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"Study of HbA1C levels and systemic blood pressure in association with diabetic retinopathy in patients attending KIMS hospital, bangalore"

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Abstract: Aim is to determine the importance of HbA1C levels and systemic hypertension in predicting the development of Diabetic Retinopathy and the relation between them
Background*: Diabetic mellitus is a important cause of avoidable blindness in both developing and developed countries.. The prevalence of diabetic retinopathy in India is 18%[1]. The risk of DR is mainly attributed to HbA1C status,systemic hypertension and diabetic duration[2]. A higher Hb1AC is associated with both increased incidence as well as progression of diabetic retinopathy[3]. 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 DR, so tight control of hypertension is mandatory[4]*
Materials and Methods*: Comparative, descriptive, non randomized clinical study comprising of two groups of 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.*
GROUP A: Men and women >40years with type 2 diabetes mellitus, HbA1C levels <7% without systemic hypertension.. GROUP B: Men and women>40 years with type 2 diabetes mellitus, HbA1C levels >7% with systemic hypertension. Patients HbA1C levels and blood pressure were measured .The diabetic retinopathy status was classified according to the ETDRS system. Statistical analysis was done.
Results*: The mean duration of diabetes in group A was 5.10±3.15 years and in group B was 12.20±6.18years.*
The average value of HbA1C levels was 6.42±0.41mmol and 9.63± 1.30mmol for group A and group B respectively
At baseline, in group A 8.8% showed mild NPDR and 1.6% moderate NPDR. Whereas in group B, 12% mild NPDR, 33.6% moderate NPDR, 28.8% severe NPDR, 10.4% very severe NPDR, 15.2% PDR. At the end of the study, in group A 10% mild NPDR, 2.4% moderate NPDR. In group B, 8.8% mild NPDR, 26.4% moderate NPDR, 24% severe NPDR, 18.4% very severe NPDR, 13.6% PDR and 8.8% progressed to high risk PDR.
All values showed statistical significance and presence of hypertension in group B patients showed a positive effect in the progression of diabetic retinopathy.

Key Word : HbA1C, Hypertension, diabetic retinopathy.

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I. Introduction

Diabetes mellitus is a 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.[5]

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.[6]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[7] . 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.[8]

The prevalence of diabetic retinopathy in India is 18%.[1] It is documented that more than 77% of patients who survive for over 20 years with DM are affected by retinopathy.[9]

The risk of DR is mainly attributable to HbA1c, systemic hypertension and diabetes duration.[2] 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[3]

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.

HYPERTENSION AND DIABETIC RETINOPATHY

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.[11,9,12]

A prospective study reported that systolic BP (SBP) reduction may improve DR and diastolic BP (DBP) increase may worsen DR[2] .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.[4]

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

II. Material And Methods

This will be a comparative clinical study comprising of two groups above 40 years of age comprising of diabetic individuals visiting for routine eye check up and clinically diagnosed diabetic retinopathy in diabetic patients visiting department of ophthalmology out patient and in-patient at Kempegowda Institute of Medical Sciences and Research Centre, Bangalore.

Study Design: Comparative descriptive non randomized study using purposive sampling
Study Location: This was a tertiary care teaching hospital based study done in Department of Ophthalmology, at kempegowda institute of medical sciences, Bangalore,Karnataka
Study Duration:. December 2017- May 2019
Sample size: 250 patients.
Sample size calculation: Formula used : $N= 4pq/ d^2$

where, N= sample size
p= expected prevalence in population based on previous studies $(18\%)^2$
q= 1-p
d= precision taken as 5%

$$\text{so, } N= \frac{4 * 0.18 * (100- 0.18)}{(0.05)^2} = \frac{0.05904}{0.025} = 236$$

