

# WORLD WIDE JOURNAL OF MULTIDISCIPLINARY RESEARCH AND DEVELOPMENT

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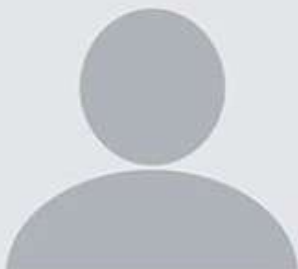
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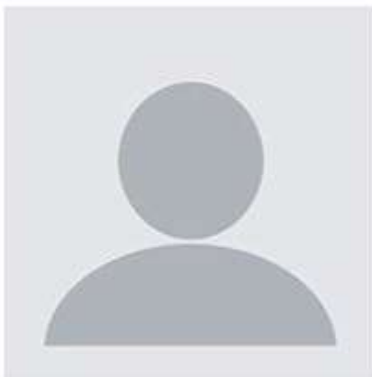
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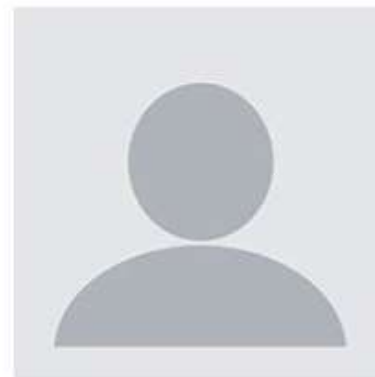
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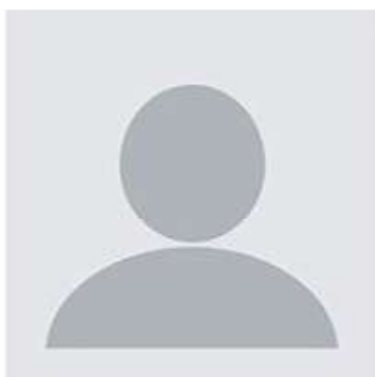
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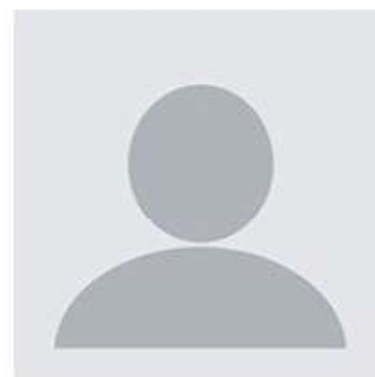
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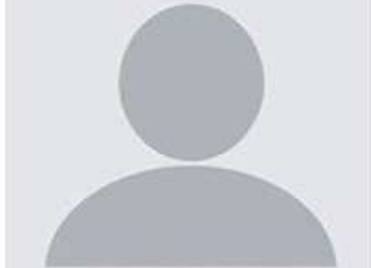
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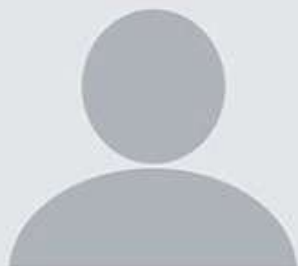
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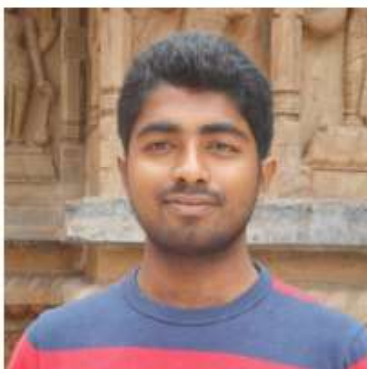
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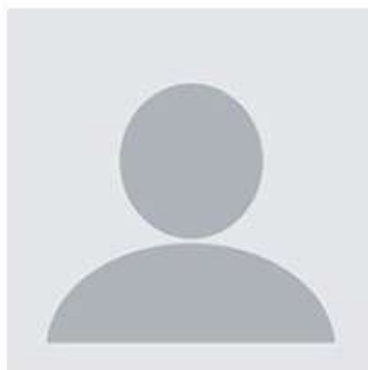
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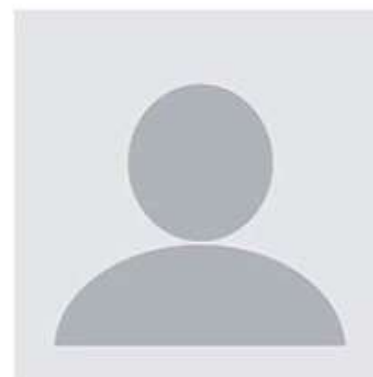
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Subject : Shariah and Law

