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DIFFERENCE IN INCIDENCE OF VISUAL THREATENING DIABETIC RETINOPATHY BETWEEN PATIENTS WITH AND WITHOUT IMPAIRED SLEEP QUALITY

Lucky Fitrada[1], Nina Ratnaningsih[1], Erwin Iskandar[1]

[1] *Department of Ophthalmology, Faculty of Medicine, Universitas Padjadjaran*
National Health Eye Center of Eye Cicendo Hospital

Abstract

Introduction: *Diabetic retinopathy (DR) is a common and major complication of diabetes mellitus (DM) and is the leading cause of preventable blindness in adults of productive age after cataracts. The global prevalence of DR is 34.6%, consisting of proliferative diabetic retinopathy (7.0%), diabetic macular edema (6.8%), and visual threatening diabetic retinopathy (VTDR) (10.2%.) The risk factors for VTDR are age, duration of diabetes, glycemic control, hypertension, obesity, HbAIC levels, and dyslipidemia. In addition, impaired sleep quality is also indicated to be connected with the incidence of VTDR. The aim of this study is to compare the incidence of VTDR between patients with and without impaired sleep quality.*

Methods: *This was a cross-sectional comparative analytic observational study involving 178 type 2 diabetes mellitus patients with DR at the National Eye Center of Cicendo Eye Hospital who met the inclusion criteria. Subject characteristic data were taken from medical records and sleep quality data were collected through a structured interview using the Indonesian version of the Shorten Pittsburgh Sleep Quality Index (PSQI) questionnaire. Subjects were distributed into poor and good sleep quality groups. The presence of VTDR was then assessed. The differences were then analyzed statistically using chi-square test with a p value of 0.05 considered statistically significant.*

Result: *Results showed that 66.2% and 71.1% of patients in the poor and good quality sleep group suffered from VTDR, respectively (p> 0.05).*

Conclusion: *There is no difference in VTDR incidence between patients in productive age with type 2 DM between those with and without impaired sleep quality.*

Keywords: Type 2 DM, DR, productive age, VTDR, impaired sleep quality
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Correspondence to:
Lucky Fitrada,
Cicendo Eye Hospital, Bandung, Indonesia,
luckyfitrada@ymail.com

INTRODUCTION

Diabetic retinopathy (DR) is a common and major complication of diabetes mellitus (DM), and is the leading cause of preventable blindness in adults of productive age after cataracts. The global prevalence of DR is 34.6% with proliferative diabetic retinopathy of 7.0%, diabetic macular edema of 6.8%, and visual threatening diabetic retinopathy (VTDR) of 10.2%.

Studies have shown that the prevalence of DR in the United States and Singapore is 40% and 10.5%, respectively. Several studies of the prevalence of DR with type 2 diabetes mellitus in adults in Indonesia have revealed that the prevalence for DR and VTDR in the Greater Bandung Area is 24.7% and 9%, respectively while in Jogjakarta, the prevalence is 43.1% and 26.3%, respectively. [1-6]

The risk factors for VTDR in DR include age, diabetes duration, and glycemic control. Other risk factors such as hypertension, obesity, HbAIC levels, dyslipidemia, nephropathy, and impaired sleep duration and quality are said to be associated with VTDR. [14,15]

Sleep is a complex and highly organized biological and behavioral process that serves many functions. When the duration of sleep is impaired and the sleep pattern is irregular, health will decline and the risk of mortality will increase. Lots of evidence from recent experimental as well as from epidemiological studies suggested that sleep duration is significantly linked with the presence of diabetes mellitus, insulin resistance, and poor glycemic control. [12,13,16]

In general population, complaints on disrupted sleep duration are given by 20% to 42.7% of the population. A study in Netherlands has demonstrated that 32% of people in the 18 to 70 year age group in the said country are identified to experience impaired sleep duration and quality. Sleep disorders have been experienced by 28 million of people or 10% of the population in Indonesia, which is currently the country with the highest prevalence of sleep disorders in Asia. [17–19]

The mechanism that links short or long sleep duration to the prevalence and severity of DR has not been well understood. A study conducted by Tan et al. suggested that in the sleep-deprived condition, the level of ghrelin increases while the level of leptin decrease, which leads to increased hunger, reduced satiety, and disrupted energy balance. This is accompanied by poorer insulin resistance and glycemic control which can increase the risk for VTDR. . [10,17–20]

