ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 12 | December - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

STUDY OF DIABETIC RETINOPATHY AND ITS ASSOCIATION WITH ANEMIA IN DIABETIC PATIENTS

Ophthalomology

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ABSTRACT

Background: Diabetic Retinopathy is one of the well-known consequences of diabetes that affects a large percentage of people with the disease. It has been suggested that anaemia(low haemoglobin levels) may be related to the onset and progression of DR. While earlier studies have suggested a connection, further study is necessary to completely comprehend the interaction between anaemia and DR, especially in individuals with diabetes. **Method:** The trial ran from July 2020 to July 2022 for two years at a western regional institute of ophthalmology. For the study, 200 diabetic patients were included, with a mean age of 58.09 ± 8.25 years. Numerous indicators were measured and examined, such as serum iron levels, haemoglobin levels, postprandial 2-hour blood sugar (PP2BS), fasting blood sugar (FBS), and HbA1c. To look for any connections between anaemia and the advancement of DR, participants were categorized according to the severity of the disease. **Result:** Within the study cohort, the females showed lower haemoglobin levels than males. Subjects with proliferative diabetic retinopathy (PDR) had lower haemoglobin and HbA1c levels, but substantially higher levels of FBS and PP2BS. Serum ferritin levels were significantly greater in PDR patients, whereas transferrin and serum iron values were shown to be correlated with the severity of DR. Anaemia has been found to have a major role in the development of diabetic retinopathy, especially in patients who are female. Additionally, a relationship was found between a higher degree of DR and a lower blood oxygen carrying capacity. **Conclusion:** The results highlight the importance of controlling haemoglobin levels in individuals with diabetes, especially those who are demonstrating acute ischemia and significant retinal degeneration. Reversing anaemia may be essential for reducing the likelihood and severity of diabetic retinopathy. It is advised that those with DR have an early diagnosis and treatment for their anaemia in order to stop future consequences. Further information on its function in the treatment of diabetic retinopathy may be obtained from prospective studies concentrating on the correction of anaemia.

KEYWORDS

Diabetic retinopathy, anaemia, Hemoglobin, diabetes

INTRODUCTION

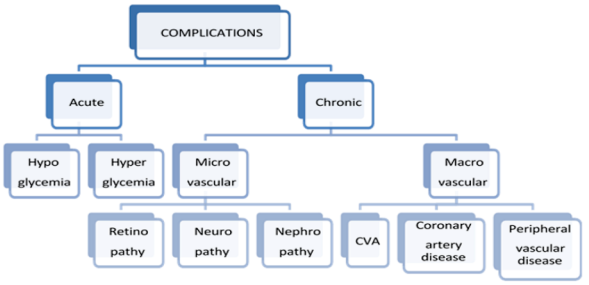
A nation's degree of development may be determined by looking at its proportion of independent people as well as the nutritional state of its populace. The poor nutrition of the typical Indian has a significant impact on his health. Anaemia is a serious public health issue since it affects a large number of people, especially those who are in their prime working years. Individuals who do not have diabetes are less prone to suffer from anemia than those who have it.[1]. Patients with diabetes also have more severe and earlier onset anaemia than those with renal impairment from other causes [2]. The guidelines of the World Health Organization (WHO) suggest looking into anaemia when the haemoglobin level is less than 12 g/dl in females and less than 13 g/dl in males. [3]. This categorization states that anaemia affects 23% of individuals with type 1 or type 2 diabetes.[1]

There is a strong correlation between gender and the frequency of anaemia in the general population.[4] The physiological variations between men and women make this group more prone to anaemia. However, little is known about the relationship between gender and diabetes-related problems, including anaemia, which has been connected to the development and course of both microvascular and macrovascular complications of diabetes[5]. Some examples of macrovascular issues are peripheral vascular, brain, and cardiovascular diseases. The microvascular effects include diabetes retinopathy, diabetic nephropathy, and diabetic neuropathy. Retinopathy is believed to be the main cause of blindness in diabetics. Individuals with diabetes have a 25-fold increased risk of blindness compared to those without the condition. Diabetic retinopathy is sixth among the leading causes of blindness in India. There are now significant issues with the degree of retinopathy's detrimental impacts on eyesight prevention, diagnosis, and therapy. Diabetes mellitus is a metabolic disease characterized by hyperglycaemia, which can be caused by insufficient insulin production, action, or both. It was also possible to see progressive macrovascular and microvascular issues. Type 2 diabetes is on the rise everywhere in the world and a major concern for public health in India. One of the most common diseases in India is diabetes mellitus, which can be attributed to a sedentary lifestyle, heredity, and other factors.Diabetic retinopathy is more frequent in older adults (relative risk highest in range30-60 years). The risk factors for vision loss include age, the severity of retinopathy, the duration of diabetes, the presence of proteinuria, and hyperglycaemia [6,7,8].The current observational study aimed to ascertain the incidence of anaemia in individuals with type-2 diabetes and its impact on the presence and severity of diabetic retinopathy in both male and female patients who had examinations at our tertiary care centre [9,10,11,12,13].

