

To study the correlation of diabetic retinopathy with glycosylated haemoglobin and body mass index in type II diabetes

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Abstract

Introduction: It is well established that chronic hyperglycaemia is one of the main risk factors for DR. There are variable reports with inconsistent findings of HbA1c values with severity of diabetic retinopathy. Overweight and obesity have become a growing public health problem in affluent societies leading to chronic diseases like diabetes. Some studies have demonstrated relationship between obesity or higher BMI and an increased risk of DR.

Aims and Objectives: To study correlation of diabetic retinopathy with glycosylated haemoglobin and body mass index (BMI) in type II diabetics having diabetes for more than 5 years.

Materials and Methods: Type 2 diabetic patients having diabetes for more than 5 years have been included in this study. We have not included patients with type I diabetes, secondary diabetes or patients who have already taken treatment for diabetic retinopathy. Detailed ophthalmic examination including fundus examination was done for all patients and severity of diabetic retinopathy was noted for every patient. HbA1c value and BMI was measured for every patient. Correlation of DR with HbA1c and BMI was analysed.

Results and Conclusion: Severity of diabetic retinopathy increases as the age and duration of diabetes increases. High BMI was risk factor for development of diabetic retinopathy and severity of DR increases as BMI value increases. Higher HbA1c values were associated with increased risk and severity of diabetic retinopathy.

Keywords: Age, Body mass index, Diabetes mellitus, Fasting blood sugar, Glycosylated haemoglobin, Obesity.

Introduction

Diabetes is a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action or both. Being a very interesting and a complicated problem, diabetes mellitus has been the subject of vigorous studies. Various risk factors have been associated with the disease. Duration of diabetes mellitus is the most important factor. The chronic hyperglycaemia of diabetes is associated with long term damage, dysfunction and failure of different organs especially the eyes, kidneys, nerves, heart and blood vessels.¹ It is well established that chronic hyperglycaemia is one of the main risk factors for diabetic retinopathy. In addition some recent analysis addressed the effect of HbA1c variability on diabetic retinopathy and related outcomes as patient may show a wide variation in their long term glycaemic control despite having similar average HbA1c values.² Other study indicates that long term fluctuation was no independent correlate of retinopathy in type 2 diabetes.³ Due to these inconsistent findings for different outcomes, further studies on the relationship between HbA1c variability and DR are needed. Overweight (body mass index BMI > 25 kg/m²) and obesity (BMI > 30 kg/m²) have become a growing global public health problem with increasing prevalence in affluent societies as well as in developing countries.⁴⁻⁶ It is projected that by 2025 there will be 380 million people with type 2 diabetes and 418 million people with impaired glucose tolerance owing to an increase in obesity, inactivity, life span extension and better detection of the disease.⁷ The evidence supporting a relationship between high BMI and increased risk of DR is inconclusive. Literature supports correlation between high BMI and risk of diabetic

retinopathy but there are isolated reports which don't support these findings.⁸⁻¹⁰ Considering that obesity is becoming increasingly prevalent in today's society and since it can be managed by lifestyle intervention namely nutrition, exercise and education. Studying its impact on diabetic complications has certain logic and benefits.

In developed countries diabetic retinopathy constitutes the leading cause of blindness in working age population¹¹ and has a considerable economic impact on society especially on healthcare systems.¹² Given that proper management of patients with DR we can prevent more than 90% of patients with visual loss. Thus the aim of the present study is to investigate whether BMI, varying HbA1C values influences DR development in type 2 diabetic patients.

Materials and Methods

The aim of our study was to find the relationship of glycosylated haemoglobin and body mass index with the risk of developing diabetic retinopathy in type II diabetic patients with history of diabetes for more than five years. The study was conducted on already diagnosed cases of type II diabetes mellitus patients who attended out patient department or got admitted in the our hospital. Out of these 100 patients, type 2 diabetic patients having diabetes for more than 5 years were taken as cases in our study.

