

**THE PROPORTION AND FACTORS ASSOCIATED WITH
DIABETIC RETINOPATHY AMONG TYPE 2 DIABETES
MELLITUS PATIENTS IN PERAK FROM 2018-2022**

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MELLITUS PATIENTS IN PERAK FROM 2018-2022**

By

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LIST OF ABBREVIATION

Adj. OR	Adjusted odd ratio
BMI	Body mass index
CVD	Cardiovascular disease
CeVD	Cerebrovascular disease
DR	Diabetic retinopathy
HbA1c	Glycated haemoglobin
OR	Odd ratio
HDL	High-density lipoproteins
LDL	Low-density lipoproteins
MOH	Ministry of Health
NCD	Non-communicable disease
NDR	National Diabetic Registry
NPDR	Non-proliferative diabetic retinopathy
OHA	Oral hypoglycaemic agents
PDR	Proliferative diabetic retinopathy
SD	Standard deviation
T2DM	Type II diabetes mellitus
TC	Total cholesterol
TG	Triglyceride
VEGF	Vascular endothelial growth factor

LIST OF SYMBOLS

$>$	More than
$\geq$	Greater than or equal to
$<$	Less than
$\leq$	Less than or equal to
β	Beta (regression coefficient)
p	p-value (probability value in hypothesis testing)
n	Sample size
$\%$	Percentage
α	Alpha (significance level in hypothesis testing)
$Z\alpha$	The Z-score associated with the level of significance
P_0	Probability of non-exposure group (literature review)
P_1	Estimated probability of exposure group (expert opinion)
m_1	Median time among non-prognostic group (by literature)
m_2	Median time among Prognostic group (by literature)
d	Detectable differences relative Precision

**PERATUSAN DAN FAKTOR-FAKTOR YANG BERKAITAN DENGAN RETINOPATI
DIABETES DALAM KALANGAN PESAKIT DIABETES MELITUS JENIS 2 DI PERAK DARI
TAHUN 2018-2022**

ABSTRAK

Pengenalan: Retinopati diabetes (DR) kekal sebagai punca utama dan boleh dicegah bagi kehilangan penglihatan dalam kalangan individu dengan Diabetes Mellitus Jenis 2 (T2DM), yang menjadi cabaran utama kesihatan awam di peringkat global dan di Malaysia. Di Perak, beban diabetes yang semakin meningkat menekankan keperluan data tempatan bagi membantu strategi saringan dan pengurusan yang lebih berfokus. Kajian ini bertujuan untuk menentukan proporsi serta mengenal pasti faktor-faktor yang berkaitan dengan DR dalam kalangan pesakit T2DM di Perak antara tahun 2018 hingga 2022.

Metodologi: Kajian rentas silang ini dijalankan menggunakan data sekunder daripada Daftar Diabetes Kebangsaan (NDR) Perak. Individu dewasa berumur 18 tahun ke atas dengan Diabetes Mellitus Jenis 2 yang didiagnosis antara Januari 2018 hingga Disember 2022 telah dimasukkan dalam kajian ini. Selepas mengenakan kriteria inklusi dan eksklusi, seramai 1160 pesakit telah dipilih melalui persampelan rawak mudah. Data mengenai ciri-ciri sosiodemografi, parameter klinikal, komorbiditi dan maklumat rawatan telah diperoleh dan dianalisis menggunakan SPSS versi 29. Analisis regresi logistik mudah dan berganda telah dijalankan untuk mengenal pasti faktor-faktor bebas yang berkaitan dengan Retinopati Diabetes.

Keputusan: Daripada 1160 pesakit Diabetes Mellitus Jenis 2 yang dikaji, proporsi keseluruhan Retinopati Diabetes adalah 25.4%. Didapati terdapat pola penurunan dalam proporsi Retinopati Diabetes dari 31.4% pada tahun 2018 kepada 13.8% pada tahun 2022. Purata umur pesakit adalah 55.3 tahun dan 59.0% adalah wanita. Regresi logistik berganda mengenal pasti beberapa faktor risiko bebas bagi Retinopati Diabetes, termasuk peningkatan umur (Adj OR 1.04; 95% CI: 1.02, 1.05), tempoh diabetes yang lebih lama (Adj OR 1.20, 95% CI: 1.07, 1.35), kawalan HbA1c yang kurang baik (Adj OR 1.10, 95% CI: 1.01, 1.19), nefropati (Adj OR 4.54, 95% CI: 2.88, 7.24), hipertensi (Adj OR 1.72; 95%CI 1.21, 2.47) dan terapi insulin (Adj OR 2.5; 95% CI 1.66, 3.77). Penemuan ini adalah selaras dengan kajian tempatan dan antarabangsa, sekali gus mengukuhkan kepentingan faktor risiko yang boleh diubah dan tidak boleh diubah ini.

Kesimpulan: Kajian ini menunjukkan penurunan yang ketara dalam prevalens Retinopati Diabetes dalam kalangan pesakit Diabetes Mellitus Jenis 2 di Perak, mencerminkan peningkatan dalam pengurusan diabetes, saringan retina berkala, serta intervensi kesihatan awam. Walau bagaimanapun, kewujudan faktor risiko yang berterusan menekankan keperluan penjagaan bersepadu dan pelbagai disiplin, saringan berkala dan keutamaan kepada individu berisiko tinggi. Penemuan ini menyokong pengukuhan strategi pencegahan dan peruntukan sumber bagi terus mengurangkan beban komplikasi diabetes yang menjejaskan penglihatan pesakit di Perak dan kawasan yang setara.

