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Correlation of depression, anxiety and stress level on dry eye disease severity

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Abstract--Dry eye disease (DED) is a multifactorial disease of the tears and ocular surface. Dry eye disease is an important public health problem which lead to ocular discomfort and disrupt on the patient's daily activity. The prevalence of DED varies with age and demographic between 5,5% - 50,1% and increased with age and has been associated with chronic illness such as diabetes melitus and hypertension. This study to investigate the correlation between DED with depression, anxiety and stress. Research location at Sanglah Hospital eye policlinic in Denpasar-Bali with 93 sample were analyzed. Data was analyzed to get correlation between DED and depression, anxiety and stress with sex, education, work, and chronic illness used SPSS program. Ninety-three patients admitted to eye policlinic, mostly female 50 (53,8%) with median age 45,00 ±12,445. The correlation between DED and depression, anxiety and stress showed inversely correlation. The correlation between OSDI score with depression, anxiety and stress showed positive correlation (depression r 0,27, p=0,008; anxiety r 0,31, p= 0,003; stress r 0,29, p=0,004). There are correlation of OSDI score with depression, anxiety and stress but not

correlated with objective DED tests. Higher OSDI score was correlated with higher depression, anxiety and stress score.

Keywords---dry eye, depression, anxiety, stress.

Introduction

Dry eye disease (DED) is a multifactorial disorder of the tear film and ocular surface. Dry eye disease is one of the health problems that still often causes discomfort in the eyes and can interfere with daily activities (Yilmaz, Gökler and Unsal, 2015). Dry eye disease is often associated with systemic diseases such as diabetes mellitus, autoimmune diseases such as Sjogren's syndrome, and rheumatoid arthritis (Vaart et al., 2015)

In general, the prevalence of DED varied by age and demographics between 5.5% - 50.1% in community-epidemiological-based studies and 7.99% - 29.9% in hospital-based studies (Yilmaz, Gökler and Unsal, 2015). In the United States, the prevalence of DED is 6.8% in the adult population and increases between the ages of 18-34 years (2.7%) and those over 75 years (18.6%). The prevalence of DED is more in women (8.8%) than in men (4.5%) (Farrand et al., 2017). Research in the Riau Archipelago showed that the prevalence of DED was 27.5% in the population over 21 years. Research conducted at Adam Malik Hospital Medan found the prevalence of DED was 76.8% in women who had experienced menopause (Chaironika, 2011). The prevalence of DED in the population aged 50 years and over in Bali is 76% in rural areas and 72.4% in urban areas (Dwipayani, 2016). In a hospital-based study by Liyue et al. in 2015 in DED patients, depression scores above 16 were 31.5%. Depression and anxiety are more related to the symptoms experienced by patients compared to the severity of the DED degree (Liyue et al., 2016)

Symptoms of DED include sore, itchy, aqueous eyes, redness, lumpiness, and pain. Factors that cause DED include old age, hormonal changes, smoking, history of eye surgery, medications, low humidity, high room temperature, wearing contact lenses, and a stressful work environment. Dry eye disease is also associated with risk factors for metabolic syndromes, such as hypertension, hyperglycemia, and hyperlipidemia, although no literature describes it in detail (Tang et al., 2016).

The aqueous layers eye is composed of 3 layers: mucin, aqueous, and lipid (Kanski, 2003). The tear film lines the eye's anterior surface and plays a role in the mechanism of transport of oxygen, carbon dioxide, and nutrients to the eye. The superficial layer is composed of a lipid layer that is 0.11 m thick and is produced by the meibomian glands. The middle layer is the aqueous layer produced by the lacrimal gland. The layer closest to the Cornea is the mucin layer produced by the conjunctival goblet cells (Tiffany, 2008). Abnormalities of the tear film can be identified through anamnesis, slit lamp examination, and some additional tests. Investigations that can be used to evaluate the presence of DED include high tear meniscus, tear break up time (TBUT), and Schirmer's test.