Inclusion Criteria

We included patients with Type II diabetes for more than five years

Exclusion Criteria

Patients with type I diabetes.

Patients with secondary diabetes (acromegaly, cushing syndrome).

Treated cases of diabetic retinopathy.

Patients whose eyes cannot be graded for retinopathy level because of opacities in the media.

All the cases were subjected to following tests and examinations:

1. Detailed history and ocular examination including slit lamp biomicroscopy and indirect ophthalmoscopic examination was done to note any signs of diabetic retinopathy.

2. The anthropometric measurements of the subjects was done. Weight was recorded on the standard weighing scale in erect position, bare feet and with no support.

Height was recorded by asking the patient to stand erect with the straight wall. Head is held in normal position and parallel to the floor with arms relaxed on the sides. Then height was measured with help of marking scale made on upright wall.

Body mass index (BMI) was calculated as:

$$\text{BMI} = \text{Weight (kg)} / \text{Height (m}^2\text{)}$$

3. Fasting venous blood sample was obtained for the determination of HbA1c

4. Dilated fundus examination was done and diabetic retinopathy was staged according to ETDRS classification:

A. Non Proliferative Diabetic Retinopathy (NPDR)

1. Mild NPDR

Presence of only microaneurysm

2. Moderate NPDR

Several retinal haemorrhages (about 20 medium large per quadrant) in 1-3 quadrants or mild IRMA.

Significant venous beading in more than 1 quadrant.

Cotton wool spots.

3. Severe NPDR

Patient will be labelled as having severe NPDR if he has any one of the following findings in the fundus.

i. Micro aneurysms and extensive intraretinal haemorrhages are present in all the four quadrants of the retina.

ii. Venous beading is there in two quadrants of the retina.

iii. IRMA in one quadrant of the retina.

4. **Very severe NPDR** -- Patient will be labelled as having very severe NPDR if he has any two of the following findings in the fundus.

i. Micro aneurysms and extensive intraretinal haemorrhages are present in all the four quadrants of the retina.

ii. Venous beading is there in two quadrants of the retina.

iii. IRMA in one quadrant of the retina.

B. Proliferative Diabetic Retinopathy (PDR)

1. Early PDR

i. When neovascularisation is there on the disc or elsewhere on the fundus without any High Risk Characteristics (HRC).

2. PDR with HRC

High risk characteristics of PDR are as follow:

i. When there is neovascularisation on the disc having diameter of 1/4 to 1/3 of disc area with or without vitreous haemorrhage (VH) or Pre retinal Haemorrhage (PRH).

ii. When there is neovascularisation on the disc having diameter of less than 1/4 disc area with VH or PRH.

iii. When there is neovascularisation elsewhere more than 1/2 disc area with VH or PRH.

3. Clinically Significant Macular Edema (CSME)

It can occur both in NPDR and PDR. It is diagnosed if one of the following three criteria are present.²¹

i. Retinal thickening at the centre of fovea or with in 500 microns of foveal centre.

ii. Presence of hard exudates at the centre of fovea or with in 500 microns associated with the adjacent retinal thickening.

iii. Retinal thickening one disc diameter or larger in size, at least a part of which is within one disc diameter of the foveal centre.

Advanced Diabetic Eye Disease

It is the end result of uncontrolled proliferative diabetic retinopathy. It is marked by complications such as:

1. Persistent vitreous haemorrhage.

2. Tractional retinal detachment.

3. Neovascular glaucoma.

4. All the cases were subjected to routine investigations

After this the data was analysed statistically.

Results and Discussion

Our study was done in a tertiary care hospital which is a government medical college in the state of Punjab. We included 100 diabetic patients. Out of these 41 were males (41%) and 59 were females (59%).

Out of 100 Type 2 diabetic patients 7(7%) fall in <50 years age group, 28(28%) fall in 51-60 years age group, 57(57%) fall in 61-70 years age group and 8(8%) fall in >70 years age group.