Kata kunci: Retinopati diabetes, Diabetes Mellitus Jenis 2, Faktor risiko

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ABSTRACT

Introduction: Diabetic retinopathy (DR) remains a leading and preventable cause of vision loss among individuals with Type 2 Diabetes Mellitus (T2DM), posing a significant public health challenge both globally and in Malaysia. In Perak, the increasing burden of diabetes underscores the need for local data to inform targeted screening and management strategies. This study aimed to determine the proportion and identify factors associated with DR among T2DM patients in Perak between 2018 and 2022.

Methodology: A cross-sectional study design was employed using secondary data from the National Diabetes Registry (NDR) of Perak. Adults aged 18 years and above with Type 2 Diabetes Mellitus diagnosed between January 2018 and December 2022 were included. After applying inclusion and exclusion criteria, 1160 patients were selected via simple random sampling. Data on sociodemographic characteristics, clinical parameters, comorbidities and treatment details were extracted and analysed using SPSS version 29. Simple and multiple logistic regression analyses were conducted to identify independent factors associated with Diabetic Retinopathy.

Results: Among the 1160 Type 2 Diabetes Mellitus patients sampled, the overall proportion of Diabetic Retinopathy was 25.4%. Notably, there was a declining trend in Diabetic Retinopathy proportion from 31.4% in 2018 to 13.8% in 2022. The mean

age of patients was 55.3 years and 59.0% were female. Multivariable logistic regression identified several independent risk factors for Diabetic Retinopathy which includes increasing age (Adj OR 1.04; 95% CI: 1.02, 1.05), longer duration of diabetes (Adj OR 1.20, 95% CI: 1.07, 1.35), poor HbA1c control (Adj OR 1.10, 95% CI: 1.01, 1.19), nephropathy (Adj OR 4.54, 95% CI: 2.88, 7.24), hypertension (Adj OR 1.72; 95%CI 1.21, 2.47) and insulin therapy (Adj OR 2.5; 95% CI 1.66, 3.77). The findings are consistent with both local and international literature, reinforcing the importance of these modifiable and non-modifiable risk factors

Conclusion: The study reveals a significant reduction in Diabetic Retinopathy prevalence among Type 2 Diabetic Mellitus patients in Perak, reflecting improvements in diabetes management, regular retinal screening and public health interventions. However, the persistence of traditional risk factors highlights the ongoing need for integrated and multidisciplinary care, regular screening and prioritisation of high-risk individuals. The findings support the strengthening of preventive strategies and resource allocation to further reduce the burden of vision-threatening diabetic complications in Perak and similar settings

Keywords: Diabetic retinopathy, Type 2 Diabetes Mellitus, Risk factors

CHAPTER 1

INTRODUCTION

1.1 Introduction

Diabetic retinopathy remains one of the most significant and preventable complications affecting individuals living with Type 2 Diabetes Mellitus, both globally and within Malaysia. In recent years, the burden of diabetes has continued to rise in Perak with serious implications for vision loss and quality of life among affected patients. Despite advancements in diabetes management, many individuals still progress to developing diabetic retinopathy underscoring the need to better understand its prevalence and the underlying factors that contribute to its onset. By focusing on the proportion and associated factors of Diabetic Retinopathy among Type 2 Diabetes Mellitus patients in Perak from 2018 to 2022, this study aims to shed light on local trends and risk determinants as well as providing valuable insights to guide targeted prevention and management strategies within the community.

1.1.1 Epidemiology of Diabetes Mellitus

Diabetes Mellitus (DM) represents a major global public health challenge, driven by factors such as an aging population, increasing urbanization, and a growing incidence of overweight and obesity (IDF,2021). According to 2021 projections from the International Diabetes Federation (IDF), it is expected that by 2045, approximately 783 million adults worldwide, or about 1 in 8, will be living with diabetes (IDF,2021). It is projected that by 2025, over 30% of the global population with diabetes will be located in the Asia Pacific region (Tajunisah *et al.*, 2011).

According to the National Health and Morbidity Survey (NHMS) 2023, the overall prevalence of diabetes was 15.6%, with the prevalence of known diabetes at 9.7%, and the prevalence of raised blood glucose among those not known to have diabetes at 5.9%. An increasing trend in the overall prevalence of diabetes was seen from 2011 (11.2%), 2015 (13.4%), and 2023, which peaked in 2019 (18.3%). Among those with diabetes, a higher proportion of raised blood glucose among those not known to have diabetes was observed among the younger age group, aged 18 to 39 years old, as compared to those with known diabetes (NHMS, 2023).

The Clinical Practice Guidelines for the Management of Type 2 Diabetes Mellitus (6th edition, MOH 2020) highlighted that Type 2 Diabetes Mellitus is the most common form of diabetes in Malaysia which accounts for over 90% of adult cases. It is often found alongside other chronic conditions such as hypertension, dyslipidemia and obesity. As the rates continue to increase both worldwide and in Malaysia, Type 2 Diabetes Mellitus creates a significant social and economic challenges primarily because of its complications such as vascular disease and the increased risk of early mortality (Khan *et al.*, 2020; Ong *et al.*, 2023). As a result, many individuals may not realize they have diabetes until complications, such as diabetic retinopathy, begin to develop (Tajunisah *et al.*, 2011). As the prevalence of diabetes grows, the risk of developing related complications, such as diabetic retinopathy, also increases.

