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Original Article

Magnesium Levels in Diabetes Mellitus: A Prospective Study

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Abstract

Background: The prevalence of retinopathy is strongly related to the duration of diabetes. After 20 years of diabetes, nearly all patients with Type 1 diabetes and >60% of patients with Type 2 diabetes have some degree of retinopathy. Diabetic retinopathy which poses a serious threat to vision should be diagnosed at an earlier stage.

Objective: The aim was to study diabetic patients and derive a relation or role of serum magnesium and glycosylated hemoglobin (HbAlc) levels in diabetic retinopathy.

Materials and Methods: A total of 100 patients who were admitted and fulfilled the inclusion/exclusion criteria were evaluated by history, physical examination, and lab tests.

Results: Serum magnesium levels are compared in the 2 groups. The mean serum magnesium level in Group 1 is 2.01 with a standard deviation of 0.28. In Group 2, the mean level is 1.86 with a standard deviation of 0.40. Using paired *t*-test, the *P* value was calculated which came to be 0.035. A value <0.05 is considered significant. Glycosylated levels are compared in the 2 groups in the study. The mean HbAlc level in Group 2 is 8.8 with a standard deviation of 2.06, while the mean HbAlc level in Group 1 is 8 with a standard deviation of 1.99. Paired *t*-test was used to calculate the *P* value.

Conclusion: Thus, from the *P* value, we can suggest that there is a significant correlation between serum magnesium level and diabetic retinopathy and hence a role of magnesium in diabetic retinopathy can be proved, and A *P* = 0.011 is derived which shows that there is a significant correlation between glycosylated hemoglobin and diabetic retinopathy. Thus, glycosylated hemoglobin can be implicated in the pathogenesis of diabetic retinopathy.

Key words: Diabetes mellitus, Diabetic retinopathy, Glycosylated hemoglobin, Magnesium, Microvascular changes

INTRODUCTION

Diabetes is one the most common non-communicable disease worldwide and has become one of the leading causes of death in most developed countries. Diabetes and its complication "diabesity" is the price paid due to increase in the life-expectancy coupled with concomitant increase in dietary affluence and decrease in physical activity.

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Today "diabetegras" (which refers to Type 2 diabetes mellitus [DM]) accounts for more than 95% of all cases of diabetes worldwide. In comparison "diabete maigre" (which refers to Type 1 DM) is seen in a small number of cases.

Type 2 DM is one of the major contributors of mortality and morbidity and has a marked social, psychological and economical implication, thus creating much interest in the medical fraternity.

It is estimated that more than 300 million people will have diabetes by 2025. India has the dubious distinction of having the maximum number of diabetics in the world which stands at 44 million today. Hence, India is called the "diabetic capital of the world."

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Aretacus of Alexandria described diabetes as "to pass through" while Shushruta of India called it large volumes of sweet urine." The understanding of the disease was in the infant stage in the 19th century after which the course and complications of the disease were better recognized.

Doctors in the 19th century were therapeutically impotent, the main role being as those who describe symptom complexes and the natural history of the disease.

The long duration of diabetes is associated with both micro- and macrovascular compilations. Diabetic retinopathy is a highly specific vascular complication of both Type 1 and Type 2 diabetes. Eduard von Jaeger is credited with the first description of diabetic retinopathy in his "atlas of disease of the ocular fundus." In 1879,[1] Stephen Mackenzie and Sir Edward Nettleship found microaneurysms in flat preparations of the retina. Nettleship went on to identify new vessels and the beaded appearance of the retinal veins.[2] The full picture of diabetic retinopathy was described in 1890 by Julius Hirschberg and classified into three types. "Central punctuate diabetic retinitis" (characterized by spots and hemorrhages). "Hemorrhagic" and "pigmentary."[3] Hirschberg was the first to claim that this retinopathy was specific to diabetes.

The prevalence of retinopathy is strongly related to the duration of diabetes. After 20 years of diabetes, nearly all patients with Type 1 diabetes and >60% of patients with Type 2 diabetes have some degree of retinopathy diabetic retinopathy poses a serious threat to vision.

