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Correlation of blood sugar and HbA1C levels in different stage of diabetes retinopathy: A hospital based prospective study

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***Abstract*---**Objectives: This present study was to evaluate the different parameters and correlation of blood sugar and HbA1C levels for the development of retinopathy in type 2 diabetes mellitus patients. Methods: A complete assessment, general physical examination and routine haematological investigations were performed to all patients. A complete fundus examination was done with the help of direct and indirect Ophthalmoscope. Biochemical investigations (Blood Sugar-Fasting and Post Prandial, HbA1C level) were performed. Patients were called for follow up after 1 month, 3 months and 6 months. Results: A total of 100 patients of diabetes retinopathy were enrolled in this study. Most of the cases 67(67%) were males with age group of 51-60 years. out of 191 eyes, most of the cases 72(37.7%) had PDR. Rest cases had 58(30.36%) severe NPDR, 46(24.08%) moderate NPDR, 9(4.71%) others and 6(3.14%) mild NPDR. HbA1c levels of the most of the cases 94(49.21%) had 6.5-8.5. Most of the patients 170(89.53%) of DR had blood glucose level > 140 mg% on PP. Fasting blood sugar level in most of the patients 97(50.78%) had >125 mg %. Conclusions: Middle age males with type 2 diabetes mellitus are more preponderance to retinopathy. Both FBS and PPBS are important to achieve optimal glycemic control, but PPBS has a closer association with HbA1c and better predictor for overall glycemic control compared to FBS. The severity of diabetic retinopathy stages increased with duration as level of HBA1C increased. Hence, increased levels of blood sugar and HbA1c are the major risk factors for the development of retinopathy in type 2 diabetic mellitus patients. Thus, it is advisable

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to include HbA1c as the investigative tool in the evaluation of diabetes mellitus, so that we can predict the development of diabetic retinopathy and treat them in early stages.

***Keywords*---**diabetic retinopathy. HbA1c, post prandial glucose level, Fasting glucose level.

Introduction

Diabetes mellitus (DM) is a metabolic disease defined by elevated blood glucose [1]. The exponential rise in the prevalence of diabetes and hence its complications has been a cause of great concern to health care providers worldwide. Prevalence of diabetic retinopathy varies widely among different ethnicity. It ranges from 29% seen in Blue mountain eye study to 50.3% in the Winconsin epidemiologic study of diabetic retinopathy [2,3]. Diabetic retinopathy is a potentially blinding complication of diabetes mellitus. Reasons for loss of vision are diabetic maculopathy and complications of proliferative diabetic retinopathy (PDR) such as vitreous hemorrhage, tractional retinal detachment, and neovascular glaucoma. By 2030 developing countries will face an increase by 69% and industrialized countries by 20% of the number of patients with diabetes compared to 2010[4]. For Africa more than 18 million, according to some estimations even 24 million, diabetic patients are predicted for the year 2030[4,5].

Type II diabetes is most dominant form of diabetes contributing for almost 90% of total burden of diabetes [5]. Diabetic retinopathy is a cause of visual loss on a global scale. The pathology is closely associated with vascular, glial, and neuronal components of the diabetic retina. Treatments for the vision-threatening complications of diabetic macular edema and proliferative diabetic retinopathy have greatly improved. As per recent studies, diabetes markedly impacts the retinal neurovascular unit and its interdependent vascular, neuronal, glial, and immune cells [6]. Laboratory and clinical evidence show that, microvascular changes, inflammation and retinal neurodegeneration may contribute to diabetic retinal damage in the early stages of diabetic retinopathy [7].

Clinically, diabetic changes in the retina can be divided into two stages: non-proliferative diabetic retinopathy and proliferative diabetic retinopathy. Early stage of DR is represented by NPDR, wherein the pathology is increased vascular permeability and capillary occlusion. During this stage, the fundus findings include microaneurysms, hemorrhages and hard exudates while the patients may be asymptomatic4. Proliferative diabetic retinopathy is an advanced type of DR, the patients may experience severe vision impairment. This stage is characterized by neovascularization [7]. However, in addition to hyperglycemia, other factors like hypertension, dyslipidemia, and particularly the genetic load, have an immense influence on the severity and clinical course of diabetic retinopathy (DR) [8]. Objectives of our study was to evaluate the correlation of blood sugar and HbA1C levels in diabetes retinopathy patients.

