Original Article

ACCURACY OF TEAR BREAKUP TIME IN CLINICALLY SUSPECTED DRY EYE DISEASE PATIENTS

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Objective: To determine the diagnostic accuracy of tear breakup time in comparison to clinical findings for the diagnosis of dry eye disease.

Methods: This cross sectional study was carried out at department of Ophthalmology, Services Institute of Medical Sciences, Services Hospital, Lahore for 6 months, from March 1st, 2016 to 31st of August 2016. The Non probability consecutive sampling technique was used. Informed consent was taken from all the patients. Complete ophthalmic examination performed prior to TBUT (Tear breakup time) evaluation. This included detailed anterior and posterior segment examination on slit lamp. TBUT measurement was done. All the collected data was entered and analyzed on SPSS for Windows, version 21.0.

Results: The mean age of patients was 44.17±15.11 years. The male to female ratio was 1:1.2.In this study the sensitivity, specificity and diagnostic accuracy of TBUT was 93.33%, 93.55% and 93.5% respectively taking clinical findings as gold standard.

Conclusions: It has been proved in our study that the tear breakup time is a useful tool with high diagnostic accuracy in diagnosis of clinical suspected cases of DED (Dry eye disease).

Keywords: dry eye disease (DED), tear breakup time (TBUT), diagnosis accuracy.

Introduction

Dry eye is a major tear deficiency disorder that affects millions of people worldwide. It causes chronic ocular irritation and is extremely distressing both for patients and ophthalmologists.[1] The accurate diagnosis and classification of DED is challenging owing to wide variations in symptoms and lack of a single reliable clinical assessment. In addition, changes and severity of clinical signs often do not correspond to patient-reported symptoms.[2]

According to the current perspective, dry eye disease (DED) is a condition that affects the health of the ocular surface, both the cornea and conjunctiva.Various epidemiological studies have used slightly different criteria to define dry eye disease.[3] A study[4] shows that the prevalence of dye eye symptoms increases with the age and has been reported in approximately 5% to 30% of the study population. In addition to age, the risk factors for the development of dry eye include race and ethnicity(greater incidence seen in Chinese, Hispanics, Asians and Pacific islands descents) female sex especially those receiving estrogen replacement therapy, presence of ocular conditions such as blephritis, meibomian gland dysfunction and conjunctival disease. Additionally a study[5] shows that DED is more prevalent among Japanese visual display terminal users. Other risk factors for DED, includes immune-mediated diseases such as rheumatoid arthritis, thyroid diseases, and atopic disorders e.g. Asthma.

The measurement of tear film stability is fundamental to the diagnosis of dry eye.[6] A variety of methods are available to assess different aspects of the tear film and provide insights into its "stability". TBUT, introduced by Norn,[7] remains the most frequently used diagnostic test to determine tear film instability.[8] Generally, assessing the TBUT involves the observation of an illuminated grid pattern reflected from the anterior tear surface. A regular image of the reflected target indicates a stable tear film. The time (in seconds) from the last blink to the appearance of the first discontinuity or break in the reflected image is recorded and graded accordingly. TBUT can also be measured by functional visual acuity assessment, corneal topography, interferometry, aberrometry, and confocal microscopy.

Methods

This cross sectional study was carried out at department of Ophthalmology, Services Institute of Medical Sciences, Services Hospital, Lahore for 6 months, from March 1st, 2016 to 31st of August 2016. The Non probability consecutive sampling technique was used. After approval from Ethical Research Board, Services Institute of Medical

Error for25.97% specificity of tear break up time. Informed consent was taken from all the patients. Complete ophthalmic examination was performed prior to TBUT evaluation. This included detailed anterior and posterior segment examination with slit lamp biomicroscopy.

Clinically diagnosed dry eye patients were included in this study and was confirmed if patient had at least 3 out of 4 of the following. i) Symptoms of dry eye i.e. any one (burning sensation, watering and occasional blurring of vision), ii) Mucous strands on slit lamp examination, iii) Corneal erosions on slit lamp examination, iv) Relief of symptoms by instillation of artificial tears. Patients having ocular inflammation, infection or neoplasia, were excluded from this study.

TBUT was measured with a strip of 2% fluorescein which was applied to the inferior conjunctival fornix. The subject was asked to blink three or four time in order to distribute fluorescein efficiently and evenly on the cornea. After that the subject was examined on slit lamp using cobalt blue light. Time between the last blink and the first appearance of dry spot was measured by stop watch. This was repeated at two different visits (2 times in succession during a single visit with at least 1hr interval in between) with at least 24hr intervals in between two visits to calculate reproducibility by taking the clinical findings as gold standard9.All the collected data was entered and analyzed on SPSS software package(SPSS for Windows, version 21.0; SPSS). Mean and standard deviation was calculated for quantitative variable like age and TBUT. Frequency and percentage was calculated for qualitative variables like diagnostic accuracy, gender, dry eye on TBUT and clinical finding. Effect modifiers like gender and age were calculated through stratification. Post stratification chi-square test was applied by taking p-value≤0.05 as significant. A 2×2 table was generated to calculate the sensitivity, specificity, PPV (Positive Predictive Value), NPV (Negative Predictive Value) and diagnostic accuracy of dry eye disease by taking clinical finding as gold standard.