In the Wisconsin Epidemiologic Study of Diabetic Retinopathy, 3.6% of younger-onset patients (aged <30 years at diagnosis, an operational definition of Type 1 diabetes) and 1.6% of older-onset patients (aged >30 years at diagnosis, an operational definition of Type 2 diabetes) were legally blind. In the younger-onset group, 86% of blindness was attributable to diabetic retinopathy. In the older-onset group, where other eye diseases were common, one-third of the cases of legal blindness were due to diabetic retinopathy. Overall, diabetic retinopathy is estimated to be the most frequent cause of new cases of blindness among adults aged 20-74 years.

Aims and Objectives

- To show a correlation between magnesium and diabetic retinopathy.
- To study the possible role of low magnesium in the microvascular change in DM leading to retinopathy.
- To study the role of glycosylated hemoglobin in diabetic retinopathy.

MATERIALS AND METHODS

The aim was to study diabetic patients and derive a relation or role of serum magnesium and glycosylated hemoglobin levels in diabetic retinopathy.

The study comprised 100 diabetic patients that were seen in the outpatient department or admitted in tertiary care hospital.

The patients were divided into 2 groups depending on the presence of absence of diabetic retinopathy.

The control group (Group A) consisted of 50 patients who are diabetic and without any diabetic retinopathy changes. Out of 50 patients, 17 are male and 33 are female.

The control group (Group B) consisted of 50 patients who are diabetic with diabetic retinopathy changes. Out of 50 patients, 29 are male and 21 are female.

The diagnosis of DM is made by standard criteria recommended by American Diabetes Association (ADA).

Inclusion Criteria

Diagnosed diabetic cases on regular treatment with oral hypoglycemic agents or insulin or both.

Exclusion Criteria

1. Hypertension
2. Chronic diarrhea
3. Alcoholism
4. Chronic use of diuretics
5. Reduced renal function.

Diabetic retinopathy was assessed using direct and indirect ophthalmoscopy. Serum magnesium levels were done on automated Dade Behring machine. Glycosylated levels were done by Nycocard kits, which is a boronate affinity assay.

RESULTS

In this study, out of 100 patients, 46 are male and 54 are female. In Group 1, out of 50 patients, 17 are male and 33 female, while in Group 2, 29 are male and 21 are female (Tables 1 and 2).

Out of the 100 patients, 10 are below 40 years of age, 18 are between 41 and 50 years, 35 are between 51 and 60 years, 34 are between 61 and 70 years, and 3 are above 70 years. The maximum prevalence of diabetes was seen in between the ages 51 and 70 years which signifies age as an important risk factor for diabetes (Table 3).

Family history is a well-known risk factor of diabetes. In my study, out of 100 patients, 40 patients had a family history of diabetes in either father, mother, brother, sister, and grandfather or grandmother while 60 patients did not have a family history of diabetes (Table 4).

Table 1: Gender wise: Distribution of 100 patients with diabetes mellitus±retinopathy

Gender	Group 1	Group 2
Male	17	29
Female	33	21
Total	50	50

P=0.33, Chi-square test

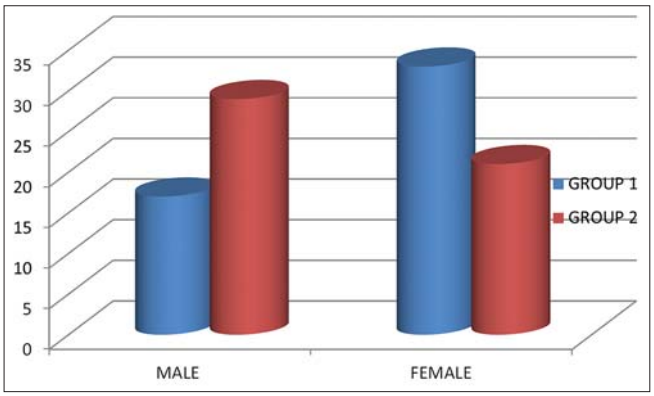
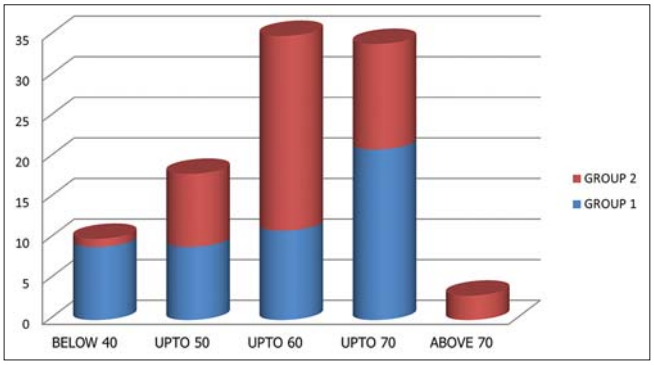


