



Diagnostic Test Schirmer and Tear Break Up Time (TBUT) in Uncontrolled Diabetes Mellitus Patient

Anang Tribowo¹, Theodorus², Junaini Laila^{3*}

¹Departement of Ophthalmology, Faculty of Medicine, Moeh. Hoesin Hospital, Universitas Sriwijaya

²Medical Research Unit, Faculty of Medicine, Universitas Sriwijaya

³Ophthalmology Fellow, Faculty of Medicine, Universitas Sriwijaya

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ABSTRACT

Dry eye syndrome is a condition with multiple characterizations characterized by the presence of symptoms of eye discomfort associated with decreased tear production and abnormalities of rapid tear evaporation. Examination of dry eye syndrome can be performed to assess the function of tears in quality and quantity such as Schirmer I and Tear break-up time (TBUT) tests. Schirmer I, examination to assess the quantity of tear production generated by the lacrimal gland while break-up time to assess the stability of the tear layer. This study aims to determine the accuracy of Schirmer I and TBUT tests in patients with diabetes mellitus in the eye outpatient and interne outpatient in General hospital Mohammad Hoesin Palembang. This diagnostic test was undertaken in the eye outpatient and interne outpatient in General hospital Mohammad Hoesin Palembang from July until September 2016. There were 30 diabetes mellitus (DM) type 2 patients who met the inclusion and exclusion criteria. Frequency and distribution of data are described in table form and sensitivity and specificity values will be cut off point using ROC curve. Accuracy value is measured by Kappa value. Data analysis was performed using SPSS version 20.0. 30 patients with diabetes mellitus have an average age of approximately 47 years, with the proportion of female sex : male is 22: 8. The majority of subjects (60%) addressed within the city of Palembang with the average length of DM suffered for approximately 8 years. The highest level of education in this study is the college (36.7%) while the most types of work is housewives (50%). With statistical analysis obtained accuracy value of Schirmer I and TBUT examination in diabetic mellitus eye patients is 0.633 which means the degree of suitability of measurement (reliability) is good. Accuracy of examination Schirmer I and TBUT examination in patients with uncontrolled diabetes mellitus had a sensitivity of 50%, 90% specificity, 90.9% positive predictive value (PPV), 47.37% negative predictive value (NPV), positive likelihood ratio 5 and a negative Likelihood ratio of 0.56. The effect of HbA1c on TBUT score was 40.7% while HbA1c effect on Schirmer I score was 10.7%. It can be concluded that the accuracy of Schirmer I and TBUT examination in Diabetes Mellitus eye patient is good with HbA1c effect on TBUT score of 40.7% while HbA1c effect on Schirmer I score of 10.7%.

Key words: Diabetes Mellitus, Diagnostic Test, HbA1c, Schierner I, TBUT

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Corresponding author: Junaini Laila

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life, rising to 10-15% in adults over the age of 65 [1-4].

INTRODUCTION

Dry eye syndrome is a condition with multiple characterizations characterized by the presence of symptoms of eye discomfort associated with decreased tear production and abnormalities of rapid tear evaporation. The prevalence of dry eye syndrome increases with age, affecting about 5% of the adult population during the fourth decade of

Examination of dry eye syndrome can be performed to assess the function of tears in quality and quantity such as Schirmer test and Tear break-up time (TBUT). Schirmer I examination to assess the quantity of tear production generated by the lacrimal gland while checking the break-up time (TBUT) to assess the stability of the tear layer [1-4].

High levels and uncontrolled of glucose can cause oxidative stress and increased expression of Advanced glycation end products (AGEs) that can affect the secretion of tears [5-8].

MATERIALS AND METHODS

A Diagnostic test was undertaken in the eye outpatient and interne outpatient in General Hospital Mohammad Hoesin Palembang from July until September 2016. There were 30 diabetes mellitus (DM) type 2 patients who met the inclusion and exclusion criteria. The protocol has been approved of Ethic Committe, Faculty of Medicine Universitas Sriwijaya.