According to the conventional sample size calculation, the estimated sample size is calculated to be 236. Considering the drop out rate of patients from the study to be 5%and 95% CI, the approximated sample size is recalculated as 250. Therefore, the sample size calculated to achieve primary objective to correlate the association between HbA1C levels, systemic hypertension with diabetic retinopathy is 250 (125 in each group).
Subjects & selection method: This will be a comparative clinical study comprising of two groups above 40 years of age comprising of diabetic individuals visiting for routine eye check up and clinically diagnosed diabetic retinopathy in diabetic patients visiting department of ophthalmology out patient and in-patient at Kempegowda Institute of Medical Sciences and Research Centre, Bangalore.
Patients were divided into two groups (each group had 125 patients) according to the following criterias.
Group A(N=125 patients) -No HTN& HbA1c <7.0
Group B (N=125 patients) - HTN& HbA1c >7.0

Inclusion criteria:

- Both men and women of >40yrs who are previously diagnosed with Diabetes Mellitus, type 2 with or without hypertension.
- Willing to give informed consent for the study

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/ hereditory ocular disorders.

- Subjects who were not willing to give informed consent for the study.

Procedure methodology:

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.

Patient's examination was then performed as per the proforma.
A general physical examination was performed followed by a complete ophthalmological examination.
All the findings were documented in the proforma and verified by the guide for the study.

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.

In our study the cut off values were as follows:
1.Hba1c levels

Less than 7%	Very good control
7-8%	Good control
8-10%	Fair control
More than 10%	Poor control

2.Blood pressure measuring
<140mmHg systoilic and <90mmHg diastolic pressure.(group A)
>140mmHg sysytolic and >90mmHg (group B).

Statistical analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%).
Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance.
Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis.
Fisher Exact test used when cell samples are very small

III. Result

Table 1: Association of age in relation to incidence of hypertension and hba1c levels of patients studied

Age in years	**Group A (n=125)**	**Group B (n=125)**	**Total (n=250)**	**P value**
• 40-50	64(51.2%)	10(8%)	74(29.6%)	<0.001**
• 51-60	57(45.6%)	40(32%)	97(38.8%)	

• 61-70	4(3.2%)	53(42.4%)	57(22.8%)	
• 71-80	0(0%)	19(15.2%)	19(7.6%)	
• >80	0(0%)	3(2.4%)	3(1.2%)	

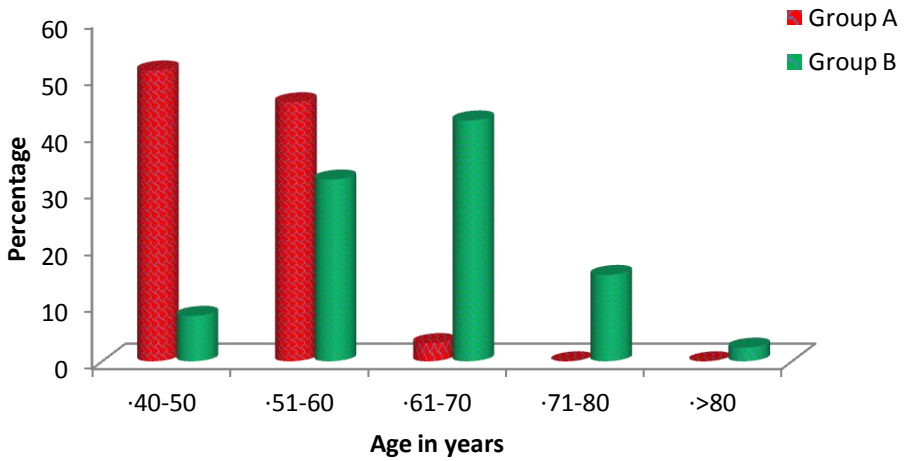

Figure no 1: Association of age

Based on the observation made on the data including both the groups, diabetic retinopathy was found most commonly in the age group of 51-70 years and the data was statistically significant.