Dry eye disease is often associated with chronic diseases that lead to a decreased quality of life and a negative impact on mood and mental health (Na et al., 2015; Yilmaz, Gökler and Unsal, 2015). According to the World Health Organization (WHO), in general, depression occurs in 4.4% of the population and tends to increase by 18.4% from 2005 to 2015 (Na et al., 2015). Anxiety is a form of psychological disorder that often coexists with physical conditions. Data analysis found that patients with DED symptoms stimulated feelings of disappointment, frustration with themselves, and emotionally unstable, which significantly affected the patient's quality of life (Li et al., 2011). Wen et al., 2012 observed an increase in the frequency of DED in 472 psychiatric patients treated with various psychiatric disorders, including depression and anxiety 60% (Wan, Chen and Young, 2016). There is a relationship between DED and post-traumatic stress, but these data are only carried out in specific populations such as old age (Basilious, Xu and Malvankar-Mehta, 2022). Patients with DED tend to experience more symptoms of Anxiety than people in general (Stevenson, Chauhan and Dana, 2012). The relationship between DED and depression, anxiety, and stress in Bali has never been studied, where DED is the third most common disease in the External Eye Disease (EED) division of Sanglah Hospital after corneal ulcers and anterior uveitis. It is interesting for researchers to research the relationship of DED with levels of depression, anxiety, and stress levels.

Method

This study is an analytical observational study that measures variables without intervention, using a cross-sectional study approach to measure the relationship (association) between DED and Depression, Anxiety, and stress scores in Eye Polyclinic, Sanglah Hospital, Denpasar. The research has obtained an ethics permit from Udayana University with No. 1626/UN14.2.2/PD/KEP/2018.

The inclusion criteria were patients aged 30 years and over who come to the Eye Clinic of Sanglah Hospital within three months or until the number of samples is met. Exclusion criteria: (1) There are eyelid, corneal, and scleral disorders, (2) Patients with a history of intraocular surgery (cataract surgery, refractive surgery, trabeculectomy, implant devices installation) less than six months, (3) Routine use of contact lenses more one year. (4) History of blunt, sharp, chemical, radiation trauma, (5) History of allergies and signs of infection and inflammation during examination, (6) Patients on antidepressant drugs, and (7) Patients who are using eye drops (artificial tears) within the last two weeks.

Samples that have the inclusion and exclusion criteria signed the informed consent, data collection on gender, age, history of diabetes mellitus, allergies, hypertension, education level, occupation, eye examination with *ocular surface disease index (OSDI)*, Schirmer test, and *tear break up time* test (TBUT). Examination of depression, anxiety, and stress with the DASS (Depression, Anxiety and Stress Scale) questionnaire. The analysis was carried out with the Statistical Package for Social Sciences (SPSS) program.

Result and Discussion

The research sample was selected consecutively from the affordable population, that is, from all patients who came to the eye polyclinic of Sanglah Hospital, Denpasar, until the desired number of samples was collected, as many as 93 samples. The characteristics of the research sample are shown in Table 1.

Table 1
Characteristics of the Research Sample

Variable	n(%)
Gender	
Female	50 (53.8%)
Male	43 (46.2%)
Age (years) mean±SD	
Diabetes mellitus History	
Yes	20 (21.5%)
No	73 (78.5%)
Cholesterol History	
Yes	6 (6.5%)
No	87 (93.5%)
Allergy History	
Yes	9 (9.7%)
No	84 (90.3%)
History of Hypertension	
Yes	20 (21.5%)
No	73 (78.5%)
Education	
Bachelor degree	36 (40.9%)
Senior High School	24 (25.8%)
Primary School	10 (10.8%)
Diploma	9 (9.8%)
Master degree	5 (5.4%)
Junior High School	4 (4.3%)
Profession	
Self-employed	29 (31.2%)
Health workers	18 (19.4%)
Civil servant	15 (16.1%)
Housewife	11 (11.8%)
Retired	8 (8.6%)
Etc	12 (12.9%)

