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Original Research Article Outline:

LITERATURE REVIEW STUDY: DETERMINANTS OF THE OCCURRENCE OF DIABETIC RETINOPATHY IN TYPE 2 DIABETES MELLITUS PATIENTS

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ABSTRACT

Introductio: Diabetic retinopathy (RD) ranks 4th as a cause of blindness globally after cataracts, glaucoma and macular degeneration. Blindness due to RD is a health problem because it will reduce a person's quality of life and decrease productivity, causing a social burden on society. Globally, around 95 million DM patients experience diabetic retinopathy (35.4%) of which one third are at risk of losing their vision and more than 75% of diabetes sufferers will experience diabetic retinopathy 20 years after diagnosis. **Methods**: The method used in this writing is literature study which aims to compile, tabulate and compare research results. Articles were collected via the PubMed and Mendeley search engines. The keywords used are diabetic retinopathy and diabetes mellitus. The articles went through an elimination and filtering process with the results being 14 articles according to the research topic. **Result & Analysis**: Results from a full text review of 14 journals containing at least 1 RD factor and in accordance with the inclusion and exclusion criteria. From the 14 articles reviewed, the risk factors were age (87.5%), hypertension (77.8%), duration/length of suffering from DM (76.9%) and HbA1c levels (87.5%), these four factors stated there is a significant relationship with the occurrence of RD in type 2 DM patients. **Discussion :** Based on the results of the study, it was concluded that most journals stated that there was a relationship between the factors age, hypertension, duration of DM and HbA1c levels on the incidence of RD in type 2 DM patients.

Keyword: Diabetic Retinopathy, Type 2 Diabetes Mellitus

INTRODUCTION

One of the non-communicable diseases that causes vision problems is diabetes mellitus or DM. Diabetes is the main cause of blindness, heart attacks, strokes, kidney failure and amputation (P2PTM, 2016). Complications that cause vision problems in the retinal blood vessels are also known as diabetic retinopathy (RD). Uncontrolled blood sugar levels in the body result in damage to the retinal blood vessels eyes which is one of the factors in the occurrence of RD (Dewi, 2019). Diabetic retinopathy ranks 4th as a cause of blindness globally after cataracts, glaucoma and macular degeneration. Dewi (2019) Blindness due

to diabetic retinopathy is a health problem because blindness will reduce a person's quality of life and reduce productivity, thereby causing a social burden on society. According to Wojciech Matuszewski *et al* (2020) stated that diabetic retinopathy was encountered in 315 (26%) patients with type 1 DM and 894 (74%) patients with type 2 DM (Matuszewski, 2020).

Globally, around 95 million DM patients experience diabetic retinopathy (35.4%) of which one third are at risk of losing their vision. Lee R (2015) The global prevalence of blindness is 1.5 billion and 0.4 million are caused by diabetic retinopathy. *International Diabetes Federation* (IDF) organization (2015), 415 million adults with DM experienced a 35% increase, by 2040 it is estimated that this will increase to 642 million. Based on gender, diabetes in 2019 was 9% for women and 9.65% for men.

In the scientific oration delivered by Prof. Arief S,K, dr, SpM(K), M.Kes, MM, PhD said that more than 75% of diabetes sufferers will experience diabetic retinopathy 20 years after being diagnosed. There are several other risk factors that are strongly related to the incidence of diabetic retinopathy, namely blood glucose levels, HbA1c levels, hypertension, dyslipidemia, duration of diabetes, pregnancy, puberty, and insulin use. I *nternational Journal of Retina and Vitreous* (2016) in its research found that individuals with poor glycemic control have three times the chance of developing diabetic retinopathy. [8] Research conducted by the Journal *of Global Health* concluded that the prevalence of any *DR* in DM patients peaks between the ages of 60 and 69 years, and increased sharply with duration of DM. A retrospective observational descriptive study at RSUP Dr. M. Djamil Padang (2021) shows that the frequency of diabetic retinopathy patients with hypertension in DM patients is higher compared to patients without hypertension with a percentage of 62.9% and 37.1% (Dewi, 2019).

The aim of this research is to determine the risk factors associated with the incidence of diabetic retinopathy in type 2 DM sufferers by conducting *a literature review study* from several related national and international journals.