There were not been many studies on the relationship between sleep disorders and DR in Indonesia. A community-based study in Jogjakarta has stated that there is no significant relationship between sleep duration and DR. With the fact that Indonesia has a high number of sleep disorder cases, this study sought to understand whether impaired sleep quality indeed a risk factor for VTDR in DR patients. [21]

METHODS

This is a retrospective cross-sectional comparative analytic observational study conducted at Cicendo Eye Hospital in September 2020. The study protocol was approved by the Research Ethics Commission of Universitas Padjadjaran, Bandung, Indonesia. Subjects were recruited based on the inclusion and exclusion criteria of the study.

The inclusion criteria used included patients diagnosed with Type 2 DM, mild NPDR, moderate NPDR, severe NPDR, PDR, and DME by an ophthalmologist and had agreed to participate in the study after informed consent. Patients with cardiovascular diseases, hypertension, chronic kidney diseases, consumption of medicine that disturbs sleep pattern, and incomplete medical record data were excluded. A medical record was considered to be incomplete when it did not contain all information needed for the study. In addition, patients without contact number, no response after three attempts of communication, and unwilling to participate in the study were also excluded. There were 178 patients diagnosed as suffering from Type 2 DM with DR who were willing to participate in the study. Interviews were then performed on these patients using the Indonesian version of the Shortened Pittsburgh Sleep Quality Index (PSQI) questionnaire.The PSQI questionnaire was translated into Indonesian using the forward-backward

translation method by two bilingual translators. A trial was then performed using the translated questionnaire to 30 subjects.

Results were then tested for validity and reliability using the Pearson Product Moment and Cronbach Alpha reliability coefficient, respectively. Structured interviews were performed by phone.

Data Processing and Analysis

There were 4,931 medical records under the code of E.11 identified in the period of January 2019 to August 2020 at the retina clinic data. However, only 368 matched the inclusion and 368 subjects, 208 could not be contacted by phone and 160 were contacted and willing to join the study. Of this number, 18 were interviewed face-to-face at the retina clinic while 160 were interviewed by phone by a trained interviewer, bringing a total of 178 subjects participating in the study.

Data collected were then processed and analyzed descriptively and analytically. For descriptive analysis on categorical data, results were presented in number and percentage while analysis on the numerical data resulted in mean, standard deviation, and range. The analytical data were performed using the chi-square test for analyzing the association between two variables of categorical data if the requirements for chi-square were met. If not, the Exact Fisher test was used.

The significance of the results was assessed using the p-value with $p \leq 0.05$ considered statistically significant or, in other words, $p > 0.05$ was considered insignificant statistically. Data collected were inputted into a specific form to be processed using the SPSS version 24.0 program for Windows.

RESULTS

From January 2016 to December 2019, a total of 4,251 people with type 2 diabetes, 1,022 (24.0%) A study to compare the incidence of VTDR in type 2 DM patients in productive age with and without impaired sleep quality has been conducted using the shortened PSQI questionnaire at the National Eye Center of Cicendo Eye Hospital in September 2020. There were 4,931 medical records under the code of E.11 identified in the period of January 2019 to August 2020 at the retina clinic data. However, only 368 matched the inclusion and from 368 subjects, 208 could not be contacted and willing to join the study. Of this number, 18 were interviewed face-to-face at the retina clinic while 160 were interviewed by phone by a trained interviewer, bringing a total of 178 subjects participating in the study.

Table 1 describes the characteristics of the study subjects that include age, gender, education background, occupation, body mass index, duration of DM, HbA1C level, FBS (fasting blood sugar) level, total cholesterol level, HDL level, LDL level, triglyceride level, night sleep duration, and sleep quality.

Most patients were in late elderly age category, females, graduated from senior high school, had normal body mass index, had been diagnosed as DM patient for less than 10 years, high fasting blood sugar profile, abnormal lipid profile, normal sleep duration, and good sleep quality.

Table 2 presents the comparison of characteristics between patients with VTDR and without VTDR. The distribution pattern between the characteristics of the two group was not too difference and could be deemed homogenous with an insignificant statistical difference.