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### Determinant Sustainability Business Perspective of The Tri Hita Karana (THK) Concept for MSMEs in Bali

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Subject : Economics and Business

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### Overcoming Academic Anxiety and Depression Using Yoga Prana Vidya Healing Protocols: A detailed case study

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### Medical countermeasures for the COVID-19 pandemic management in India

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**Ahmad Helman Hamdani**

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Subject : Geology

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**Noviani Prasetyaningsih**

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## Prevalence of Dry Eye Syndrome and its Relationship with Blood Sugar (HbA1C) Levels in the Elderly

**Husnun Amalia, Anggraeni Adiwardhani, Ida Effendi, Nashita Amira Zaina, Farah Mufidah, Chikita Nur Mustika Rahmaditya, David Tjahyadi, Emad Yousif**

### Abstract

Dry eye syndrome (DES) is an eye disorder that occurs in the elderly and has a risk of decreased vision and interference with daily activities. Risk factors are age over 40 years, female sex and diabetes mellitus. Currently, the incidence of DES is very high in the elderly, and based on research, there is a relationship with diabetes mellitus. Hence, researchers are interested in research to assess the prevalence of DES, risk factors and its relationship with blood sugar levels (HbA1C). This study will determine the prevalence and risk factors that influence the incidence of DES and analyze the relationship between DES and HbA1C levels. The results of this study will likely be an effort to prevent the occurrence of dry eyes in people with risk factors. The study was carried out in a cross-sectional in three hospitals in Jakarta and Bekasi from March to April 2022. The study subjects consisted of 104 respondents with no history of Steven Johnson Syndrome (SSJ), Sjogren's Syndrome, or chronic disorders such as scars due to trauma to the conjunctiva or cornea, history of chemical burns and trauma to the eye area. Analysis was performed univariately and bivariate using the Chi-Square statistical test and Fisher's test with a significance value  $<0.05$ . The result is HbA1C levels did not show a significant relationship with DES ( $p=0,681$ ). There was no significant relationship between DES risk factors, HbA1C levels and DES.

**Keywords:** Dry Eye Syndrome, DES, Risk factors, HbA1C.

### 1. Introduction

Dry eye syndrome (DES) or dry eye is a tear film disorder due to a lack of tears or excessive tear evaporation. This causes damage to the surface of the eye inter palpebra and is associated with symptoms such as eye discomfort.<sup>[1,2]</sup> Complaints from DES are in the form of a foreign body sensation in the eye; the eye feels dry, irritated, itchy, to blurred vision.<sup>[1,3]</sup> This condition will have a risk of decreasing visual function and interference with daily activities.<sup>[4]</sup> The prevalence of DES is influenced by age and gender.<sup>[3,5]</sup> Yazdani et al. found that most studies show that individuals over 40 have a higher risk than younger individuals.<sup>[5,6]</sup> Increasing a person's age causes changes in all organs, including the eyes. Decreased vision in older people will impact their quality of life and independence.<sup>[3,7]</sup> Research in 2018 in India showed that age  $63.25 \pm 6.95$  is a risk factor for severe DES.<sup>[8]</sup> Syanti et al. conducted research in 15 countries in 2016-2017 and found the highest prevalence of DES at age  $>45$  years.<sup>[9]</sup> So, there can be a decreased quality of life due to dry eyes, especially in older people.<sup>[7,10]</sup> Septivianti R. et al. reported that the incidence of dry eyes at the age of  $> 60$  reached 26.2%.<sup>[11]</sup> The prevalence of DES was reported to be higher in women than in men.<sup>[11]</sup> The incidence of DES in women is around 1.33 to 1.74 times higher than in men.<sup>[5]</sup>