Methodology

Aim of the study is to study the association between anaemia and diabetic retinopathy. And the objectives are to estimate the prevalence of anaemia in patients with Type 2 diabetes mellitus, to establish association between anaemia and presence of diabetic retinopathy. It is a hospital based prospective cross-sectional study. The study is carried out from July 2020 to July 2022 in Type 2 Diabetes patient with Diabetic retinopathy. Data was collected after approval from Ethics Committee, B.J. Medical College. This study will be carried out in department of ophthalmology, M and J Institute of ophthalmology (Government medical College), Civil Hospital, Ahmedabad. Consecutive sampling method adopted, the entire subject meeting the criteria of inclusion were included in study. The study is carried out for 200 patients.

The inclusion criteria were Patients having diabetic retinopathy and who gave consent. The exclusion criteria were patients who does not give consent for the examination or unwilling for follow-up, Pediatric patients, Anemia due to chronic kidney disease and blood loss.



After taking into consideration the inclusion and exclusion criteria, type 2 diabetes patients whose having diabetic retinopathy enrolled for our study. An excel sheet was used to assemble, tabulate, and gather data. Qualitative data were expressed as percentages in numbers. The standard deviation and mean were used to express quantitative data. The statistical analysis was conducted using IBM, SPSS, Inc.'s SPSS 26.0 version of software. A value of less than 0.05 is regarded as statistically significant. Ethical Committee Clearance was taken before starting the study. Written and informed consent was taken from all patients who participated in the study. At the M&J Institute of Ophthalmology, prospective observational research was carried out in a hospital setting. Every patient involved in the research had their best corrected visual acuity (BCVA), non-contact tonometry (NCT), both eyes dilated with phenylephrine and tropicamide, and their fundus examined using slit lamp biomicroscope and indirect ophthalmoscopy. DR data were used to determine the worldwide clinical diabetic retinopathy disease severity scale's classification of mild, moderate, severe, and proliferative retinopathy. Using a colorimetric hemoglobinometer and the capillary technique, haemoglobin was estimated. Haemoglobin levels below 13 mg/dl for men and <12 mg/dl for women were considered anaemia. Anaemia profiles, comprising blood levels of iron, ferritin, and transferrin, should be performed on all participants in order to assess the degree of diabetic management. Every individual had measurements of their FBS, PP2BS, and HbA1c. Recently, the Early Treatment of Diabetic Retinopathy Study (ETDRS) classification has been regarded as the "gold standard" for many years due to its ability to predict the risk of progression to proliferative disease and vision loss. In numerous clinical investigations, the ETDRS stereoscopic seven-field (7F) has become the accepted imaging and grading protocol for determining the diabetic retinopathy (DR) severity score. To the best of our knowledge, there is no published literature comparing montage and stereoscopic 7F. Six classes areidentified from the DDR DR images:proliferative DR, mild non proliferative DR, moderate non proliferative DR, severe non proliferative DR, andungradable. The first database that represents the Indian population is called the Indian Diabetic Retinopathy Image Dataset, or IDRiD for short. The two main types of diabetic retinopathy (DR) are proliferative and non proliferative, which are distinguished by the presence or absence of aberrant new blood vessels that emerge from the retina. The Early Treatment of Diabetic Retinopathy Study (ETDRS) has unveiled the ETDRS chart, a standardized visual acuity (VA) testing chart. It makes use of 14 lines with a logarithmic progression of 5 Sloan letter optotypes per line.

RESULTS AND DISCUSSION

We registered 200 patients based on the exclusion and inclusion criteria from October 2021 to October 2022, all of whom had diabetic retinopathy. We measured haemoglobin level with severity of diabetic retinopathy in our study as well as associated factors.

Table: 1: Study of 200 patients as per their age group

Age Group	Frequency	Percent
20-30	1	0.5
31-40	6	3.0
41-50	31	15.5
51-60	87	43.5
61-70	75	37.5
Total	200	100.0

The average age in our study was 58.09 ± 8.23 years. In our study maximum patients were the age group 51-60 years followed by the age group 61-70 years. Least number of patients were found in 20-30 years group.

Table 2: Study of 200 patients according to their Gender and results of haemoglobin amongst them.