METHOD AND ANALYSIS

The method used in this research is literature study. Journals were searched via the PubMed and ScienceDirect search engines . The inclusion criteria for journal articles reviewed were: scientific articles published in national and international journals accredited by Sinta or Scopus in the last 5 years; review at least one form of factor associated with diabetic retinopathy and diabetes mellitus; quantitative research using a cross sectional approach; in the form of original research articles and full text can be downloaded. The keywords used are *diabetic retinopathy AND Risk Factor* . Selection is carried out using the PRISMA chart.

The identification results on PubMed and ScienceDirect showed 1,469 for PubMed and 1,068 for ScienceDirect. Article search data and search results with the keyword *diabetic retinopathy* and *Risk Factors* . Results are limited to the last 5 years or published under 2018 as many as 893 for PubMed and ScienceDirect 17 journals. Next, through the process of eliminating topic linkages in PubMed 204 and ScienceDirect 2. Eligibility assessment of a total of 206 journals using *tools* *https://www.rayyan.ai/* There were 195 journals excluded and 14 journals were found that matched the topic and purpose for review.

RESULTS

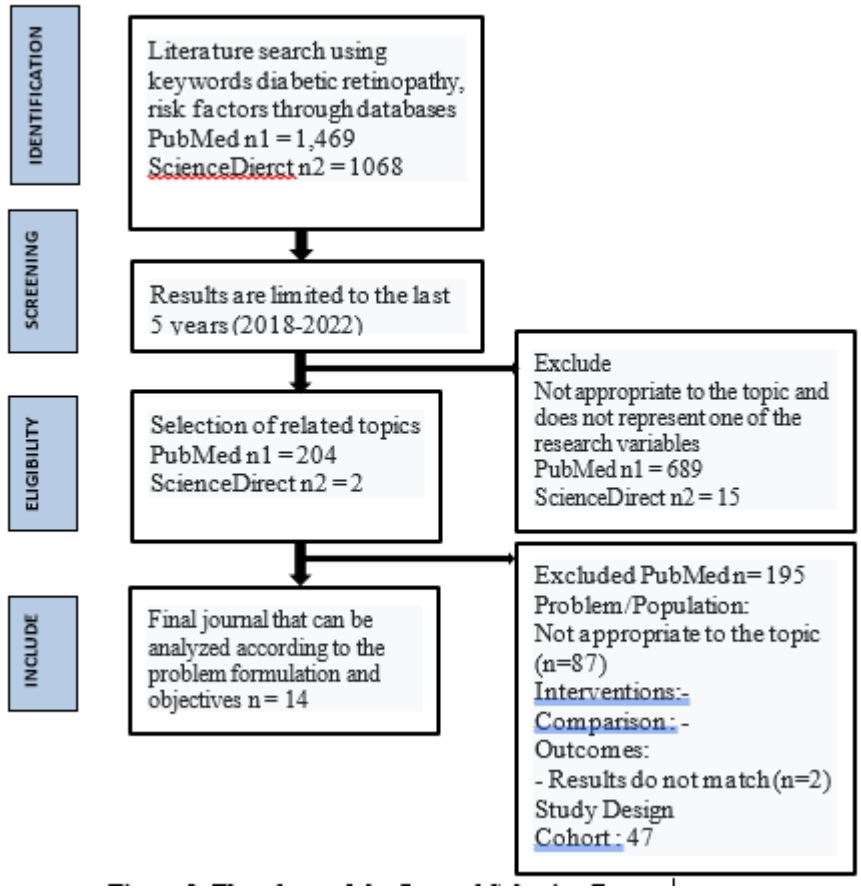

Figure 1. Flowchart of the Journal Selection Process

Based on the study results, a total of 14 articles were found that met the inclusion criteria. There were 7 out of 8 journals (87.5%) regarding age that stated there was a relationship between age and the incidence of RD, and 1 journal (12.5%) stated there was no relationship. There were 7 journals (77.8%) regarding hypertension which stated that it was significant for the incidence of diabetic retinopathy and 2 journals (22.2%) stated that there was no relationship with the incidence of diabetic retinopathy. The duration factor / length of suffering from DM was found (76.9%) stating that there was a significant relationship between the duration of DM and RD. There were 7 out of 8 journals (87.5%) regarding HbA1c levels that were related to the incidence of RD and 1 journal (12.5%) stated that there was no significant relationship. The characteristics of each journal will be explained in Table 1. All journals used use the *cross sectional method* with a publication time range between 2017-2022. The risk factors for the occurrence of RD from each journal include at least one factor for the occurrence of RD in type 2 DM sufferers.

