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Assessment of Anaemia in Patients with Diabetic Retinopathy: A Cross-Sectional Study

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ABSTRACT
Diabetes mellitus (DM) is a globally escalating medical concern, with Diabetic retinopathy (DR) emerging as the foremost cause of acquired yet potentially preventable blindness. Anaemia presents as an independent risk factor in the progression of cardiovascular disease, chronic renal disease DR. Our study aims to establish anaemia as a risk factor for DR among patients diagnosed with type 2 diabetes This hospital-based cohort study involved 267 patients of both genders diagnosed with type 2 DM and DR. Blood investigations, including hemoglobin levels determined by colorimetric methods, glycosylated hemoglobin (HbA1c), blood urea nitrogen serum creatinine, were conducted. Statistical analysis was performed using SPSS version 18. The mean age of the participants was 57.86±10.12 years. Among the 267 patients, 102 patients (38.20%) had diabetes for <5 years, 138 (51.69%) for 5-10 years 27 (10.11%) for over 10 years. Among the 534 eyes examined, 209 (39.14%) exhibited mild non-proliferative diabetic retinopathy (NPDR), 155 (29.03%) moderate NPDR, 157 (29.40%) severe NPDR 13 (2.43%) proliferative diabetic retinopathy (PDR). 23 (15.86%) male patients had hemoglobin levels below 13g/dl 85 (69.67%) female patients had hemoglobin levels below 12g/dl. Regular screening for DR among all patients with type 2 DM is crucial, especially for those with longer durations of diabetes, elevated blood glucose levels, inconsistent glycemic control, renal disorders, or anaemia resulting from any cause.

INTRODUCTION

Diabetes mellitus (DM) has emerged as a significant global health concern, with its prevalence escalating at an alarming rate worldwide. India, in particular, has witnessed a surge in diabetic cases, earning the title of "diabetes capital of the world." DM is a metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Type 2 DM, also known as non-insulin-dependent DM, involves individuals with insulin resistance and typically relative, rather than absolute, insulin deficiency accompanied by inadequate insulin production. Prolonged hyperglycemia due to DM can lead to micro vascular and macrovascular complications. Micro vascular complications encompass retinopathy, nephropathy neuropathy, whereas coronary artery disease, cerebrovascular disease peripheral artery disease are considered macrovascular complications[1]. Diabetic Retinopathy (DR) stands out as a leading cause of acquired yet preventable blindness. It is characterized by microangiopathy affecting retinal arterioles, capillaries venules. The progression of DR is influenced by factors such as defective carbohydrate metabolism, duration of the disease, control of hyperglycemia oxidative stress. Anaemia serves as an independent risk factor contributing to the advancement of DR due to retinal tissue hypoxia, exacerbating the severity and progression of retinopathy in diabetic individuals[2,3]. The Early Treatment Diabetic Retinopathy Study (ETDRS) conducted in the United States demonstrated that prompt diagnosis and management of anaemia could attenuate the rate of retinopathy progression in type 2 DM patients. It is crucial to implement more frequent screenings for diabetic patients, especially those with anaemia or renal predictors of diabetic nephropathy, to avert swift progression of retinopathy and potential vision-threatening complications[4,5]. Therefore, the objective of our study is to establish anaemia as a risk factor for DR, with low hemoglobin levels serving as predictors of diabetic nephropathy.