Dry eye syndrome is also influenced by systemic risk factors, namely diabetes mellitus (DM).<sup>[7,12]</sup> The reported prevalence of DES in DM sufferers is around 15-33% at the age of over 65 and increases with age. In DM sufferers, DES is 50% more common in women than men. The incidence of DES correlates with the level of glycated hemoglobin, the higher the level of glycated hemoglobin, the higher the incidence of DES.<sup>[5]</sup>

With the high incidence of DES in the elderly and associated with DM at this time, researchers are interested in research to assess the prevalence of DES and its relationship with age, sex and HbA1C levels.

**2. Materials and methods**

The research was carried out from September 2021-July 2022 in 3 hospitals in Jakarta and Bekasi, Indonesia. The research design was cross-sectional, with the sampling technique being consecutive non-random sampling. The number of samples in this study was 104 people, the inclusion criteria were age >40 years, and the exclusion criteria were a history of Steven Johnson syndrome, Sjogren's syndrome, chronic disorders such as scars due to trauma to the conjunctiva/cornea, eye area burns, chemical trauma to the eye area.

The research instrument was a questionnaire for

demographic data and a DEQ5 questionnaire for establishing a diagnosis of DES. An ophthalmological examination was performed to exclude exclusion criteria. A laboratory examination was carried out to assess HbA1C levels. The data analysis method is presented in the table, and coding is then given to test the data normality of all variables using the Kolmogorov-Smirnov test. A parametric test will be used if the data is normally distributed, while a non-parametric test will be used if it is not normal. Data will be analyzed univariately and bivariate using the SPSS program with the Chi-Square test with a significance value <0.05.

Ethical Clearance was obtained from the Research Ethics Committee of the Faculty of Medicine, Universitas Trisakti, with number 033/KER/FK/III/2022.

**3. Results & Discussion**

**Table 1:** Characteristics of Respondents (n=104).

Variable	Frequency (n)	Percentage (%)
Gender		
Male	49	47,1
Female	55	52,9
Age		
< 65-year-old	63	60,6
≥ 65-year-old	41	39,4
DES		
Yes	40	38,5
No	64	61,5
HbA1C level		
Normal (<6 %)	24	23,1
Pre-Diabetes Mellitus (6-6,4 %)	12	11,5
Diabetes Mellitus (>6,4 %)	68	65,4

Characteristics of the respondents in this study were that the majority of respondents were women (52.9%), aged <65 years (52.9%). In this study, 61.5% of respondents did

not suffer from DES, and 65.4% had HbA1C levels >6.4%, which was classified as a diagnosis of Diabetes Mellitus.

**Table 2:** The relationship of DES risk factor and DES.

Variable	Dry Eye Syndrome		p
	Yes (n (%))	No (n (%))	
Age			0,924*
<65-year-old	24 (38,1)	39 (61,9)	
≥65-year-old	16 (39,0)	25 (61,0)	
Gender			0,641*
Male	20 (40,8)	29 (59,2)	
Female	20 (36,4)	35 (63,6)	
HbA1C level			0,681*
Diabetes Mellitus (>6,4%)	9 (37,5)	15 (62,5)	
Pre DM (6,0-6,4%)	6 (50,0)	6 (50,0)	
Not DM (<6,4%)	25 (36,8)	43 (63,2)	

\* Chi-square test

Based on the results of the study showed that high HbA1C levels showed that most were not diagnosed with DES (62.5%) and did not show a significant relationship between DES and HbA1C levels with a p-value = 0.681.