Table 1. List of synthesized articles

No	Author, Year	Research Title	Research result
1.	DVC Nagasree, Ramakrishna Rachakonda, 2018	Study of Prevalence of Diabetic Retinopathy and Correlation with Risk Factors	Sample of 302 RD patients. Female gender is significant for DR. There is an increase related to age, duration of diabetes on the prevalence of DR but the value is not statistically significant. The average age was around 54. Systolic blood pressure, albuminuria and smoking history were correlated with the severity of RD (p-value < 0.05).
2.	Guihua Zhang, Haoyu Chen, Weiqi Chen, Mingzhi Zhang, 2017	Prevalence and risk factors for diabetic retinopathy in China: a multi-hospital-based cross-sectional study	Results of 16,305 patients. Age prevalence, longer duration of diabetes, (OR, 1.093), higher hemoglobin A1c (OR, 1.115), higher fasting plasma glucose (OR, 1.074), higher systolic blood pressure (OR, 1.014), higher low -density lipoprotein (OR, 1.149), lower triglycerides (OR, 0.975), higher blood urea nitrogen (BUN) (OR, 1.012) and increased serum creatinine level (OR, 1.003) were associated with DR factors.
3.	Enrique O Graue-Hernandez,1 David Rivera-De-La-Parra et al. 2020	*Prevalence and associated risk factors of diabetic retinopathy and macular edema in patients recently diagnosed with type 2 diabetes* .	A sample of 1232 patients (mean age 51.5 years) with diabetes duration of 0-5 years was examined. The prevalence of DR and adjusted for age and sex was 17.4% (95% CI 15.3% to 19.6%) and. DR was associated with duration of diabetes and systolic blood pressure (SBP).
4.	Tsion Shibru, Fekadu Aga and Abdisa Boka. 2019	Prevalence of Diabetic Retinopathy and Associated Factors among Type 2 Diabetes Patients at Tikur Anbessa Hospital, Ethiopia	Sample of 191 type 2 diabetes patients, average age 57 years. A total of 98 patients (51.3%) had diabetic retinopathy. Glycemia (HbA1c), hypertension, uisa, gender, routine control of clinic visits were associated with the incidence of RD
5.	Thirajit Boonsaen, Sawaraj Choksakunwon	Prevalence of and Factors Associated with Diabetic Retinopathy in Patients with Diabetes Mellitus at Siriraj	Sample of 1130 patients undergoing retinal examination. The overall prevalence of RD was 34.78%. Multivariate analysis revealed

	g Raweewan Lertwattanarak. 2021	Hospital	diabetes duration, glycated hemoglobin (HbA1c) levels, albuminuria to be independent risk factors for RD. The prevalence of DR increased with longer duration of diabetes ($p < 0.001$), decreased glucose control ($p = 0.006$ for HbA1c) and the presence of significant albuminuria ($p = 0.010$).
6.	Mukharram M Bikbov, Timur R Gilmanshin et al. 2021	Prevalence and Associated Factors of Diabetic Retinopathy in a Russian Population	Total population 5105. RD was present in 99/5105 individuals (1.9%). The prevalence increased from 6/657 (1.0%) in the 45-50 year age group to 24/680 (3.5%) in the 65-70 year age group, and decreased to 3/153 (2.0%) in age group 80+ years. The prevalence of DR in 577 (11.4%) individuals with diabetes was 99/577 (17.2%). In multivariable analysis, higher prevalence of RD was associated with higher serum glucose concentration (OR: 1.30, longer duration of diabetes (OR: 1.06).
7.	Sajid Adhi Raja, Vui Heng Chong, Noor A. Rahman. 2021	Prevalence and Associated Factors of Diabetic Retinopathy among Type 2 Diabetes Mellitus Patients in Brunei Darussalam: A Cross-sectional Study	The sample was 341 patients (female, 58.9%; mean age 55.3 years) with a mean duration of DM of 9.4 years and a mean serum HbA1c of 8.4%. Multivariate analysis showed that RD was significantly associated with certain age groups (reduced in older age groups), longer duration of DM (11 years or more), poor control (HbA1c >9.0%).
8.	Ying Cui, Min Zhang, Liang Zhang. 2019	Prevalence and risk factors for diabetic retinopathy in a cross-sectional population-based study from rural southern China	Of 8952 Han Chinese, 1500 were diagnosed with type 2 DM (T2DM) with a mean age of 59.51 years. The prevalence rate of male DR was significantly higher than female DR (23.0% vs 14.1%, $p<0.001$). No significant differences were found in the age-specific prevalence of DR. Male gender, higher education, long-term diabetes mellitus (DM), higher systolic blood pressure and glycosylated hemoglobin are independent risk factors for DR.

