

A prospective study on effect of controlled hba1c levels and normotension in the development of diabetic retinopathy in type 2 diabetics

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Abstract

Aim: To determine the importance of HbA1C levels and normotension in predicting the development of diabetic retinopathy and the relationship between them.

Method: Prospective clinical study comprising of a group of 125 diabetics above 40 years visiting for routine eye checkup and clinically diagnosed diabetic retinopathy including both out-patient and in-patients at Department of Ophthalmology, KIMS, Bangalore. Men and women >40years with type 2 diabetes mellitus with HbA1C levels <7.5% and non-hypertensives (<140mmHg systolic and <90mmHg diastolic pressure) were included. Patient's HbA1C levels and blood pressure were measured. The diabetic retinopathy status was classified according to the ETDRS system. Statistical analysis was done.

Results: At 3rd month follow up, the mean HbA1C levels was 7.25±0.22. At the end of 12th month, the mean HbA1C was 7.42±0.11. At baseline, in group A 8.8% showed mild NPDR and 1.6% moderate NPDR. At the end of the study it was 8.8% mild NPDR, 1.6% moderate NPDR. No further progression was seen in a year span. All values showed statistical significance and absence of hypertension also goes in favour of mild diabetic retinopathy changes.

Conclusion: HbA1C levels and systemic hypertension are the two major modifiable risk factors in the development and progression of diabetic retinopathy.

Key words: HbA1C, Hypertension, diabetic retinopathy.

Introduction

Diabetes mellitus is an important cause of avoidable blindness in both the developing and the developed countries. Patients with diabetic retinopathy (DR) have 25 times more likely chances to become blind than non-diabetics [1].

It is estimated that diabetes mellitus affects 4 per cent of the world's population, almost half of whom have some degree of DR at any given time [2]. India is already being termed as the "Diabetic capital of the world", with the number of patients with diabetes expected to rise from 40.9 million, at present, to a whopping 60.9 million by 2025 [3]

According to the latest World Health Organization (WHO) report, India has 31.7 million diabetic subjects, and the number is expected to increase to a staggering 79.4 million by 2030 [4].

The prevalence of diabetic retinopathy in India is 18% [5]. It is documented that more than 77% of patients who survive for over 20 years with DM are affected by retinopathy [6].

The risk of DR is mainly attributable to HbA1c, systemic hypertension and diabetes duration [7]. Glycated haemoglobin is a commonly used marker for monitoring glycaemic control. Multiple studies have frequently shown HbA1c to be an independent risk factor for diabetic retinopathy. A higher HbA1c is associated with both increased incidence as well as progression of diabetic retinopathy [8].

Patients with type 1 diabetes may show evidence of retinopathy as early as 5 years after the onset of diabetes, and almost all patients will show varying degrees of retinopathy 20 years after the onset of diabetes.

Diabetic retinopathy may even be present at the time of diagnosis of type 2 patients, consistent with the usually long duration of subclinical hyperglycemia in such patients and more than 60% of type 2 diabetic patients will have some degree of retinopathy after 20 years of onset of diabetes [9]. The introduction of insulin by Banting and Best seemed to offer the ideal therapy for the treatment of diabetes. The first oral hypoglycemic agents were introduced in the mid 50's. However, despite the continual use of these agents, diabetic retinopathy still develops and continues to cause morbidity and vision loss.

One of the main difficulties in establishing whether there is a relationship between the degree of hyperglycemia and the long term complications of diabetes is the lack of a reliable and objective method for assessing diabetic control. The clinician at present has no quick and simple way of ascertaining whether his patient is well controlled or of telling whether modification of the therapeutic regimen has altered control for better or worse.

Blood glucose and urine glucose testing and urine ketone testing provide useful information for day to day management of diabetes. However these tests cannot provide the patient and the health care team with a quantitative and reliable measure of glycemia over an extended period of time. These tests also demand patient compliance and frequent assessments.