Materials and Methods

This study was conducted in Department of Ophthalmology of SKMCH, Muzaffarpur, Bihar India during a period from November 2021 to May 2022. Entire patients signed an informed consent approved by institutional ethical committee of Shri Krishna Medical College and Hospital (SKMCH), Muzaffarpur, Bihar, India was sought. All patients attended Ophthalmology outpatient department were enrolled in this study. A complete assessment, general physical examination and routine haematological investigations were performed to all patients. Assessment of visual acuity [Distant and near vision]. Fundus examination was done by using Direct and Indirect ophthalmoscope (Using 20D lens). Biochemical investigations (Blood Sugar- Fasting and Post Prandial, HbA1C level) were performed. Follow up: we had routinely followed up all the patients after 1 month, 3 months and 6 months. Any therapeutic intervention in the form of retinal laser, intravitreal anti VEGF/Steroid injection, or V-R surgery if required were done according to the need of patient. At every follow up all the below Investigations like assessment of visual acuity, biochemistry investigations(FBS,PPBS and HbA1c), fundus Examinations were done.

Observations

A total of 100 patients of diabetes retinopathy were enrolled in this study. Most of the cases 67(67%) were males. Majorities of patients 40(40%) were in age group of 51-60 years. Out of 200 eyes, 191 eyes had diabetic retinopathy.