Out of 100 patients, 78 diabetic patient had diabetic retinopathy (78%) and 22 diabetic patient does not have diabetic retinopathy (22%).

Among 78 patients, severity of diabetic retinopathy was as:

Mild NPDR – 26 (33.33%),

Moderate NPDR -- 20 (25.64%)

Severe NPDR -- 14 (17.94%)

Very Severe NPDR 11(14.10%)

Proliferative diabetic retinopathy (PDR) -- 7(8.9%)

Body Mass Index (BMI)

Table 1

BMI	Total no of patients	%age
<24.9kg/m ²	39	39%
25-29.9kg/m ²	29	29%
30-34.9kg/m ²	23	23%
>35kg/m ²	9	9%

Out of total 100 patients 39(39%) patient had BMI<24.9kg/m², 29(29%) between 25-29.9 kg/m², 23(23%) between 30-34.9 kg/m², and 9(9%) above 35 kg/m².

Glycosylated Haemoglobin (HbA1c)

Table 2

Glycosylated haemoglobin (HbA1c)	Total no. of patients	% age
<6%	32	32%
6.1%-7.9%	39	39%
8%-9.9%	17	17%
>10%	12	12%

Table 2 shows that out of 100 patients 32(32%) patients fall in group of patients having HbA1c value <6%, 39(39%) fall in group having HbA1c value between 6.1%-7.9%, 17(17%) fall in group having HbA1c value between 8%-9.9% and 12(12%) fall in group having HbA1c value above >10%.

In our study out of 100 patients it was found that 41(41%) patients had duration of diabetes between 5-10 years, 48(48%) patient had 10-15 years duration of diabetes and 11(11%) patient had >15 year duration of diabetes.

Table 3: Association of BMI with diabetic retinopathy

BMI (Kg/m ²)	Patients with DR	Patients without DR
<24.9	23 (59%)	16 (41%)
25-29.9	25 (86.2%)	4 (13.8%)
30-34.9	21 (91.3%)	2 (8.7%)
>35	9 (100%)	0
Total	78	22

$\chi^2 = 14.276$, $df=3$, $p=0.003$, Statistically Significant.

Table 3 shows the association of diabetic retinopathy with the levels of BMI. In our study it was observed that as the level of BMI increases the percentage of subjects having diabetic retinopathy increases. Out of 100 patients 59% of the subjects having BMI<25kg/m² had diabetic retinopathy. 86.2% of the subject having BMI levels between 25-29.9 kg/m² had diabetic retinopathy. 91.3% of the subject having BMI levels between 30-34.4 kg/m² had diabetic retinopathy and 100% of the subjects having BMI >35kg/m² had diabetic retinopathy. A statistically significant relationship was found between BMI and presence of diabetic retinopathy. ($p<0.003$)

We also found association of BMI levels with severity of diabetic retinopathy. It was observed that as level of BMI increases the severity of diabetic retinopathy in patients increases. Among the subjects having BMI level <24.9kg/m², 41% had no diabetic retinopathy, 38.5% had mild NPDR, 15.4% had moderate NPDR, 5.1% had severe

NPDR. Among the subjects having BMI between 25-29.9kg/m², 13.8% had no diabetic retinopathy, 27.6% had mild NPDR, 41.4% had moderate NPDR, 13.8% had severe NPDR and 3.4% had very severe NPDR. Among the subjects having BMI levels between 30-34.9kg/m², 8.7% had no diabetic retinopathy, 13% had mild NPDR, 4.3% had moderate NPDR, 30.4% had severe NPDR, 34.8% had very severe NPDR and 8.7% had PDR. Among the subjects having BMI levels >35kg/m², 11.1% had moderate NPDR, 11.1% had severe NPDR, 22.2% had very severe NPDR and 55.6% had PDR.