Recordings of glycated proteins, primary hemoglobin and serum proteins have added a new dimension to the assessment of glycemia. With a single measurement of each of these parameters, we can get a quantitative estimate of the average glycemia over weeks and months, there by complementing day to day testing.

Expert opinion recommends A1c testing at least two times a year in patients who have stable glycemic control [10]. HbA1C has been known to be a marker to assess the long term control of diabetes mellitus. Studies in the past have shown that HbA1C levels could be correlated with the severity of diabetic retinopathy as well.

At the age of 45 almost 40% of patients with type 2 diabetes are hypertensive, the proportion increasing to 60% by the age of 75. Hypertension increases the high risk of cardiovascular disease associated with type 2 diabetes and is also a risk factor for the development of retinopathy [12, 6, 11].

A prospective study reported that systolic BP (SBP) reduction may improve DR and diastolic BP (DBP) increase may worsen DR [7]. It has been observed that prevalence of hypertension is higher in diabetic subjects than in the general population and as it also plays a major role in the progression of diabetic retinopathy, so tight control of hypertension is mandatory [13].

Therefore this study helps us to know the association between HbA1C levels and systemic blood pressure in development and progression of diabetic retinopathy.

Methods

Prospective clinical study comprising of a group of 125 diabetics above 40 years visiting for routine eye check up and clinically diagnosed diabetic retinopathy including both out-patient and in-patients at Department of Ophthalmology, KIMS, Bangalore. Men and women >40years with type 2 diabetes mellitus with HbA1C levels <7.5% and non-hypertensives

(<140mmHg systolic and <90mmHg diastolic pressure) were included.

Exclusion criteria

- Age of the subjects below 40 years.
- Subjects with history of ocular infection.
- Subjects with history of ocular trauma.
- Subjects with complications due to ocular surgeries.
- Subjects with CSME (of any cause), macular degenerations, retinal detachments, glaucoma.
- Subjects with history of congenital/hereditary ocular disorders.
- Subjects who were not willing to give informed consent for the study.

Relevant data about the patient's diabetes was taken:

- Age of onset of diabetes (first diagnosed)
- Duration of diabetes
- History regarding patient's glycemic control.
- History of hypertension was collected.

A general physical examination was performed followed by a complete ophthalmological examination.

The fundii were evaluated by

- Direct ophthalmoscopy
- Indirect ophthalmoscopy
- Slit lamp biomicroscopy using +90Dlens.
- Fundus fluorescein angiography was performed only when clinically necessary.

Manual measurement of blood pressure was done.

HbA1C levels were determined in all patients by the Immunoinhibition technique.

In case of patients with asymmetric fundus findings the eye with a more severe grade of diabetic retinopathy was taken into consideration.

Based on the ETDRS criteria, patients were graded according to the severity of their retinopathy.

Results

Table 1: diabetic retinopathy at baseline

	Group A (n=13)
Mild NPDR	11(8.8%)
Moderate NPDR	2(1.6%)
Severe NPDR	0(0%)
Very Severe NPDR	0(0%)
PDR	0(0%)
High risk PDR	0(0%)

In group A, maximum patients had mild NPDR. These were statistically significant. Very severe NPDR and PDR were insignificant at the initial checkup.

Table 2: Diabetic Retinopathy Status

Diabetic Retinopathy Status	Group A (N=13)
3months	
Mild NPDR	11(8.8%)
Moderate NPDR	2(1.6%)
Severe NPDR	0(0%)
Very Severe NPDR	0(0%)
PDR	0(0%)
High Risk PDR	0(0%)
6months	
Mild NPDR	11(8.8%)
Moderate NPDR	2(1.6%)
Severe NPDR	0(0%)
Very Severe NPDR	0(0%)
PDR	0(0%)
High Risk PDR	0(0%)
9months	
Mild NPDR	11(8.8%)
Moderate NPDR	2(1.6%)
Severe NPDR	0(0%)
Very Severe NPDR	0(0%)
PDR	0(0%)
High Risk PDR	0(0%)
12months	
Mild NPDR	11(8.8%)
Moderate NPDR	2(1.6%)
Severe NPDR	0(0%)
Very Severe NPDR	0(0%)
PDR	0(0%)
High Risk PDR	0(0%)