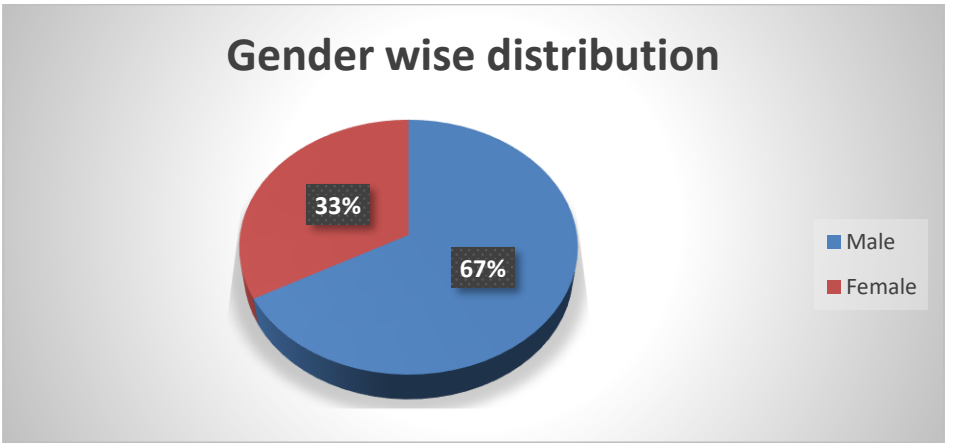

Figure 1. Gender wise distribution of diabetic retinopathy patients

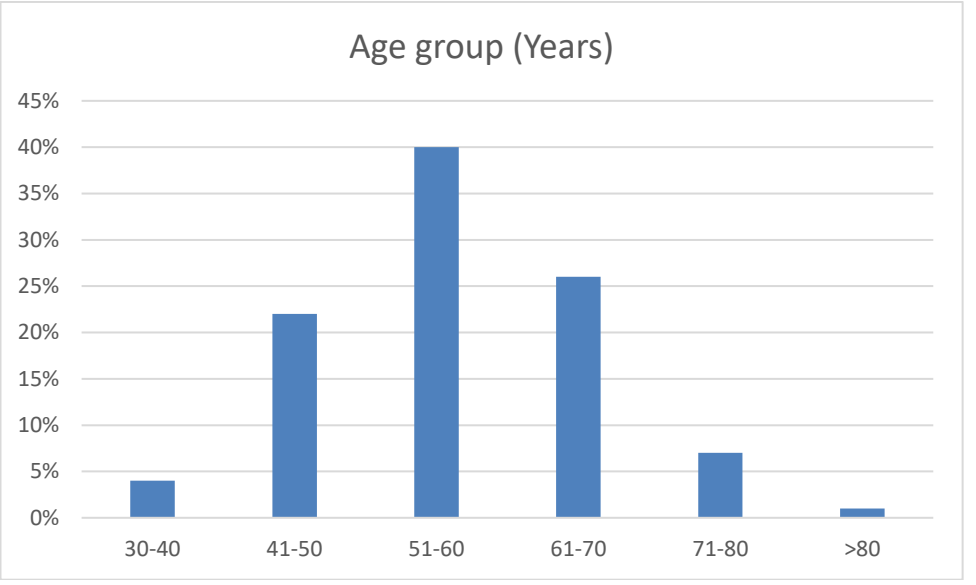

Figure 2. Age wise distribution of diabetes retinopathy patients.

In this study, out of 191 eyes, majorities of cases (36.65%) had PDR. 32.46% had severe NPDR. Duration of diabetes retinopathy in most of the cases (38.74%) had 0 to 5 years.

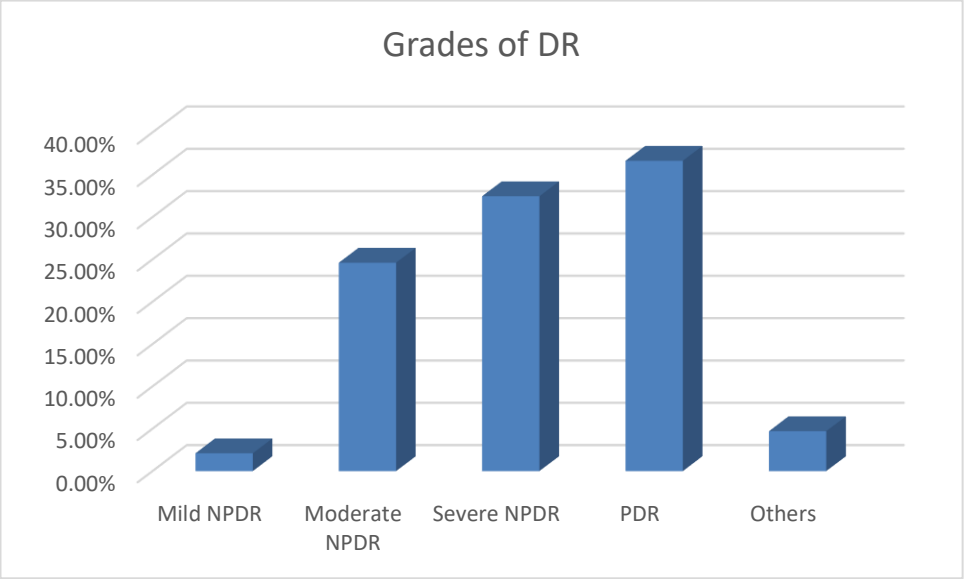

Figure 3. Different grades of diabetes retinopathy patients (N=191)