Table 2: Association of gender in relation to incidence of hypertension and hba1c levels of patients studied

Gender	Group A	Group B	Total (250)	
• Female	36(28.8%)	32(25.6%)	68(27.2%)	0.570
• Male	89(71.2%)	93(74.4%)	182(72.8%)	

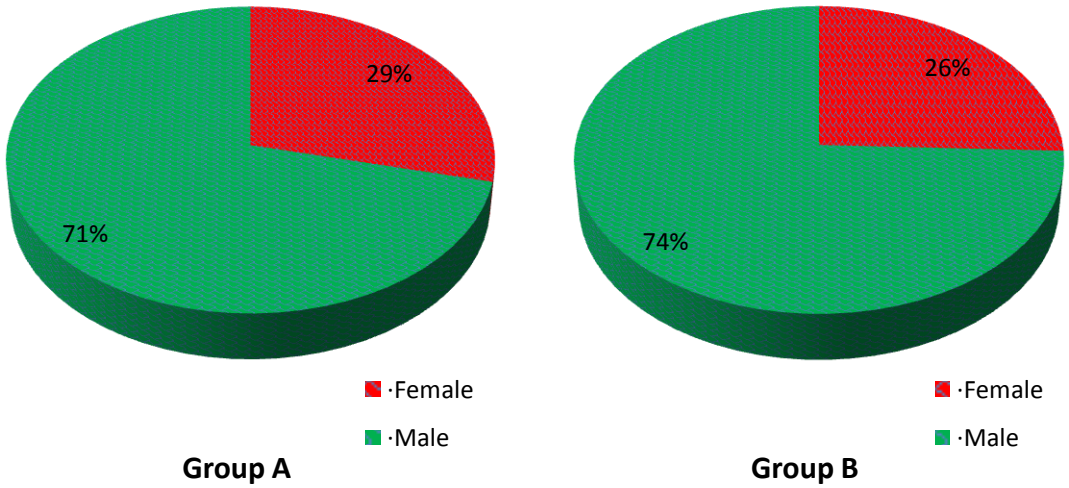

Figure no 2: Association of gender

In our study, group A had 71% males,29% females and in group B, there were 74%males, 26% females . Both the groups showed male predominance. But the data was not statistically significant.

Table 3: Association of duration of diabetes in relation to incidence of hypertension and hba1c levels of patients studied

Duration of DM (years)	Group A (n=125)	Group B (n=125)	Total (n=250)
• <12	120(96%)	67(53.6%)	187(74.8%)
• 12-24	5(4%)	54(43.2%)	59(23.6%)
• >24	0(0%)	4(3.2%)	4(1.6%)

P<0.001**, Significant, Chi-Square Test

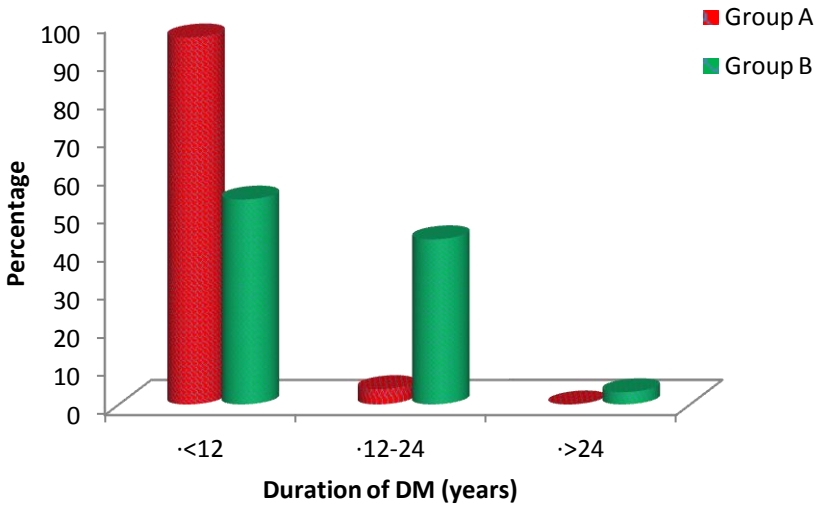

Figure no 3: Association of duration of diabetes

In <12years duration of diabetes, group A had 96% patients and group B had 53.6%.
From 12-24years , group A had 4% and group B had 43.2% and in >24 years, group A did not had any patients and in group B it was 3.2%.All these were significant statistically.

