Risk Factors for Diabetic Retinopathy
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Abstract

Introduction.
Diabetic retinopathy is a progressive microangiopathy characterized by damage and occlusion of small blood vessels. The earliest pathologic changes are thickening of the capillary endothelial basement membrane and a reduction in the number of pericits. Diabetic retinopathy is the main cause of vision loss in type 1 of DM patients and has various risk factors such as chronic hyperglycemia, hypertension, hypercholesterolemia, and elevated HbA1C levels.

Methods.
This research was conducted using a descriptive observational analytic method with a cross sectional approach at The Eye Polyclinic (RSUP) Dr. Mohammad Hoesin Palembang used secondary data on diabetic retinopathy patients. The sample consisted of 64 patients with a total sampling technique, there were 50 patients who met the inclusion criteria.

Results.
There was a significant relationship between HbA1C levels (p value = 0.050) with a PR value = 1.463 and total cholesterol (p value = 0.038) with a PR value = 1.667 for diabetic retinopathy.

Conclusion.
HbA1C levels and total cholesterol are significant risk factors for diabetic retinopathy.

Keywords. diabetic retinopathy, DR risk factors
Introduction

Diabetic retinopathy is a chronic progressive disease which potentially vision-threatening for the retinal microvascularis associated with prolonged hyperglycemia and other conditions associated with diabetes mellitus such as hypertension.\(^1\) The main cause of diabetic retinopathy is diabetic which can damage the small blood vessels that supply nutrients to the retina.\(^2\)

The estimated prevalence rate of vision-threatening diabetic retinopathy in the United States is 4.4\% (0.7 million people). The prevalence rate of diabetic retinopathy in patients with diabetics ranges from 10\% in India to 43\% in Indonesia.\(^3\) The risk factors for diabetic retinopathy are various, such as chronic hyperglycemia, hypertension, hypercholesterolemia, and smoking (Vaughan and Asbury’s, 2011). Other risk factors are a long period of suffering from diabetes, increased levels of HbA\(_1\)C, increased systolic blood pressure, male gender, and increased levels of lipid profile.\(^4\)

The DiabCare Asia 2008 Study involving 1785 DM patients in 18 primary and secondary health centers in Indonesia reported that 42\% of DM sufferers experienced complications of retinopathy and 6.4\% of them were proliferative diabetic retinopathy. The prevalence of vision-threatening diabetic retinopathy in Indonesia is about 26.3\%.\(^5\)

Glycated hemoglobin (HbA\(_1\)C), also known as glycohemoglobin, is one of the blood tests to evaluate blood sugar control.\(^6\) For every 10\% decrease in HbA\(_1\)C, there is a 39\% reduction in the risk of developing retinopathy in the range of HbA\(_1\)C values.\(^3\)

Chronic hypertension found in DM patients can affect the incidence and severity of diabetic retinopathy by 1-1.2 times. This is due to the condition of retinal hyperperfusion which causes damage to the retinal capillaries which leads to increased blood flow and worsens diabetic retinopathy.\(^7\)

Methods

This research is a descriptive analytic observational study with a cross sectional approach using secondary data from medical records. Data were collected at the medical record installation in RSUP Dr. Mohammad Hoesin Palembang from August to October 2020.
The data collection technique was total sampling, namely all members of the population who met the inclusion criteria were taken as samples. Medical record data that meet the criteria are 50 data from 64 medical record data. Medical record data are collected and will be examined according to research variables and then statistical calculations are carried out.

Results

The frequency distribution shown in Table 1 shows that patients with more diabetic retinopathy are in the age group ≥40 years as many as 48 people (96%), with the same sex between men and women are 25 people each (50%). 31 people (62%) had more diabetic retinopathy with diabetes mellitus duration > 5 years, 33 people (66%) for uncontrolled HbA1C levels, 45 people (90%) for hypertension, and 15 people (30%) for high total cholesterol.