Table 2: Distribution of patients according to age group

Age (years)	Group 1	Group 2
Mean	54.1	57.5
Standard deviation	12.1	9.4
Range	29.70	38-80
Total	50	50

Age (years)	Group 1	Group 2	Total
Below 40	9	1	10
Up to 50	9	9	18
Up to 60	11	24	35
Up to 70	21	13	34
Above 70	0	3	3
Total	50	50	100

P=0.11, Paired *t*-test



Serum magnesium levels are compared in the 2 groups. The mean serum magnesium level in Group 1 is 2.01 with a standard deviation of 0.28. In Group 2, the mean level is 1.86 with a standard deviation of 0.40. Using paired *t*-test, the *P* value was calculated which came to be 0.035. A value <0.05 is considered significant. Thus, the from the *P* value, we can suggest that there is a significant correlation

Table 3: Distribution of patients according to number of diabetic years

Number of diabetic years	Group 1	Group 2	Total
Below 5	18	8	26
Up to 10	23	18	41
Up to 20	7	16	23
Up to 30	2	6	8
Above 30	0	2	2
Total	50	50	100

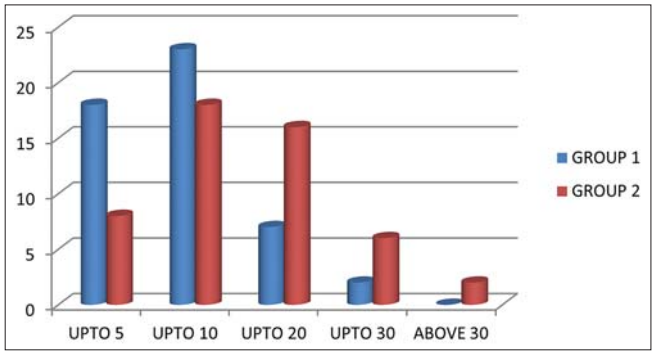
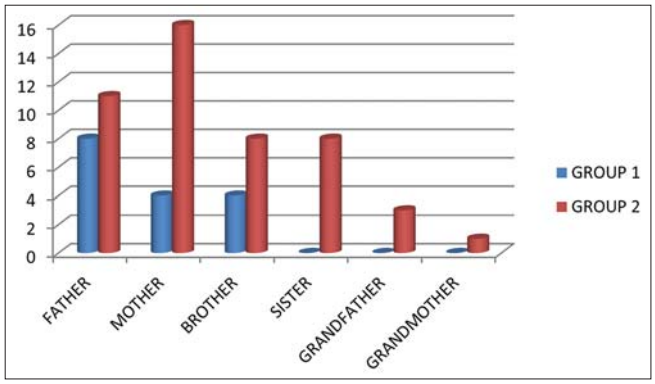


Table 4: Distribution of patients according to family history of diabetes

Family history	Group 1	Group 2	Total
Father	8	11	19
Mother	4	16	20
Brother	4	8	12
Sister	0	8	8
Grandfather	0	3	3
Grandmother	0	1	1
None	38	22	60
Total	50	50	100



between serum magnesium level and diabetic retinopathy and hence a role of magnesium in diabetic retinopathy can be proved (Table 5).

Glycosylated levels are compared in the 2 groups in the study. The mean glycosylated hemoglobin (HbAlc) level in Group 2 is 8.8 with a standard deviation of 2.06 while the mean HbAlc level in Group 1 is 8 with a standard deviation of 1.99. Paired *t*-test was used to calculate the *P* value. A $P = 0.011$ is derived which shows that there is a significant correlation between glycosylated hemoglobin and diabetic retinopathy. Thus, glycosylated hemoglobin can be implicated in the pathogenesis of diabetic retinopathy (Table 6).