Table 4: Association of glycosylated haemoglobin with diabetic retinopathy

Hb1Ac Levels	Diabetic Retinopathy	
	Absent	Present
≤6%	16 (50%)	16 (50%)
6.1%-7.9%	6 (15.4%)	34 (85%)
8% - 9.9%	0	17 (100%)
≥10%	0	11 (100%)
Total	22	78

$\chi^2 = 23.660$, $df=3$, $p<0.001$, Highly Significant.

Table 4 shows the association of diabetic retinopathy with the level of Glycosylated Haemoglobin. There are more chances of having diabetic retinopathy in patients having high value of glycosylated haemoglobin. 50% of the subjects having Glycosylated Haemoglobin <6% had diabetic retinopathy. 85% of the subject having Glycosylated Haemoglobin levels between 6.1%-7.9% had diabetic retinopathy and 100% of the subject having Glycosylated Haemoglobin levels between 8%-9.9% and > 10% had diabetic retinopathy. A statistically significant relationship was found between Glycosylated Haemoglobin and presence diabetic retinopathy. ($p<0.001$)

It was observed that as the duration of diabetes increases, the percentage of subjects having diabetic retinopathy increases. In our study 46.3% of the subjects having duration of diabetes between 5-10 years had diabetic retinopathy while 53.7% of the patients had no diabetic retinopathy. It was found that 100% of the subjects having duration of diabetes between 10-15 years and >15 years had diabetic retinopathy. A statistically significant relationship was observed between diabetic retinopathy and duration of diabetes. ($p<.001$)

Above table shows association of severity of diabetic retinopathy with duration of diabetes. It was observed that as the duration of diabetes increases the severity of diabetic retinopathy increases. Among the subjects having duration of diabetes between 5-10 years, 53.7% of the patients had no diabetic retinopathy, 34.1% had mild NPDR and 12.2% had moderate NPDR. Among the subjects duration of diabetes between 10-15 years 25% had mild NPDR, 31.3% had moderate NPDR, 25% had severe NPDR, 16.7% had

very severe NPDR and 2.1% had PDR. Among the subjects of duration >15 years 18.2% had severe NPDR, 27.3% had very severe NPDR and 54.5% had PDR.

Table 5: Association of FBS levels with diabetic retinopathy

FBS Levels	Diabetic Retinopathy	
	Absent	Present
80-120mg/dl	18 (45%)	22 (55%)
120-160mg/dl	4 (12.9%)	27 (87.1%)
160-200mg/dl	0	19 (100%)
>200mg/dl	0	10 (100%)
	22	78

$\chi^2 = 22.005$, $df=3$, $p<0.001$, Highly Significant.

There was association of diabetic retinopathy with FBS (Fasting Blood Glucose) levels. It was observed that as the FBS level increases the percentage of subjects having diabetic retinopathy increases. In our study it was found that subjects having FBS level between 80-120mg/dl 55% had diabetic retinopathy and 45% had no Diabetic Retinopathy. Among subjects having FBS levels between 120-160mg/dl, 87.1% had diabetic retinopathy and 12.9% had no Diabetic Retinopathy. Among subjects having FBS levels between 160-200mg/dl and FBS levels >200mg/dl 100% of the subjects had diabetic retinopathy. A statistically significant relationship was observed between FBS levels and presence of diabetic retinopathy ($p<.001$)

We also found association of FBS levels with severity of diabetic retinopathy. It was observed that as level of FBS increases the severity of diabetic retinopathy increases. Among the subjects having FBS level between 80-120mg/dl, 45% had no diabetic retinopathy, 40% had mild NPDR, 12.5% had moderate NPDR, 2.5% had severe NPDR. Among the subjects having FBS between 120-160mg/dl, 12.9% had no diabetic retinopathy, 32.3% had mild NPDR, 35.5% had moderate NPDR, 16.1% had severe NPDR and 3.2% had PDR. Among the subjects having FBS levels between 160-200mg/dl, 21.1% had moderate NPDR, 31.6% had severe NPDR, 42.1% had very severe NPDR and 5.3% had PDR. Among the subjects having FBS levels >200mg/dl 20% had severe NPDR, 30% had very severe NPDR and 50% had PDR.