Table 3 depicts the comparison of sleep quality between patients with VTDR and without VTDR. No difference in the incidence of VTDR was identified between the groups with good and poor sleep quality based on the statistical results with a probability value of above 0.05.

DISCUSSION

Diabetic retinopathy (DR) is one of the most common complications of diabetes mellitus (DM). It is also the leading cause of preventable blindness in adults of productive age. Ryan Lee et al. reported that around one third of DM patients will experience VTDR. The global prevalence of DR is 34.6% while the prevalence of the visual threatening diabetic retinopathy (VTDR) is 10.2%.[1,2,9]

Sample in this study has characteristics that match the previous study on DR patient characteristics except for the duration of DM. Several studies on DR degree development in type 1 and 2 diabetes mellitus discovered that the duration of disease is a factor that significantly trigger the risk for DR as it is related to increased risk of poor glycemic control that worsens the inflammation condition and microvascular damages in retina. In this study, DR, both VTDR and non-VTDR, was seen more frequently on patient who has had DM for less than 10 years. This may be due to several factors, such as the low awareness of Indonesian people on the signs and symptoms of diabetes which leads to delayed laboratory examination. This will make it more difficult to identify the exact duration of the disease.[9,14,49–56]

This study found no difference in the incidence of VTDR between type 2 DM patients with and without sleeping disorders. This supports the results of Morjaria et al. who studied the link between impaired sleep quality and severity of DR, stating that there is no relationship between DR degree and sleep quality. Morjaria et al. suggested that the lack of connection between DR degree and sleep quality might be due to inaccurate DRM duration data, since the longer the patient has diabetes, the higher the risk for VTDR. This issue is similar to the situation in this study. The fact that the sleep disorder is assessed using a retrospective questionnaire is also considered to be the cause of the lack of association between DR and sleep quality according to Morjaria et al.[57]

Another study by Tan et al. suggested the relationship between sleep quality and VTDR, which is in contrast with the result of this study as well as the results of Morjaria et al. and Banerjee et al. Tan et al. assessed sleep quality using STOP Bang questionnaire, which is more specific for Obstructive Sleep Apnea (OSA). This present study used the PSQI questionnaire where questions on sleep apnea are also included but it is not sensitive to assess sleep disorders caused by OSA. Another difference between the two questionnaires is that the PSQI can be considered more subjective as it records the subject's own answers while the STOP Bang questionnaire is more objective as it involves other persons who observe the patient's condition. These differences may contribute to the difference results between the studies using the two questionnaires.[10,58,59]

Table 1 Subject Characteristics

Variable	N=178
Age Category	
Early adulthood	1(0.6%)
Late adulthood	17(9.6%)
Early elderly	79(44.4%)
Late elderly	81(45.5%)
Gender	
Male	76(42.7%)
Female	102(57.3%)
Education	
No formal education	1(0.6%)
Elementary school	25(14.0%)
Junior high school	32(18.0%)
Senior high school	99(55.6%)
Academy	1(0.6%)
Graduate	19(10.7%)
Postgraduate	1(0.6%)
Occupation	
Have occupation	81(45.5%)
Unemployed	97(54.5%)
Body Mass Index	
Underweight	9(5.1%)
Normal	110(61.8%)
Overweight	48(27.0%)
Obese	11(6.2%)
Duration of DM	
10 years or less	119(25.84%)
11-20 years	52(5.06%)
More than 20 years	7(1.69%)
HbA1c	
High	168(94.4%)
Normal	10(5.6%)
FBS	
Low	1(0.6%)
Normal	66(37.1%)
High	111(62.4%)
Total Cholesterol	
Normal	77(43.3%)
Abnormal	101(56.7%)
HDL	
Normal	43(24.2%)
Abnormal	135(75.8%)
LDL	
Normal	29(16.3%)
Abnormal	149(83.7%)
Triglyceride	
Low	2(1.1%)
Normal	73(41.0%)
High	103(57.9%)
Night Sleep Duration	
Short	53(29.8%)
Normal	116(65.2%)
Long	9(5.1%)
Sleep Quality	
Good	133(74.7%)
Poor	45(25.3%)

Note : Categorical data are presented in number/frequency and percentage.

