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Co-relation between HBAIC levels and Prevalence of Retinopathy among Patients Attending our Hospital

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Abstract

Purpose: To determine the Co- relation between HBA1C levels and prevalence of retinopathy among patients attending our hospital.

Methods: This is a prospective observational study of patients attending the outpatient department and those referred to department of Ophthalmology. Patients were recruited on the basis of history, clinical examination and blood investigations. Along with detailed demographic history, all subjects underwent complete slit lamp anterior segment, posterior segment examination. Estimation of RBS at admission and FBS and PPBS second day of admission along with Urine sugar, Albumin and Microscopy. If necessary based on the indication Fundus Fluorescein Angiography was also performed.

Results: Out of 250 patients evaluated, 151 were males (60.3%) and 99 (39.7%) were females. Diabetic retinopathy was the most common complication (36.8%). The strongest predictor for the prevalence of retinopathy in persons with type 2 diabetes is the duration of diabetes and was proven statistically significant. Both prevalence and severity of retinopathy correlates with HBA1C level in our study group.

Conclusion: Diabetic retinopathy was the commonest ocular complication of diabetes. The prevalence and severity of diabetic retinopathy was higher in patients with longer duration of diabetes.

Keywords: Ocular complications, Diabetes, Diabetic retinopathy, Cataract.

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INTRODUCTION

Diabetes mellitus has progressed from a pathology affecting primarily people in developed countries into a true worldwide epidemic in the last few decade.[1] In 1999, the World Health Organization (WHO) gave the definition of diabetes mellitus as "a metabolic syndrome with multiple etiologies characterized by chronic hyperglycaemic state along with disturbances of carbohydrate, fat and protein metabolism resulting

from defects in insulin secretion, action, or both."[2] Uncontrolled diabetes mellitus can manifests as long term damage, dysfunction and failure of various organs, resulting microvascular and macrovascular complications.[2] It was estimated that in 2005 approximately 200 million people had diabetes mellitus globally. Most of these patients are classified as having type 2 diabetes mellitus and the metabolic syndrome.[3] Most of the increase in total numbers of diabetic patients is expected to occur in developing countries. As per the global statistics, about 300 million people are expected to have diabetes by 2025, affecting approximately 5.4% of the world's population.[3] Changing dietary and exercise trends tend to play a leading role in the increasing prevalence of diabetes mellitus. It is unfortunate that India is known as the Diabetes Capital of the World. A decade back, India reported 62.4 million people with type 2 diabetes, compared to 50.8 million the previous year, according to the International Diabetes Federation (IDF) and the Madras Diabetes Research Foundation. India now tops with prevalence of diabetes about 9%. By 2030, India will have 100 million people with diabetes.[4] Diabetes Mellitus being a lifestyle disease, is on the rise in urban areas; Shankar Netralaya reported that the prevalence of Diabetes Mellitus in the population older than 40 years, in urban India, was around 28% in 2014.[5]

Diabetic eye disease refers to a group of eye problems that people with diabetes may face as a complication of diabetes ranging from subtle lid xanthomas to vision threatening condition.[6] Diabetic retinopathy is the commonly ocular sequalae of uncontrolled diabetes and the most common cause of blindness among people 20–64 years of age in the U.S.[7] It is also 6th most common cause of blindness in India (NPCB).[7] A Meta-analysis by Yau JVY[8] estimated that among individuals with diabetes, the overall prevalence of any DR was 34.6%, PDR was 7.0%, DME was 6.8%, and VTDR was 10.2%. The Chennai Urban Rural Epidemiology (CURES) Eye Study from South India reportedprevalence of DR about 17.6 per cent, significantly lower than age-matched western counterparts.[9] Detailed literature analysis reveals that diabetic complications can be reduced with strict glucose control. It has been seen that intensive blood glucose control alleviates the risk of developing retinopathy by 54%. Neuropathy was reduced by 60% and albuminuria by 54%, respectively.[10] With regards to type 2 diabetes mellitus, the United Kingdom Prospective Diabetes Study (UKPDS) showed a 21% reduction in risk for progression of diabetic retinopathy over a 12-year period in the intensive group.11 Skyler and associates have demonstrated that HBA1C levels correlate in a direct relationship with the relative risk of diabetic microvascular complications.[12] Strict glucose control, weight control, and exercise, remain the essential elements to prevent the complications of diabetic disease.[13]

The burdenof blindness due to diabetic retinopathy can be ameliorated by intervening at early stages of diabetic retinopathy.[14] With the available cost-effective methods of early screening, appropriate strategies/models need to be developed.[14] These models need to have a well-developed mode for screening, diagnosis and referral at eachlevel beginning from primary health centres to tertiary institutes for eye care. The National Program for Control of Blindness of India suggests opportunistic screening for early identification of diabetic retinopathy.[15] The participation ofcommunity can play a major role in improving the health status among diabetics in order to reach to a major proportion of population and increasing the compliance for continued care. It is the responsibility of ophthalmology community in creating awareness in the society so as to prevent and or delay these complications and to treat them at the earliest. It is in this context, we have studied the prevalence of diabetic retinopathy at our hospital in Southern India.