**Age and DES**

The incidence of DES in the elderly in this study reached 38.5%. This is a higher number when compared to research by Farrand et al. reaches 2%.<sup>[13]</sup> Morthen et al. reported the prevalence of DES at age > 50 years, namely 72% compared to age < 50, with a total of 78,165 respondents.<sup>[3]</sup> Rouen PA et al. states that the prevalence of DES at the age

of 40 years reaches 75%.<sup>[14]</sup> Our study showed no significant results for the two age groups (p=0.924) because the division of the age groups was not based on the classification of young age. All respondents were aged > 40 years. In contrast to the study of Farrand et al. which had respondents from adolescents and classified them into two age groups, namely 18-49 and > 50 years.<sup>[13]</sup> Syanti et al.<sup>[9]</sup> also found a significant relationship between age and DES (p=0.001). This is also because this study has respondents with a wide age range, namely 18-90 years and divides them into three age groups (18-25 years, 26-45 years, and > 45 years). This age grouping difference can

cause significant differences.

The incidence of DES according to age based on its pathophysiology will increase in prevalence with age with an odds ratio of 1.2x (1.1-1.3) at each additional ten years of age.<sup>[15]</sup> The prevalence of symptomatic dry eye is reported to increase progressively with age. The frequency of DES is 8.4% at ages <60 years, 15% at 70-79 years and 20% at ages >80 years. This can be caused because, in old age, the frequency of blinking decreases, the quality of the meibomian glands also decreases, involuntal palpebral malposition, horizontal lid laxity, and eyelid malposition lead to corneal exposure, poor tear film distribution and abnormal tear outflow with induce joint eye dryness.<sup>[16]</sup>

### Gender and DES

In our study, gender was not a risk factor for DES ( $p=0.641$ ). A different thing was reported by Syanti et al.<sup>[9]</sup>, which showed a significance level of  $p=0.001$  with an odds ratio of 0.524. This difference could be because the study had a wide age range and a large number of samples and was carried out in a multi-centre manner in 15 countries, so it had excellent sample variations.

Stapleton F. et al.<sup>[15]</sup> also stated minimal and inconsistent relationships in gender relations with DES. At the age above 50, there is a relationship between the incidence of DES based on gender. With increasing age, women show a higher prevalence of DES. Whereas in men, an increased prevalence of meibomian gland dysfunction was found.

Malet F. et al.<sup>[17]</sup> also showed an association between DES diagnosis and female gender, as females have a 1.5 times higher risk of developing DES than males. This finding could be explained by the use of hormones for contraception or infertility in the younger women age group and the impact of these hormones on the female's lacrimal gland, goblet cell function, Meibom Gland and ocular surface sensitivity that may contribute to dry eye symptoms. In women in the older age group, lower levels of estrogens and androgens may lead to inadequate lacrimal gland secretion associated with aqueous deficient DES.<sup>[18]</sup> The impact of gender on the development of DES varies across studies. Consistent with the current study, most studies reported that DES occurs more likely among females.<sup>[19]</sup>

### HbA1C levels and DES

High HbA1C levels indicated that most were undiagnosed with DES (62.5%). This is different from the theory, which states that the incidence of dry eye correlates with the level of glycated hemoglobin, the higher the level of glycated hemoglobin, the higher the incidence of dry eye syndrome.<sup>[5]</sup> The prevalence of DES at HbA1C levels >6.4% is 8.6%. This result is lower than the study by Lukandy A. et al.<sup>[5]</sup>, which stated that the prevalence reached 15-33%.

This study showed no relationship between DES obtained using the DEQ5 questionnaire and HbA1C levels with  $p=0.681$ . This is different from several studies that state a relationship between DES and Diabetes Mellitus. Goebels stated a significant difference in the Schirmer examination in the diabetes mellitus group and without diabetes mellitus ( $p=0.001$ ), and reflex tearing was demonstrated to be significantly decreased.<sup>[20]</sup> Moreover, their tear protein composition differs from that of healthy subjects. In long-lasting diabetes, damage to the lacrimal gland's

microvasculature and autonomic neuropathy might impair lacrimation. Diabetic sensory neuropathy of the cornea can also play a role in decreased tear secretion.<sup>[21]</sup>