Table 4: Comparison of clinical variables in relation to incidence of hypertension and hba1c levels of patients studied

Variables	Group A (n=125)	.Group B (n=125)	Total (n=250)	P value
Age in years	51.17±5.69	63.70±9.57	57.43±10.05	<0.001**
Duration of DM (years)	5.10±3.15	12.20±6.18	8.65±6.05	<0.001**
HbA1c	6.42±0.41	9.63±1.30	8.02±1.88	<0.001**

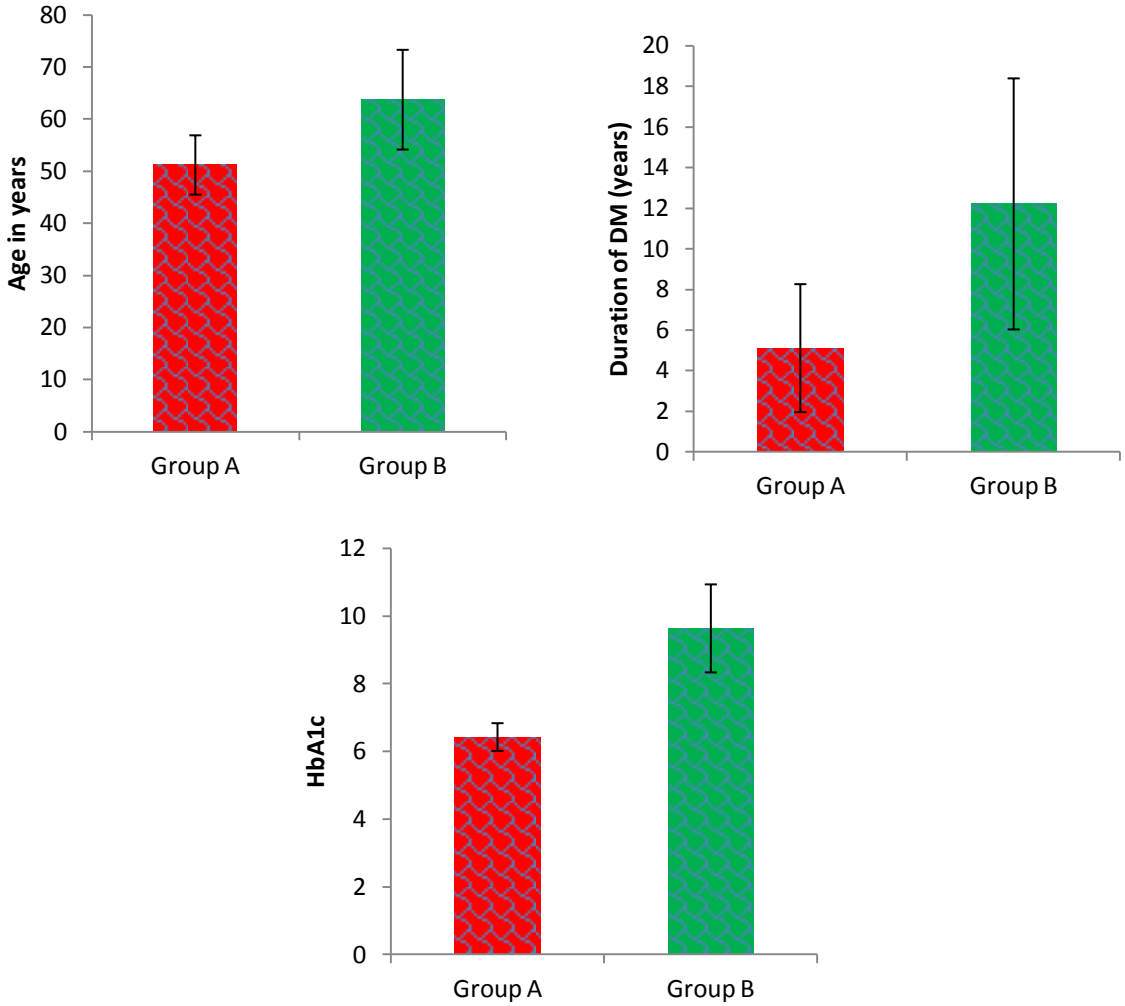

Figure no 4 : Comparison of clinical variables

The mean age in group A and group B was 51.17±5.69 and 63.70±9.57 respectively. The duration of diabetes was 5.10±3.15 and 12.20±6.18 and HbA1C levels was 6.42±0.41 and 9.63±1.30 in group A and group B respectively.
All data was statistically significant.

Table 5: diabetic retinopathy at baseline (including both the groups, 138 patients had diabetic retinopathy)

	Group A (n=13)	**Group B (n=125)**	**Total (n=138)**	**P value**
Mild NPDR	11(8.8%)	15(12%)	26(18.8%)	<0.001**
Moderate NPDR	2(1.6%)	42(33.6%)	44(31.9%)	<0.001**
Severe NPDR	0(0%)	36(28.8%)	36(26.1%)	<0.001**
Very Severe NPDR	0(0%)	13(10.4%)	13(9.4%)	0.222
PDR	0(0%)	19(15.2%)	19(13.8%)	0.130
High risk PDR	0(0%)	0(0%)	0	-