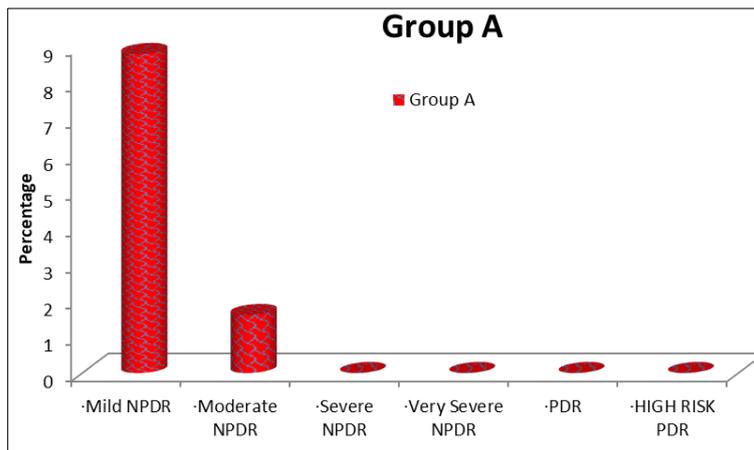


Fig 1: Diabetic Retinopathy status-3 months

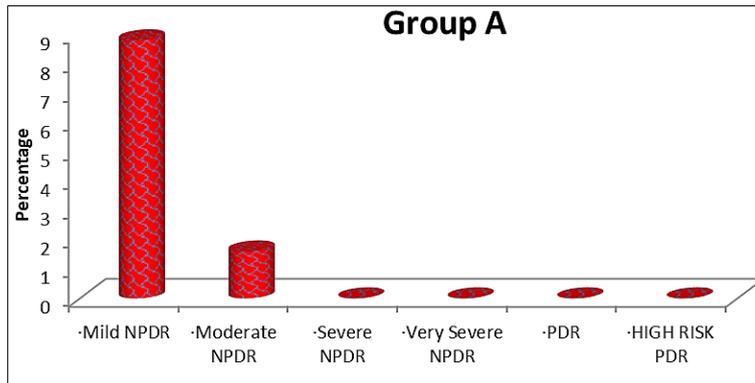


Fig 2: Diabetic Retinopathy Status- 6 months

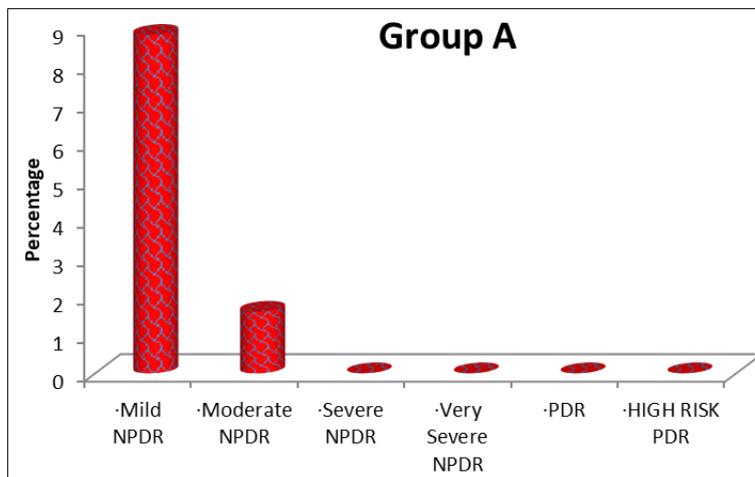


Fig 3: Diabetic Retinopathy Status- 9 months

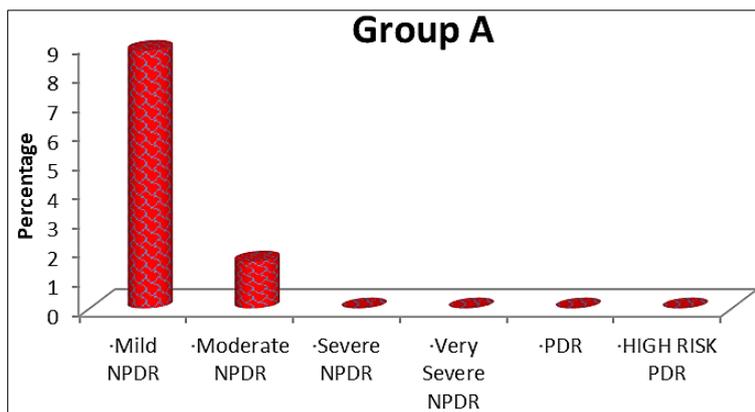


Fig 4: Diabetic Retinopathy Status- 12 months

At first follow i,e at 3months in group A, 8.8% had mild NPDR, 1.6% had moderate NPDR. At the end of 12months it was the same.

Table 3: HbA1c% -Comparison

HbA1c%	Group A (n=13)
3months	7.25±0.22
6months	7.24±0.23
9months	7.30±0.15
12months	7.42±0.11

At 3rd month follow up, the mean HbA1C levels in group A was 7.25 ± 0.22
At the end of 12th month, the mean HbA1C was 7.42 ± 0.11

Discussion

Accuracy about the type and severity of diabetic retinopathy and associated risk factors are of utmost importance in planning a well-planned approach to the public health problem like this sight threatening complication of diabetes. Identifying the patient who may be at high risk of severe retinopathy is important in advising ophthalmic care. Such accurate data are also helpful in planning future studies such as controlled clinical trials of treatment of diabetes and of diabetic retinopathy [14].

This is a prospective study done on 125 patients known diabetics with good HbA1C levels (<7.5%) and no other comorbidities.

HbA1C levels was constantly between 7-7.5% (very good control). These data were significant statistically and it strengthens the fact that the development and progression of DR is mainly influenced by the level of hyperglycemia [15].

Intensive glycemc control was effective in substantially reducing the incidence and progression of retinopathy in the Diabetes Control and Complication Trial (DCCT) group. The UKPDS also showed that intensive glucose control reduced the risk of a two-step change in retinopathy by 21% at 12 years follow up. WESDR also found that risk of retinopathy is related to the control of blood glucose levels. The CURES Eye Study observed a linear trend between prevalence of DR and poor glycemc control [16].