METHODOLOGY

This was a prospective observational study of patients attending the outpatient department and those referred to department of Ophthalmology at a tertiary care hospital. The study adhered to the tenets of Declaration of Helsinki. The study approval was obtained from the Institutional Review Board of the Institutional Ethics Committee and informed consent was taken from all the study participants. Patients were recruited on the basis of history, clinical examination and blood investigations. Patients were labelled as type 2 diabetes mellitus based on the criteria laid down by the American Diabetes Association. All subjects were interviewed as per the prepared proforma and the complete slit lamp anterior segment , posterior segment examination. Estimation of RBS at admission and FBS and PPBS second day of admission along with Urine sugar, Albumin and Microscopy. If necessary based on the indication Fundus Fluorescein Angiography was also performed in required subjects. The Inclusion criteria was a) Patients who have been diagnosed type 2 Diabetes Mellitus. b) Patients more than 30 years of age. The following patients were excluded

from the study (a) Patient with type 1 diabetes (b) Patients with hypertension. Data was analyzed using following statistical method diagrammatic presentation and mean +/- SD.

RESULTS

A total of 250 patients of NIDDM were analyzed. Out of 350, 151 were males (60.3%) and 99 (39.7%) were females (Table 1a). Among both the sexes, the age groups between 51 to 60 years had maximum number of patients (33.7%) (Table 1a). Seven patients had vitreous hemorrhage at presentation (2.8%), while there were another 9 patients having asteroid hyalosis. 92 patients were affected by some form of retinopathies (36.8%) making it the most common pathological condition found in the study population. 80 of them (32.6%) had NPDR while 12 had PDR (4.3%). In the NPDR group, 20 of them had mild NPDR (25.6%), 31 had moderate (39.5%) and 19 had severe NPDR (23.5%) {Table 3a}. 14 of these patients had CSME (5.6%). In this study, most of the patients were found to be in the age group of 51-60 years (33%). The average age of the patients studied was 50.9 yrs. A significant association was found between age group and retinal complication of diabetes mellitus. (p value=0.001) {Table 3b). In the present study 151 patients were male while 99 patients were female. We found significant association between sex and ocular complication of diabetes mellitus (p-value < 0.001) wherein both mild NPDR and severe NPDR were more common in males than in females. Our study showed no difference in prevalence of PDR in either sexes (9% each), while slightly more common CSME in men (11.7%) than in females (9.1%). The prevalence of combined retinal lesions were however more common in males (131, 52.6%) than females (99, 39.6%). 11.7% of people are affected by Mild NPDR within 5 years of getting type 2 Diabetes, which increases significantly to 23.7% and 25% by 10 years and thereafter (Table 4b). Similarly, Moderate NPDR rises from 25% to 28.9% and 36.8% in same interval. The severe NPDR type prevalence rises from 8.3% to 18.8% within 5 years to more than 10 years of diabetes. Also, PDR prevalence increased from 1.7% to 13.2%. Our study found that with increasing HBA1C levels, the prevalence of retinopathies increases. From Table No 5a, it is clear that 16.1%, 65.8% and 95.5% prevalence was observed for HBA1C of 6-7%, 7-8% and > 8 % respectively. It is also seen that the mild NPDR (87.9%) is found clustering at lower levels of HBA1c (<8 %), moderate NPDR(68.6%) is most prevalent between 7-8 % of HBA1C levels and Severe NPDR (73.3%) is most common at > 8 % levels. Apparently, 60.6% of Mild NPDR patients were on regular treatment than 39.3% who were not. In the same way, both moderate and severe variety of NPDR were found more commonly with regular treatment than irregular ones (Table 5b). The p-value of this is 0.964, which indicates dissociation between the two.

Table 1: Distribution of Patients according to Age and Sex

Age in years	Male (%)	Female (%)	Total (%)
31 – 40	7(4.7%)	06(6.5%)	13(5.1%)
41 – 50	39(26.1%)	24(24.5%)	63(25.4%)
51 – 60	47(31.3%)	37(37.4%)	84(33.7%)
61 – 70	37(25.1%)	24(25.2%)	61(10.6%)
71 and above	21(13.7%)	08(5.8%)	29(25.1%)
Total	151(100%)	99(100%)	250(100%)

Table 2: Distribution ofpatients according to type of retinopathy.