This research was conducted at the Eye Clinic of Sanglah Hospital with 50 patients (53.8%) were female and male 43 (46.2%) . Schaumberg et al., (2013) found that the prevalence of women with dry eyes was 72% compared to men, which was 28% The prevalence of DED in studies conducted in the United States was more in women (8.8%) than men (4.5%) (Farrand et al., 2017). Research conducted at Adam Malik Hospital Medan found the prevalence of DED was 76.8% in women who had experienced menopause (Chaironika, 2011). The influence of the female gender is a significant risk factor for the occurrence of

DED. In addition to having sensitivity to acute pain responses, female hormones such as estrogen can increase the risk of pain. Androgen hormones regulate the functioning of the meibomian glands, improve the quality and quantity of fat produced by tissues and increase the fat layer in the tear film. The decrease in this hormone causes an increase in the prevalence of DED in women and in old age.

The prevalence of dry eye in this study showed the mean age of the patients was 45.00 ± 12.445 years. Research Bron AJ et al. (2014), the prevalence of dry eye increases with age, where the prevalence in veterans over 80 years is 19.0%. Basiliou et al. research showed that the prevalence of DED ranged from 5-30% of the population over 50 years. The study conducted in the United States on adults over 18 years found the prevalence of DED in the age range 18-34 years by 2.7% and increased at the age above 75 years, which is 18.6%. Dry eyes are more common at the age above 40 years where at this age there is a decrease in tear secretion, lacrimal gland instability, an increase in the prevalence of abnormalities in the meibomian glands, and an increase in the likelihood of developing diseases that attack the elderly such as diabetes mellitus, hypertension, hypercholesterolemia (Bron et al., 2014; Farrand et al., 2017; Basiliou, Xu and Malvankar-Mehta, 2022)

Chronic diseases such as diabetes mellitus, cholesterol, a history of allergies, and hypertension are among the comorbidities that elderly patients often experience. In this study, 20 patients (21.5%) had a history of DM and 73 (78.5%). A history of cholesterol was obtained in 6 (6.5%) patients, and in those who did not there is a history of cholesterol of 87 (93.5%). There was a 9 (9.7%) history of allergies and 84 (90.3%) with no allergies. The history of hypertension was 20 (21.5%) and those who did not suffer from hypertension were 73 (78.5%). Diabetes mellitus (DM) is a health problem in many countries and a systemic disease that often causes complications of diabetic retinopathy, cataracts, glaucoma, and dry eyes. People with diabetes often experience tear dysfunction and have a different composition of tears from ordinary people due to high blood sugar levels for a long time. DM patients also experience microvascular damage and neuropathy which causes impaired secretion of the lacrimal gland (Achtsidis et al., 2014; Zou et al., 2018).

The education level of the sample in this study was obtained at the most Bachelor degree at 40.9%. A person's level of education does not affect the occurrence of DED, this is evidenced in several studies that found no significant correlation between the two, such as the research by Muna'aim et al. in 2016, where the highest percentage of education level was obtained at the secondary educational level, but this does not have a statistically significant association with the incidence of DED (Muna'Aim et al., 2016)

This study found that most of the jobs are in the private sector. The field of work is thought to influence the occurrence of DED, especially work carried out outdoors, windy and exposed to direct sunlight, or work indoors that is exposed to air conditioning or associated with long-term computer use. In a study conducted by Kluizenaar et al. in 2016, 34% of workers in the room complained of dry eyes such as discomfort, itching, and watering in the last four weeks.

Environmental factors such as high temperature, low humidity, and air regulation can cause eye discomfort, but other studies have shown no statistically significant correlation to the occurrence of DED (de Kluzenaar et al., 2016).

Characteristics of dry eyes degrees, depression, anxiety, and stress in Table 2 found that the highest degree of dry eye in the right eye was in grade one, as many as 57 (61.3%), in grade two as 20 (21.5%), and in grade three, as many as 12 (12.9%), grade four as many as 4 (4.3%). The highest degree of dry eye assessment in the left eye was found in the first degree, as many as 55 (59.1%), then the second degree as much as 21 (22.6%), the third degree as many as 13 (14.0%) and the fourth degree as much as 4 (4.3%). The bivariate analysis results showed that the degree of dry eye in the right and left eyes was not correlated with depression, anxiety and stress. The relationship of dry eye degrees based on subjective assessment using OSDI (Ocular Surface Disease Index) obtained a positive correlation strength value between OSDI on depression, anxiety, and stress which shows the more significant the OSDI value, the greater the depression score, anxiety and stress in the sample. Research conducted by (Wan, Chen and Young, 2016).