Table 1. Frequency Distribution of Risk Factors in Patients with Diabetic Retinopathy

| Variable                  | Result | Percentage |
|---------------------------|--------|------------|
| Age                       |        |            |
| <40 Year                  | 2      | 4          |
| ≥40 Year                  | 48     | 96         |
| Gender                    |        |            |
| Male                      | 25     | 50         |
| Female                    | 25     | 50         |
| Duration of DM            |        |            |
| ≤5 Year                   | 19     | 38         |
| >5 Year                   | 31     | 62         |
| HbA1C Level               |        |            |
| ≥6.5 %                    | 33     | 66         |
| < 6.5 %                   | 17     | 34         |
| Blood Pressure            |        |            |
| Hypertension              | 45     | 90         |
| Normal                    | 5      | 10         |
| Total Cholesterol         |        |            |
| High                      | 15     | 30         |
| Normal                    | 3      | 6          |
| No data                   | 32     | 64         |

In table 3, patients with diabetic retinopathy with PDR classification were 49 eyes (61.3%) and NPDR classification were 31 eyes (38.8%).
Diabetic retinopathy patients with age $\geq 40$ years experienced PDR as many as 48 eyes (60%). There was no significant relationship between age and diabetic retinopathy ($p = 0.556$) which is attached to table 3.

**Table 3. Relationship between Age and Diabetic Retinopathy**

| Age       | Classification of Diabetic Retinopathy | Total | $p$  |
|-----------|----------------------------------------|-------|------|
|           | PDR         | NPDR |     |      |
| <40 Year  | n  | %     | n  | %     | n  | %     | 0.556 |
| ≥40 Year  | 48 | 60    | 29 | 36.3  | 77 | 96.3  |

The most diabetic retinopathy patients with male gender experienced PDR as many as 27 eyes (33.8%). There is no significant relationship between gender and diabetic retinopathy ($p = 0.359$) attached to table 4.

**Table 4. Relationship between Gender and Diabetic Retinopathy**

| Gender | Classification of DR | Total | $p$  |
|--------|----------------------|-------|------|
|        | PDR          | NPDR |     |      |
| Male   | n  | %     | n  | %     | n  | %     | 0.359 |
| Female | 27 | 33.8  | 13 | 16.3  | 40 | 50    |
|        | 22 | 27.5  | 18 | 22.5  | 40 | 50    |

Diabetic retinopathy patients with a duration of mellitus $> 5$ years experienced PDR as many as 29 eyes (36.3%). There was no significant relationship between the duration of diabetes mellitus and diabetic retinopathy ($p = 0.809$) which is attached to table 5.
Diabetic retinopathy patients with uncontrolled HbA1C levels most experienced PDR as many as 37 eyes (46.3%). There was a significant relationship between HbA1C levels and diabetic retinopathy (p = 0.050) which is attached to table 6.

**Table 6. Relationship between HbA1C Levels and Diabetic Retinopathy**

| HbA1C Level | Classification of DR | Total | p   | PR |
|-------------|----------------------|-------|-----|----|
| ≥ 6.5 %     | n %                  | n %   |     |    |
| < 6.5%      | 37 46,3 16 20 53 66,3 | 0,050 | 1,463 |

The most diabetic retinopathy patients with hypertension experienced PDR as many as 47 eyes (58.8%). There was no significant relationship between blood pressure and diabetic retinopathy (p = 0.102) which is attached to table 7.

**Table 7. Relationship between Blood Pressure and Diabetic Retinopathy**

| Blood Pressure | Classification of DR | Total | p |
|----------------|----------------------|-------|---|
| Hypertension   | n %                  | n %   |   |
| Normal         | 2 2,5                 | 5 6,3 | 7 8,8 |

Diabetic retinopathy patients with high total cholesterol experienced PDR as many as 20 eyes (71.4%). There is a significant relationship between total cholesterol and diabetic retinopathy (p = 0.038) attached to table 8.
Table 8. Relationship between Total Cholesterol and Diabetic Retinopathy

| Total Cholesterol | Classification of DR | Total | $p$ | PR |
|-------------------|----------------------|-------|-----|----|
|                   | PDR                  | NPDR  | n   | %  | n   | %   |     |     |
| High              | 20                   | 14.3  | 24  | 85.7| 0.038| 1.667|
| Normal            | 1                    | 3.6   | 4   | 14.3|     |      |     |     |

Discussion

Diabetic retinopathy patients in this study with the age group $\geq$40 years, experienced the most PDR (60%). This result is not different from the results of Gapur, A (2016), which is that patients with diabetic retinopathy have the most PDR, namely the age range of 51-60 years (26.32%).$^9$ Diabetic retinopathy occurs because of a long history of diabetes mellitus due to hyperglycemia conditions, inflammatory reactions, and oxidative stress which accelerates apoptosis in retinal cells which results in diabetic retinopathy.