Hypertension has been consistently demonstrated to have a positive association with the development of diabetic retinopathy.

In our study absence of hypertension did not had any additive effect in promoting development and progression of diabetic retinopathy. Patients had very less incidence of diabetic retinopathy (13 patients out of 125). The association with hypertension with the elevated risk of DR was in conformity with other studies [17].

The landmark UKPDS 69 study has showed the importance of blood pressure control in patients with diabetic retinopathy. The authors demonstrated that tight control of blood pressure with a target level of 150/85 mm Hg, rather than loose control of less than 180/105 mm Hg, statistically significantly decreased the development of microaneurysms (relative risk [RR]=0.66; $P < 0.001$), hard exudates (RR=0.53; $P < 0.001$), and cotton-wool spots (RR=0.53; $P < 0.001$) [18].

Conclusion

The present study demonstrated statistically significant correlation between diabetic retinopathy, HbA1C levels. Controlled blood glucose levels was significantly associated with the lesser occurrence of all grades of retinopathy especially severe NPDR, very severe NPDR and PDR. It also showed that absence of hypertension had an additive effect in development and progression of diabetic retinopathy.

- These data can lend additional support to current treatment guidelines recommending aggressive lowering of elevated blood glucose levels and tight blood pressure control among diabetic patients, in addition to its known health benefits in preventing cardiovascular disease, may also lessen ocular morbidity and thereby potentially improving quality of life and vision among patients with type 2 diabetes.
- Good glycemc and blood pressure control remain the most important modifiable risk factors to reduce the risk of progression of diabetic retinopathy and vision loss.

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