Table 2
Characteristics of Dry Eyes Degrees, Depression, Anxiety, and Stress

Variable	n(%)
Degree of DED Right	
I	57 (61.3%)
II	20 (21.5%)
III	12 (12.9%)
IV	4 (4.3%)
Degree of DED Left	
I	55 (59.1%)
II	21 (22.6%)
III	13 (14.0%)
IV	4 (4.3%)
Depression	
Normal	74 (79.6%)
Mild	10 (10.8%)
Moderate	7 (7.5%)
Severe	2 (2.2%)
Anxiety	
Normal	84 (90.3%)
Mild	3 (3.2%)
Moderate	5 (5.4%)
Severe	1 (1.1%)
Stres	
Normal	76 (81.7%)
Mild	6 (6.5%)
Moderate	5 (5.4%)
Severe	6 (6.5%)

DED: Dry eyes disease

The relationship between the degree of DED with depression, anxiety, and stress in Table 3 was determined by using a non-parametric test. Spearman. The results show the Spearman correlation value of the right eye DED degree to depression of 0.068. The correlation value of the right eye DED degree to Anxiety is -0,057. The correlation value of the right eye DED to stress was 0.012, which showed no relationship between the degree of right eye DED and depression, anxiety, and stress, with a p-value > 0.05. spearman correlation value of left eye DED degree to depression is 0.014, anxiety - 0.050 and stress - 0.026, with p-value > 0.05. Scatter plot of the relationship between depression and OSDI in Figure 1, relationship between anxiety and OSDI in Figure 2 and relationship between stress and OSDI in Figure 3.

Table 3
Relationship of Dry Eye Degrees with Depression, Anxiety, and Stress

Degree of DED right eye	Correlation coefficient	p
Depression	0.068	0.516
Anxiety	- 0.057	0.585
Stress	0.012	0.906
Degree of left eye DED		
Depression	0.014	0.891
Anxiety	- 0.050	0.632
Stress	- 0.026	0.805

DED: Dry eyes disease

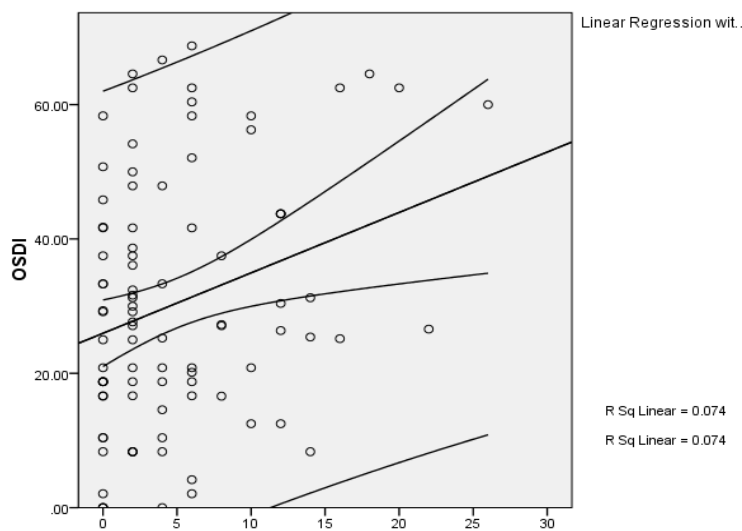


Figure 1 Scatter plot of the relationship between depression and OSDI ($r = 0.27$; $r^2 = 0.74$; $p = 0.008$) with the linear equation $OSDI = 25.96 + 0.899$ (Depression score)

