



## DIFFERENCES OF SCHIRMER'S TEST RESULT IN PATIENTS WITH CONTROLLED AND UNCONTROLLED DIABETES MELLITUS

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### ABSTRACT

**Background:** Diabetes Mellitus (DM) is a metabolic disease whose prevalence continues to increase every year. Peripheral neuropathy, as a microvascular complication of DM, can cause dry eye syndrome. Uncontrolled DM can cause microvascular complication. **Objective:** To determine the differences of the Schirmer's test result for patients with controlled and uncontrolled diabetes mellitus. **Methods:** This study was an analytic observational study with a cross-sectional design. The study subjects were 44 diabetes mellitus patients, consisting of 22 patients with controlled DM and 22 patients with uncontrolled DM, who were selected based on inclusion and exclusion criteria, using the consecutive sampling method. Data were collected from primary data that consists of name, age, gender, duration of DM, medical history, Hb, MCV, HbA1c, and the Schirmer's test result. The data were analyzed using the non-parametric Mann-Whitney test, and  $p < 0.05$  was taken as significance. **Results:** The Schirmer's test result  $< 10$  mm, which indicated the presence of dry eye syndrome, was mostly found in females (71.4%), aged  $> 45$  years (85.7%), with a duration of DM  $> 10$  years (78.6%), and patients with uncontrolled DM. The non-parametric Mann-Whitney test showed that there was a significant difference in the Schirmer's test result ( $p < 0,05$ ) between patients with controlled and uncontrolled DM. **Conclusion:** Schirmer's test result in patients with controlled DM was higher than patients with uncontrolled DM.

**Keywords:** Diabetes mellitus, Schimer test, dry eye syndrome

### INTRODUCTION

Diabetes mellitus (DM) is a health problem that is experienced throughout the world.<sup>1</sup> Diabetes mellitus is a metabolic disorder whose prevalence continues to increase.<sup>2</sup> According to the International Diabetic Federation in 2019, the world population aged 20-79 years had a diabetes prevalence of 9.3% or 463 million people. This number is expected to increase by 10.2%, or 578.4 million people in 2030 and 10.9% or 700.2 million people in 2045. In 2019, the prevalence of DM in Indonesia was 10.7 million people, and is estimated to increase by 13.7 million people in 2030.<sup>3</sup>

There are two types of complications due to DM in general, those are macrovascular and microvascular complications. Microvascular complications of DM in the eye are diabetic retinopathy, cataracts, glaucoma, keratopathy, and *dry eye syndrome*.<sup>4</sup> According to the *American Diabetes Association* (ADA), the control of blood glucose levels can be assessed by HbA1c levels. Patients with controlled DM have HbA1c level  $\leq 7\%$ , while in uncontrolled DM have HbA1c level  $> 7\%$ .<sup>5</sup> If blood glucose levels are well controlled, the complications of diabetes can be reduced.<sup>6</sup>

Peripheral neuropathy in DM patients occurs when there are changes in the nerves that innervated the corneal, thereby reducing corneal sensitivity.<sup>7</sup> Based on previous research, it was explained that corneal sensitivity in patients with controlled DM was better than in patients with uncontrolled DM.<sup>8</sup> The decrease in corneal sensitivity would cause a decrease in the protection reflex and blinking reflex. Therefore, dry eye syndrome occurred due to a reduction of tear secretion and an increase in the evaporation of the tear film.<sup>9</sup>

In a previous study, it was explained that the prevalence of *dry eye syndrome* in patients with DM was 54.3%. *Dry eye syndrome* can be influenced by several factors such as age, current use of medication, history of eye surgery, and blood glucose levels control.<sup>10</sup> *Dry eye syndrome* affect the patient's quality of life especially on work productivity, economic, social, and psychology.<sup>11</sup>

*Dry eye syndrome* can be diagnosed using the Schirmer test and the Ocular Surface Disease Index (OSDI) score. The Schirmer test aims to objectively measure total tear secretion. Previous studies have explained that there is a difference between tear production in patients with DM and non-DM as



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measured by the Schirmer test, which there is a decrease in the Schirmer's test result in patients with DM.<sup>11</sup> Therefore, this study aims to determine the differences of the Schirmer's test results in patients with controlled and uncontrolled DM.

## METHODS

This was an analytic observational study with a cross sectional design. This study was conducted at Diponegoro National Hospital, Manyaran Health Center, and Safira Clinic in Semarang from April to July 2021. The study subjects were 44 patients with DM consisting of 22 patients with controlled DM and 22 patients with uncontrolled DM who were selected based on inclusion and exclusion criteria, using the consecutive sampling method.

The inclusion criteria for this study were DM patients, aged 35-60 years, and willing to participate in the study. Exclusion criteria for this study were the use of drugs that affect tears, history of systemic disease (thyroid disease and autoimmune disease), use of contact lenses, history of eye surgery, history of allergic conjunctivitis, eye trauma, ptosis, exophthalmos, and anemia with Hb levels < 9 gr/dl and MCV < 80 fl.