Table 2 Comparison of Subject Characteristics between Patients with and Without VTDR

Variable	Group		p-value
	VTDR N=120	Without VTDR N=58	
Age Category			**0.214**
Early adulthood	1(0.8%)	0(0.0%)	
Late adulthood	13(10.8%)	4(6.9%)	
Early elderly	58(48.3%)	21(36.2%)	
Late elderly	48(40.0%)	33(56.9%)	
Gender			**0.805**
Male	52(43.3%)	24(41.4%)	
Female	68(56.7%)	34(58.6%)	
Education			**0.347**
No formal education	1(0.8%)	0(0.0%)	
Elementary school	16(13.3%)	9(15.5%)	
Junior high school	23(19.2%)	9(15.5%)	
Senior high school	60(50.0%)	39(67.2%)	
Academy	1(0.8%)	0(0.0%)	
Graduate	18(15.0%)	1(1.7%)	
Postgraduate	1(0.8%)	0(0.0%)	
Occupation			**0.276**
Have occupation	58(48.3%)	23(39.7%)	
Unemployed	62(51.7%)	35(60.3%)	
Body Mass Index			**0.859**
Underweight	6(5.0%)	3(5.2%)	
Normal	78(65.0%)	32(55.2%)	
Overweight	29(24.2%)	19(32.8%)	
Obese	7(5.8%)	4(6.9%)	
Duration of DM			**0.164**
10 years or less	73(60.83%)	46(79.31%)	
11-20 years	43(35.83%)	9(15.52%	
More than 20 years	4(3.33%)	3(5.17%)	
HbA1c			**0.858**
High	113(94.2%)	55(94.8%)	
Normal	7(5.8%)	3(5.2%)	
FBS			**1.000**
Low	0(0.0%)	1(1.7%)	
Normal	44(36.7%)	22(37.9%)	
High	76(63.3%)	35(60.3%)	
Total Cholesterol			**0.113**
Normal	47(39.2%)	30(51.7%)	
Abnormal	73(60.8%)	28(48.3%)	
HDL			**0.452**
Normal	31(25.8%)	12(20.7%)	
Abnormal	89(74.2%)	46(79.3%)	
LDL			**0.812**
Normal	19(15.8%)	10(17.2%)	
Abnormal	101(84.2%)	48(82.8%)	
Triglyceride			**0.996**
Low	1(0.8%)	1(1.7%)	
Normal	47(39.2%)	26(44.8%)	
High	72(60.0%)	31(53.4%)	
Night Sleep Duration			**0.201**
Short	35(26.7%)	21(36.2%)	
Normal	80(66.7%)	36(62.1%)	
Long	8(6.7%)	1(1.7%)	

Note: For numerical data, p-value was tested using unpaired t-test if data were normally distributed and Mann-Whitney test as an alternative if the data were not distributed normally.

For categorical data, p-value was calculated using the Chi-Square with Kolmogorov Smirnov and Exact Fisher tests as alternatives if the requirements for the *Chi-Square* were not met. Results were considered significant when $p<0.05$.

Table 3 Comparison of Sleep Quality between Patients with and without VTDR

Variable	Group		p-value
	VTDR N=120	Without VTDR N=58	
Sleep Quality			**0.541**
Good	88(66.2%)	45(33.8%)	
Poor	32(71.1%)	13(28.9%)	

Note: the p-value for categorical data was calculated using the Chi-Square with Kolmogorov Smirnov and Exact Fisher tests as alternatives if the requirements for the *Chi-Square* were not met. Results were considered significant when $p<0.05$.

Dutta et al. suggested the relationship between sleep quality and DR in their study. This is different from the result of this study which may be due to the differences in the inclusion criteria between the two studies.[59]

This study has several limitations. The first was the use of the cross-sectional retrospective method that may lead to recall bias. This approach was selected because it is impossible to do a prospective study during the pandemic. The fact that the sample size was small might also contribute to this limitation. Another limitation is that this study used a subjective questionnaire based on self-report.

CONCLUSION

There is no difference in VTDR incidence between patients in productive age with type 2 DM between those with and without impaired sleep quality.

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