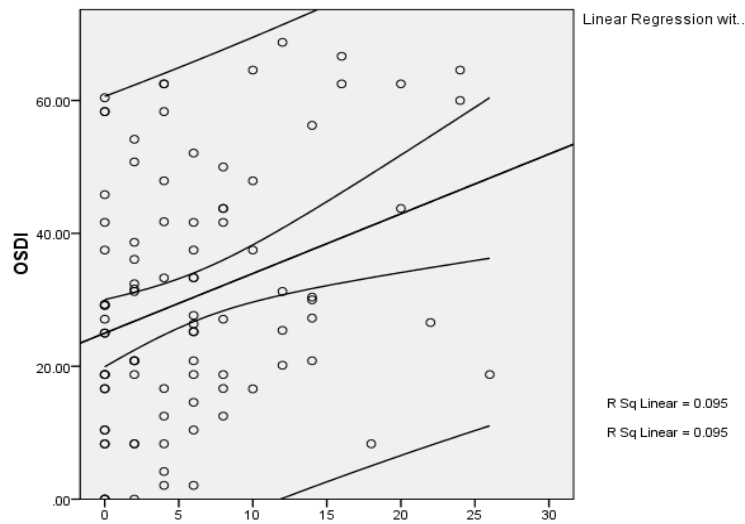


Figure 2 Scatter plot of the relationship between Anxiety and OSDI ($r = 0.31$; $r\ sq = 0.095$; $p = 0.003$) with the linear equation $OSDI = 24.98 + 0.898$ (Anxiety Score)

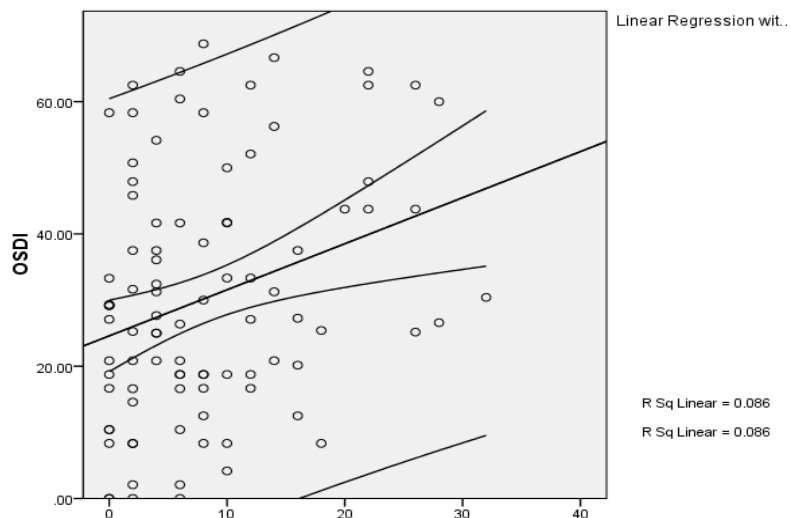


Figure 3 Scatter plot of the relationship between stress and OSDI ($r = 0.29$; $r\ sq = 0.086$; $p = 0.004$) with the linear equation $OSDI = 24.59 + 0.697$ (Stress Score)

A meta-analysis found that DED was associated with an increase in depression and anxiety scores. Retrospective studies show that chronic discomfort and pain from DED symptoms impact cognitive, mood, sleep, and psychological disorders. However, the correlation between reported subjective symptoms was not by the severity of DED. Thus, several psychological factors showed a positive correlation with the occurrence of DED. Factors that can affect the ocular surface and cause DED symptoms to include hormonal changes, smoking, previous surgery history, drugs such as antihistamines, α -blockers, antispasmodics, diuretics, antidepressants, a low humidity environment, room temperature high, the use of

contact lenses is a factor that can reduce the production of the tear film (Alves et al., 2014; Yilmaz, Gökler and Unsal, 2015; Szakáts et al., 2016).

