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Assessment of anaemia and hyperglycaemic status in progression of diabetic retinopathy along with macular changes: A case control study

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ABSTRACT

Background: Diabetes-related visual impairment is preventable through control measures. As diabetic retinopathy and maculopathy lack effective treatment, prevention is key. This study examines glucose, HbA1c, and hemoglobin to assess their impact on disease development and severity.
Materials and Methods: Study includes 100 case (diabetic retinopathy) and 100 control (diabetes without retinopathy)subjects. Further, case group was subdivided into subgroups according to its severity and depending on the presence of maculopathy. Thereafter, values of different renal parameters were compared between these sub groups.
Result: The mean FBS and PPBS values significantly correlate with diabetic retinopathy (DR) severity (P<0.001 for FBS, P=0.012 for PPBS). Uncontrolled diabetes compounds DR risk. All very severe NPDR and PDR patients had HbA1c >7.0. No significant relationship between HbA1c and DR severity (P=0.302) was found. Elevated HbA1c in cases (P<0.001) underscores hyperglycemia's role. CSME, F/PP blood sugar, and HbA1c show no significant correlation. DR group has higher anemia likelihood (P=0.001), increasing with severity (P=0.017). Hemoglobin's relation to CSME is statistically insignificant.
Conclusion: Elevated FBS, PPBS, and HbA1C levels in diabetic retinopathy (DR) cases link hyperglycemia to DR development. Severity correlates with these parameters. HbA1C rises notably in severe NPDR and PDR. Anemia risk increases, but CSME shows no significant correlation. Monitoring biochemistry is vital due to limited DR treatment options.

1. Introduction

Diabetes is an endocrinopathy caused by insulin secretion, action, or both. Long-term hyperglycemic state causes nerve, eye, heart, and blood vessel dysfunction. Diabetic retinopathy (DR), the most prevalent microvascular condition, may cause substantial vision loss.[1,2] Diabetic retinopathy causes 3%–7% of Asian blindness, according to WHO.[3] Diabetic retinopathy causes 3.5% of blindness in India and affects 18% of diabetes patients.[4] A research in south India found diabetic retinopathy in 1.78% of diabetics.[5,6]

Non-proliferative and proliferative diabetic retinopathy are the main types. Increased vascular permeability causes mild to moderate NPDR, then severe to extremely severe NPDR with vascular closure. Growth of new blood vessels on the retina and post-vitreous surface indicates PDR risk.[7] Diabetic maculopathy causes vision loss owing to macular oedema. Preventing diabetic retinopathy or maculopathy is preferable than treating it, which has a dismal prognosis.

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Thus, risk factors for DR and CSME (Clinically significant macular oedema) must be identified and controlled to prevent future vision loss.

The UKPDS and DCCT clinical trials found a strong association between uncontrolled diabetes and diabetic retinopathy progression, but the pathophysiology that causes microvascular damage in hyperglycaemia is unknown.[8,9] UKPDS and DCCT clinical investigations have shown biochemical routes for diabetic retinopathy in hyperglycemic patients. These include increased polyol pathway flux, oxidative stress, increased expression of growth factors like VEGF and IGF-1, haemodynamic changes, activation of the diacylglycerol- (DAG-)PKC pathway, accelerated AGE formation, RAAS activation, and subclinical inflammation and leukostasis.[10–13]

The process by which diabetic retinopathy loses pericytes early is uncertain. Since retinal capillary pericytes have aldose reductase but endothelial cells do not, the sorbitol pathway may be involved. This adequately explains pericyte loss in retinal microcirculation and elsewhere. Another research suggests that persistent hyperglycemia or galactosemia may specifically affect pericyte viability, leading to apoptosis.[14]

Anaemia may be a risk factor since retinal tissue needs less oxygen.15 Singh et al.16 observed spontaneous microaneurysm closure in type 1 diabetics with nutritional anaemia after anaemia correction and metabolic management.[15] In the ETDRS, low haematocrit independently predicted high-risk PDR and visual impairment.[16] Even after controlling for serum creatinine, proteinuria, and other diabetes prognostic factors, a Finnish study found that subjects with a haemoglobin level of less than 12 g/dl had a two-fold higher odds ratio of having any retinopathy. In addition, DR patients with low haemoglobin levels had a fivefold greater risk of serious retinopathy.

DM-related visual handicap is a major public health issue that may be prevented. Controlling the aforementioned parameters may prevent diabetes-related visual loss. Our research aims to determine how glycemic management and anaemia affect diabetic retinopathy and maculopathy.

2. Materials and Methods

This year-long case-control study conducted at KPC Medical College & Hospital and Techno India DAMA Healthcare & Medical Centre involved 200 participants. The case group comprised 100 patients with diabetic retinopathy categorized into subgroups based on severity and maculopathy presence. Controls included 100 age-matched diabetic patients without retinopathy. Sample size was convenient.