Frequency and distribution of data are described in table form and sensitivity and specificity values will be cut off point using ROC curve. Accuracy value is measured by Kappa value. Data analysis using SPSS version 20.0.

RESULTS

There were 30 patients with diabetes mellitus have an average age of approximately 47 years, with the proportion of female sex : male is 22: 8.

Table 1 shows that the majority of subjects (60%) addressed within the city of Palembang with the average length of DM suffered for approximately 8 years. The highest level of education in this study is the college (36.7%) while the most types of work is housewives (50%).

Table 1: Characteristics Demographics of Research Subject

Characteristics	N = 30
Age (years). Mean ± SD (Min-Max)	48.03±4.63 (40-55)
Sex (n.%)	
Male	22 (73.3%)
Female	8 (26.7%)
Education (n.%)	
Elementary School	6 (20%)
Junior High School	3 (10%)
Senior High School	10 (33.3%)
Bachelor Degree	11 (36.7%)
Occupation. (n.%)	
Housewives	15 (50%)
Private Employees	5 (16.7%)
Traders	1 (3.3%)
Government Employees	9 (30%)
Address (n.%)	
In the City	18 (60%)
Out of Town	12 (40%)
Length of Diabetes Mellitus Suffered (years). Mean ± SD (Min-Max)	8.33±3.56 (5-20)

The ophthalmological characteristics of research subjects with uncontrolled diabetes mellitus are shown in Table 2. Diabetes Mellitus patients had a right eye vision of 0.49 ± 0.39 with a range of 0.1 to 1, a mean left eye visus of 0.58 ± 0.42 with a range of 0 to 1.1. The mean of intraocular pressure of right eye 16.18 ± 2,16 with range 13,1 to 18,5 and mean of intraocular pressure of left eye 15,91 ± 2,24 with range 13,1 to 18.5. HbA1c average of 9.98 ± 1.78 with range 7.3-14, average of Schirmer I right eye 9.6 ± 4.69 with range 2 to 20, average Schirmer I left eye 8.77 ± 5.22 with range 2 to 20, the mean TBUL of the right eye was 5.83 ± 2.65 with a range of 1 to 10 and the mean left eye TBA 5.43 ± 2.67 with range 1 to 10.

Table 2: Ophthalmological Characteristics of Research Subjects

Characteristic	Mean ± Standard deviation
Right Eye Vision	0.49±0.39 (0-1.1)
Left Eye Vision	0.58±0.42 (0-1.1)
Right Eye Intraocular Pressure	16.18±2.16 (13.1-18.50)
Left Eye Intraocular Pressure	15.91±2.24 (13.1-18.50)
HbA1c (%)	9.98±1.78 (7.3-14.0)
Right Eye Schirmer I (mm)	9.6±4.69 (2-20)
Left Eye Schirmer I (mm)	8.77±5.22 (2-20)
Right Eye TBUT (second)	5.83±2.65 (1-10)
Left Eye TBUT (second)	5.43±2.67 (1-10)

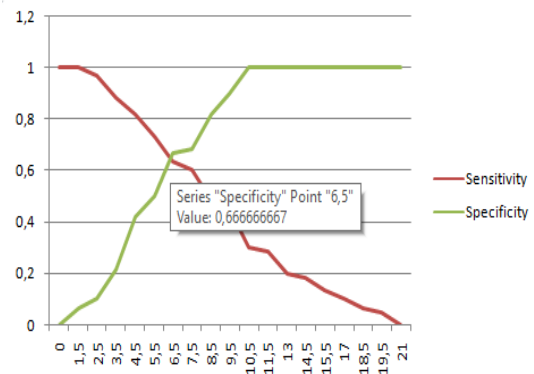


Figure 1: Intersection Curve of Sensitivity, Specificity, Dry Eye Syndrome of DM Patients

Analyzes of receiver operating curve (ROC) curves were performed to find the cut off point to obtain sensitivity and specificity of dry eye syndrome in Diabetes Mellitus eye. Figure 1 is the ROC curve of dry eye syndrome of Diabetes Mellitus patients. Determination of the point of intersection of dry eye syndrome, done by making a curve between the sensitivity, specificity and the results of examination of dry eye syndrome.