Type 2 Diabetes Mellitus is a condition characterized by a gradual decline in the functionality of the insulin-producing cells within the pancreas accompanied by reduced insulin responsiveness in the body's muscle and fat tissues (Solis-Herrera *et*

al., 2000). This physiological shift results in an increased hepatic glucose output and impaired glucose utilization by various bodily organs. Consequently, blood glucose levels become elevated, both in fasting states and postprandial periods.

Furthermore, dysregulation of specific gut hormones known as incretins interferes with the normal secretion of insulin and the post-meal regulation of glucagon, thereby intensifying postprandial hyperglycemia (Nauck and Meier, 2018). The kidneys can also contribute to elevated blood glucose levels through excessive glucose reabsorption (Vallon and Thomson, 2020).

Type 2 Diabetes Mellitus is recognized as a major independent risk factor for cardiovascular disease and can lead to severe microvascular and macrovascular complications affecting the eyes with retinopathy, kidneys with nephropathy, and nerves with neuropathy (Dilworth *et al.*, 2024). Despite these significant health implications, a considerable proportion of individuals remain undiagnosed with a reported undiagnosed rate of 5.9% during the specified period (Naserrudin *et al.*, 2022). This often leads to diagnoses occurring only after the development of complications (Ogurtsova *et al.*, 2022). Diabetic retinopathy is indeed one of the most common complications associated with diabetes mellitus. It affects an estimated 382 million individuals globally, with nearly one-third of patients over 40 years old in the U.S. experiencing this condition (Stephen and Stanley, 2019)

1.1.2 Diabetic Retinopathy

Diabetic Retinopathy (DR) is the primary cause of irreversible blindness in working-age adults. Chronic hyperglycemia results in both retinal vascular damage and neuronal injury, both of which play a role in vision impairment. Approximately

20% of individuals newly diagnosed with type 2 Diabetes Mellitus also show signs of Diabetic Retinopathy at the time of diagnosis (Hao *et al.*, 2020).

Diabetic Retinopathy is a serious complication of diabetes that damages the blood vessels in the retina and can lead to significant vision loss or even blindness (Mounirou *et al.*, 2022; Kropp *et al.*, 2023). This condition is primarily driven by prolonged high blood sugar levels and tends to be more prevalent among individuals with a longer duration of diabetes. Persistently elevated glucose levels promote the formation of advanced glycation end products and trigger the activation of protein kinase C, both of which contribute to the progressive damage of retinal capillaries (Seewoodhary, 2021). Such changes can result in plasma leakage, retinal hemorrhage, fibrosis and in severe cases, tractional retinal detachment and irreversible loss of sight (Hao *et al.*, 2020).

As retinal blood flow decreases, the body attempts to compensate by increasing the production of vascular endothelial growth factor (VEGF) in the oxygen-deprived retina (Li *et al.*, 2023). Higher VEGF levels are strongly associated with the development and progression of diabetic retinopathy (Ahuja *et al.*, 2019). VEGF stimulates the growth of new blood vessels on the retinal surface but these vessels are fragile and prone to bleeding thus leading to scar tissue formation. This scarring can cause the retina to detach which results in further vision impairment. In addition, lipid deposits which may appear as yellowish exudates and macular edema can develop, both of which pose further risks to visual function.

The global prevalence of Diabetic Retinopathy is estimated to be 27.0%, which leads to 0.4 million blindness in the world (Zegeye *et al.*, 2023). The

prevalence of Diabetic Retinopathy among diabetic patients in Malaysia in 2023 was 11.12% (NDR Report, 2023). In Malaysia, recent statistics indicate that 36.8% of individuals with diabetes are affected by Diabetic Retinopathy. Additionally, Diabetic Retinopathy is a leading cause of blindness in the country, contributing to 10.4% of blindness cases among elderly patients (Naserrudin *et al.*, 2022). Findings from a study examining diabetes control and its complications in Malaysian private primary care clinics revealed that Diabetic Retinopathy ranked as the second most common complication immediately succeeding neuropathy among diabetic patients (Mafauzy, 2005).

The rising incidence of Diabetic Retinopathy especially among younger patients has become a significant public health concern (Romero-Aroca *et al.*, 2016). Diabetic Retinopathy affects approximately 30 to 50 % of people living with diabetes and is the leading cause of legal blindness among adults aged 20 to 74 in developed countries (Lee *et al.*, 2015). Beyond its physical complications, Diabetic Retinopathy can also contribute to considerable psychological distress including heightened anxiety, depression and an overall decline in quality of life for those affected (Deswal *et al.*, 2020).

Diabetic Retinopathy is generally classified into two main types which are non-proliferative and proliferative. Non-proliferative diabetic retinopathy (NPDR) represents the earlier stage of the disease and is further divided into mild, moderate and severe forms. At this stage, timely intervention and improved diabetes management can be most effective in preventing further progression to the more advanced proliferative diabetic retinopathy (Naserrudin *et al.*, 2022). Proliferative

diabetic retinopathy (PDR) is characterized by the growth of new, abnormal blood vessels in the retina, a process known as neovascularization (Huda *et al.*, 2023). Unfortunately, patients are often unaware of disease progression since early retinal damage usually does not cause noticeable symptoms (Nwanyanwu *et al.*, 2021). Therefore, early detection and prompt treatment are essential, underscoring the importance of regular eye examinations for individuals with diabetes (MOH, 2017).