Results

In this study we included, 200 patients with the mean age of 44.17±15.11 years. The minimum age of patients was 18 years while maximum age of patients was 70 years. **(Table-1)**. In our study 93(46.50%) patients were male and 107(53.50%) patients were females. The male to female ratio was 1:1.2 **(Fig-1)**. The mean average TBUT of the patients was 11.09±2.80. The minimum TBUT was observed as 5 while maximum TBUT was 15. **(Table-2)**. On TBUT, positive dry eye was diagnosed in 52(26%) patients while 148(74%) patients were negative for dry eye or having normal eye **(Fig-2)**. On clinical examination, symptoms of dry eye were noted in 109(54.5%) patients and the symptoms were absent in 91(45.5%) patients out of 200 patients **(Table-3)**. Mucous strands were noted in 91(45.5%) patients and were absent in 109(54.5%) patients **(Table-4)**. In this study the corneal erosion was found in 92(46%) patients and was absent in 108(54%) patients **(Table-5)**. The relief of symptoms was observed in 96(48%) patients while remaining patients did not show relief of symptoms **(Table-6)**. The clinical examination diagnosed 45(22.50%) patients as having positive dry eye and was negative in 155(77.50%) **(Fig-3)**. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of TBUT was 93.33%, 93.55%, 80.77%, 97.97% and 93.5% respectively taking clinical findings as gold standard. **(Table-7)**. In ≤ 50 years patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy was 93.55%, 91.67%, 78.38%, 97.78% and 92.13% respectively. In the patients of more than50 years of age the sensitivity, specificity, PPV, NPV and diagnostic accuracy was 92.86%, 96.61%, 86.67%, 98.28% and 95.89% respectively **(Table-8)**.

Table-1: Descriptive statistics of age (years).

	N	200
	Mean	44.17
Age (Years)	SD	15.11
	Minimum	18
	Maximum	70

35
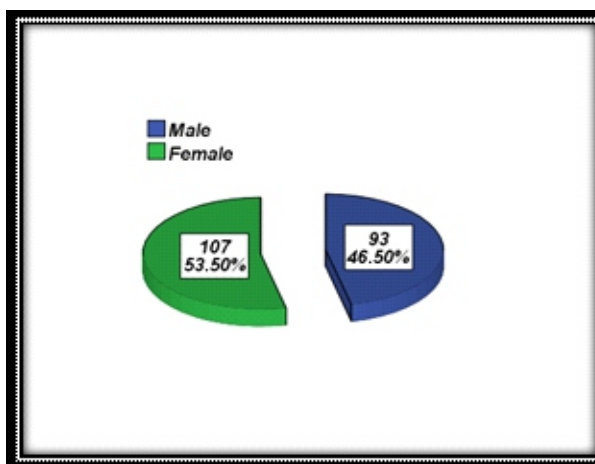
Table-2: Descriptive statistics of average TBUT.

	N	200
	Mean	11.09
Average TBUTT	SD	2.80
	Minimum	05
	Maximum	15
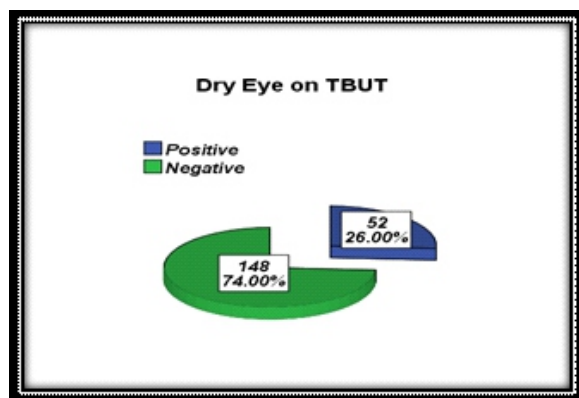
Fig-2: Frequency distribution of gender.

Table-3: Frequency distribution of symptoms.

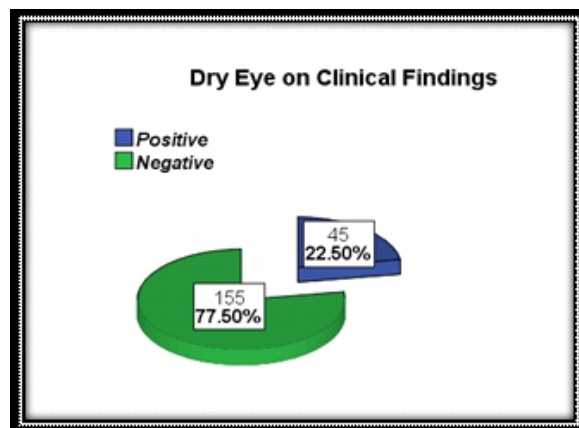|		Frequency	Percent
	Yes	109	54.5
Symptoms	No	91	45.50
	Total	200	100.0

Fig-3: Frequency distribution of dry eye on clinical findings.

