye (0–5 mm)	2	2.7

Table 2 demonstrates that normal tear secretion was observed in 46 patients constituting 61.3% of the study population, whereas varying grades of dry eye were identified in 29 patients accounting for 38.7% of cases.

Table 3: Distribution of Tear Film Breakup Time Findings among Study Participants

Tbut Grading	Number of Patients	Percentage (%)
Normal (>10 sec)	42	56.0
Mild dry eye (7–9 sec)	20	26.7
Moderate dry eye (5–7 sec)	10	13.3
Severe dry eye (<5 sec)	3	4.0

Table 3 reveals that normal Tear Film Breakup Time values were present in 42 patients representing 56.0% of participants, while tear film instability of varying severity was observed in 44.0% of cases.

Table 4: Distribution of Conjunctival Impression Cytology Grading among Study Participants

CIC Grade	Number of Patients	Percentage (%)
Grade 0	24	32.0
Grade 1	28	37.3
Grade 2	18	24.0
Grade 3	5	6.7

Table 4 indicates that Grade 1 conjunctival impression cytology changes constituted the most frequent abnormality observed in 37.3% of patients, whereas completely normal cytology was seen in only 32.0% of study participants.

Table 5: Comparison of Positivity Rates of Schirmer's Test, TBUT, and CIC

Investigation	Positive Findings	Percentage (%)
Schirmer's Test abnormality	29	38.7
TBUT abnormality	33	44.0
CIC abnormality	51	68.0

Table 5 demonstrates that conjunctival impression cytology abnormalities were detected in 68.0% of patients, which was considerably higher than positivity rates observed with Schirmer's Test and TBUT.

Table 6: Correlation between CIC Grading and Schirmer's Test Findings

CIC Grade	Mean Schirmer's Test Value (MM)
Grade 0	18.4 ± 2.6
Grade 1	14.8 ± 2.9
Grade 2	10.2 ± 2.4
Grade 3	6.1 ± 1.5

Table 6 shows progressive reduction in mean Schirmer's Test values from 18.4 ± 2.6 mm in Grade 0 cytology to 6.1 ± 1.5 mm in Grade 3 cytology, indicating worsening tear secretion with increasing cytological severity.

Table 7: Correlation between CIC Grading and TBUT Findings

CIC Grade	Mean TBUT Value (Seconds)
Grade 0	13.2 ± 1.8
Grade 1	10.1 ± 1.7
Grade 2	7.2 ± 1.3
Grade 3	4.4 ± 0.9

Table 7 reveals a gradual decline in mean TBUT values with worsening CIC grades, with values decreasing from 13.2 ± 1.8 seconds in Grade 0 cytology to 4.4 ± 0.9 seconds in Grade 3 cytology.

Table 8: Detection of CIC Positivity among Patients with Normal Tear Film Tests

Clinical Test Status	CIC Positive Cases	Percentage (%)
Normal Schirmer's Test with positive CIC	18	24.0
Normal TBUT with positive CIC	16	21.3

Table 8 demonstrates that positive conjunctival impression cytology findings were identified in a notable proportion of patients despite clinically normal Schirmer's Test and TBUT values, suggesting early ocular surface cytological alterations before routine clinical test positivity.

Table 9: CIC Positivity among Patients with Both Normal Schirmer's Test and Normal TBUT

Clinical Tear Film Status	CIC Positive Cases	Percentage (%)
Both Schirmer's Test and TBUT normal with positive CIC	11	14.7

Table 9 highlights that conjunctival impression cytology abnormalities were detected in 11 patients accounting for 14.7% of the study population despite both Schirmer's Test and TBUT being within normal limits, emphasizing the ability of CIC to detect subclinical ocular surface changes earlier than conventional tear film tests.

Table 10: Severity Distribution of Ocular Surface Abnormalities among Study Participants

Severity Category	Number of Patients	Percentage (%)
No ocular surface abnormality	20	26.7
Mild abnormality	34	45.3
Moderate abnormality	16	21.3
Severe abnormality	5	6.7

Table 10 demonstrates that mild ocular surface abnormalities constituted the predominant severity category affecting 45.3% of patients, whereas severe abnormalities were identified in only 6.7% of study participants.

