Risk Factors for developing Diabetic Retinopathy: A Review of Literature

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***Abstract*—One of the most prevalent non-communicable diseases (NCDs) worldwide is diabetes mellitus (DM). In India, the prevalence of diabetes mellitus (DM) is increasing exponentially. Although it is impractical with the current infrastructure, it is ideal for all individuals with diabetes mellitus to undergo periodic screening for diabetic retinopathy (DR). However, many studies globally reported that about 10-30 % from total population with diabetes has prevalence of Diabetic Retinopathy (DR). The objectives of this review were to estimate the prevalence of DR, and identify the associated risk factors for developing DR.**

The prevalence of DR in India has risen substantially in recent decades. Significant risk factors associated with DR includes Older age, longer duration of diabetes , poor glycemic control, Hypertension (either systolic & diastolic) , High Body Mass Index (BMI) , Metabolic abnormalties, Fasting Blood Glucose (FBS), and High HbA1c. A high-risk group-based targeted screening of people with DM might be given priority in a resource-constrained nation like India, although the existing opportunistic screening could continue until India implements universal screening for all DM patients.

Categories: Endocrinology / Diabetes/ Metabolism, Ophthalmology, Public Health

***Index Terms*—Diabetes mellitus, Diabetic Retinopathy, Risk factors for Diabetic Rretinopathy, Prevalence.**

I. INTRODUCTION AND BACKGROUND

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels.[1]

The global prevalence has increased nearly 8 times in the last five decades; from 1.2% in 1971 to 9.3% in 2019.[2] Prevalence has increased disproportionately in low- and middle-income nations. A substantial public health burden has been created in India as a result of the rise in the prevalence of diabetes mellitus among those aged 20 to 79 from 61.3 million in 2011 to 77 million in 2019, with an additional 77 million people classified as prediabetic.[2,3] It is anticipated that 101 million people in India would develop diabetes by 2030.[4-6]

Among the many complications most often asymptomatic until late, diabetic retinopathy (DR) is the most prevalent consequence of diabetes. DR screening is therefore required, either through fundus examination or fundus photography. Retinal specialists and qualified healthcare professionals are needed for assessment. India's human resources for health (HRH) and infrastructure are now inadequate, and the knowledge, attitude, and self-care practices of diabetics are not at their best. [7] There is a series of factors related to the development and progression of diabetic retinopathy; some more or less related to the severity of the disease. Even while recent research has shown that high blood pressure, poor glycemic control, and a lengthy history of diabetes are risk factors for the progression of DR, it is yet unknown how demographic and clinical traits affect DR patients' recurring hospitalizations.[8]

The pathophysiology of DR is not well understood, but a number of theories have been postulated. The most probable among them is the intraocular formation of reactive oxygen species (ROS) and the activation of protein kinase C that cause hyperpermeability of the retinal vasculature and the subsequent alterations in retinal blood flow. Protein kinase C also causes the thickening of the basement membrane, leading to ischemia and cellular signaling by vascular endothelial

growth factors (VEFs) causing ocular neovascularization. [9]

In fact, type 2 diabetes affects middle-aged and older people who are more likely to develop hypertension and to die from cardiovascular disease. Thus, in addition to the traditional DR risk factors (such as the length of diabetes mellitus or glycated hemoglobin A1C [HbA1c] it is crucial to investigate the effects of other systemic risk factors (such as age, sex, body mass index [BMI], blood pressure, and pertinent venous blood test parameters) on the retinal microvasculature in patients with type 2 DM, as these effects are still unknown.[10] Even though the early treatment of DR could reduce severe vision loss by 90 % , there are some factors that pose difficulty for patients to seek the care they need. There is lack of awareness regarding risk factors that results in increase prevalence of development of DR and cost of treatment is quite high. Hence this study aims to estimate the prevalence and identify risk factors for developing DR that helps to lower physical and financial burden.

A. Aim of the study

The aim of this review of literature is to summarize the available literature on to estimate the prevalence and identify risk factors for developing DR among diabetic patients.