Gender	Frequency	Percent	Haemoglobin
Female	109	54.5	6.98 ± 1.90
Male	91	45.5	9.02 ± 2.60
Total	200	100.0	p-value <0.0001

Out of 200 patients, 54.5% were males whereas 45.5% were females observed in our study. Haemoglobin was significantly lower among females compared to males in Diabetic retinopathy affected patients. (p=<0.0001).

Table 3: Result based on the Duration of Diabetes

	Mean	S. D
Duration of Diabetes	9.82	6.02

Overall mean duration of diabetes was 9.82 ± 6.02 years

Table 4: Results for 200 patients on study of Other Systemic Illness

	Number of Cases	Percentage
Hypertension	86	43
Ischemic Heart Disease	11	5.5
Hypothyroidism	5	2.5

In our study, 43% had hypertension, 5.5% had ischemic heart disease and 2.5% had Hypothyroidism.

Table 5: Results of patients on the base of Visual Acuity

Visual acuity	RE	LE
< 6/60	41	59
6-60 – 6/18	98	93
>6/18	61	48
Total	200	200

In our study, majority of patient had visual acuity with 6-60 – 6/18 than visual acuity <6/60 and >6/18.

Table 6: Results of Fundus Findings: for patients

	RE		LE	
	Case	%	case	%
MILD NPDR	37	18.5	42	21
MODERATE NPDR	63	31.5	60	30
SEVERE NPDR	45	22.5	37	18.5
PDR	55	27.5	61	30.5

In our study, Moderate NDPR cases were higher in right eye whereas PDR cases were higher in left eye of patients.

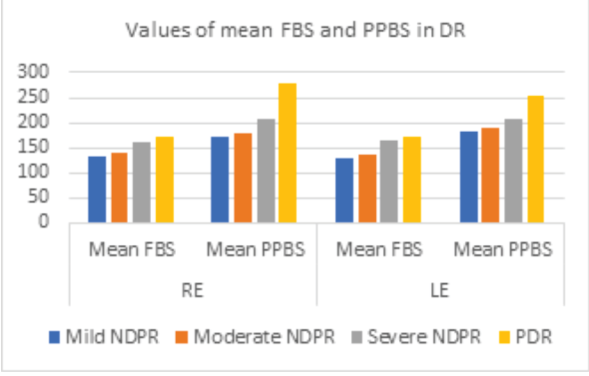


Chart no.1: Results of FBS and PPBS in mg/dl Based on Diabetic Retinopathy: We were observed that FBS and PP2BS was higher in PDR cases whereas FBS and PP2BS was lower in mild NPDR cases.

Table 7: Results of HbA1c in mmol/mol Based on Diabetic Retinopathy

	RE		LE	
	Mean	S. D	Mean	S. D
Mild NDPR	6.83	0.34	7.12	1.01
Moderate NDPR	7.41	0.49	7.40	0.55
Severe NDPR	7.56	0.74	7.64	0.76
PDR	7.88	1.46	7.67	1.25

We were observed that HbA1c was higher in PDR cases whereas HbA1c was lower in mild NPDR cases.

Table 8: Result of Ferritin in micrograms/litter and Transferrin in mg/dl Based on Diabetic Retinopathy

	RE		LE	
	Mean Ferritin	Mean transferrin	Mean Ferritin	Mean transferrin
Mild NDPR	116.43	291.16	120.69	291.88
Moderate NDPR	123.75	283.87	122.05	282.15
Severe NDPR	124.53	269.84	127.38	268.19
PDR	131.36	266.55	128.33	268.02

We observed that Ferritin was higher in PDR cases whereas Ferritin was lower in mild NPDR cases. Ferritin was significantly higher among PDR cases compared to NPDR cases. (p=0.0040)

We observed that transferrin was lower in PDR cases whereas transferrin was higher in mild NPDR cases. Transferrin had no

significant relationship between NPDR and PDR cases. (p=0.0520)

Table 9: Results of Iron in mcg/dl and Hemoglobin in g/dl based on Diabetic Retinopathy

	RE		LE	
	Mean Iron	Mean Haemoglobin	Mean Iron	Mean Haemoglobin
Mild NDPR	92.22	10.14	93.07	10.09
Moderate NDPR	82.56	8.75	79.93	8.96
Severe NDPR	75.89	6.85	75.43	6.83
PDR	73.96	6.32	75.41	6.02

We observed that serum iron was lower in PDR cases whereas iron decreased respectively from mild to severe cases of NDPR cases. Serum iron had not significant relationship between PDR and NDPR cases. (p=0.0700). We observed that Haemoglobin was lower in PDR cases whereas it decreased respectively from mild to severe cases of NDPR.