1.2 Problem statement and rationale of study

The prevalence of Diabetic Retinopathy has increased by over a 25% within a mere decade is expected to further strain on healthcare systems that already overstretched (Tan and Wong, 2022). Morbidity related to diabetic retinopathy, though often neglected, is a crucial aspect of the issue that requires prompt reforms in public health programs (Teo *et al.*, 2021). Diabetic retinopathy can significantly impact vision, hindering daily activities, reducing independence, and affecting overall well-being. Diabetic Retinopathy can drive up healthcare expenses, decrease workplace productivity, create a greater need for caregiver support, place additional demands on social services, and require increased investment in public health programs and accessibility measures for individuals with vision loss (Khandekar, 2012).

Diabetic Retinopathy typically develops as type 2 Diabetes Mellitus progresses over time. Research indicates that around 60% of individuals with T2DM will be diagnosed with DR after 20 years of living with the condition. Additionally, studies suggest that 2% of patients will become blind and 10% will experience some

form of visual impairment due to Diabetic Retinopathy within 15 years of Type 2 Diabetes Mellitus diagnosis (Naserrudin *et al.*, 2022). There is limited study about the proportion of Diabetic Retinopathy and its associated factors among Type 2 Diabetes Mellitus (Zegeye *et al.*, 2023).

Our research findings wish to add to evidence to form future prevention strategy on diabetes in general and Diabetic Retinopathy specifically. The outcome of this research could offer significant support to the Perak State Health Department and healthcare practitioners in enhancing diabetes management strategies, developing community education programs and implementing screening initiatives for the early detection of diabetic retinopathy.

1.3 Research Questions

1. What is the proportion of Diabetic Retinopathy among Type 2 Diabetes Mellitus patients in Perak?
2. What are the factors associated with Diabetic Retinopathy among Type 2 Diabetes Mellitus patients in Perak?

1.4 Objectives

1.4.1 General Objective

To study the proportion and factors associated with Diabetic Retinopathy among Type 2 Diabetes Mellitus patients in Perak from 2018-2022.

1.4.2 Specific Objectives

1. To determine the proportion of Diabetic Retinopathy among Type 2 Diabetes Mellitus patients in Perak from 2018-2022
2. To determine the factors associated with Diabetic Retinopathy among Type 2 Diabetes Mellitus patients in Perak from 2018-2022

1.5 Research Hypothesis

Null Hypothesis (H_0) : There is no significant associations between sociodemographic characteristics, clinical factors, blood parameters and treatment-related factors with Diabetic Retinopathy among Type 2 Diabetes Mellitus patients in Perak from 2018 to 2022

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

A thorough literature review was undertaken using a systematic approach, drawing on multiple reputable online databases such as PubMed, Scopus, and EBSCOhost as well as university-subscribed resources. The review primarily focused on studies published between 2015 and 2025 to ensure the inclusion of the most current and relevant research. Nevertheless, several earlier studies were also considered due to their significant contribution to the topic. Various search strategies were applied, including the use of advanced Boolean operators (AND, OR, NOT) to effectively combine and refine key search terms. This structured methodology was intended to capture a wide and comprehensive array of literature related to the research area, thereby strengthening the quality and scope of the review. The main keywords used during the search process included Diabetic Retinopathy, Type 2 Diabetes Mellitus, proportion and risk factors.

2.2 Prevalence of Diabetic Retinopathy

According to the International Diabetic Federation (IDF) 2021, the global diabetes population is expected to reach 783 million by 2045. The 2023 National Health and Morbidity Survey (NHMS) reported an overall diabetes prevalence of 15.6%, with 9.7% of individuals diagnosed with known diabetes and 5.9% showing elevated blood glucose levels despite not being previously diagnosed. The survey also observed a rising trend in the prevalence of diabetes, which increased from

11.2% in 2011 to 13.4% in 2015, peaking at 18.3% in 2019 before reaching 15.6% in 2023. In Malaysia, 1 in 5 adults is affected by diabetes, and many individuals remain unaware of their condition until complications arise, with diabetic retinopathy being one of the most common associated issues (Tajunisah *et al.*, 2011).

Diabetic Retinopathy is a microvascular disease defined by damage to the retinal capillaries, which can result in subsequent visual impairment (Kropp *et al.*, 2023). Diabetic Retinopathy is a leading cause of preventable blindness, particularly prevalent among individuals with diabetes in low- and middle-income countries (Ngah *et al.*, 2020). The prevalence of Diabetic Retinopathy among diabetic patients in Malaysia in 2023 was 11.12% compared to 10.29% in 2022 (NDR Report, 2023). In the state of Perak, the prevalence of Diabetic Retinopathy was reported as 13.65% in 2023 compared to 13% in 2022 (NDR Report, 2023).