MATERIAL AND METHODS

This hospital-based study spanned two years and involved 267 patients diagnosed with Type 2 DM who sought treatment at the outpatient clinic within the ophthalmology department of a tertiary care center in India. Patients with a confirmed diagnosis of Type 2 DM, either established or recently diagnosed, exhibiting clinical evidence of diabetic retinopathy (DR) changes were included in the study. Patients with pre-existing renal diseases or diabetic nephropathy, those with Type 1 DM, hypertension, dyslipidemia, pregnancy, chronic liver disease, malignancy, blood disorders, or significant media opacities that hindered fundus examination were excluded. All participants were thoroughly informed about the study consent was obtained from each participant. Patients with fasting blood sugar levels exceeding 126 mg/dl, postprandial blood sugar levels above 140 mg/dl, or HbA1c levels exceeding 5.7% were classified as diabetic. Additionally, haemoglobin levels below 13g/dl in males and below 12g/dl in females were considered anaemic. The background data collected included age, gender, occupation, type and duration of diabetes, blood pressure, personal and lifestyle histories treatment history. Ophthalmic clinical data encompassed best-corrected visual acuity (BCVA), slit-lamp examination, intraocular pressure measurement fundus examination. Fasting and postprandial blood sugar levels were determined using the glucose oxidase method. Haemoglobin levels were assessed via the colorimetric method, while blood urea nitrogen, serum creatinine glycosylated haemoglobin were measured using high-performance liquid chromatography. Proliferative retinopathy was confirmed through fundus fluorescein angiography.

RESULTS AND DISCUSSIONS

This study included a total of 534 eyes from 267 patients, comprising 145 males (54.31%) and 122 females (45.69%). The average age of the participants was 57.86±10.12 years. The visual acuity of these 267 patients upon presentation is detailed in (Table 1). Diabetic retinopathy (DR) grading was performed using the ETDRS classification. Among the 534 eyes with DR, 209 (39.14%) exhibited mild non-proliferative diabetic retinopathy (NPDR), 155 (29.03%) moderate NPDR, 157 (29.40%) severe NPDR 13 (2.43%) proliferative diabetic retinopathy (PDR). Regarding the duration of diabetes,

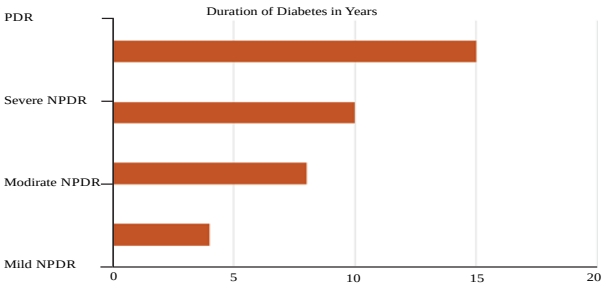

Fig. 1: Comparison of Duration of Diabetes and Severity of DR

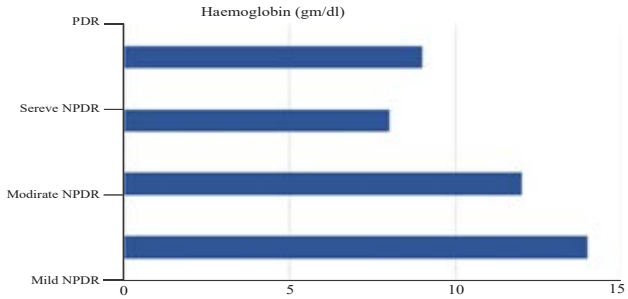

Fig. 2: Comparison of Haemoglobin Level and Severity of DR

Table 1: Visual Acuity of eyes in patients of DR at presentation

Visual Acuity at Presentation	No. of Eyes	Percentage
6/9	78	14.61
6/12	60	11.24
6/18	86	16.10
6/24	56	10.49
6/36	65	12.17
6/60	52	9.74
3/60	63	11.80
2/60	50	9.36
1/60	13	2.43
CFCF	7	1.31
HMCF	4	0.75
Total	534	100.00

102 patients (38.20%) had diabetes for < 5 years, 138 (51.69%) for 5-10 years 27 (10.11%) for over 10 years. The mean duration of diabetes was 3.1±1.09 years for mild NPDR, 7.1±1.9 years for moderate NPDR, 9.5±4.3 years for severe NPDR 15.1±1.7 years for PDR (Fig. 1). Among the 240 patients evaluated for haemoglobin levels, 108 (40.45%) had low haemoglobin. Specifically, 23 (15.86%) of the male patients had haemoglobin levels below 13g/dl 85 (69.67%) of the female patients had haemoglobin levels below 12g/dl. The mean haemoglobin values for mild NPDR, moderate NPDR, severe NPDR PDR were 14.3±1.8, 13.5±2.2, 9.3±1.1 9.85±0.7, respectively (Fig. 2).