Figure 1 shows dry eye syndrome index curve of the uncontrolled DM. From the figure we get the value that has the best sensitivity and spesifisitas is at value 6.5.

Based on Table 3, the above Schirmer I and TBUT tests have a 50% sensitivity, 90% specific predictive value (PPV), negative predictive value (NPV) of 47.37%, Likelihood positive ratio 5 and negative Likelihood ratio 0,56. Accuracy of examination Schirmer and TBUT examination in Diabetes Mellitus patient's eye is 0,633 which means degree of conformity measurement (reliabilitas) is good.

Table 3: Diagnostic test table of Schirmer I and TBUT examination

Examination	TBUT		Total
	Positive > 6.5	Negative > 6.5	
Schirmer I	Positive > 6.5	20 ^a	22
	Negative > 6.5	20 ^c	38
Total	40	20	60

Table 4: Result Of Correlation Analysis Of Dry Eye Syndrome Based On TBUT and Schiemer I With HbA1c

Correlation	N	Mean ± SD	R	P
TBUT Score	60	5.633 ± 2.65	-0.638*	0.407**
HbA1c	60	9.98 ± 1.76		
Schirmer I Score	60	9.18 ± .,94	-0.327*	0.107**
HbA1c	60	9.98 ± 1.76		

*Uji Pearson Correlation; **Regresi Linier

In this study, there was a significant negative correlation between HbA1c and dry eye syndrome based on TBUT ($r = -0.638$; $p = 0,000$). This shows the percentage of HbA1c effect on TBUT score of 40,7% and a significant negative correlation between HbA1c and dry eye syndrome based on Schirmer I ($r = -0.327$; $p = 0,005$). This shows the percentage of HbA1c influence on Schirmer I score of 10,7%.

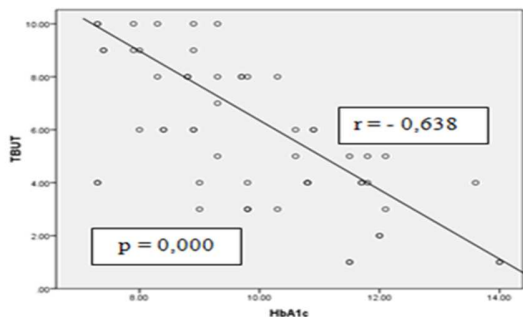


Figure 2: Linear regression TBUT and HbA1c

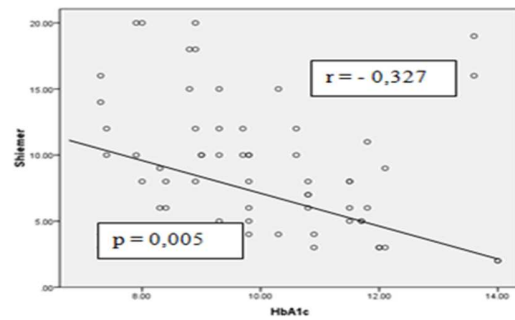


Figure 3: Linear regression Schirmer I and HbA1c

DISCUSSION

Dry eye syndrome (DES) is a group of circumstances characterized by symptoms of ocular discomfort and is associated with a rapid decrease in tear production and or tear vapor abnormalities. Teardrop disorders may be associated with other systemic and autoimmune diseases. One of the diseases that can interfere with the secretion of tears is Diabetes mellitus [1, 4-9].