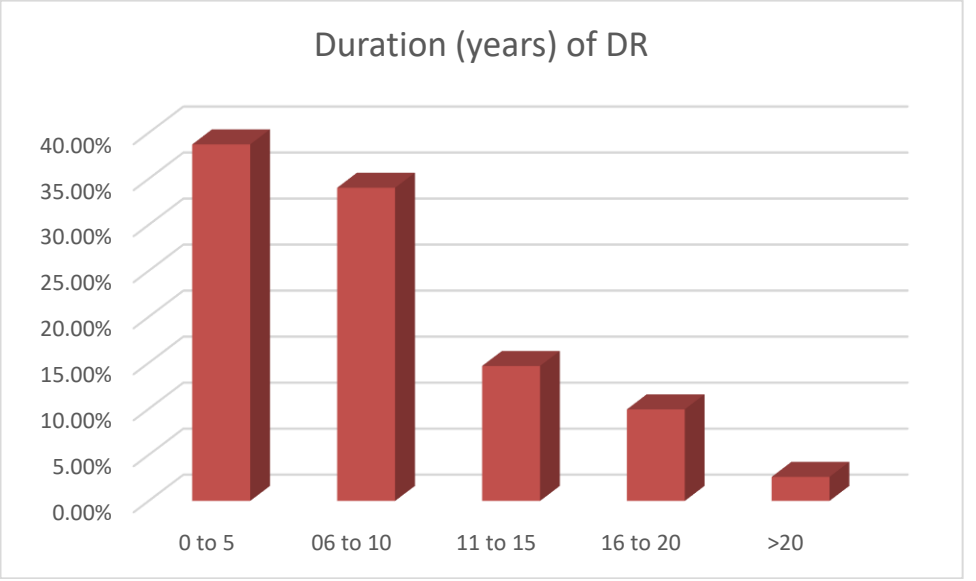

Figure 4. Duration of diabetes retinopathy

Table 5
Association between HbA1C and diabetic retinopathy stages

HbA1C level	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Others	Total
Upto 5.7	0	1	2	1	0	4(2.09%)
5.7-6.4	3	5	13	5	0	26(13.61%)
6.5-8.5	3	30	31	28	2	94(49.21%)
8.5-11.2	0	10	12	38	7	67(35.07%)
Total	6(3.14%)	46(24.08%)	58(30.36%)	72(37.7%)	9(4.71%)	191(100%)

In this present study, out of 191 eyes, most of the cases 72(37.7%) had PDR. Rest cases had 58(30.36%) severe NPDR, 46(24.08%) moderate NPDR, 9(4.71%) others and 6(3.14%) mild NPDR. HbA1c levels of the most of the cases 94(49.21%) had 6.5-8.5.

Table 6
Association between Post-prandial glucose level and diabetes retinopathy stages

PP (mg%)	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Others	Total
Upto 140	2	5	11	2	1	21(10.99%)
>140	4	41	47	70	8	170(89.53%)
Total	6(3.14%)	46(24.08%)	58(30.36%)	72(37.7%)	9(4.71%)	191(100%)

In this present study, most of the patients 170(89.53%) of DR had blood glucose level > 140 mg% on PP. Fasting blood sugar level in most of the patients 97(50.78%) had >125 mg %.

Table 7
Association between Fasting glucose level and Diabetic retinopathy stages

Fasting glucose (mg%)	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Others	Total
Upto 125	5	26	30	27	6	94(49.21%)
>125	1	20	28	45	3	97(50.78%)
Total	6(3.14%)	46(24.08%)	58(30.36%)	72(37.7%)	9(4.71%)	191(100%)

Discussions

Diabetic retinopathy (DR) is a chronic progressive, potentially sight-threatening disease of the retinal microvasculature, and is associated with prolonged hyperglycemia and other conditions linked to diabetes mellitus such as hypertension [9], hyperlipidemia, dysregulated hormones levels and growth factors. These induce a cascade of biochemical and physiological changes that lead to neurovascular damage in the retina through oxidative stress, inflammation and apoptosis [10]. High blood sugar levels (hyperglycemia) in diabetes mellitus is considered the most causative etiology for DR [11]. A hyperglycemia environment in the retina can stimulate the accumulation of inflammatory mediators and reactive oxygen species (ROS), which induce the activation of microglia cells [12]. D2

In this present study, majorities of patients (40%) of diabetic retinopathy were seen in age 51-60 years. Most of the cases (67%) were males**.** These findings are relevant to previous studies done on Diabetic Retinopathy screening, where most of participants were middle aged patients with median age of 58.1years and 54 years respectively [13]. In this study, out of 191 eyes, majorities of cases (36.65%) had PDR. 32.46% had severe NPDR. Duration of diabetic retinopathy in most of the cases (38.74%) had 0 to 5 years. The duration of diabetes was shown to be significantly different between the two diabetic groups, namely, the diabetic subjects without retinopathy, and those with mild-to-moderate NPDR. There are many studies that suggest that the duration of diabetes is closely linked to the prevalence of diabetic retinopathy (DR) [14,15]. According to the World Health Organization (2016), less than 5% of patients will have retinopathy at diagnosis, while its prevalence can rise up to 40%–50% after ten years. After 20 years of diabetes, most patients with type 1 diabetes, and 60% of patients with type 2 diabetes have some degree of DR. The duration of diabetes is significantly associated with the development and severity of DR, with the odds ratio (OR) ranging from 1.00 to 8.74 in a study conducted by Lim et al. [16].