Data were taken from primary data consisting of name, age, gender, medical history, Hb levels, MCV, HbA1c and Schirmer's test result. The non-parametric test, Mann Whitney, was used to determine the significance of this study variables with  $p < 0.05$  was taken as significance.

## RESULTS

Data obtained from 44 study subjects consisted of 7 male and 15 female patients with uncontrolled DM, and 6 male and 16 female patients with controlled DM. The table also showed that the age of the study subjects with uncontrolled DM are mostly (90.9%) at the age of > 45 years, and all controlled DM (100%) are at the age of > 45 years. In terms of duration of DM, patients with uncontrolled DM were mostly (59,1%) had duration of DM > 10 years, while most of patients with controlled DM (95,5%) had a duration of DM  $\leq 10$  years

**Table 1.** Characteristics by gender and age

Character		Uncontrolled DM				Controlled DM	
		Uncontrolled DM		Controlled DM			
		Frequency	%	Frequency	%		
Gender	Male	7	31.8	6	27.3		
	Female	15	68.2	16	72.7		
Age (years old)	45	2	9.1	0	0		
	> 45	20	90.9	22	100		
Duration of DM (years)	10	9	40.9	21	95.5		
	> 10	13	59.1	1	4.5		

Distribution of Schirmer's test result by gender and age based on the table below, there are 4 males and 10 females with a Schirmer's test result < 10 mm, and there are 9 males and 21 females with a Schirmer's test result  $\geq 10$  mm. The table showed that the majority (85.7%) of the Schirmer's test result < 10 mm is in patients that aged > 45 years, and the Schirmer's test result  $\geq 10$  mm (100%) is in patients that aged > 45 years. In duration of DM, patients with Schirmer's test result < 10 mm were mostly (78,6%) had a duration of DM > 10 years, and patients with Schirmer's test result 10 mm were mostly (90%) had as duration of DM 10 years.

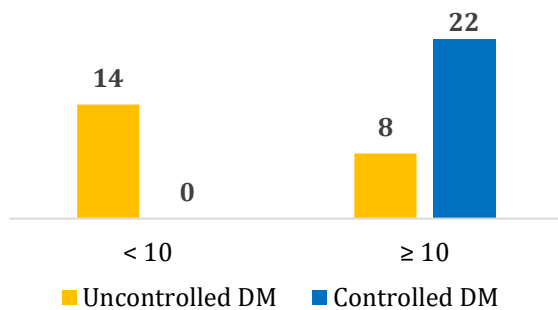
**Table 2.** Distribution of Schirmer's test result according to gender and age

Character		Distribution of Schirmer's test result			
		< 10 mm		10 mm	
		Frequency	%	Frequency	%
Gender	Male	4	28.6	9	30.0
	Female	10	71.4	21	70.0
Age (years old)	45	2	14.3	0	0
	> 45	12	85.7	30	100.0
Duration of DM (years)	10	3	21.4	27	90.0
	> 10	11	78.6	3	10.0

Distribution diagram of Schirmer's test result in patients with DM showed that the Schirmer's test result < 10 mm was found in 14 patients with uncontrolled DM, while the Schirmer's test result  $\geq 10$  mm was found in 8 patients with uncontrolled DM and 22 patients with controlled DM.



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**Fig 1.** Distribution diagram of Schirmer's test result according to type of DM

The result of normality test showed that most of the data were not normally distributed ( $p < 0.05$ ). The result of homogeneity test showed that the data was homogeneous ( $p > 0.05$ ),

**Table 3.** Mann-Whitney test

Mean Rank		P-Value
Uncontrolled	Controlled	
12,32	32,68	0,000

The results of Mann-Whitney test showed that there was a significant difference in Schirmer's test result ( $p < 0.05$ ) in patients with controlled and uncontrolled DM. Mean rank value showed that the Schirmer's test result in patients with controlled DM was higher (32.68 mm) than in patients with uncontrolled DM (12.32 mm).

## DISCUSSION

This study involved 44 patients with diabetes mellitus, consisting of 22 patients with controlled DM and 22 patients with uncontrolled DM, who were selected based on inclusion and exclusion criteria at Diponegoro National Hospital, Manyaran Health Center, and Safira Clinic in Semarang.

The results of this study indicate that there is a significant difference between the Schirmer's test results in patients with controlled and uncontrolled diabetes mellitus. The results of this study are related to the researcher's hypothesis that Schirmer's test results in patients with controlled DM were higher than in patients with uncontrolled DM. The result of normal Schirmer test is  $\geq 10$  mm, while the result of the Schirmer test  $< 10$  mm indicates the presence of *dry eye syndrome*.<sup>11</sup>

In the distribution of the Schirmer's test result in gender, there are 4 male and 10 female with the Schirmer's test result  $< 10$  mm. This showed that the percentage of *dry eye syndrome* is more common in female (71.4%) than male (28.6%). The results obtained are in accordance with the research by Intira *et al.* which states that the risk of *dry eye syndrome* is higher in female.<sup>12</sup>

*Dry eye syndrome* can be influenced by androgen hormones. Androgen hormone function is to regulate the secretory function of the meibomian gland and the function of the lacrimal gland. Androgen hormones levels are higher in males than females, therefore the prevalence of *dry eye syndrome* was higher in females than males.

