Effect of duration of illness and lipid profile of type 2 Diabetes Mellitus patients on diabetic retinopathy

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Abstract. Diabetic retinopathy (DR) is one of complication chronic of Diabetes Mellitus (DM). The purpose of this study is to analyze the impact of duration and lipid profile (dyslipidemia) on the prevalence of DR complications in patients with type 2 DM in Medan. This research is a cross-sectional study. The population was typed 2 DM patients at primary care in Medan with sample of 89 patients. The research data are primary, assessment of lipid profile by taken venous blood and examination by the Enzymatic Colorimetric method, while the determination of DR complications using indirect fundoscopy. Data were processed with SPSS with Independent T-test analysis. The results showed the duration of illness and triglyceride levels had a strong relationship with DR in type 2 DM patients (p <0.05), while total cholesterol, HDL-C, LDL-C levels had a weak relationship (p> 0.05).

1. Introduction

The microvascular complication such us Diabetic Retinopathy (DR) can cause blindness and visual disturbances in the occupational age population [1-2]. RD is a progressive multifactorial disease of the retina with very complex pathogenesis involving many cells, molecules, and factors. RD slowly occurs damage to the retinal blood vessels or nerve lining of the eye, causing leakage so that the accumulation of fluid (exudate) containing fat and bleeding on the retina that can gradually cause blurred vision, even blindness [3]. It is estimated that around 60-70% of type 2 DM patients experience DR after 20 years [4]. Other studies suggest that progressive capillary occlusion often causes severe retinopathy within 15-20 years of the onset of DM [5].

Visual impairment in RD is often characterized by a sharp reduction in vision, blurred vision, dark areas when viewing, reduced night vision, and disruption of color vision function [6]. Some risk factors that influence the occurrence of RD include sex, age, duration of diabetes, hyperglycemia, hypertension, and hyperlipidemia. Early detection and adequate medical and ophthalmological management can prevent blindness. It is estimated that up to 90% of cases can be appropriately handled [7].
The risk of DM patients are 25 times more likely to develop blindness than non-diabetics. The risk of experiencing retinopathy in diabetic patients increases with the duration of diabetes. The opinion states that the prevalence of diabetic retinopathy based on WHO data is 5.2-30.8% of the DM population [8]. DR is the leading cause of cases of blindness in adults in the United States [9]. It is estimated that 4 percent of the world's population and almost half suffer from DR [10]. The purpose of this study was to analyze the effect of duration of diabetes and lipid profile (dyslipidemia) with the prevalence of DR in type 2 DM patients in Medan.

2. Materials and Method
This study is an analytic study with a cross-sectional approach, and the study population is type 2 DM patients who come to primary health services in the city of Medan, the study sample numbered 89 people using a single sample formula to hypothesis the proportion of a population. Sampling was performed by consecutive sampling, patients who took were who met the inclusion and exclusion criteria. Inclusion criteria were patients who were willing to participate in this study (signed informed consent), while the inclusion criteria were: DM patients in pregnancy, patients suffering from mature cataracts at the time of the study examination, patients who had a history of glaucoma (before suffering from DM), patients who had to have a history of eye disorders (especially the retina) either due to trauma or infectious disease or due to other factors (known through interviews).

Previously conducted research, the USU ethics commission approved the research protocol. Sources of research data are primary data (characteristic of the patient) lipid profile (total cholesterol, HDL, LDL, and triglyceride) and determination of DR complications. The determination of the lipid profile is done by the Enzymatic Colorimetric method. Fundoscopy examination is carried out using Indirect fundoscopy under the Keeler brand. The measurement results will be determined abnormalities in the retina found and classified DR and no DR. Data were processed with SPSS and data analysis using descriptive statistics and Independent t-test.

3. Results and Discussion
From 89 patients of type 2 DM, the following characteristics were conveyed including sex, age, nutritional status, duration of diabetes, and type of diabetes treatment, for more details, see Table 1.