In our study out of 191 eyes, most of the cases 72(37.7%) had PDR. Rest cases had 58(30.36%) severe NPDR, 46(24.08%) moderate NPDR, 9(4.71%) others and 6(3.14%) mild NPDR. So, this shows that with increase in biochemical

parameters, there is also increase in severity of Diabetic Retinopathy grade. However, we had also proved that with increase in duration of DM, number of patients of Diabetic Retinopathy also increased. Consistently high blood glucose levels can lead to macrovascular and microvascular complication that will eventually affect patient's quality of life. The costs related to diabetes include increased use of health services, disability and productivity loss, which can be a considerable burden to the patient, families and society [13].

Our results correlate well with the study of Sabanayagam et al. [17] which mentioned that in subjects with mild-to-moderate NPDR, HbA1c levels in the range of 7.0%–7.9% and ≥8.0% had a nine-fold and 30-fold higher prevalence, respectively, than in subjects with HbA1c ≤ 6.9%. In their study, the optimal cut-off points with maximum sensitivity and specificity to detect mild to moderate DR were 6.6% and 7.0%, and the AUCs were 0.899 and 0.904, respectively. The two cut-off points of sensitivity and specificity were in agreement with other studies which recommended the HbA1c cut-off points of ≥6.5% and 7.0%, respectively [18,19]. However, another two studies showed different cut-off points, which were in the range of 6.0% to 7.0% [20,21]. In our present study, HbA1c levels of the most of the cases 94(49.21%) had 6.5-8.5. Raman R et al [22] studied, a strong association of HbA1c with sight 14 threatening Diabetic retinopathy (P-value < 0.001).

In our study, most of the patients 170(89.53%) of DR had blood glucose level > 140 mg% on PP. Fasting blood sugar level in most of the patients 97(50.78%) had >125 mg %. Our study revealed that both FBS and PPBS are important to achieve optimal glycemic control, but PPBS has a closer association with HbA1c and better predictor for overall glycemic control compared to FBS, which shows similarity to that of the study done by Rosediani [23] and Monnier et al. [24] Based on the findings of this study, it is recommended that stringent measures must be adopted to control modifiable risk factors associated with development and progression of DR in order to reduce the morbidity related with this disease. Another study examining 2,551 Chinese patients reported that the prevalence of diabetic retinopathy significantly increased in patients with HbA1c levels of 6.4% or higher [25]. A study of 3,010 Iranian patients reported that the optimal cut-off point of HbA1c was 6.2% [26]. Our study revealed that the retinopathy significantly increased when the HbA1c level exceeded 6.8%, which is slightly higher than the values reported by the other studies. A study done by Leske et al, [27] in Barbodose eye study, they found that every 1% increase in HbA1C from baseline was associated with a >2-fold risk of DR, upto 4 years of follow up. Many other epidemiological studies also confirm that uncontrolled sugars which is assessed by HbA1c is important risk factor for DR [28,29].

Conclusions

This present study concluded that the middle age males with type 2 diabetes mellitus are more preponderance to retinopathy. Both FBS and PPBS are important to achieve optimal glycemic control, but PPBS has a closer association with HbA1c and better predictor for overall glycemic control compared to FBS. The severity of diabetic retinopathy stages increased with duration as level of HBA1C increased. Hence, increased levels of blood sugar and HbA1c are the

major risk factors for the development of retinopathy in type 2 diabetic mellitus patients. Thus, it is advisable to include HbA1c as the investigative tool in the evaluation of diabetes mellitus, so that we can predict the development of diabetic retinopathy and treat them in early stages.

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