Chi-Square/Fisher Exact Test

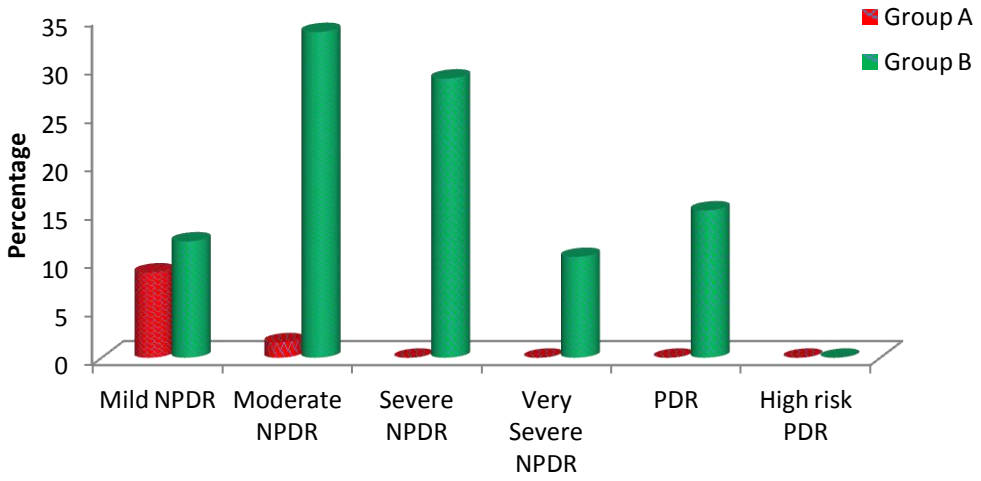

Figure no 5: diabetic retinopathy at baseline

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

Table 6: Diabetic Retinopathy progression status – in every 3months follow up

Diabetic Retinopathy Status	Group A (n=13)	Group B (n=125)	Total (n=138)	P value
3MONTHS				
• Mild NPDR	11(8.8%)	15(12%)	26(10.4%)	<0.001**
• Moderate NPDR	2(1.6%)	43(34.4%)	45(18.%)	
• Severe NPDR	0(0%)	34(27.2%)	34(13.6%)	
• Very Severe NPDR	0(0%)	15(12%)	15(6%)	
• PDR	0(0%)	14(11.2%)	14(5.6%)	
• HIGH RISK PDR	0(0%)	4(3.2%)	4(1.6%)	
6MONTHS				
• Mild NPDR	11(8.8%)	15(12%)	26(10.4%)	<0.001**
• Moderate NPDR	2(1.6%)	42(33.6%)	44(17.6%)	
• Severe NPDR	0(0%)	18(14.4%)	18(7.2%)	
• Very Severe NPDR	0(0%)	30(24%)	30(12%)	
• PDR	0(0%)	16(12.8%)	16(6.4%)	
• HIGH RISK PDR	0(0%)	4(3.2%)	4(1.6%)	
9MONTHS				
• Mild NPDR	11(8.8%)	13(10.4%)	24(9.6%)	<0.001**
• Moderate NPDR	2(1.6%)	42(33.6%)	44(17.6%)	
• Severe NPDR	0(0%)	24(19.2%)	24(9.6%)	