Fasting sugar level is compared between the 2 groups. A mean FBS of 191.1 is seen in Group 2 with a standard deviation of 93.3 versus a mean level of 155.8 in Group 1 with a standard deviation of 48.8. The $P = 0.02$ by paired *t*-test which is significant showing the significance of elevated fasting sugar levels and occurrence of diabetic retinopathy (Table 7).

Postprandial sugar levels in the 2 groups are compared and a $P = 0.11$ is derived which shows there is no significant correlation between postprandial sugar levels and diabetic retinopathy (Table 8).

Serum creatinine levels are higher in Group 2 as compared to Group 1 with mean value of 0.88 with standard deviation of 0.23 in Group 1 and a mean value of 1.2 with a standard deviation of 1.04 in Group 2. The calculated $P = 0.0086$ is significant establishing a correlation between diabetic retinopathy and serum creatinine levels (Table 9).

In Group 1 (above) and Group 2 (below), the serum magnesium levels were compared with serum creatinine levels. A regression plot was made for their comparison. Since the values in both the graphs fall within the 95% confidence interval a straight line is plotted and no significant correlation is established between the two (Table 10).

Table 5: Comparison of serum magnesium levels in diabetics without retinopathy (Group 1) with diabetic with retinopathy (Group 2)

Serum magnesium	Group 1	Group 2
Mean	2.01	1.86
Median	1.97	1.76
Standard deviation	0.28	0.40
Range	1.6-3.2	1.43-3.14

P=0.035, paired *t*-test

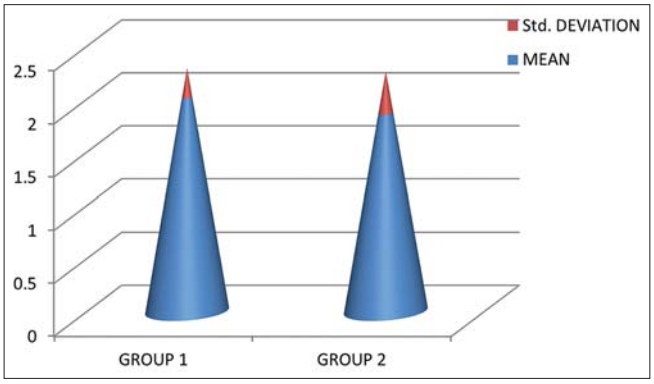


Table 6: Comparison of HbAlc levels in patients without retinopathy (Group 1) and patients with retinopathy (Group 2)

HbAlc	Group 1	Group 2
Mean	8.0	8.8
Median	8.11	8.45
Standard deviation	1.99	2.06
Range	5.6-13.1	6.2-12.2

P=0.011, paired *t*-test

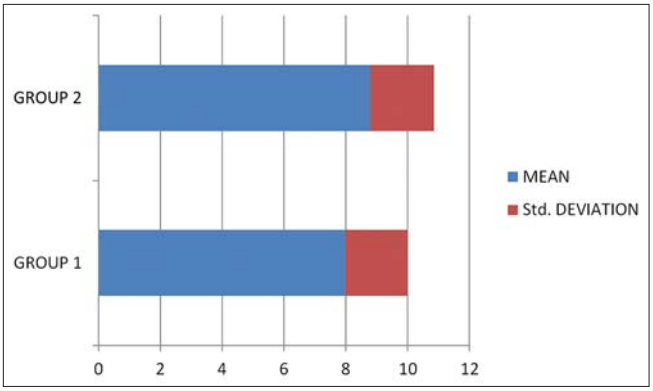
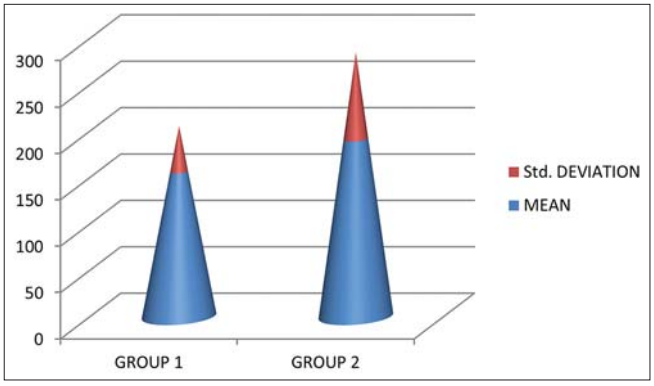