Type 2 diabetes mellitus is emerging as epidemic in developed as well as developing countries and is a multiorgan disease affecting almost each and every system in the human body. In developed countries, working age population is becoming visually disable by sight threatening complications of diabetic retinopathy.¹³ more than 50% of patients having diabetes for more than 20 years develop diabetic retinopathy.¹⁴ In our study, the mean duration of diabetes was 12.95+/-6.68. Out of 100 patients in our study

78 had diabetic retinopathy and 22 had no diabetic retinopathy, this percentage of patients having diabetic retinopathy is more than the previous studies because in our study we have taken the patients who have history of diabetes for more than 5 years and moreover our patients are the mostly referred patients as our hospital is a tertiary care centre. It has been reported many times in the literature that prevalence and progression of diabetic retinopathy is directly related to the duration of diabetes mellitus. More is the duration of diabetes; more are the chances of developing diabetic retinopathy.¹⁵ We also got similar type of results in our study. According to our study, the chances of diabetic retinopathy increases with increase in duration of diabetes, DR was significantly positively correlated with diabetes duration ($P<0.001$). Our study also shows that as the duration increases the severity of diabetic retinopathy increases. Our study also find poor glycaemic control as a risk factor for development and severity of diabetic retinopathy ($p<0.001$). In our study the patients are divided into four groups having different Hb1Ac levels and it was found that 50% of the patients having Hb1Ac levels <6% had no diabetic retinopathy while 50% had diabetic retinopathy, while all the patients having HbA1c values more than 10% had diabetic retinopathy. The long-term benefits of improving the glycaemic control on DR have been explored by studies like the Diabetes Control and Complications Trial (DCCT), the Stockholm Interventional Study, and the United Kingdom Prospective Diabetes Study UKPDS).¹⁶

The results of our study also demonstrated a positive correlation between BMI and diabetic retinopathy ($p<0.003$), BMI and severity of retinopathy ($p<0.001$). In our study, in patients having BMI value of < 24.9kg/m², 16 (41%) had no diabetic retinopathy and 23 (59%) had diabetic retinopathy and in patients having BMI value of > 35kg/m², 9 (100%) had diabetic retinopathy. It was also found that high BMI values were related to increased severity of retinopathy, 5 (55.6%) patients having BMI value >35kg/m² had Proliferative Diabetic Retinopathy. There are various hypotheses which explain the association of higher body mass index and development of diabetic retinopathy but none have been proved so far. Researchers have explained the role of platelet dysfunction, aldose reductase activity and vasoproliferative parameters such as vascular endothelial growth factor (VEGF) in the progression of diabetic retinopathy in patients with high BMI values.¹⁷⁻¹⁹ Now a days, pathogenesis of diabetic retinopathy is revolving around vascular endothelial growth factor (VEGF), Various anti VEGF drugs are being used intravitreally to treat diabetic retinopathy. Moreover people have reported higher values of VEGF in vitreous of eyes with proliferative diabetic retinopathy.²⁰ Similarly, obese individuals having high BMI have more serum levels of angiogenic factors including VEGF which may be due to oxidative stress.²¹ These similar findings support the association of obesity with proliferative diabetic retinopathy.

Conclusion

We conclude from our study that high values of body mass index (BMI) are associated with the development and moreover progression of diabetic retinopathy. These results indicate that if we try to adapt measures to reduce body mass index of diabetic patients, we can delay onset or even decrease the severity of diabetic retinopathy in these patients. Thus one of the sight threatening complication of diabetes can be prevented by simple weight reduction management programmes. This will be new area of interest which has not been studied in detail so far.¹⁷ Modifications in the life style including weight reduction programmes have been advised to prevent and treat diabetes and its associated complications including diabetic retinopathy.²²⁻²³

Conflict of Interest: None.

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