The prevalence of Diabetic Retinopathy has increased by over 25% in the past decade, a trend that is likely to place additional pressure on already overburdened healthcare systems (Tan *et al.*, 2018). Despite its significance, the morbidity associated with Diabetic Retinopathy is often underrecognized, highlighting the need for urgent reforms in public health strategies (Teo *et al.*, 2021). Diabetic Retinopathy can severely affect vision, impairing daily functioning, diminishing independence, and overall well-being. This can complicate the management of diabetes and contribute to higher risks of social isolation, depression, and anxiety (Hussein *et al.*, 2016)

The proportion of Diabetic Retinopathy among Type 2 Diabetes Mellitus patients are reported according to a few studies. A study by (Al-Sarraf *et al.*, 2010)

done in Kuwait noted that among the 704 diabetic patients who participated in the study, 216 were diagnosed with diabetic retinopathy, resulting in an overall prevalence rate of 30.7%. Whereas, in a study done in Ethiopia, at the study period of January 2009 until May 2017, among the 377 adult diabetes patients, the proportion of Diabetic Retinopathy was 18.57% (Azeze *et al.*, 2018). Another study done in China from 2018 till 2020 found out that the prevalence of Diabetic Retinopathy was 16.3% among 50,564 participants (Hou *et al.*, 2023). Compared to a study in South Africa, the prevalence of Diabetic Retinopathy was 35.4% among they 416 Diabetes Mellitus patients (Maluleke *et al.*, 2024). These discrepancies suggests that the progression of Diabetic Retinopathy varies according to different regions and potentially other factors.

2.3 Risk factors

2.3.1 Age

In context to age as an associated factor, a study from Kuwait identified that patients in the age group 50 to 59 had double risk of Diabetic Retinopathy than those under forty (OR = 2.2, 95% CI: 1.1, 5.2) and those more than 60 years had more than four times risk (OR = 4.6, 95% CI: 2.0, 11.0) (Al-Sarraf *et al.*, 2010). In a study done in Korea, the prevalence of any Diabetic Retinopathy in Koreans was 15.8% (95% CI:14.1, 17.5) in those more than 40 years old and increased with age from those aged 40 to 49 years [10.2% (95%CI 6.2, 14.2)], to those aged 60 to 69 years [18.4% (95%CI 15.3, 21.5)], and then decreased in those aged ≥ 70 years [15.3% (95%CI 12.0, 18.6)] (Jee *et al.*, 2013). Most of the elderly group are also the

group of patients with a physiological decline in functions and high risk of many chronic disease. These findings suggest that advancing age is a consistent and significant associated factor for the development of Diabetic Retinopathy across different populations.

2.3.2 2.3.2 Gender

Diabetic Retinopathy is more common among males compared to females as reported by a few studies. In a study done among the Swedish population in January 2015 until December 2019 noted that Diabetic Retinopathy was more common in men compared to women OR 1.10 (95% CI: 1.05, 1.14, $p < 0.001$) (Sofizadeh *et al.*, 2024). Furthermore, a study from Ethiopia noted that for males, the odds of diabetic retinopathy were 3.25 times that of females (Adj OR=3.25, 95% CI:1.80, 6.69) (Zegeye *et al.*, 2023). One possible explanation for these findings is that neuroretinal function is more disrupted in males than in females with type 2 diabetes. This suggests that, relative to males, females may have a certain level of protection or resistance to the neurodegenerative changes that precede the development of background retinopathy in type 2 diabetes.

2.3.3 Race

A study done in Malaysia among diabetic patients who screened for Diabetic Retinopathy between March 2015 till December 2016 found that Malay was a predominant race group to have Diabetic Retinopathy at approximately 62.6%, whereas non-Malay which consisted of Chinese and Indian, comprised about 37.4% (Ngah *et al.*, 2020). Malays have approximately twice the risk to develop diabetic retinopathy compared to non-Malays in Malaysia (Adj OR 1.69; 95%CI 1.34, 2.13). In

a study done between May 2008 to December 2008, Chinese people had a better blood sugar control (HbA1c less than 6.5%) compared to Malays and Indians ($p < 0.001$) (Boon How *et al.*, 2011).

2.3.4 Body Mass Index (BMI)

Increased Body Mass Index (BMI) has an impact on the risk of developing Diabetic Retinopathy. According to a study done in Southeast Ethiopia in June to July 2021, the likelihood of developing Diabetic Retinopathy were higher in overweight or obese diabetic patients than those with normal BMI (AOR 2.65, 95% CI 1.02, 6.92) (Sahiledengle *et al.*, 2022). A recent large scale study using data from the US Behavioral Risk Factor Surveillance System (BRFSS) involving over 21,000 adults with diabetes found that the prevalence of Diabetic Retinopathy increased gradually with higher BMI categories. Specifically, the weighted prevalence of Diabetic Retinopathy was 0.8% in underweight individuals, 13.8% in normal weight, 29.7% in overweight and 55.7% in the obese group. After adjusting for confounders such as age, gender, hypertension, hypercholesterolemia and insulin therapy, both overweight BMI (Adj OR = 1.004, 95% CI 1.003, 1.004) and obesity (Adj OR = 1.051, 95% CI 1.048, 1.055) remained significantly associated with increased Diabetic Retinopathy risk (Guang-Ran *et al.*, 2021).

2.3.5 Duration of diabetes

The risk of retinopathy increases significantly with the duration of diabetes. It is found from a study done in China between 2018 to 2020 where the prevalence of Diabetic Retinopathy was 8.2% (95% CI: 6.7, 9.7) among those with diabetes duration of less than one year and climbed to 38.6% (95% CI: 35.8, 41.4) among

those with diabetes duration of longer than 20 years (Hou *et al.*, 2023). In Kuwait, it was found that patients who had diabetes for 10 to 19 years had more than double the risk as compared with those who had diabetes for less than ten years (OR = 2.6, 95% CI: 1.6, 4.2) and patients with diabetes for 20 years or more had about triple the risk of DR (OR = 2.8, 95% CI: 1.5, 5.5) (Al-Sarraf *et al.*, 2010). This is likely due to the impact of diabetes on small blood vessels, which can lead to diabetic microvascular complications.