The results in our study were similar to those found in the study of Olanian SI et al.<sup>[22]</sup>, which stated that there was no relationship between dry eye and HbA1C levels in people with diabetes in Nigeria ( $r=0.086$ ,  $p=0.239$ ). Control of HbA1C levels also affects dry eye; in our study, we did not evaluate this. So that it can lead to meaningless results in this study, we recommend that controlling HbA1C levels be assessed in future studies. Poor glycemic control is associated with microvascular complications of the lacrimal gland, impairs lacrimal gland function, causing dry eye among people with diabetes.<sup>[22]</sup>

The prevalence of dry eye in people with diabetes mellitus is 37.5%, which is not much different from research by Olanian SI et al.<sup>[22]</sup>, who found a prevalence of 21.7% and Kaiserman et al.<sup>[21]</sup> 20.6%. The longer duration of diabetes mellitus has been documented to correlate with an increase in the prevalence of dry eye among patients ( $p=0.01$ ).<sup>[23]</sup>

### 4. Conclusions

Our research showed there was no significant relationship between DES risk factors, HbA1C levels and DES. However, the prevalence of DES is higher in women and people with diabetes mellitus based on HbA1C measurements.

### 5. Acknowledgments

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### 7. Conflict Of Interest

The authors declare no competing interests.

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*by* Ida Effendi FK

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**Keywords:** Dry Eye Syndrome, DES, Risk factors, HbA1C.

### 18 Introduction

Dry eye syndrome (DES) or dry eye is a tear film disorder due to a lack of tears or excessive tear evaporation. This causes damage to the surface of the eye inter palpebra and is associated with symptoms such as eye discomfort.<sup>[1,2]</sup> Complaints from DES are in the form of a foreign body sensation in the eye; the eye feels dry, irritated, itchy, to blurred vision.<sup>[1,3]</sup> This condition will have a risk of decreasing visual function and interference with daily activities.<sup>[4]</sup> The prevalence of DES is influenced by age and gender.<sup>[3,5]</sup> Yazdani et al. found that most studies show that individuals over 40 have a higher risk than younger individuals.<sup>[5,6]</sup> Increasing a person's age causes changes in all organs, including the eyes. Decreased vision in older people will impact their quality of life and independence.<sup>[3,7]</sup> Research in 2018 in India showed that age  $63.25 \pm 6.95$  is a risk factor for severe DES.<sup>[8]</sup> Syanti et al. conducted research in 15 countries in 2016-2017 and found the highest prevalence of DES at age  $>45$  years.<sup>[9]</sup> So, there can be a decreased quality of life due to dry eyes, especially in older people.<sup>[7,10]</sup> Septivianti R. et al. reported that the incidence of dry eyes at the age of  $> 60$  reached 26.2%.<sup>[11]</sup> The prevalence of DES was recorded to be higher in women than in men.<sup>[1]</sup> The incidence of DES in women is around 1.33 to 1.74 times higher than in men.<sup>[5]</sup>

Dry eye syndrome is also influenced by systemic risk factors, namely diabetes mellitus (DM).<sup>[7,12]</sup> The reported prevalence of DES in DM sufferers is around 15-33% at the age of over 65 and increases with age. In DM sufferers, DES is 50% more common in women than men. The incidence of DES correlates with the level of glycated hemoglobin, the higher the level of glycated hemoglobin, the higher the incidence of DES.<sup>[5]</sup>

With the high incidence of DES in the elderly and associated with DM at this time, researchers are interested in research to assess the prevalence of DES and its relationship with age, sex and HbA1C levels.

**2. Materials and methods**

The research was carried out from September 2021-July 2022 in 3 hospitals in Jakarta and Bekasi, Indonesia. The research design was cross-sectional, with the sampling technique being consecutive non-random sampling. The number of samples in this study was 104 people, the inclusion criteria were age >40 years, and the exclusion criteria were a history of Steven Johnson syndrome, Sjogren's syndrome, chronic disorders such as scars due to trauma to the conjunctiva/comea, eye area burns, chemical trauma to the eye area.