Wan KH et al. in 2016 found that the prevalence of depression and anxiety in DED patients was three times higher than in patients without DED and population found an increase in DED in 472 psychiatric patients suffering from depression and anxiety. Basilious, Xu, and Malvankar-Mehta, (2022) found an association between DED and post-traumatic stress disorder (PTSD) in a veteran population. Vaart et al. (2015) found that the odds ratio of DED to Depression was 2.9 (95% CI 2.7-3.1), and the odds ratio of DED to Anxiety was 2.8 (95% CI 2.6-3.0). Stress is a negative emotional experience accompanied by biochemical, physiological, cognitive, and behavioral changes. Changes occur in the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system. Activation of the release of glucocorticoids in the form of cortisol. The effects of cortisol are mobilizing proteins from muscle and fatty acids from adipose tissue, increasing liver fat, and anti-inflammatory response. Psychosomatic disorders, depression, can contribute to physical complaints and lower pain thresholds and can interact with each other (Oka and Raka-Widiana, 2015)

In theory, OSDI is a questionnaire that assesses the frequency of DED to diagnose DED. From previous studies, OSDI and TBUT have a significant correlation in assessing DED compared to Schirmer. Subjective complaints of DED are related to psychological factors that underlie subjective complaints that cause therapy failure in DED. Gender, age, and history of chronic disease are essential factors for the occurrence of depression, anxiety and stress decreased quality of life, and harmed mood and mental health, but this study found a statistically insignificant relationship (Özcura, Aydin and Helvaci, 2007; Na et al., 2015; Yilmaz, Gökler and Unsal, 2015).

Psychosomatic disorders are adverse psychological factors, affecting the patient's medical condition. Someone who experiences stress or emotional disturbance due to psychosocial or other stressors will experience psychological, physiological, biochemical, and other changes, which are the body's response to ongoing stressors. This situation will cause psychological and somatic symptoms at a particular stage, generally known as psychosomatic disorders. Hormonal factors can be a mediator between stress and disease. The mediators between cognitively based stress and illness may be hormonal. In Hans Selye's generalized adaptation syndrome, in which hydrocortisone is the mediator, mediators may alter the function of the anterior pituitary-adrenal hypothalamic axis and lymphocyte shrinkage. In the hormonal chain, hormones are released from the hypothalamus and into the anterior pituitary, where tropic hormones interact directly with or release hormones from other endocrine glands. Another causative variable is the work of monocytes of the immune system. Monocytes interact with brain neuropeptides, which act as messengers between brain cells so that they can affect psychological states and moods. Complaints and symptoms can arise from a multiorgan system or only stand out in one of the organ systems in the body, such as the tear gland system, so that the perceived symptoms such as impaired perception of foreign body sensations, a discomfort that occur in DED patients can be influenced by disorders psychosomatic so that it exacerbates depression, anxiety and stress (Wan, Chen and Young, 2016).

The occurrence of DED and depression, anxiety, and stress is a multifactorial process. The characteristics of the patients in this study did not include DE and the intensity of the patient's length of time and worked both inside and outside the room, as well as the factors thought to influence the incidence of DED could not be known. In this study, first-degree dry eye was found, measured by a subjective scale with OSDI examination and objectively by Schirmer examination, TBUT, and associated with subjective examination scale with DASS (Depression, Anxiety, stress scale).

Conclusion

There is a correlation between OSDI scores with depression, anxiety, and stress, but it is not correlated with objective DED tests. A Higher OSDI score was associated with higher depression, anxiety, and stress scores. The occurrence of DED and depression, anxiety, and stress is a multifactorial process, there are many variables involved, and this study only included gender, age, occupation, and history of chronic disease as variables to be adjusted. Should future studies include other variables that are also suspected to affect the degree of DED, such as a history of smoking and the use of drugs. The Ocular Surface Disease Index (OSDI) can be used as a screening tool for psychosomatic disorders to provide holistic management of psychosomatic patients, especially those with DED disorders. Suppose it is found that the OSDI score increases not by the degree of DED. In that case, it is better to think about the existence of a state of depression, anxiety, and stress so that they can immediately get special treatment related to these conditions from the relevant doctor. Further research is needed to determine the relationship between DED and psychosomatic disorders compared to patients without DED

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