2.3.6 Smoking

Smoking may increase the risk of Diabetic Retinopathy among others. It is found in China that the incidence of Diabetic Retinopathy in severe smokers was significantly higher than that in non-smokers (OR=1.664, $p=0.043$) (Hao *et al.*, 2020). This was also found in a study done in Jordan from January to December 2019 where the current smokers were at significantly higher risk of Diabetic Retinopathy than those who had never smoked (OR: 1.7, 95% CI: 1.2, 2.4, $p < 0.01$) (Roto *et al.*, 2022). A major study using data from the Malaysian National Diabetic Registry (NDR) analyzed over half a million diabetic patients attending government primary care clinics. The study found that smoking was independently associated with a higher risk of diabetes complications including retinopathy. Specifically, diabetic patients who smoked had a significantly increased hazard of developing complications with an adjusted hazard ratio (Adj HR) of 1.10 (95% CI: 1.07, 1.14, $p < 0.001$) compared to non-smokers. This finding persisted even after adjusting for other sociodemographic and clinical factors underscoring the contribution of smoking to the overall burden of diabetic complications in Malaysia (Nor Asiah *et al.*, 2018)

2.3.7 Nephropathy

Additionally, nephropathy is also a powerful indicator of worsening retinopathy. This is supported by the study done in Jordan where all the later stages of chronic kidney disease (classified using eGFR) were associated with significantly higher risks of DR than stage 1. Specifically, chronic kidney disease stages 4 and 5 were associated with the highest risks of Diabetic Retinopathy (OR: 5.8, 95% CI: 2.7, 12.3, $p < 0.01$ and OR: 3.5, 95% CI: 1.3, 9.7, $p < 0.01$, respectively) (Roto *et al.*, 2022). Another study done in Brazil found that the risk to Diabetic Retinopathy in patients with diabetic nephropathy was 3.32 (95 % CI 1.62, 6.79) (Lima *et al.*, 2016). Serum creatinine also serves as one of the risk factors in Diabetic Retinopathy. Higher serum creatinine is associated with increased risk of Diabetic Retinopathy (OR=1.18 per $\mu\text{mol/L}$ increase, $P=0.0001$) (Zhang *et al.*, 2013)

2.3.8 Hyperlipidemia

Hyperlipidemia was shown to increase the risk of Diabetic Retinopathy (OR=2.19, 95% CI 1.09, 4.38, $P=0.03$) (Zhang *et al.*, 2013). Lipid profile also has significant associative value for Diabetic Retinopathy; higher levels of total cholesterol (2.94 mg/dL, 95% CI 1.32, 4.56) at baseline were observed in patients with later onset of Diabetic Retinopathy (Li *et al.*, 2023), whereas the likelihood of developing Diabetic Retinopathy among patients with lower HDL was almost six times (AOR 5.82, 95% CI 1.86, 18.24) that of their counterparts (Sahiledengle *et al.*, 2022). Furthermore, higher triglyceride (OR=1.18, $P=0.02$) is significantly associated with increased risk of Diabetic Retinopathy (Zhang *et al.*, 2013).

2.3.9 Hypertension

Hypertensive patients had about 2.56 times the chance of diabetic retinopathy than non-hypertensive patients [AOR=2.56, 95% CI (1.01, 6.45)] from a study conducted in Northwest Ethiopia in 2021 (Zegeye *et al.*, 2023). From a study done in Sweden, the risk of Diabetic Retinopathy increased with higher SBP with an OR of 1.33 (95% CI 1.20, 1.46, $p < 0.001$) for an SBP ≥ 140 mm Hg compared with those having an SBP of 110–119 mm Hg (Sofizadeh *et al.*, 2024). Hypertensive patients suffer from abnormal retinal autoregulation, thus making them unable to protect the changes in blood pressure due to the hyperglycaemia in Diabetes Mellitus patients that impairs the regulation of retinal perfusion.

2.3.10 Cerebrovascular disease and ischemic heart disease

Additionally, Diabetic Retinopathy was significantly more common in participants with history of myocardial infarction, congestive heart failure and coronary artery disease (Roto *et al.*, 2022). Previous stroke is one of the variable associated with Diabetic Retinopathy [OR 1.18 (95% CI 1.07, 1.30, $p = 0.001$)] (Sofizadeh *et al.*, 2024). A cross-sectional study conducted in Sabah, investigated 22,345 Type 2 Diabetes Mellitus patients and found a significant association between Ischemic heart disease (IHD) and the risk of developing Diabetic Retinopathy. The prevalence of Diabetic Retinopathy was higher among Type 2 Diabetes Mellitus patients who had IHD (26.7%) compared to those without IHD (17.8%). The analysis showed that the odds of having Diabetic Retinopathy were 1.7 times higher in patients with IHD compared to those without (OR 1.7, 95% CI 1.29, 2.19, $p < 0.05$) (Naserrudin *et al.*, 2022).