Type of Retinopathy	No. of Patients	Percentage
Mild NPDR	20	25.6
Moderate NPDR	31	39.5
Severe NPDR	19	23.2
Total NPDR	70	88.3
PDR	12	11.6
Total Retinopathies	82	100

Table 3: Distribution of patients according to age group.

Diagnosis		Age					Total
		31-40	41-50	51-60	61-70	>71	
Mild NPDR	Frequency	01	01	10	7	03	20
	Percentage	6.3	10.7	24.6	23.3	22.7	19.9
Moderate NPDR	Frequency	00	7	19	10	05	31
	Percentage	00	35.7	35.1	27.9	40.9	30.7
Severe NPDR	Frequency	12	02	06	08	02	19
	Percentage	75.0	7.1	10.5	18.6	9.1	18.1
PDR	Frequency	01	02	03	03	03	12
	Percentage	6.3	10.7	7.02	9.3	13.6	9.03
CSME	Frequency	0	5	6	2	1	14
	Percentage	00	21.4	12.3	9.3	4.5	10.8
Others	Frequency	2	4	6	5	2	19
	Percentage	12.5	14.3	10.5	11.6	9.1	11.4
Total	-	16	28	57	43	22	166

p-value = 0.0001

Table 4: Distribution of patients according to sex

Diagnosis		Sex		Total
		Female	Male	
Mild NPDR	Frequency	08	22	20
	Percentage	14.5	22.5	19.9
Moderate NPDR	Frequency	12	19	31
	Percentage	40.0	26.1	30.7
Severe NPDR	Frequency	04	15	19
	Percentage	14.5	19.8	18.1
PDR	Frequency	03	9	12
	Percentage	9.1	9.0	9.03
CSME	Frequency	05	9	14
	Percentage	9.1	11.7	10.8
Others	Frequency	02	7	9
	Percentage	12.7	10.8	11.4
Total		34	81	115

p-value= 0.001

Table 5 (a): Correlationbetween duration of diabetes and type of retinopathy

Diagnosis		Duration of DM			Total
		0-5	6-10	>10	
Mild NPDR	Frequency	03	07	10	20
	Percentage	11.7	23.7	25.0	19.9
Moderate NPDR	Frequency	7	9	15	31
	Percentage	25.0	28.9	36.8	30.7
Severe NPDR	Frequency	6	07	06	19
	Percentage	8.3	12.4	18.8	18.1
PDR	Frequency	01	02	09	12
	Percentage	1.7	13.2	13.2	9.03

CSME	Frequency	05	02	07	14
	Percentage	11.7	5.3	13.2	10.8
Others	Frequency	13	04	02	19
	Percentage	21.7	10.5	2.9	11.4
Total		35	29	18	82

p-value = 0.002

Table 5 (b): Severity of NPDR versus regular and irregular treatment

Treatment		Mild NPDR	Mod NPDR	Severe NPDR	Total
Regular	Frequency	12	19	11	42
(250/350)	%	60.6	62.7	60.0	73.6
Irregular	Frequency	8	12	8	28
(90/350)	%	39.3	37.3	40.0	39.4
Total	Frequency	20	31	19	70
(350)	%	100	100	100	100

Chi square=0.07 p-value=0.964

Table 6: Co- relation between HBA1C levels and prevalence of retinopathy

HBA1C	No. of Patients	Mild NPDR	Mod NPDR (%)	Sev NPDR (%)	PDR (%)	Total
6-7%	140	17(87.9)	4(11.7)	01(6.7)	00(0)	22(16.1%)
7-8%	70	01(6.1)	21(68.6)	04(20.0)	05(46.7)	10(65.8%)
>8%	40	02(6.1)	6(19.6)	14(73.3)	07(53.3)	29(95.5%)
Total	250(100)	20(100)	31(100.)	19(100)	12(100)	82(100)

p-value <0.0001

DISCUSSION

In this study most of the patients were found to be in the age group of 51-60 years (33.7%). All the patients were aged above 30 years. There were 151 males and 99 females in the study group. The average age of the patients studied was 54.9 years for males and 56.2 years for females. Comparable age distribution was found in the Wisconsin epidemiologic study of diabetic retinopathy.[16] The average duration of diabetes in the study group was 6.4 years in males and 7.3 years in females. In the present study we found retinal lesions were the most common ocular complication occurring in diabetes subjects (40.6%), of which retinopathies of all kind constituted majority of them (36.8%). The prevalence of cataract was 35.4% followed by glaucoma (4.6%) and other ocular pathologies like conjunctivitis, recurrent horeolum, dacrocystitis, etc. Stanga PE,[17] in their review of literature in 1999, have found that retinopathy is the most common ocular complication of long standing diabetes mellitus followed by other lesions like cataract, uveitis, neuro-ophthalmitis, etc.