2.1. Exclusion criteria included

1. Patients who have had an episode of chronic inflammatory syndrome, alcoholism or malnutrition will not be included in the study.
2. Non-diabetic cases of retinopathy (e g infective cause of retinal dystrophy, trauma, toxic maculopathy, ARMD.
3. Subjects not willing for consent

After ethical approval and authorization, data collecting began utilising a pre-designed and proven routine. Interviews, clinical exams, anterior segment biomicroscopic evaluations, and lab tests were done. Written agreement was acquired, and topical medicine dilated pupils. Slit lamp biomicroscopy and direct and indirect ophthalmoscopy were used for detailed fundoscopy. Patients having retinopathy in at least one eye were studied by DR grade and maculopathy presence. Blood was analysed using SPSS 20. Normal distribution data were analysed using independent 't' tests and One-Way ANOVA, with a 5% significance level ($p<0.05$).

3. Results

In this research, 40 of 100 patients had mild NPDR, 33 moderate, 12 severe, 4 extremely severe, and 11 PDR. 31 of these 100 individuals had CSME on fundus examination. The study group had a significantly higher mean FBS value (151.78±54.23) compared to the control group (108.12±21.44) (P<0.001). The mean PPBS value in case (219.32±80.39) was substantially higher than control group (172.23±40.24) with P<0.001.16 patients in the case group had ideal HbA1c levels (<6.5), whereas 60% of the control group (60 out of 100) had optimal levels. Most patients in the case had HbA1c >7.0, 67 out of 100. 12 patients (12%) in control group were above. A higher HbA1c score is substantially linked to the case group (P<0.001). This research found that 14% of the control group had Hb% <10, whereas 35% of the case group did. Thus, diabetic retinopathy increases anaemia risk (p=0.001).

Table 1 shows the mean value of FBS and PPBS has significant correlation with severity of diabetic retinopathy (P<0.001 for FBS and P=0.012 for PPBS).

Table 2 shows the mean value of FBS in study group had no significant correlation (P=0.193) with development of CSME. The mean value of PPBS in patients with CSME (209.33±72.50) was lower than patients without CSME (223.60±83.67) but without any statistical significance. (P=0.649).

Table 3 shows the distribution of HbA1c values among 5 stages of retinopathy. All patients of very severe NPDR and PDR had HbA1c value >7.0 (suboptimal). But still there was no statistically significant relationship between HbA1c and severity of diabetic retinopathy (P=0.302).

Table 1: Mean values of the Glucose parameters in subjects categorized according to severity of diabetic retinopathy

	Mild NPDR		Moderate NPDR		Severe NPDR		Very Severe NPDR		PDR			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	p Value	Significance
FBS	134.15	39.05	153.24	60.91	171.58	69.97	160.75	85.28	186.64	25.30	<0.001	Significant
PPBS	200.15	63.85	219.24	89.44	232.58	111.21	291.75	82.37	248.45	46.11	0.012	Significant

Table 2: Comparison of Glucose parameters depending on presence of CSME

	Negative		Positive			
	Mean	Std. Deviation	Mean	Std. Deviation	p Value	Significance
FBS	156.24	54.04	141.37	54.14	0.193	Not Significant
PPBS	223.60	83.67	209.33	72.50	0.649	Not Significant

Table 3: Glycemic control and severity of diabetic retinopathy

		Mild NPDR	Moderate NPDR	Severe NPDR	Very Severe NPDR	PDR	p Value	Significance
Hba1c	Optimal (<6.5)	8(20)	5(15.15)	3(25)	0(0)	0(0)	0.302	Not Significant
	Fair (6.5-7)	9(22.5)	7(21.21)	1(8.33)	0(0)	0(0)		
	Suboptimal (>7.0)	23(57.5)	21(63.64)	8(66.67)	4(100)	11(100)		
Total		40(100)	33(100)	12(100)	4(100)	11(100)		

Table 4: Distribution of patients in 2 subgroups of case (with CSME and without CSME) as per HbA1c value

		Negative	Positive	p Value	Significance
Hba1c	Optimal(<6.5)	10(14.49)	6(19.35)	0.683	Not Significant
	Fair(6.5-7)	13(18.84)	4(12.9)		
	Suboptimal(>7.0)	46(66.67)	21(67.74)		
Total		69(100)	31(100)		

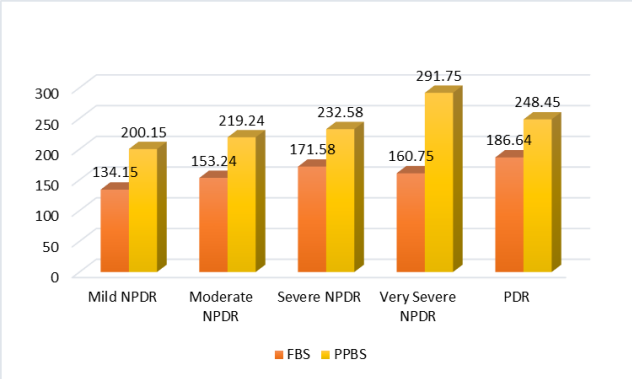

Fig. 1: Comparison of mean value of FBS & PPBS in 5 sub grades of diabetic retinopathy

Table 4 shows the distribution of HbA1c values among 2 sub group of case (with CSME and without CSME). There was no statistically significant relationship between HbA1c and CSME(P=0.683).