Table 7: Comparison of FBS levels in patients without retinopathy (Group 1) and patients with retinopathy (Group 2)

FBS	Group 1	Group 2
Mean	155.8	191.1
Median	149	167.5
Standard deviation	48.86	93.3
Range	74-304	79-498

P=0.020, paired *t*-test



DISCUSSION

Diabetes is becoming an emerging health problem in both developed and developing countries. The much-gained focus on the disease is due to the various complications that can occur secondary to diabetes. Diabetes itself increases the incidence of myocardial infarction and stroke and hence strict control is of utmost importance.[4]

Table 8: Comparison of PLBS levels in patients without retinopathy (Group 1) and patients with retinopathy (Group 2)

PLBS	Group 1	Group 2
Mean	217.7	253.1
Median	201	229.5
Standard deviation	72.1	135.5
Range	91 – 673	114 – 482

P=0.011, paired *t*-test

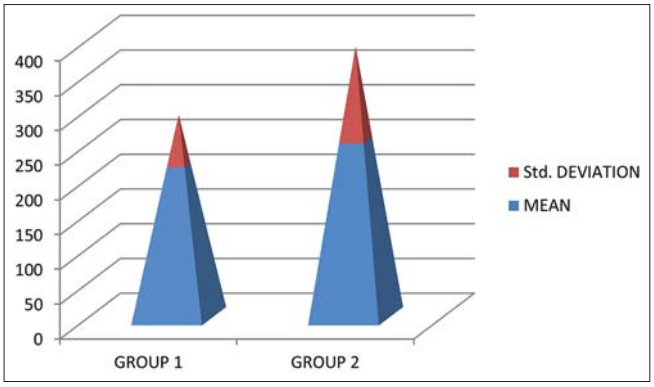
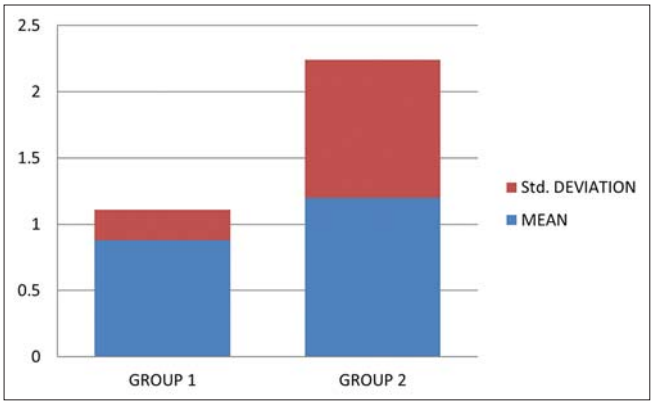


Table 9: Comparison of serum creatinine in patients without retinopathy (Group 1) and patients with retinopathy (Group 2)

Serum creatinine	Group 1	Group 2
Mean	0.88	1.2
Median	0.89	1.01
Standard deviation	0.23	1.04
Range	0.4-1.5	0.7-6.64

P=0.0086, paired *t*-test



Diabetic retinopathy is one of the most common microvascular complications of diabetes second to diabetic nephropathy. Diabetic retinopathy is also one of the leading causes of blindness in the developed world.[5]

Magnesium, its role in the progression of diabetes and its complications is not yet well established, but a number of studies show a lower level of magnesium in diabetic patients compared to their nondiabetic counterparts. Since use of magnesium is in multiple processes in the body, it is difficult to suggest that low magnesium levels itself lead to diabetes and its complications.[6]

Glycosylated hemoglobin which reflects the 3-month control of diabetes is also a strong predictor for diabetic retinopathy. A strict blood sugar control with HbAlc <7%, preprandial capillary plasma glucose between 70 and 130 mg% and postprandial capillary plasma glucose <180 mg% is recommended by ADA.