| Table 1. Characteristics of type 2 DM patients |
|-----------------------------------------------|
| Characteristics | Frequency (people) (n=89) | Percentage (%) |
| Gender          |                             |                |
| Male            | 20                          | 22.5           |
| Female          | 69                          | 77.5           |
| Age, years (mean, SD) | 55.2 (8.9) |                        |
| Age group       |                             |                |
| <36 years       | 1                           | 1.1            |
| 36-45 years     | 12                          | 13.5           |
| 46-55 years     | 37                          | 41.6           |
| 56-65 years     | 29                          | 32.6           |
| >65 years       | 10                          | 11.2           |
| Nutritional status |                             |                |
| Mild Thinness   | 3                           | 3.4            |
| Normal          | 44                          | 49.4           |
| Overweight      |                             |                |
| Grade 1 overweight | 25                      | 28.1           |
| Grade 2 overweight | 14                      | 15.7           |
| Grade 3 overweight | 3                       | 3.4            |
| Medication History |                             |                |
| Oral anti diabetic | 20                     | 22.5           |


The results of table 1 revealed that the majority of DM patients were female with 69 people (77.5%), the most age group in the age of 46-55 years as many as 37 people (41.6%), the normal majority nutritional status was 44 people (49.4%). Based on the history of treatment, it is known that they are more conventional treatments using glibenclamide as many as 26 people (29.2%). Determination of DR complications in patients with type 2 DM is done by indirect fundoscopy, in that examination determined abnormalities that are found on the retina, such as the existence of exudates, new vascularization, and bleeding, for more details we can see in the following table:

Table 2. Diabetic retinopathy in type 2 DM patients

| Complications          | Frequency (people) | Percentage (%) |
|------------------------|--------------------|----------------|
| Diabetic Retinopathy   | 61                 | 68.5           |
| Normofundus            | 28                 | 31.5           |

Based on Table 2, it is known that there are 61 (68.5) people who experience complications from the DR, and there are 28 people with a healthy retinal condition. To see what factors, play a role in the occurrence of complications of DR in DM patients, then an analysis using an independent T-test can be seen below:

Table 3. Risk factors for diabetic retinopathy in type 2 DM patients

| Variable                | Group 1 with DR (n=61) | Group 2 No DR (n=28) | p     |
|-------------------------|------------------------|----------------------|-------|
| Duration of Diabetes    | 5.31 ± 4.47            | 2.52 ± 3.02          | 0.003 |
| Total Cholesterol (mg/dl)| 220.69 ±45.81         | 220.25 ±33.19        | 0.959 |
| HDL-C (mg/dl)           | 46.33 ±12.69           | 47.46 ±9.26          | 0.636 |
| LDL-C (mg/dl)           | 125.72 ±38.03          | 127.96 ±26.58        | 0.779 |
| Triglyceride (TG)       | 254.67 ±137.46         | 221.93 ±85.99        | 0.004 |

Results from Table 3 showed that duration of DM and Triglyceride levels are associated with the prevalence of complications of DR, while levels of total cholesterol, HDL-C, and LDL-C are not related to the prevalence of DR complications in type 2 DM patients in Meidan. DR is one of the chronic complications in patients with type 2 DM. Several risk factors are considered to determine the occurrence of DR complications, such as the duration of diabetes. The results showed that the duration of diabetes affected the prevalence of DR (p< 0.05). The results of this study are in line with other studies that the longer DM patients suffer from illness, the more they are at risk for suffering from DR, even when 25 years after suffering from DM, it is confirmed that they experience DR. [11-13].

Although the etiology of microvascular diabetes is still unexplained, long-term exposure to hyperglycemia is believed to change biochemistry and physiology, leading to endothelial damage [14]. The activity of various protein kinase C isoforms will be increased because of hyperglycemia. This situation will cause cell changes resulting in ischemia and cellular signaling by vascular endothelial growth factors (VEGF) to neovascularization of ocular. VEGF causes macular capillary hyperpermeability, which contributes to macular edema and endothelial proliferation, leading to microaneurysm and the formation of neovascular membranes that prevent apoptosis of capillary endothelial cells. Hyperglycemia increases the conversion of glucose into sorbitol, which causes osmotic damage to the retinal blood vessels. Eventually, hyperglycemia results in plasma protein leakage and bleeding in the retina and vitreous [15] So the longer a person has diabetes, especially those that are not well controlled so that it will increase the risk of complications from DR.
In addition, blood lipid levels are also a risk factor for complications of RP [16]. The strong correlation between dyslipidemia and diabetic retinopathy has been reported in various studies. An increase in cholesterol levels is significantly associated with the occurrence of all levels of diabetic retinopathy [10] [17]. Endothelial dysfunction has a strong correlation with high blood lipid, due to reduced bioavailability of nitric oxide, and endothelial dysfunction is thought to play a role in the formation of retinal exudates in diabetic retinopathy. It has also been reported that lipid peroxidation in lipoproteins in blood vessel walls leads to local production of reactive carbonyl species that mediate macrophage recruitment, cell activation and proliferation, and also chemical modification of vascular proteins by the end product of sorbitol that affects both the structure and function of blood vessel walls.