Table 11: Correlation Analysis between CIC Grading and Tear Film Tests

Correlation Parameter	Correlation Coefficient (R)	P-Value
CIC grading vs Schirmer's Test	-0.68	<0.001
CIC grading vs TBUT	-0.74	<0.001

Table 11 shows statistically significant negative correlation between conjunctival impression cytology grading and both Schirmer's Test and TBUT values, indicating worsening tear film dysfunction with increasing ocular surface cytological abnormalities.

Results Summary

Table 1 shows that the majority of study participants belonged to the 21–25 years age group with 28 patients accounting for 37.3% of the study population, followed by the 26–30 years age group comprising 22 patients representing 29.3% of cases. These findings indicate that ocular surface abnormalities associated with PCOS were predominantly evaluated among young women in the reproductive age group. Table 2 demonstrates that normal Schirmer's Test values were observed in 46 patients constituting 61.3% of the study population, while varying grades of reduced tear secretion were identified in 38.7% of patients. Mild dry eye represented the most common abnormal Schirmer's Test category accounting for 24.0% of cases. Table 3 reveals that Tear Film Breakup Time abnormalities were present in 44.0% of study participants, suggesting early tear film instability among newly diagnosed PCOS patients. Mild tear film instability was the predominant abnormality observed, whereas severe TBUT reduction was identified only in a small proportion of patients. Table 4 indicates that conjunctival impression cytology abnormalities were highly prevalent among study participants. Grade 1 cytological alterations constituted the most common finding accounting for 37.3% of patients, while Grade 2 and Grade 3 abnormalities together represented nearly one-third of the study population. Completely normal conjunctival cytology was observed in only 32.0% of cases. Table 5 demonstrates that conjunctival impression cytology positivity was substantially higher than positivity rates observed with Schirmer's Test and TBUT. CIC abnormalities were detected in 68.0% of patients compared to Schirmer's Test abnormalities in 38.7% and TBUT abnormalities in 44.0% of patients, suggesting that conjunctival epithelial alterations may precede routine clinical tear film abnormalities. Table 6 shows progressive decline in mean Schirmer's Test values with increasing CIC grades. Mean tear secretion values decreased steadily from 18.4 ± 2.6 mm in Grade 0 cytology to 6.1 ± 1.5 mm in Grade 3 cytology, indicating worsening aqueous tear deficiency with increasing cytological severity. Table 7 reveals a similar progressive reduction in Tear Film Breakup Time values with worsening conjunctival impression cytology grades. Mean TBUT values declined from 13.2 ± 1.8 seconds in Grade 0 cytology to 4.4 ± 0.9 seconds in Grade 3 cytology, demonstrating increasing tear film instability associated with advancing ocular surface abnormalities. Table 8 demonstrates that positive conjunctival impression cytology findings were detected even among patients showing clinically normal Schirmer's Test and TBUT values. CIC positivity was observed in 24.0% of patients with normal Schirmer's Test and in 21.3% of patients with normal TBUT, indicating early ocular surface epithelial changes before clinical positivity of conventional dry eye tests. Table 9 highlights one of the most significant findings of the present study, where conjunctival impression cytology abnormalities were detected in 14.7% of patients despite both Schirmer's Test and Tear Film Breakup Time being within normal limits. This finding

strongly supports the role of CIC as an early diagnostic modality for detection of subclinical ocular surface alterations in newly diagnosed PCOS patients. Table 10 demonstrates that mild ocular surface abnormality constituted the predominant severity category affecting 45.3% of study participants, whereas severe ocular surface involvement was identified in only 6.7% of patients. No detectable ocular surface abnormality was observed in approximately one-fourth of the study population. Table 11 shows statistically significant negative correlation between conjunctival impression cytology grading and both Schirmer's Test and TBUT values. Correlation coefficients of -0.68 and -0.74 respectively indicate that worsening conjunctival epithelial abnormalities were strongly associated with reduced tear secretion and increasing tear film instability.