The research instrument was a questionnaire for

demographic data and a DEQ5 questionnaire for establishing a diagnosis of DES. An ophthalmological examination was performed to exclude exclusion criteria. A laboratory examination was carried out to assess HbA1C levels. The data analysis method is presented in the table, and coding is then given to test the data normality of variables using the Kolmogorov-Smirnov test. A parametric test will be used if the data is normally distributed, while a non-parametric test will be used if it is not normal. Data will be analyzed univariately and bivariate using the SPSS program with the Chi-Square test in a significance value <0.05.

Ethical Clearance was obtained from the Research Ethics Committee of the Faculty of Medicine, Universitas Trisakti, with number 033/KER/FK/III/2022.

**3. Results & Discussion**

**Table 1:** Characteristics of Respondents (n=104).

Variable	Frequency (n)	Percentage (%)
Gender		
Male	49	47,1
Female	55	52,9
Age		
< 65-year-old	63	60,6
> 65-year-old	41	39,4
DES		
Yes	40	38,5
No	64	61,5
HbA1C level		
Normal (<6 %)	24	23,1
Pre-Diabetes Mellitus (6-6,4 %)	12	11,5
Diabetes Mellitus (>6,4 %)	68	65,4

Characteristics of the respondents in this study were that the majority of respondents were women (52.9%), aged <65 years (52.9%). In this study, 61.5% of respondents did

not suffer from DES, and 65.4% had HbA1C levels >6.4%, which was classified as a diagnosis of Diabetes Mellitus.

**Table 2:** The relationship of DES risk factor and DES.

Variable	Dry Eye Syndrome		p
	Yes (n (%))	No (n (%))	
Age			
<65-year-old	24 (38,1)	39 (61,9)	0,924*
>65-year-old	16 (39,0)	25 (61,0)	
Gender			
Male	20 (40,8)	29 (59,2)	0,641*
Female	20 (36,4)	35 (63,6)	
HbA1C level			
Diabetes Mellitus (>6,4%)	9 (37,5)	15 (62,5)	0,681*
Pre DM (6,0-6,4%)	6 (50,0)	6 (50,0)	
Not DM (<6,4%)	25 (36,8)	43 (63,2)	

\* Chi-square test

Based on the results of the study showed that high HbA1C levels showed that most were not diagnosed with DES (62.5%) and did not show a significant relationship between DES and HbA1C levels with a p-value = 0.681.

**Age and DES**

The incidence of DES in the elderly in this study reached 38.5%. This is a higher number when compared to research by Farrand et al. reaches 2%.<sup>[13]</sup> Morthen et al. reported the prevalence of DES at age > 50 years, namely 72% compared to age < 50, with a total of 78,165 respondents.<sup>[3]</sup> Rouen PA et al. states that the prevalence of DES at the age

of 40 years reaches 75%.<sup>[14]</sup> Our study showed no significant results for the two age groups (p=0.924) because the division of the age groups was not based on the classification of young age. All respondents were aged >40 years. In contrast to the study of Farrand et al. which had respondents from adolescents and classified them into two age groups, namely 18-49 and > 50 years.<sup>[13]</sup> Syanti et al.<sup>[9]</sup> also found a significant relationship between age and DES (p=0.001). This is also because this study has respondents with a wide age range, namely 18-90 years and divides them into three age groups (18-25 years, 26-45 years, and > 45 years). This age grouping difference can

cause significant differences.