This study shows that diabetic retinopathy patients based on gender with a ratio of 1: 1 between men (50%) and women (50%). This result is not much different from the results of Funatsu, et al. (2011), namely 50% male and 50% female.$^{10}$ Diabetic retinopathy patients in this study shows that male had the most PDR (33.8%). This result is not much different from the research of Amin & Ansyori (2015), which shows that most diabetic retinopathy patients are male (54.4%).$^8$ The results of the study by Suryathi, et al (2020) showed that most male patients with diabetic retinopathy experienced PDR (51%). Based on the theory, diabetic retinopathy affects lifestyle and economic status associated with many men who smoke, consume coffee, alcohol, soft drinks and low activity increases the progressiveness of PDR diabetic retinopathy. Another factor that causes it is men often ignore the initial symptoms of diabetic retinopathy, so that patients come in a more severe condition.$^{12}$

Diabetic retinopathy patients based on the length of suffering from diabetes mellitus in this study were found to be the most $> 5$ years (62%). Diabetic retinopathy patients with diabetes mellitus duration $> 5$ years in this study most experienced PDR (36.3%). The results of this study are not different from the results of research by Gapur, A (2016), namely that diabetic retinopathy patients with a duration of diabetes mellitus $> 10$ years experience the most PDR.$^9$ Prolonged hyperglycemia conditions can trigger the formation of many free radicals, namely AGE products, sorbitol and reactive oxygen species which excessive so that causing circulatory disorders, hypoxia, and inflammation of the retina.$^3$
The results of this study showed that most diabetic retinopathy patients had uncontrolled HbA₁C levels (66%). The results of this study showed that diabetic retinopathy patients with uncontrolled HbA₁C levels experienced the most PDR (46.3%). This result is not different from the results of the study by Suryathi et al. (2020), namely that diabetic retinopathy patients with the highest levels of HbA₁C experienced PDR (83.8%). HbA₁C is a chemokinesis secretion of Hb and adhesion molecules on the cell membrane in glycosylated retinal blood vessels, formed when glucose in the blood attaches to hemoglobin (Hb). High HbA₁C levels indicate uncontrolled hyperglycemia over the past 3 months. Controlled HbA₁C levels (<7%) can reduce the progression of complications that occur.

This study shows that most diabetic retinopathy patients based on blood pressure had hypertension (90%). Diabetic retinopathy patients who experienced hypertension most experienced with PDR (58.8%). The results of the study by Dewi, et al (2019) that diabetic retinopathy patients who had the most hypertension experienced PDR (37.3%). In diabetics patient, hypertension can cause endothelial damage to retinal blood vessels and increase the expression of VEGF receptors. VEGF can bind directly to vascular endothelial cells, causing increased vascular permeability and forming ischemic neovascularization in diabetic retinopathy. VEGF will also stimulate the expression of Intracellular Adhesion Molecule-I (ICAM-I) which triggers the formation of bonds between leukocytes and blood vessel endothelium. These bonds cause retinal blood barrier damage, thrombosis, and retinal capillary occlusion.

Conclusion

Diabetic retinopathy patients were found mostly in the age group ≥40 years (96%) and had the most PDR (60%), for male (50%) and for female (50%), duration of diabetes mellitus > 5 years (62%).) and experienced the most PDR (36.3%), uncontrolled HbA₁C levels (66%) and the most experienced PDR (46.3%), hypertension (90%) and the most experienced PDR (58.8%), high total cholesterol (30%) and experienced the most PDR (25%). There was a significant relationship between HbA1C levels (p value = 0.050) with a prevalence ratio (PR) = 1.463 and total cholesterol (p value = 0.038) with a prevalence ratio (PR) = 1.667 for diabetic retinopathy.

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