Table 5 shows with the severity of diabetic retinopathy the chance of developing anemia increased significantly (P=0.017). In mild and moderate NPDR distribution of patients with Hb<10 was 20% and 33.33% respectively. But in severe, very severe NPDR and in PDR this distribution was more (58.33%, 75%, 54.55% respectively).

Table 6 shows distribution of patients with Hb%<10 was slightly lower in CSME negative patients(34.29%) than CSME positive (36.67%) but without any statistical significance (P=0.946).

4. Discussion

Westernisation, weight gain, and sedentary lifestyle have increased diabetes in India. Due to the growing incidence of diabetes, problems including diabetic retinopathy are rising.

There is significant evidence that long-term glycaemic management delays DR development and slows progression. Most subjects in this research had poor glycaemic control, indicating high FBS and PPBS levels. Diabetic retinopathy severity is significantly correlated with FBS and PPBS mean values (P<0.001 for FBS and P=0.012 for PPBS). 16% of case patients had optimum HbA1c (<6.5), whereas 60% of control group patients (60 out of 100) did. All extremely severe NPDR and PDR patients exhibited poor HbA1c values. HbA1c did not significantly affect diabetic retinopathy severity

Table 5: Distribution of patients based on haemoglobin level among various grades of diabetic retinopathy

		Mild NPDR	Moderate NPDR	Severe NPDR	Very Severe NPDR	PDR	p Value	Significance
HB%	<10	8(20)	11(33.33)	7(58.33)	3(75)	6(54.55)	0.017	Significant
	≥10	32(80)	22(66.67)	5(41.67)	1(25)	5(45.45)		
Total		40(100)	33(100)	12(100)	4(100)	11(100)		

*() signifies in percentage

Table 6: Distribution of patients based on haemoglobin level among two sub groups of case (with CSME and without CSME)

		Negative	Positive	p Value	Significance
HB%	<10	24(34.29)	11(36.67)	0.946	Not Significant
	≥10	46(65.71)	19(63.33)		
Total		70(100)	30(100)		

(P=0.302). Higher mean HbA1c values in case compared to control (P<0.001) suggest that hyperglycemia levels impact the onset and progression of DR. In the Diabetes management and Complication Trial (DCCT), intensive glycaemic management significantly reduced retinopathy incidence and development.[17] At 12 years follow-up, stringent glucose management decreased the chance of a two-step retinopathy change by 21% in the UKPDS.[18] The Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) likewise believed blood glucose levels caused diabetic retinopathy.[19] The CURES Eye Study found a linear relationship between DR and poor glycemic control.[20] The mean FBS value in the study group did not correlate with CSME development (P=0.193). The link between HbA1c and CSME was not significant (P=0.683). Ong Ming Jew et al. found that HbA1c increased the risk of CSME.[21] However, this investigation found no significant correlation between CSME and glycaemic control.

The research found that 14% of the control group had Hb% <10, whereas 35% of the case group did. Anaemia is more likely in diabetic retinopathy (P=0.001). Anaemia risk increased with diabetic retinopathy severity (P=0.017). CSME negative patients had a little lower Hb%<10 distribution (34.29%) than CSME positive patients (36.67%), however the difference was not statistically significant (P=0.946) Bahar A, Kashi Z, Amiri AA et al. found that diabetics with retinopathy had lower haemoglobin and more anaemia.

5. Conclusion

Mean FBS, PPBS, and HbA1C levels were significantly higher in case group than control group, confirming that hyperglycaemia affects DR onset and progression. These metrics significantly correlated with diabetic retinopathy severity. HbA1c values spike to inadequate levels only in extremely severe NPDR and PDR patients. Anaemia is also common in diabetic retinopathy patients.

Despite the previous paragraph, CSME does not affect F/PP Blood Sugar, HbA1C, or Hb%. Diabetic retinopathy, especially diabetic maculopathy, has no cure and a bad prognosis. Better to prevent its growth. Thus, metabolic markers must be monitored to track diabetic retinopathy and maculopathy severity and prevent morbidity.

6. Source of Funding

None.

7. Conflict of Interest

None.

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