2.3.11 HbA1c

Elevated HbA1c levels are a significant association factor for Diabetic Retinopathy. A study done in Africa found that poor glycemic control (HbA1c >7%) was associated with an increased risk of diabetic retinopathy when compared with good glycemic control (OR = 1.25; 95% CI; 1.14, 1.38) (Shiferaw *et al.*, 2020). The finding is also further supported with a study done in Jordan where they found out high HbA1c level was associated with a significantly higher risk of Diabetic Retinopathy (OR: 1.4, 95% CI: 1.3, 1.5, $p < 0.01$) (Roto *et al.*, 2022). A 2023 study conducted at Cicendo Eye Hospital, Bandung examined the relationship between HbA1c levels and the severity of Diabetic Retinopathy in patients with Type 2 Diabetes Mellitus. In this cross-sectional analytic study of 70 patients, most participants (74.3%) had uncontrolled HbA1c (>7%). Among them, 62.9% were diagnosed with proliferative diabetic retinopathy (PDR), the more severe form, while 37.1% had non-proliferative diabetic retinopathy (NPDR). Statistical analysis revealed a significant association between HbA1c levels and the degree of Diabetic Retinopathy ($p = 0.018$) indicating that higher HbA1c is correlated with greater severity of Diabetic Retinopathy (Farhani *et al.*, 2023).

2.3.11 Type of medication

In Kuwait, patients with type 2 insulin treated diabetes had an increased risk of Diabetic Retinopathy as compared with type 1 (OR = 8.0, 95% CI: 3.5, 19.4) (Al-Sarraf *et al.*, 2010). A possible explanation is that Diabetic Retinopathy may result from prolonged hyperglycemia, which is more commonly observed in patients receiving insulin treatment. It is also important to note that insulin therapy is

typically initiated after oral antidiabetic drugs fail, meaning these type 2 diabetes patients often have a longer duration of the disease. On the other hand, the odds ratio of metformin associated with severe non-proliferative diabetic retinopathy (SNPDR)/ proliferative diabetic retinopathy (PDR) was 0.37 in all cases ($p < 0.001$), 0.35 in sulfonylurea use cohort ($p < 0.05$), 0.45 in non-sulfonylurea use cohorts ($p < 0.01$) (Li *et al.*, 2023). However, Diabetic Retinopathy progressed in 67% of statin non-users and 37% of statin users with a statistically significant difference ($P < 0.001$) at 12 months (Priyadarshini *et al.*, 2022). Low-dose statins have been shown to support vascular integrity by promoting the survival of retinal capillary endothelial cells, facilitating healing and repair, and preventing neovascularization.

2.4 Conceptual framework

The literature review highlights several significant factors influencing the progression to Diabetic Retinopathy among patients with Type 2 Diabetes Mellitus. The factors are categorized into four main groups: socio-demographic characteristics, clinical characteristics, blood parameters, and treatment factors. Socio-demographic factors include age, sex, and race. Clinical factors comprise duration of DM, body mass index (BMI), and comorbidities like hypertension, heart disease, nephropathy, stroke and smoking status. Blood parameters include HbA1c level, TC, HDL-C, LDL-C, and total TG. Creatinine level was excluded because it was already represented by the status of nephropathy. Socioeconomic status were not included due to incomplete secondary data in the National Diabetes Registry (NDR) line listing. Treatment comprise of those on insulin and on statin.