The Aravind Eye Disease Survey in southern India reported a retinopathy prevalence of 27% in a population aged 30 years or older with self-reported diabetes,[24] similar to the 22% prevalence reported from another population based study in an urban population in Hyderabad, India.[25] The prevalence of retinopathy in our study population was 36.8%, of which NPDR were 32.6% and PDR were 4.3%. In the younger onset group in the WESDR, the prevalence of any retinopathy was 8% among participants with diabetes duration of 3 years, 25% for 5 years, 60% for 10 years, and 80% for 15 years.[16] In the present study, the prevalence of proliferative retinopathy was 1.7% for those with diabetes duration of 5 years, increasing to 13.2% for 10 years. In our study, the prevalence of NPDR varied from 26.1% in persons who had diabetes for less than five years to 32.3% in persons who had diabetes for 5 to 10 or more years and 78.7% in more than 10 years. Increased incidence of CSME was noted as the duration of diabetes increased (11.7% to 13.2% over the same duration intervals of diabetes.) Similar increased incidence of CSME with increased duration of diabetes was noted in a study by Varma.[26] The findings are thus consistent with the fact that the strongest predictor

for the prevalence of retinopathy in persons with type 2 diabetes is the duration of diabetes and was proven statistically significant (p-value <0.002). The WESDR showed that both the younger-onset and older-onset patients with diabetes who had no retinopathy had significantly lower mean glycosylated haemoglobin values than those patients with retinopathy.[16] Patients with higher glycosylated haemoglobin values were shown to have a higher risk of retinopathy, such that those with mean HbA1c levels over 12% were 3.2 times more likely to have retinopathy after 4 years than subjects with HbA1c levels under 12%.[27] Our study population exhibits a similar pattern : 16.1% of diabetic patients with HBA1C between 6-7% had some form of DR, while the prevalence rises to 65.8% and 95.5% with HBA1C of 7-8% and more than 8% (i.e. uncontrolled type) respectively. It is also seen that the mild NPDR is found clustering at lower levels of HBA1c (<7 %), moderate NPDR is most prevalent between 7-8 % of HBA1C levels and Severe NPDR is most common at > 8 % levels. Thus, both prevalence and severity of retinopathy correlates with HBA1C level in our study group. In our study, subjects taking regular treatment (oral tablets/insulin) had a combined NPDR prevalence of 24% which is lower when compared to the group not taking treatment regularly (48.9%). The essentials for managing a diabetes mellitus patient are regular treatment and follow up. In a study conducted by Alan MJ.[27] Compared with individuals with continuous follow-up, patients with irregular clinical visits were more likely to be from families of lower socioeconomic class, have a family history of separation and divorce, and were members of families that reported being least openly expressive of positive emotions. Rush JA showed that diabetes is the underlying cause in 25–30% of patients aged 45 years and older who develop acute extra ocular muscle palsy.[28] In a study by Watanabe K, 1% of patients with diabetes were found to have cranial nerve palsies, compared with only 0.13% of control subjects.[29] 1.1% of our patients (i.e. 4 of them) had cranial nerve palsy, same as with the Watanabe study. We found a prevalence of 0.3% BRVO amongst diabetics in our study while BRVO were detected in 0.79% in a study conducted by Kawasaki R.[30]

CONCLUSION

Retinal lesions (like Retinopathies, CSME, BRVO, BRAO, ARMD and RD) were the most common ocular complication occurring in diabetes subjects (40.6%), of which retinopathies of all kind constituted majority of them (36.8%). The prevalence of retinopathy in our study population was 36.8%, of which NPDR were 32.6% and PDR were 4.3%. The strongest predictor for the prevalence of retinopathy in persons with type 2 diabetes is the duration of diabetes and was proven statistically significant (p-value <0.0001). It is also seen that the mild NPDR is found clustering at lower levels of HBA1c (<7 %), moderate NPDR is most prevalent between 7-8 % of HBA1C levels and Severe NPDR is most prevalent at > 8 % levels. Thus, both prevalence and severity of retinopathy correlates with HBA1C level in our study group.

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