Haemoglobin was significantly lower among PDR cases compared to NPDR cases (p=<0.0001) It has been found that 14–48% of DM patients had anemia.[14-16] In people with diabetes mellitus, anaemia is thought to be a separate risk factor for the onset and advancement of cardiovascular problems, heart failure, chronic renal disease, and DR [21-31]. Anaemia is more common and more severe in DM patients with any level of glomerular filtration than in non-DM patients with the same renal function. [16,20,23]

Younger age, low serum albumin, high glycosylated haemoglobin, diabetic neuropathy, and low haemoglobin have all been linked to an increased risk of developing a more severe type of DR (high risk proliferative DR) and vision loss. The cross-sectional All-India Ophthalmological Society DR Eye Screening Study, which examined 6218 people in 2014, revealed a 21.7% prevalence of DR. [27] Urban (18.0%) versus rural (10.8%) prevalence was found in the Sankaran Nethra Laya DR Epidemiology and Molecular Genetics Study Report 2 (SN-DREAMS 2), which was carried out in Chennai [28]. The causes of and connections between anaemia and diabetic retinopathy were also demonstrated by SN DREAMS, Padmaja Kumar et al.56 in type 2 diabetes patients. Anaemia is a risk factor for the development of diabetic retinopathy. Therefore, we want to investigate the relationship between anaemia and diabetic retinopathy. Of the instances of diabetic retinopathy in this research, 42% are NDPR cases and 58% are PDR patients.

According to research by Yanfeng Li and colleagues, there is a higher risk of progression to VTDR, PDR, and DME in cases of mild and moderate/severe anaemia. Our results were similar in a way that patients with PDR had lower haemoglobin levels than those with NPDR, (p value significant <0.0001). We found that, in our study, females had more anaemia than males (p<0.0001). Additionally, the majority of the patients in our research were found to be anaemic. However, there was no difference in the anaemia observed in men and women beyond the fifth decade. The literature indicates that one of the potential causes might be the start of menopause in women at this age.

We found in our study that the severity of diabetic retinopathy increased in tandem with increases in fasting blood glucose levels and HbA1c. Matsushita Y. et al. observed that there was a 4.87-fold increase in the severity of retinopathy with an increasing fasting glucose level.[29]He discovered that the FPG's area under the ROC curve was 0.735 and the HbA1c's was 0.837. By comparison, only two research [30,31] have indicated that FPG is a better indication than HbA1c. We also saw comparable outcomes, with the severity of diabetic retinopathy increasing with rising HbA1c or FBS values, respectively. In our investigation, we found that while serum iron and transferrin were trending downward, the severity of diabetic retinopathy increased in tandem with an increase in ferritin values.

The results of Acton's study [32] revealed a substantial correlation between serum ferritin levels and fasting blood sugar levels, as well as a constant difference between serum ferritin levels in patients with diabetes and those in good health. Transferrin and iron levels decreased as the severity of diabetic retinopathy increased, according to Elis A. et al.'s research [33]. In a similar vein Serum iron was also found to be lower in PDR cases (p value 0.0700) while serum transferrin was found to be greater in NPDR cases (p value 0.0520) in our study. As DR severity increases, lower serum iron and transferrin levels imply that DR is impacted by anaemia severity. Ferritin levels in PDR patients were notably greater in our investigation than in NPDR cases. Our study's results were comparable to those of studies conducted by Li Zhou et al.[34] and Elis A. et al.[33] Since serum ferritin is an inflammatory biomarker, elevated levels of serum ferritin in PDR patients can be explained by the interaction of endothelial dysfunction, oxidative stress, and inflammation in diabetic retinopathy.

In our investigation, we found that in comparison to moderate and mild NDPR cases, severe anaemic patients were more frequently reported in PDR and severe NDPR cases. More long-term studies are needed in the near future, even though this work and other research have demonstrated the link between anaemia and diabetic retinopathy.

CONCLUSION

The current study looks at the connection between anaemia and diabetic retinopathy. The study's average age was 58.09 ± 8.25 years. When compared to men, females' haemoglobin levels were much lower. While haemoglobin and HbA1c were considerably reduced in PDR patients, FBS and PP2BS were significantly greater. We found that when DR severity increases, transferrin and serum iron levels fall. PDR sufferers had noticeably increased serum ferritin levels. Diabetic retinopathy has been shown to be significantly influenced by anaemia in both its development and progression. Patients with anaemia were more often female.

Anaemia has been discovered to be often linked to diabetic retinopathy, and there is a correlation between higher severity of diabetic retinopathy and reduced blood oxygen carrying capacity as measured by haemoglobin concentration. These results must have practical ramifications, such as efforts to better regulate diabetes patients' haemoglobin concentrations, especially when there is severe damage and substantial ischemia. For this reason, it is best to identify, treat, and avoid anaemia in individuals with diabetic retinopathy. The function of treating anaemia in DR will be clarified by prospective research on anaemia correction.

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