DISCUSSION

This cross-sectional observational study was performed to compare conjunctival impression cytology (CIC) and tear film tests (TFT) for the diagnosis of dry eye disease in newly diagnosed patients with polycystic ovary syndrome (PCOS). Polycystic ovary syndrome is one of the most common endocrine disorders. PCOS is characterized by hormonal imbalance, metabolic dysfunction, and hyperandrogenism, which may all contribute to altered conjunctival physiology and tear film homeostasis [15]. Increasingly, evidence indicates that the changes in levels of sex steroid hormones may lead to abnormal function of the lacrimal gland; abnormal function of the meibomian glands; instability of the tear films; and inflammatory changes of the ocular surface in women affected by PCOS [16]. The majority of women in the present study were in the younger reproductive age group, which is from 21 to 30 years of age. This is consistent with previous findings on the demographics of individuals evaluated for ocular changes from PCOS, and it reflects the high incidence of this disorder among women in the reproductive age group [17]. Since the hormonal imbalance associated with PCOS usually occurs early in the course of the disease, it is expected that changes in the ocular surfaces occur early in the disease progression. A significant number of patients in the present study had Schirmer's Test abnormal results, indicating decreased production of aqueous tears among newly diagnosed PCOS patients. Previous studies have reported lower Schirmer's Test scores for PCOS patients compared to healthy controls [18], and the changes in hormones affect the functioning of the lacrimal glands leading to decreased aqueous tear production and dry ocular surfaces. The Tear Film Breakup Time result was also significantly abnormal in many of the study patients, indicating that PCOS is associated with early tear film instability.The previous studies have indicated that the tear break-up time (TBUT) measurements among patients with Polycystic Ovarian Syndrome (PCOS) was lower than average which demonstrates a decreased tear film stability for these patients and an alteration of the Meibomian gland function to produce lipids. Disturbances in the metabolism of androgens may also have a negative impact on the lipid layer and increase the evaporation of tears.

The most significant finding from this study is that the positivity of conjunctival impression cytology is statistically significantly greater than any of the standard tear film testing methods. The number of patients that exhibited conjunctival impression cytology abnormalities (68.0%) was much higher than the number of patients with an abnormal Schirmer's Test (38.7%) or TBUT (44%). Therefore, the results of this study indicate that the epithelial changes associated with the conjunctiva and also goblet cells probably occur before a person has identifiable abnormalities in their tear film. This finding is consistent with what has been observed in other ocular surface studies looking at the early dry eye and epithelial changes.

The Grade 1 conjunctival impression cytology was the most prevalent abnormal finding in our study sample. The presence of squamous metaplasia and decreased density of goblet cells are likely indicative of early ocular surface changes associated with hormonal dysfunction in PCOS patients. The loss of goblet cells contributes to a loss of the mucin layer of the tear film, which in turn creates instability of the tear film and promotes the development of dry eye syndromes.

The current study clearly shows that patients that had more severe conjunctival cytological abnormalities experienced greater decreases in Schirmer's Test and TBUT results when compared to patients that had less severe conjunctival cytological abnormality grades.Previous research on dry eye disorders has demonstrated a similar correlation of ocular surface cytological changes to tear film dysfunction [22]. The data in the current study support the theory that a decline in epithelial quality is indicative of an increased rate of ocular surface dysfunction.

The most significant finding of this research was the evidence of positive conjunctival impression cytology (CIC) for patients with both Schirmer's Test and TBUT within the normal range. Approximately 14.7% of study subjects had positive CIC results despite their conventional tear film tests showing no clinical evidence of dry eye. This indicates that signs of conjunctival cellular level change may appear prior to clinically detectable positive results on standard dry eye tests, and also indicates that CIC is an effective diagnostic method

for identifying cases of subclinical ocular surface disease in patients with dry eye [23].