9.	Raba Thapa, Shankha N Twyana et al. 2018	Prevalence and risk factors of diabetic retinopathy among an elderly population with diabetes in Nepal	Diabetes was found in 168 (9%) subjects (mean age 69.6 years), 31 (18.5%) of whom were newly diagnosed. The prevalence of DR was 23.8% among people with diabetes. The prevalence of DR among newly diagnosed subjects with diabetes was 6.5%. The prevalence of DR was 83.3% among those who had diabetes for more than 20 years. In multivariable logistic regression analysis, duration of diabetes, hypertension, and alcohol consumption were significantly associated with DR.
10	Intan Lamy Manao, Hesti Triwahyu Hutami, Fifin Luthfia Rahmi, Arnila Novitasari Saubig. 2021	The Association of Diabetes Duration with the Severity of Diabetic Retinopathy	The research subjects were 51 patients. The prevalence was greater in the age group 51-60 years (45.1%), women (58.8%), diabetes sufferers <5 years (41.2%), and PDR (72.6%). Chi Square analysis showed there was no statistically significant relationship between the duration of diabetes and the severity of diabetic retinopathy (p = 0.881).
11.	Sukma Sahreni, Isramilda, Andi Ipaljri Saputra. 2020	The Relationship between the Duration of Diagnosis of Type 2 Diabetes Mellitus and Current Blood Sugar Levels with the Incidence of Diabetic Retinopathy at Budi Kemuliaan Hospital, Batam City in 2017-2018	The research sample consisted of 66 people. A total of 38 (57.6%) people had diabetes mellitus duration ≤5 years. The results of the Risk Estimate Test show an OR value: 6.5. OR > 1. This means that the chance of RD patients ≤5 years having a risk of type 2 DM is 6.5 higher than patients > 5 years. This research can be concluded that there is a significant relationship between Diabetes Mellitus type 2 and the incidence of Diabetic Retinopathy at Budi Kemuliaan Hospital, Batam City in 2017 - 2018.
12.	Yun Peng, Xianxian Guo, Junan Liu. 2021	Incidence and risk factors for diabetic retinopathy in the communities of Shenzhen	Sample of 904 patients with DM in Shenzhen. The prevalence of DR among diabetes sufferers in Shenzhen was 18.58%. And the prevalence of VTDR is 2.43%. The prevalence of DR and VTDR was higher in men than in women. Logistic regression

			analysis showed that age, disease, duration, treatment mode, and occurrence of diabetic peripheral neuropathy (DPN) were associated with the occurrence of DR in DM patients, and disease duration, occurrence of DPN, and diabetic nephropathy were associated with the occurrence of VTDR.
13.	Yan Liu, Jiarui Yang et al. 2017	Risk factors of diabetic retinopathy and sight-threatening diabetic retinopathy: a cross-sectional study of 13 473 patients with type 2 diabetes mellitus in mainland China	The sample was 13304 patients with type 2 DM. Younger age, longer duration of diabetes, high SBP, higher FBG and high HbA1c were independent risk factors for DR. In analysis of all factors, younger age, longer duration of diabetes, higher SBP, oral medication use and insulin use were independent risk factors for DR.

DISCUSSION

Age Factors in the Occurrence of Diabetic Retinopathy

Based on the results in table 1, it was found that there were 8 journals that discussed the age factor with the incidence of RD. There were 7 journals (87.5%) stating there was a significant relationship and 1 journal (12.5%) stating there was no relationship so the majority showed there was a significant relationship. significant relationship between age and the incidence of RD. The highest age of occurrence of RD is at the age of 50-60 years (47.3%), 40-50 years (24.1%) and (16.5%) at the age of >60 years (Nagasree, 2018). In line with research by Raja SA et al (2021) that the highest age is 51-60 years (34.6%) 61-70 years (26.9%) and 41-50 (19.0%). 14 Apart from that, the results of the study conducted by Yun Peng et al (2020), Guihua Zhang *et al* (2017) and Tsion Shibru (2019), with an average age of 65, 63 and 57 years.