Table-4: Frequency distribution of mucous strands.

		Frequency	Percent
	Yes	91	45.5
Mucous Strands	No	109	54.5
	Total	200	100.0

Table-5: Frequency distribution of corneal erosion.

		Frequency	Percent
	Yes	92	46.0
Comeal Erosion	No	18	54.0
	Total	200	100.0

Table-6: Frequency distribution of relief of symptoms.

		Frequency	Percent
	Yes	96	48.0
Relif of Symptoms	No	104	52.0
	Total	200	100.0

Table-7: Comparison of dry eye on TBUT with on clinical findings.

Frequency		On clinical findings Positive	Negative	Total
	Positive	42	10	52
On TBUT	Negative	03	145	148
	Total	45	155	200

Table-7: Comparison of dry eye on TBUT with on clinical findings.

Frequency		On clinical findings Positive	Negative	Total
	Positive	42	10	52
On TBUT	Negative	03	145	148
	Total	45	155	200

Sensitivity	**93.33%**
Specificity	93.55%
PPV	80.77%
NPV	97.97%
Diagnostic Accuracy	93.5%

Table-8: Comparison of dry eye on TBUT with on clinical findings stratified by age.

Age (Years)	On TBUT	On clinical findings Negative	Negative	Total
=50	Positive	29	08	37
Dry Eye	Negative	02	88	90
>50	Positlve	14	02	15
	Negative	01	57	58

TBUTT	Age (Years)	
	=50	>50
Sensitivity	91.67%	92.86%
Specificity	91.67%	96.61%
PPV	78.38%	86.67%
NPV	97.78%	98.28%%
Diagnostic accuracy	92.13%%	95.89%%

Table-9: Comparison of dry eye on TBUT with on clinical findings stratified by gender.

Age (Years)	On TBUT	On clinical findings		Total
		Negative	Negative	
Male	Positive	22	04	27
Dry Eye	Negative	02	64	66
Female	Positlve	20	05	25
	Negative	01	81	88

TBUTT	Gender	
	Male	Female
Sensitivity	91.67%	95.24%
Specificity	92.75%	94.19%
PPV	81.48%	80%
NPV	96.97%	98.78%%
Diagnostic accuracy	92.47%%	94.39%%

In male patients the sensitivity, specificity, PPV,NPV and diagnostic accuracy was 91.67%, 92.75%, 81.48%, 96.97% and 92.47% respectively, similarly in female patients the sensitivity, specificity, PPV, NPV and diagnostic accuracy was 95.24%, 94.19%, 80%, 98.78% and 94.39% respectively **(Table-9).**

Discussion

TBUT is can be regarded as one of the simplest and the most efficient test for the diagnosis of the dry eye syndrome. It has however, received a certain amount of criticism. Lemp[10] has reported that TBUT has high reproducibility in dry eye disease patients while Norn[11] has questioned its clinical significance.

Our results are in agreement with the study by Rehman A et al.[12] demonstrated sensitivity of the TBUT test was found to be 88.88%.

Another study by Lee JH et al[9] presented the high reproducibility of TBUT in DED patients i.e. 95%.

In an epidemiological study of dry eye in elderly Chinese in Taiwan, Lin et al[13] found that of the 1361 participating in the study, 33.7% had symptoms of the condition (reporting one or more dry eye symptoms often or all time). Among those with symptoms, 78.9% had a low TBUT (<10s). This finding is comparable to our results.

Study by Bhatnagar KR et al[14] concluded that there is strong correlation between MS (Mc Monnies Index scores) and TBUTin normal as well as marginal and pathological dry eye.

Lin P et al. has shown that the most frequently used diagnostic test to determine tear film abnormality was the tear breakup time test which was done on 93% of the participants.[8] Similar results have been reported by Kilic A et al.[15]

In our study the clinically diagnosed positive dry eyes were 45(22.50%) patients and the TBUT diagnosed dry eye patients were 52 (26%) patients. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of TBUT was 93.33%, 93.55%, 80.77%, 97.97% and 93.5% respectively taking clinical findings as gold standard.

We stratified our data for age of patients. In ≤ 50 years patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy was 93.55%, 91.67%, 78.38%, 97.78% and 92.13% respectively. In >50 years patients the sensitivity, specificity, PPV, NPV and diagnostic accuracy was 92.86%, 96.61%, 86.67%, 98.28% and 95.89% respectively. Thus showing that age has no impact on findings of TBUT and in all age groups, TBUT has high accuracy rate.

We stratified our data for The gender stratification of patients showed that In male patients the sensitivity, specificity, PPV, NPV and diagnostic accuracy was 91.67%, 92.75%, 81.48%, 96.97% and 92.47% respectively, similarly in female patients the sensitivity, specificity, PPV, NPV and diagnostic accuracy was 95.24%, 94.19%, 80%, 98.78% and 94.39% respectively. Thus showing that gender has no impact on findings of TBUT and for both genders, TBUT has high accuracy rate.

Conclusion

It has been proved in our study that the tear breakup time is a useful tool with high diagnostic accuracy in diagnosis of clinical suspected cases of DED.

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