Dry eye condition is a disorder due to lack of tear production or excessive tear evaporation. The low secretion of tears can be caused by various factors that interfere with the function of the lacrimal gland such as disorders of the innervation that regulate lacrimation reflexes. Uncontrolled blood sugar conditions can accelerate the occurrence of microvascular damage that will cause tissue hypoxia and then will disrupt the metabolic and mitogenic cells. If the condition persists then there will be damage to lacrimal gland cells that cause decreased aqueous production of the lacrimal gland. In diabetic patients, decreased blink reflexes are a result of peripheral nerve damage (diabetic neuropathy) that regulates synchronization between corneal and conjunctival sensitivity with tear glands. This results in decreased stimulation signals from the surface of the eyeball to the lacrimal gland thus disrupting the regulation of tear secretion [9-11].

In this study, Schirmer I and TBUT were examined. This is in accordance with research conducted by Jin *et al* and Xinyaun *et al* explain the examination Schirmer and TBUT is a routine examination performed on patients Diabetes mellitus.41 Schirmer I test is the assessment of the function of reflex secretion from the lacrimal gland and basal secretion of the glands Krause and Wolfring. The Schirmer I test is said to be normal

if wetted 10-30 mm and dry eyes when wetted 10 mm or less. In the average Schirmer I study of right and left eyes have a range of 2 to 20 mm with a mean of approximately 8-9 mm. This suggests that with the average Schirmer I Test of Diabetes Mellitus patients suffering from dry eyes.

Statistical analysis shows significant negative correlation between dry eye syndrome based on TBUT ($r = -0.638$ and $p = 0,000$) and Schirmer I ($r = -0.327$ and $p = 0,005$) with HbA1c. This shows that the higher the HbA1c level of Diabetes Mellitus patient, the lower the Schirmer I test score and the TBUT test, which means the degree of dry eye syndrome is greater. The results of this study were not much different from Ni Made Ayu's research results (2014) showed that Diabetes Mellitus patients with HbA1c ≥ 7 mg / dl had a risk of dry eye (Schirmer I test <10 mm) compared to Diabetes Mellitus patients with HbA1c <7 mg / dl. The results of this study were also supported by one study performed by Chiranjit Bal et al in which a correlation was found between the hemoglobin (HbA1c) in the presence of dry eye syndrome where the higher the HbA1c value, the higher the rate of dry eye syndrome.

From the statistical analysis, the percentage of HbA1c effect on the TBUT score is 40.7%. The percentage of HbA1c effect on Schirmer I score is only 10,7%, so it can be concluded that TBUT test is more correlated with HbA1c than Schirmer I test.

Schirmer I and TBUT accuracy point accuracy in the eyes of Diabetes mellitus patients in this study was 6.5 where the accuracy value of Schirmer I and TBUT examination in Diabetes mellitus patient's eye was 0.633, which means the degree of conformity of measurement (reliability) is good. In this study obtained 50% sensitivity and 90% specificity. this means the ability of Schirmer I to diagnose dry eye in Diabetes Mellitus patients is equal to 50% of TBUT while Schirmer I ability to rule out dry eye diagnosis in Diabetes Mellitus eye is equal to TBUT by 90%

In this study, uncontrolled eye predictive value (PPV) was 90.9% and negative predictive value (NPV) of 47.37%, which explains that a person has a dry eye diagnosis by examination of TBUT if the results of Schirmer I the result of diagnosis of dry eye is 90,9% whereas the possibility of someone having diagnosis instead of dry eye with TBUT examination if the result of Schirmer I

examination gives the result of dry eye diagnosis is 47.37%.

On the right eye of the positive Likelihood ratio of 5 and the negative Likelihood ratio of 0.56 it can be explained that the ratio between the proportion of dry eye diagnoses with Schirmer I and TBUT examinations is 5 and the comparison between the proportion of non-dry eye diagnoses with Schirmer I and TBUT examinations is 0.56.

CONCLUSION

Accuracy of examination Schirmer I and TBUT examination in uncontrolled Diabetes mellitus eye patient was 0.633 (good) and had a sensitivity of 50%, 90% specificity, 90.9% positive predictive value (PPV), negative predictive value (NPV) 47.37 %, a positive Likelihood ratio of 5 and a negative Likelihood ratio of 0.56.

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