In our study, 100 patients of diabetes either attending the outpatients department or admitted hospital were included. A detailed history with special importance to family history and number of years of diabetes was taken. A complete clinical examination and required investigations as per the pro forma were done. The patients were divided into 2 groups on the basis of presence of diabetic retinopathy (Group 1) or the absence of diabetic retinopathy (Group 2).[7]

In the study out of the 100 patients, 46 are male and 54 are females. Group 1 consisted of 17 male and 33 female while Group 2 consisted of 29 male and 21 female patients. Most of the patients were in the age group of 51-70 years with 32 patients in Group 1 and 37 patients in Group 2. The mean age in Group 1 is 54.1 years and in Group 2 is 57.5 years.[8]

In our study, 41% patients had a history of diabetes up to 10 years with 26% and 23% patients with a history of 5 and 20 years of diabetes. Kahn *et al.* in their study of 965 patients at Joslin clinic showed a strong positive association between retinopathy and duration of diabetes of more than 10 years. A similar result was shown by Soto-Pedre *et al.* in their study. Wisconsin epidemiological study of diabetic retinopathy. 40% of the patients had a family history of diabetes while 60% did not have a family history.[9]

Serum magnesium levels in Groups 1 and 2 are compared. A mean value of 2.0 and standard deviation of 0.28 is seen in Group 1 while a mean of 1.86 with a standard deviation of 0.40 is seen in Group 2. The calculated $P = 0.035$ showed a significant correlation of serum magnesium with diabetic retinopathy. A low level of magnesium was seen in diabetic

Table 10: Correlation between serum magnesium and creatinine (within group)

Group	Correlation	Regression equation	R^2	*P*-value
Group 1	0.290	Serum magnesium = 1.70 + 0.355 creatinine	0.084 (no correlation)	0.041
Group 2	0.565	Magnesium = 1.57 + 0.223 creatinine	0.32 (no correlation)	0.001

retinopathy patients as compared to non-retinopathy diabetics. This is in sync with studies conducted by Hatwal *et al.* which showed similar results with a hypomagnesemia in diabetic retinopathy. Kareem *et al.* and Soto-Pedre *et al.* showed significant correlation between low serum magnesium and diabetic retinopathy.[9]

In our study, glycosylated hemoglobin levels are higher in Group 2 patients as compared to Group 1 with mean value of 8.8 in Group 2 and a mean value of 8 in Group 1. The $P = 0.011$ showed a significant correlation between glycosylated hemoglobin and diabetic retinopathy suggesting a strict blood sugar control to prevent the onset as well as the progression of diabetic retinopathy. The study was conducted by Klein *et al.* suggests a similar result with a consistent relationship between hyperglycemia and incidence and progression of diabetic retinopathy. Singh *et al.* also showed higher levels of glycosylated hemoglobin in diabetic retinopathy as compared to diabetics without retinopathy. However, their study did not show a significant correlation ($P = 0.6$) of glycosylated hemoglobin in proliferative diabetic retinopathy with background retinopathy. Raman *et al.* showed a glycosylated hemoglobin >8% was associated with sight-threatening diabetic retinopathy.[10]

The fasting blood sugar levels were higher in Group 2 as compared to Group 1. The $P = 0.020$ shows higher fasting sugar levels correlation with diabetic retinopathy (Group 2). Cheng *et al.*, in their study showed increase Wong *et al.* showed FBS >7 mmol/l having a sensitivity of only 40% for detecting diabetic retinopathy. However, the postprandial levels, in our study, in both the groups were similar with a $P = 0.11$, showing no significant correlation. This is against study conducted by Shiraiwai *et al.* who showed a significant correlation between postprandial sugar levels and progression of diabetic retinopathy.

The creatinine levels in the 2 groups showed a higher serum creatinine level in diabetic retinopathy patients (Group 2) as compared to non-retinopathy diabetics (Group 1). The $P = 0.0086$ was significant indicating the presence of renal involvement in diabetic retinopathy patients.[11]

Comparison within diabetic retinopathy patients showed a lower serum magnesium levels in proliferative diabetic retinopathy as compared to non-proliferative diabetic retinopathy patients. This is supported by evidence from studies by Hatwal *et al.* and Mcnair *et al.* who showed lower serum magnesium levels in the severest form of diabetic retinopathy as compared to background retinopathy.[12]

CONCLUSION

The final conclusion is that serum magnesium is low in patients in diabetic retinopathy and can be considered a risk factor for the development of the same in patients with diabetes. Correlation of magnesium should be considered, but long-term perspective trials will be required to prove the benefit.

Glycosylated hemoglobin levels correlate with the severity of diabetic retinopathy indicating strict control as hyperglycemia increases the risk for the development as well as the progression of the disease.

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