Thus, hyperlipidemia can contribute to DR and macular edema (ME) because of endothelial dysfunction and blood-retinal barrier damage that causes exudation of serum lipids and lipoproteins [12], [18-19]. The results of this study showed total cholesterol, HDL-C, and LDL-C had a weak relationship with the occurrence of DR, while Triglyceride had a very strong relationship for the occurrence of DR (p <0.05). The results of this study are in line with research conducted by Prakash et al., On traditional lipid measurements, higher TG and lower HDL cholesterol showed a significant relationship (P <0.05) with the severity of DR, while the study of Liu, et al. also proved that triglycerides and LDL-C are strong risk factors for DR. [20-22].

4. Conclusions
The results of this study said the duration of illness of diabetes and blood triglyceride levels had a strong relationship with the occurrence of complications of DR in patients with Type 2 diabetes. In contrast, TC, HDL-C, LDLC levels had a weak relationship. Reasonable glycemic control is expected to be able to prevent complications, especially microvascular associated with blindness that will be experienced by type 2 DM patients.

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References
[1] Krishnamoorthy R, Kaliaperumal R, Venkatachalam R, Poovitha R, RAJAGOPALAN G 2017 Journal of Clinical & Diagnostic Research 1:11(10)
[2] Wang W and Lo AC 2018 International journal of molecular sciences 19(6) p1816.
[3] Tarr JM, Kaul K, Chopra M, Kohner EM, Chibber R 2013 ISRN Ophthalmol 343560
[4] Department of Health and Human Services. Diabetic Retinopathy. National Eye Institute. [Internet]. 2010. [cited 2020 Feb 12]. Available from: https://nei.nih.gov/eyedata/diabetic#4.
[5] Ankit BS, Mathur G, Agrawal RP, and Mathur KC Indian journal of endocrinology and metabolism 21(1) p 102.
[6] Nasralah Z, Robinson WF, Jackson GR, and Barber A 2013. Journal of Clinical and Experimental Ophthalmology 4(6).
[7] Amelia R, Damanik HA, Lindarto D, and Mutiara E 2017 Advanced Science Letters 23(4) p 3610-3613.
[8] Amelia R, Ariga RA, Sari MI, and Savira M 2018 In Journal of Physics: Conference Series (Vol. 1116 No. 5, p. 052003)
[9] Nentwich MM and Ulbig MW 2015 World journal of diabetes 6(3) p 489
[10] Hegde, S.S., 2013. Association of Lipid Profile with Diabetic Retinopathy-A Comparative Study (Doctoral dissertation).
[11] Hegde SS & Vekategowda HT 2016 International Journal of Health Science and Research 6(7) p 74-81.
[12] Bansal P, Gupta RP and Kotecha M 2013 Medical Journal of Dr. DY Patil University 6(4) p
366.

[13] Agroiya P, Philip R, Saran S, Gutch M, Tyagi R, and Gupta KK 2013 Indian journal of endocrinology and metabolism 17(Suppl1) p S335.

[14] Pande SS and Chutani A 2018 International Journal of Clinical and Biomedical Research p 14-22.

[15] Kern TS, Berkowitz BA 2015 Journal of diabetes investigation 6(4) p 371-80.

[16] Deschler EK, Sun JK and Silva PS 2014 In Seminars in ophthalmology 29 (5) p. 290-300

[17] Utami DR, Amin R, Zen NF 2017 Majalah Kedokteran Sriwijaya 49(2) p 66-74.

[18] Amelia R 2018 Open access Macedonian journal of medical sciences 6(9) p 1762.

[19] Amin ZA, Islam QU, Mehboob MA 2016 Pakistan journal of medical sciences 32(6) p 1349

[20] Voigt M, Schmidt S, Lehmamn T, Köhler B, Kloos C, Voigt UA, Meller D, Wolf G, Müller UA, Müller N 2018 Experimental and Clinical Endocrinology & Diabetes. 2018 126(09) p 570-6

[21] Prakash G, Agrawal R, Satsangi SK, Prakash S 2016 Middle East African journal of ophthalmology. 23(2) p 212.

[22] Liu, Y., Yang, J., Tao, L., Lv, H., Jiang, X., Zhang, M. and Li, X., 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. BMJ open, 7(9).