II. MATERIALS AND METHODS

A comprehensive search from international journals, Pubmed, Google Search, MEDLINE and Cochrane database were carried out. A systematic review of the published literature has been used. the search terms or key words used were Diabetes mellitus (DM), Diabetic Retinopathy (DR), Risk factors for Diabetic retinopathy. The reference lists of articles were checked for further relevant publications. systemic mixed review approach is used. This approach integrates study findings from studies conducted within and outside country.

A. Study Selection

Articles were screened to determine whether the studies found in the search met following inclusion and exclusion criteria.

B. Inclusion Criteria

Studies related to prevalence and risk factors for DR Studies published between 2011 to 2024.

C. Exclusion criteria

Studies with prevalence of DR due to secondary complications of primary eye conditions.

D. Quality assessment methods

The two reviewers simultaneously evaluated the risks of bias for the included articles, and any differences in opinion were resolved through discussion. In this paper, Newcastle-Ottawa Scale (NOS) is used to evaluate the methodological quality of the included literature. The score of NOS scale is 0–9, including 3 parts and 8 points: selection (4 points), comparability (2 points), and outcome (2 points) [11]. You can get up to one star in the selection and exposure of a study, and up to two stars in the comparability. 0–3 points are considered as low quality, 4–6 points as medium quality and 7–9 points as high quality.

E. Reviews related to risk factors for Diabetic Retinopathy

In a cross-sectional study conducted among Palestinian Adults by Shrateh ON, Abdelhafez M, Ereqat S, Dein LNE, Iriqat Son identification of risk factors for the development of Diabetic Retinopathy with Type 2 Diabetes Mellitus. T2DM duration was associated with a 45% increase in the likelihood of developing DR. Patients with DR had higher odds of using insulin, being physically inactive, and having a HbA1c >7%. [12]

Berrabeh S, Elmehraoui Q, Benouda S, Assarrar I, Rouf S, and Latreach H has demonstrated that poor glycemic control, age, and the length of diabetes all increase the occurrence of diabetic retinopathy. For this reason, early diagnosis and treatment are dependent upon collaboration between diabetologists and ophthalmologists. For this reason, early diagnosis and treatment are dependent upon collaboration between diabetologists and ophthalmologists. [13]

A retrospective study to identify risk factors and evaluate outcomes of patients with delayed presentation and advanced diabetic retinopathy in our safety – net country hospital population among 562 patients who presented with a new diagnosis of diabetic retinopathy. Patients who originally reported with PDR were the most likely to lack a primary care provider (PCP), at 28.8%; this was higher than the rates for moderate/severe NPDR patients (14.3%),

mild NPDR patients (12.4%), and no DR patients (7.6%) (P < 0.001). A number of risk variables, such as not having a PCP, not having a screening referral, and being uninsured or underinsured, were identified as contributing to the delayed presentation of DR. [14]

In a study investigate among 7462 residents on prevalence and risk factors of diabetic retinopathy (DR) in a Chinese population with type 2 diabetes mellitus in a suburb (Qingpu) of Shanghai from January to December 2020. The subjects were instructed to provide a blood and urine sample, as well as photographs of the macula and disc of the central retina. Age, weight, BMI, duration of type 2 diabetes, FPG, HbA1c, TC, HDL-C, BUN, Ucr, U-Alb, and UACR were found to be connection factors supporting the outcome.The subjects were instructed to provide a blood and urine sample, as well as photographs of the macula and disc of the central retina. The study found that while there is no correlation between lipid indicators and DR, a number of renal function indicators, such as elevated urea nitrogen and urine albumin, were risk factors for DR. [15]

Repeated hospitalization is caused by a variety of causes and risk factors, which places a heavy financial and physical strain on DR patients. In the study done on DR patients who were readmitted to the Guangdong Provincial People's Hospital's Department of Ophthalmology for treatment between January 2012 and July 2021 to determine the reasons for and risk factors for patients with diabetic retinopathy (DR) who frequently require hospitalization. A deeper comprehension of these reasons and readmission risk factors could result in a reduction of these risks and a lighter load for patients.[16]