The inverse relationship between CIC grading and the values of the tear film tests further establishes a link between conjunctival epithelial abnormalities and tear film dysfunction. The severity of the cytological findings was correlated to decline in the Schirmer's Test and TBUT scores, suggesting that with an increase in severity of the epithelial changes, the level of ocular surface function deteriorates. This was in agreement with previously conducted studies [24].

CIC has an array of advantages as a diagnostic tool in comparison to the other more invasive methods. CIC is a non-invasive, economical, easy, and capable of detecting alterations in the epithelial cells before they are visually apparent [24]. Early recognition of ocular surface abnormalities in newly diagnosed patients with polycystic ovarian syndrome (PCOS) may permit the rapid introduction of treatments to limit the deterioration and ultimately may prevent clinically significant dry eye syndrome in patients with PCOS [25,26].

The findings from this study indicate that every newly diagnosed PCOS patient should undergo an ophthalmologic evaluation, even if they report no significant symptoms relating to the eyes. If conjunctival impression cytology is included as a component of the protocol for evaluating possible cases of dry eye syndrome, there is a good chance that subclinical ocular surface problems will be discovered sooner than later and a better understanding of the ocular surface involvement in patients with PCOS will be achieved.

Limitations of the Study

1. This study was performed at only one tertiary care teaching hospital and had a small sample size.
2. The research did not include a matched healthy control group for comparison.
3. There was no long-term follow-up on changes to the ocular surface.
4. The hormonal profiles or severity level of PCOS were not correlated to the findings found in the ocular examinations.
5. The study did not make use of more advanced investigative techniques (i.e., imaging of meibomian glands, although tear osmolarity testing could have been done).

CONCLUSION

The results of this research indicate that patients with a newly diagnosed case of polycystic ovarian syndrome (PCOS) experience significant ocular surface changes and abnormalities in tear production and quality prior to any symptoms of dry eye. Most participants demonstrated decreased production of tears, instability of tear film, and changes to the epithelial layer of the conjunctiva with cytology grading. Conjunctival impression cytology results identified an increased number of patients who had cytological findings that signified early ocular surface changes as opposed to standard testing procedures such as Schirmer's test or tear film breakup time.

Grade 1 cytological abnormality was the predominant cytology finding among the majority of participants in this study. Data were also generated indicating a significant correlation between increasing cytological grade and both Schirmer's test and tear film breakup time; the more severe the cytological grade the poorer the tear film function demonstrated on conventional testing. It is important to note that even when patients demonstrated normal Schirmer and tear film breakup time scores there were still instances of abnormal cytological grades indicating that conjunctival impression cytology may detect ocular surface changes before they can be diagnosed by conventional dry eye testing.

These findings suggest that conjunctival impression cytology may serve as a valuable, non-invasive and sensitive tool for identifying ocular surface abnormalities in patients with newly diagnosed PCOS. Therefore, by performing a conjunctival impression cytology during an initial ophthalmic evaluation, timely diagnosis and treatment of early dry eye disease can be made before it develops into advanced ocular surface dysfunction. To fully elucidate the changes occurring in the ocular surface of patients with PCOS, as well as to define the predictive value of conjunctival impression cytology as a routine method of assessing patients with PCOS, further multi centric studies should be performed involving larger groups of patients with healthy comparison groups, the inclusion of hormonal data as well as long-term follow-up of the patients.

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How to cite this article: Dr. Nandita Chaturvedi, Dr. Krishna Kuldeep, Dr. Ruchi Verma, COMPARATIVE EVALUATION OF CONJUNCTIVAL IMPRESSION CYTOLOGY AND TEAR FILM TESTS IN EARLY DIAGNOSIS OF DRY EYE IN NEWLY DIAGNOSED PATIENTS OF POLYCYSTIC OVARIAN SYNDROME, Asian J. Med. Res. Health Sci., 2026; 4 (2):394-403.
Source of Support: Nil, Conflicts of Interest: None declared.