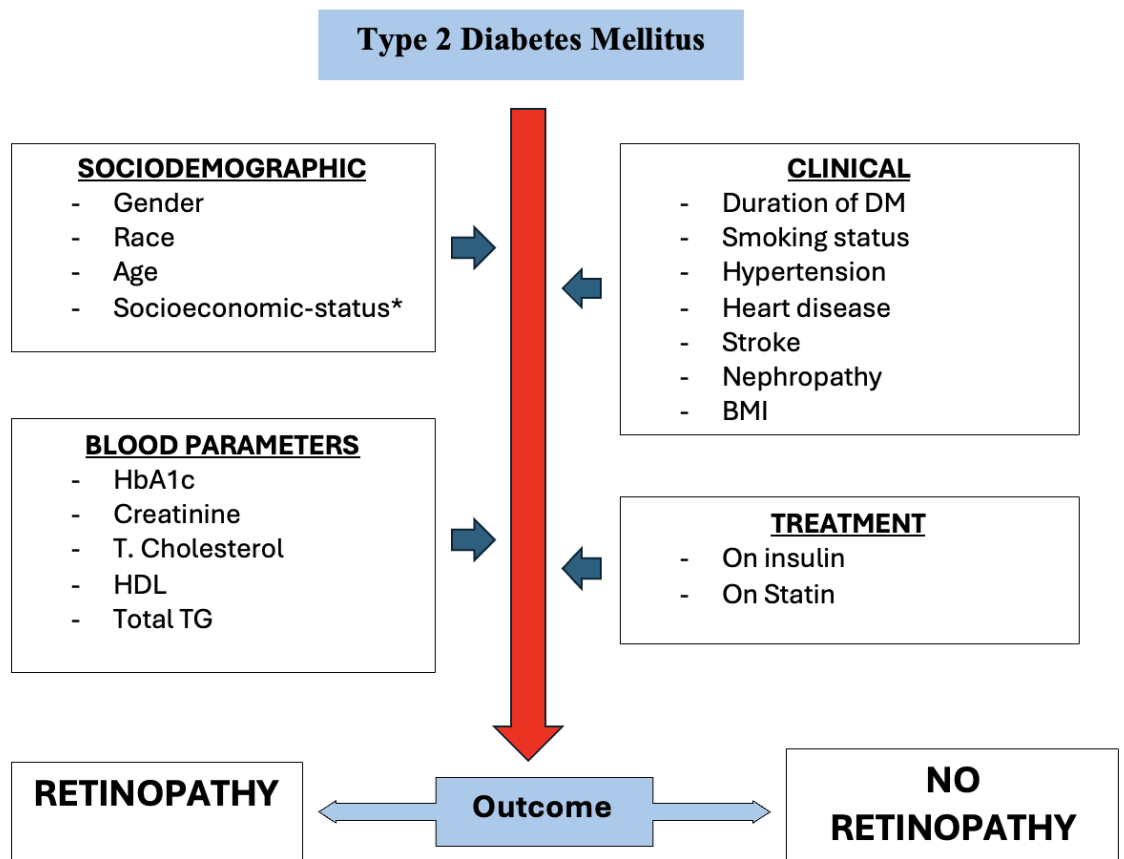


Figure 2.1 Conceptual framework

CHAPTER 3

METHODOLOGY

3.1 Study design

This study was a cross-sectional study using secondary data

3.2 Study duration

The study was conducted from November 2024 until June 2025

3.3 Study area

The study was carried out in the state of Perak. Perak is located in the north side of the Peninsular Malaysia which has a total land area of 21,146 km² with a total population of 2,515,800 in 2021 (Department of Statistics Malaysia, 2021). It is divided into 13 districts which are Hulu Perak, Larut Matang, Selama, Kuala Kangsar, Kerian, Kinta, Kampar, Perak Tengah, Hilir Perak, Manjung, Muallim, Batang Padang and Bagan Datuk (Figure 3.1). The data collection was done at the NCD unit of the Perak Health Department.

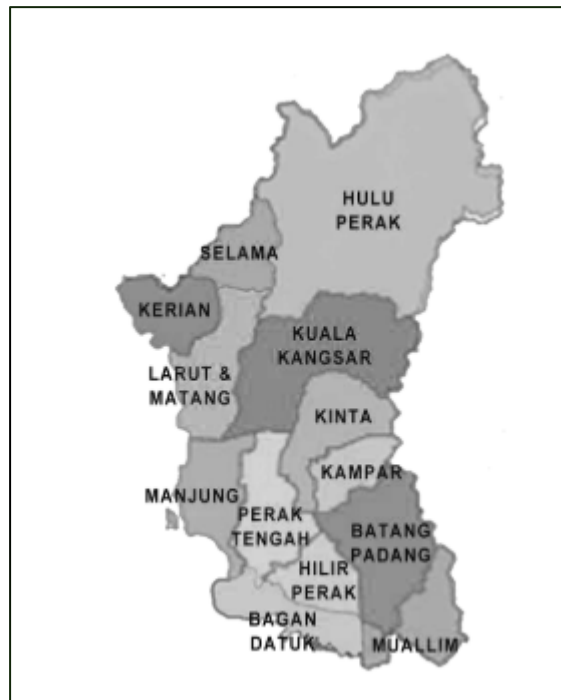


Figure 3.1 Map of districts in Perak (Source: Department of Statistics Malaysia, 2021)

3.4 Study population

3.4.1 Reference population

The reference population were adult patients with Type 2 Diabetes Mellitus in Perak

3.4.2 Source population

The source population for the study were adult patients with Type 2 Diabetes Mellitus registered in National Diabetic Registry in Perak

3.4.3 Sampling frame

The sampling frame for this study were adult patients with Type 2 Diabetes Mellitus registered in National Diabetic Registry in Perak from 1st January 2019 till 31st December 2023 and fulfilled the study criteria.

3.5 Subject data criteria

3.5.1 Inclusion criteria

1. Malaysian
2. Adult patients (≥ 18 years old)
3. Patients who were diagnosed with type 2 diabetes mellitus from 1/1/2018 and 31/12/2022
4. Patients who were registered in NDR (Clinical audit datasets Negeri Perak 2023)

3.5.2 Exclusion criteria

1. Cases with incomplete data >20%
2. Cases who already have diabetic retinopathy at the time of their DM diagnosis

3.6 Sample size estimation

The calculation of the sample size was determined according to the study objectives as follows:

3.6.1 Objective 1

Objective 1 sample size calculation was calculated for the proportion of Diabetic Retinopathy among Type 2 Diabetes Mellitus patients in Perak from 2018-2022. The sample size was calculated by using the single-proportion formula. The parameters used for the sample size calculation were P, d and Z_{α} . With an additional of 20% allowance of potential data input errors, the sample size for the proportion was calculated. Table 3.1 shows the sample size calculation for the proportion of Diabetic Retinopathy among Type 2 Diabetes Mellitus patients in Perak from 2018 to 2022.

$$n = \left(\frac{Z_{\alpha/2}}{d} \right)^2 * P(1 - P)$$

Table 3.1 Sample size estimation

Variables	Value
Significance (α)	0.05
P : Reference Population according to Literature (NDR report,2023)	0.11
d: detectable differences relative Precision	0.05
Z α = normal deviates that reflects Type I error; (level of significance at 5%; 95% CI)	1.96
Total Sample Size calculated	151