Based on the data above, it can be concluded that there is a significant relationship between the age factor and the occurrence of RD. The highest average age is 50-60 years. So the increasing age of DM sufferers becomes a risk factor for the occurrence of RD. Based on the age category of DM sufferers, it is the largest and reaches its peak at the age of 55-64 years and decreases after passing that range. Apart from that, DM is also one of the main causes of blindness in people under 65 years of age (P2PTM, 2020). According to several theories, diabetic retinopathy occurs because of its long duration. have a history of diabetes mellitus (P2PTM, 2020). Regarding those aged 50-60 years who are more likely to experience diabetic retinopathy because as age increases, glucose intolerance also increases so that people with a long history of diabetes mellitus at the age of >45 are more likely to experience diabetic retinopathy (Dewi, 2019).

Hypertension factors with the incidence of Diabetic Retinopathy

Hypertension is a non-communicable disease. Hypertension and DM that occur simultaneously can increase the risk of microvascular

complications, one of which is retinopathy. The results of a literature study regarding hypertension factors on the incidence of RD found that 7 journals (77.8%) stated that there was a significant relationship and 2 journals (22.2%) stated that there was no significant relationship between hypertension and RD. Research conducted by DVC Nagasree et al in a *cross sectional descriptive study* stated SBP (*systolic blood pressure*) with the degree of RD. where the highest was (13.9%) *grade* 2 160-190 mmHg, (11.9%) *grade* 1 160-190 mmHg and (10.5%) *grade* 3 130-160 mmHg. In research by Enrique O Graue-Hernandez et al (2020) stated that the SBP factor had a value of OR=1.16 per 5mmHg, which shows that the increase in SBP was 1.16 times greater than the occurrence of RD. The risk value of hypertension for the occurrence of RD is OR: 1.113 (Cui, 2019). OR: 1, 191 (Shibru, 2019). OR: 1.1. (Thapa, 2018). Comparison of DM patients with hypertension had a risk of experiencing retinopathy 12 times greater than non-hypertension and the increased risk was statistically significant (OR = 12.3; 95% CI = 3.7- 56.5) (Dewi, 2019).

The emergence of hypertension in diabetes is caused by hyperglycemia in diabetes mellitus. The emergence of hypertension can cause further complications such as diabetic retinopathy.

Duration/Length of suffering from DM factors with the incidence of Diabetic Retinopathy

Several studies show that suffering from diabetes for a long time is one of the factors causing RD. The results of the journal study showed that the majority (76.9%) stated that there was a significant relationship between the duration of DM and RD. Patients who have a diagnosed duration of DM > 5 years with Retinopathy of (75.0%) have a higher value compared to those with a duration of < 5 years, namely (13.6%) with a value of (OR: 6.5), OR > 1 means patients with DM duration >5 years who experience RD have a 6.5 times higher risk than patients <5 years (Sahreni, 2020). This figure shows a significant number for the relationship between DM duration and RD. Another study conducted by Graue-Hernandez, EO et al. (2020) stated that the highest duration of DM was 3–5 years (48.8%) <1 year (29.1%) and 1–2 (22.1%), so it can be concluded from the results above that the risk of experiencing RD increases in line with the length of time suffering from DM so that long-standing hyperglycemia is a major risk factor.

HbA1c Level Factors with Diabetic Retinopathy

The results of the literature review showed that 7 out of 8 journals (87.5%) were related to HbA1c levels with the incidence of RD and 1 journal (12.5%) stated that there was no significant relationship. Sajid AR et al (2022) in their research on 341 patients stated that HbA1c control >7% (76%) had a higher value compared to HbA1c levels <7% (24%) with an OR value (1.95) which means the higher the number HbA1c >7% has a 1.95 times chance of RD occurring (Raja, 2022). In line with previous research, HbA1C levels >7% (67.5%) have a higher value compared to HbA1C levels <7% (34.5%) (Shibru, 2019). From The results of these two studies can be concluded that the higher the HbA1c number, it indicates that there is a possibility that the body has uncontrolled diabetes and increases the risk of retinopathy complications.

CONCLUSION

Diabetes Mellitus (DM) is a non-communicable disease that has many complications, one of which is idiabetic retinopathy (RD). Several factors that are mostly related to the occurrence of RD are age, hypertension, duration of DM

and levels/amounts of HbA1c. Ages 50-60 years are more likely to experience RD because as age increases, glucose intolerance also increases so that people with a history of DM or long duration at age >45 and duration >5 years are more likely to experience RD, HbA1c levels have an influence on the occurrence of RD, Apart from that, the risk of DM patients with hypertension is 12 times greater than that of non-hypertensive patients with retinopathy.

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