The mean HbA1c levels for mild NPDR were 6.21±0.5, for moderate NPDR 7.6±0.57, for severe NPDR 8.9±0.9 for PDR 9.95±0.5. A history of smoking was reported by 63 patients (23.60%), indicating a significant positive relationship between smoking and DR ($p<0.05$). Similarly, 83 patients (31.09%) reported a history of alcohol intake, also showing a significant association with DR ($p<0.05$). Additionally, 155 patients (58.05%) had a sedentary lifestyle, suggesting a notable correlation between sedentary behavior and DR. Diabetic Retinopathy (DR) represents a distinctive vascular complication associated with diabetes, characterized by progressive changes in the retinal microvasculature. These changes lead to retinal hypoperfusion, increased vascular permeability abnormal retinal vessel proliferation. The chronic elevation of blood glucose levels, known as hyperglycemia, serves as the primary instigating factor for various microvascular alterations in diabetes[6,7].

In individuals with diabetes, abnormalities in red blood cells (RBC), oxidative stress, renal sympathetic denervation causing hypoxia in the renal interstitium reduced erythropoietin production contribute to the progression of anaemia. Anaemia is more prevalent among diabetic patients compared to non-diabetic individuals, with estimates ranging from 14%-48%. It is a common coexisting condition with diabetes and plays a potential role in the pathogenesis of retinopathy. Anaemia tends to develop earlier and is more severe in diabetic patients compared to those with renal impairment from other causes[8,9]. The presence of anaemia can lead to falsely low levels of HbA1c, a marker used to assess average blood glucose levels over time. This misinterpretation may result in inadequate treatment of hyperglycemia, thereby contributing to the progression of retinopathy. Early detection and management of anaemia have been shown to reduce the number of microaneurysms and promote the resolution of hard exudates in the retina[10]. The objective of our study was to investigate the correlation between anaemia and DR in patients with type 2 diabetes mellitus (DM) attending the Ophthalmology outpatient clinic. Our findings indicated a positive correlation between the duration of diabetes and the severity of retinopathy, consistent with previous studies that identified the duration of diabetes as a key predictor for retinopathy[11]. Anaemia emerged as a risk factor for DR in our study, with anaemic patients being more likely to develop retinopathy, possibly due to the contribution of anaemia to retinal hypoxia, which can influence angiogenesis, capillary permeability, vasomotor response cell survival[12].

Studies such as the Early Treatment Diabetic Retinopathy Study (ETDRS) have evaluated the impact of moderate levels of anaemia on the development of retinopathy. They found that anaemia was an independent risk factor for high-risk proliferative retinopathy and severe visual loss over a 5-year follow-up period[4]. Other studies have reported similar associations, including increased odds of severe retinopathy with the presence of anaemia[13,14]. Treatment with erythropoietin in anaemic diabetic patients has shown promising results in resolving macular hard exudates and improving tissue oxygenation, which may reduce Vascular Endothelial Growth Factor (VEGF) production and the stimulus for neovascularization[15]. These findings underscore the importance of evaluating anaemia in the routine screening of diabetic patients and initiating early treatment to mitigate the risk of micro vascular complications, including DR. Our study also highlighted correlations between age, retinopathy stage, gender, lifestyle factors the prevalence of DR, consistent with previous research[16,18]. However, the study's limitations, such as a small sample size and lack of

follow-up, suggest the need for larger-scale studies with longitudinal assessments to provide more definitive insights into the impact of anaemia correction on DR progression.

CONCLUSION

The incidence of DR was higher in males and in individuals aged between 40-60 years. Our study underscores that anaemia serves as a significant risk factor for DR, with haemoglobin levels emerging as a primary predictor of reduced erythropoietin levels, which could indicate early signs of diabetic nephropathy. Incorporating healthy lifestyle modifications complements efforts to reduce the risk of DR. Therefore, more frequent screening for DR, along with monitoring haemoglobin levels and addressing underlying anaemia, could substantially contribute to preventing disease progression. This emphasizes the importance of holistic care for the overall well-being of the patient.

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