The incidence of DES according to age based on 12's pathophysiology will increase in prevalence with age with an odds ratio of 1.2x (1.1-1.3) at each additional ten years of age.<sup>[15]</sup> The prevalence of symptomatic dry eye is reported to increase progressively with age. The frequency of DES is 8.4% at ages <60 years, 15% at 70-79 years and 20% at ages >80 years. This can be caused because, in old age, the frequency of blinking decreases, the quality of the meibomian glands also decreases, involutional palpebral malposition, horizontal lid laxity, and eyelid malposition lead to corneal exposure, poor tear film distribution and abnormal tear outflow with induce joint eye dryness.<sup>[16]</sup>

#### Gender and DES

In our study, gender was not a risk factor for DES (p=0.641). A different thing was reported by Syanti et al.<sup>[9]</sup>, which showed a significance level of p=0.001 with an odds ratio of 0.524. This difference could be because the study had a wide age range and a large number of samples and was carried out in a multi-centre manner in 15 countries, so it had excellent sample variations.

Stapleton F. et al.<sup>[15]</sup> also stated minimal and inconsistent relationships in gender relations with DES. At the age above 50, there is a relationship between the incidence of DES based on gender. With increasing age, women show a higher prevalence of DES. Whereas in men, an increased prevalence of meibomian gland dysfunction was found.

Malet F. et al.<sup>[17]</sup> also showed an association between DES diagnosis and female gender, as females have a 1.5 times higher risk of developing DES than males. This finding could be explained by the use of hormones for contraception or infertility in the younger women age group and the impact of these hormones on the female's lacrimal gland, goblet cell function, Meibom Gland and ocular surface sensitivity that may contribute to dry eye symptoms. In women in the older age group, lower levels of estrogens and androgens may lead to inadequate lacrimal gland secretion associated with aqueous deficient DES.<sup>[18]</sup> The impact of gender on the development of DES varies across studies. Consistent with the current study, most studies reported that DES occurs more likely among females.<sup>[19]</sup>

#### HbA1C levels and DES

High HbA1C levels indicated that most were undiagnosed with DES (32.5%). This is different from the theory, which states that the incidence of dry eye correlates with the level of glycated hemoglobin, the higher the level of glycated hemoglobin, the higher the incidence of dry eye syndrome.<sup>[5]</sup> The prevalence of DES at HbA1C levels >6.4% is 8.6%. This result is lower than the study by Lukandy A. et al.<sup>[5]</sup>, which stated that the prevalence reached 15-33%.

This study showed no relationship between DES obtained using the DEQ5 questionnaire and HbA1C levels with p=0.681. This is different from several studies that state a relationship between DES and Diabetes Mellitus. Goebels stated a significant difference in the Schirmer examination in the diabetes mellitus group and without diabetes mellitus (p=0.001), and reflex tearing was demonstrated to be significantly decreased.<sup>[20]</sup> Moreover, their tear protein composition differs from that of healthy subjects. In long-lasting diabetes, damage to the lacrimal gland's

microvasculature and autonomic neuropathy might impair lacrimation. Diabetic sensory neuropathy of the cornea can also play a role in decreased tear secretion.<sup>[21]</sup>

The results in our study were similar to those found in the study of Olanian SI et al.<sup>[22]</sup>, which stated that there was no relationship between dry eye and HbA1C levels in people with diabetes in Nigeria (r=0.086, p=0.239). Control of HbA1C levels also affects dry eye; in our study, we did not evaluate this. So that it can lead to meaningless results in this study, we recommend that controlling HbA1C levels be assessed in future studies. Poor glycemic control is associated with microvascular complications of the lacrimal gland, impairs lacrimal gland function, causing dry eye among people with diabetes.<sup>[22]</sup>

The prevalence of dry eye in people with diabetes mellitus is 37.5%, which is not much different from research by Olaniyan SI et al.<sup>[22]</sup>, who found prevalence of 21.7% and Kaiserman et al.<sup>[21]</sup> 20.6%. The longer duration of diabetes mellitus has been documented to correlate with an increase in the prevalence of dry eye among patients (p=0.01).<sup>[23]</sup>

#### 4. Conclusions

Our research showed there was no significant relationship between DES risk factors, HbA1C levels and DES. However, the prevalence of DES is higher in women and people with diabetes mellitus based on HbA1C measurements.

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#### 7. Conflict Of Interest

The authors declare no competing interests.

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