The Schirmer's test result based on the ages of the study subjects showed that the majority (85.7%) of the Schirmer's test result  $< 10$  mm were aged  $> 45$  years. This was in accordance with the research of Michael *et al.* which showed that with increasing age, the risk of *dry eye syndrome* increases.

Increasing in ages causes a decrease in tear production and also causes meibomian gland atrophy, which produces a lipid layer in the tear film so that tear evaporation increases.<sup>13</sup> Previous research by Cintia *et al.* explained that the prevalence of dry eye syndrome increases in females and males every 5 years after the age of 50, and it is more common in females.<sup>14</sup>

In duration of diabetes mellitus, it was found that the Schirmer's test result  $< 10$  mm were mostly found (78,6%) in the duration of DM  $> 10$  years. These showed that the duration of DM affects the occurrence of *dry eye syndrome*. In accordance with the research of Ying Iyu *et al.* which showed that there was a significant relationship between the duration of suffering from DM and *dry eye syndrome*, which the longer a person suffers from DM, the higher risk of experiencing *dry eye syndrome*. The Schirmer's test result was lower in duration of DM  $> 10$  years than duration of DM  $\leq 10$  years.<sup>15</sup>

The relationship between duration of DM and dry eye syndrome was also found in the study of Galvani *et al.* The study found that peripheral neuropathy as a complication of DM that causes a decrease in corneal sensitivity, was influenced by the duration of DM. The longer the duration of suffering from DM, the sensitivity of the corneal will decrease and cause *dry eye syndrome*.<sup>16</sup>



The Schirmer's test result  $< 10$  mm were found in 14 patients with uncontrolled DM, while the Schirmer's test result  $\geq 10$  mm were found in 22 patients with controlled DM and 8 patients with uncontrolled DM. Based on these results, it can be said that the incidence of *dry eye syndrome* mostly occurs in patients with uncontrolled DM. Control of blood glucose levels affects tear secretion.

Uncontrolled blood glucose levels can accelerate the complications of diabetes mellitus, especially microvascular complications. Previous research by Jian *et al.* showed that an increase in HbA1c levels was significantly associated with the incidence of peripheral neuropathy as one of the microvascular complications in diabetes mellitus.<sup>17</sup>

Peripheral neuropathy can affect the nerves that innervate the corneal from the ophthalmic nerve, which is a branch of the trigeminal nerve. Nerve damage will cause a decrease in corneal sensitivity so that there is a decrease in the protective reflex with reduced tear secretion from the lacrimal gland and a decrease in the blinking reflex so that tear evaporation increases. Eva *et al.* showed that patients with controlled DM had better corneal sensitivity than patients with uncontrolled DM.<sup>18</sup>

Microvascular complications in the eye can also cause hypoxia. A decrease in oxygen supply to cells and tissues causes metabolic and proliferation disorders in lacrimal gland cells. This will cause the function of the lacrimal gland in regulating tear secretion to decrease, causing *dry eye syndrome*.

Based on this study that has been done, it was found that there was a significant difference in the Schirmer's test result ( $p < 0.05$ ) between patients with controlled and uncontrolled DM. The results of this study are relevant to the research by Akbar *et al.* that said the Schirmer's test results of patients with uncontrolled DM are lower than those patients with controlled DM.<sup>19</sup>

The results obtained can prove that the researcher's hypothesis can be accepted. The results showed that there was a difference in the quantity of tear secretion on the Schirmer test between patients with controlled and uncontrolled DM, with the quantity of tear secretion on the Schirmer test in patients with controlled DM was higher than in patients with uncontrolled DM.

Further research is expected to pay attention to other factors that can affect the Schirmer's test result, such as temperature and humidity.

## CONCLUSION

Based on the results of this study that have been obtained, it can be concluded that:

1. The distribution of the Schirmer's test result  $< 10$  mm which indicated the presence of dry eye syndrome, was mostly found in females, age  $> 45$  years, duration of DM  $> 10$  years, and patients with uncontrolled DM.
2. There was a significant difference in the Schirmer's test result between patients with controlled and uncontrolled DM ( $p < 0.05$ ). The Schirmer's test result in patients with controlled DM was higher than in patients with uncontrolled DM

## ETHICAL APPROVAL

This study received Ethical Clearance from the Health Research Ethics Commission, Faculty of Medicine, Diponegoro University with ethical clearance number No. 187/EC/KEPK/FK-UNDIP/VI/2021.

## CONFLICTS OF INTEREST

There are no conflict of interest in this study.

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