The study done among Dutch patients with type 1 diabetes mellitus (T1DM) to investigate risk factors for the development and progression of diabetic retinopathy (DR) and long-term visual outcomes. The cumulative incidences of DR, VTDR, and visual impairment are comparatively insignificant, according to the data. The risk of developing DR was found to be independently correlated with higher mean HbA1c, HbA1c variability, age of onset of T1DM, and total cholesterol; HDL cholesterol was found to be protective in T1DM participants. The progression of DR has been demonstrated to mean HbA1c and albuminuria. [17]

Tan GS, Gan A, Sabanayagam C, Tham YC, Neelam K, Mitchell P conducted a study to evaluate the prevalence and risk factors for diabetic retinopathy (DR) in the Singapore Epidemiology of Eye Diseases (SEED) Study in 2019. Participants were Persons of Malay, Indian, and Chinese ethnicity aged 40+ years, living in Singapore. The prevalence of any DR was greater in Indians (30.7% vs. 26.2% in Chinese and 25.5% in Malays, P = 0.012); any DME (P = 0.001) and CSME (P = 0.032) showed a similar pattern. The odds ratio [OR], 1.41; 95% CI, 1.09-1.83, vs. Chinese, the length of diabetes (OR, 1.10; 95% CI, 1.08-1.11, per year), the percentage of HbA1c (OR, 1.25; 95% CI, 1.18-1.32), the serum glucose (OR, 1.03; 95% CI, 1.00-1.06, per mmol/l), and the systolic blood pressure (OR, 1.14; 95% CI, 1.09-1.19, per centile) were independent risk factors for any DR. The three ethnic groups in this study had comparable major risk factors for DR. Regardless of ethnicity, addressing these risk factors may lessen the burden of DR in Asia. [18]

In the study done by Alramadan et al., advancing age was found to be significantly associated with DR. The prevalence in patients aged $\leq$ 60 years, 61-70 years, and $\geq$ 71 years was 38.5%, 46.8 % and 55.4% respectively. A significant association with physical inactivity was also observed. In the study Alramadan , the reference for physical inactivity was < 150 min/week. The prevalence of DR in patients who were physically inactive patients was 31.4% and 47.6 % respectively (p: < 0.001). The odds of having DR was increased by 60 % (p=0.002). [19]

In the study done by Magliah, 44.7% of DR patients had nephropathy. The duration of DM for > 10 years and older age were the most significant risk factor for DR. Male gender was significantly associated with DR, with male having prevalence of 61.2% compared to 38.8% for Female but there isno significant correlation between gender and DR. The use of insulin and poor glycemic control were found to be significant risk factors of DR. Moreover, hypertension was reported in 78.9% of DR cases. While smoking & BMI was not associated with DR while hyperlipidemia was found to have a significant association(p=0.002).[20]

In subjects with recent diagnosis of diabetes and without incapacitant complications due to this condition, haemoglobin A1c, albuminuria and hypertension constitute key factors in the development of DR and DME. DR was associated with diabetes duration (OR per year=1.20, p<0.001), haemoglobin A1c (HbA1c) from 7.0 to 8.9 (OR=2.19, p<0.001),

HbA1c≥9 (OR=2.98, p<0.001) and systolic blood pressure (SBP) (OR=1.16 per 5mm Hg, p<0.001). [21]

III. CONCLUSION

Diabetic Retinopathy (DR) is a serious complication of diabetes mellitus. It is also a leading cause of blindness worldwide. The prevalence of DR in India has been risen subtantially in recent decades, as a consequence of the dramatic increase in the prevalence of diabetes mellitus. Significant risk fcators for DR include older age, longer duration of diabetes, poor glycemic control, metabolic abnormalties, hypertension, BMI, Cataract surgery, lipid control, lack of screening referral, High HbA1c, High Fasting Blood Glucose (FBS), High Uric acid, LDL-C & BUN. Therefore, awareness camping and practice of opportunistic screening for DR in India and recommends universal systemic screening in the coming year are linked to better outcomes and fewer problems.

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VI. CONFLICTS OF INTEREST

Nil.

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