• Very Severe NPDR	0(0%)	25(20%)	25(10%)	
• PDR	0(0%)	16(12.8%)	16(6.4%)	
• HIGH RISK PDR	0(0%)	5(4%)	5(2%)	
12MONTHS				
• Mild NPDR	11(8.8%)	11(8.8%)	22(8.8%)	<0.001**
• Moderate NPDR	2(1.6%)	33(26.4%)	35(14%)	
• Severe NPDR	0(0%)	30(24%)	30(12%)	

• Very Severe NPDR	0(0%)	25(20%)	25(10%)	
• PDR	0(0%)	16(12.8%)	16(6.4%)	
• HIGH RISK PDR	0(0%)	10(8%)	10(4%)	
15MONTHS				
• Mild NPDR	10(8%)	11(8.8%)	21(8.4%)	
• Moderate NPDR	3(2.4%)	33(26.4%)	36(14.4%)	
• Severe NPDR	0(0%)	30(24%)	30(12%)	<0.001**
• Very Severe NPDR	0(0%)	23(18.4%)	23(9.2%)	
• PDR	0(0%)	17(13.6%)	17(6.8%)	
• HIGH RISK PDR	0(0%)	11(8.8%)	11(4.4%)	
18MONTHS				
• Mild NPDR	10(8%)	11(8.8%)	21(8.4%)	
• Moderate NPDR	3(2.4%)	33(26.4%)	36(14.4%)	
• Severe NPDR	0(0%)	30(24%)	30(12%)	<0.001**
• Very Severe NPDR	0(0%)	23(18.4%)	23(9.2%)	
• PDR	0(0%)	17(13.6%)	17(6.8%)	
• HIGH RISK PDR	0(0%)	11(8.8%)	11(4.4%)	

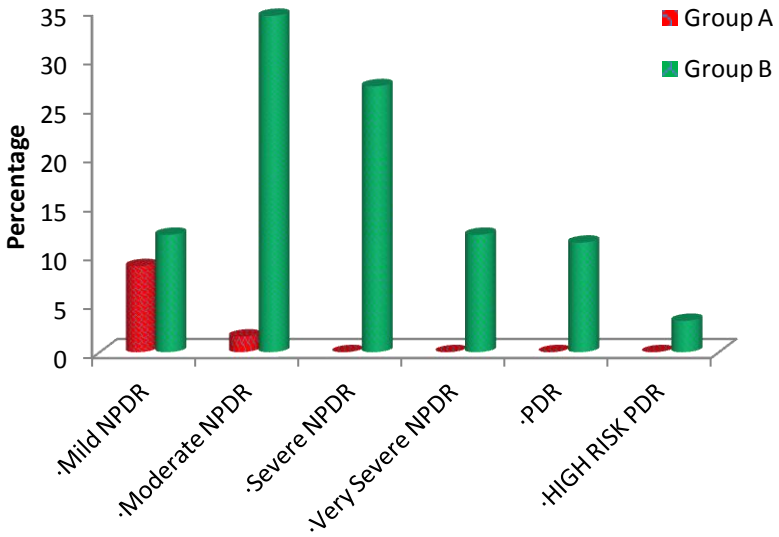

Figure no 6a: Diabetic Retinopathy status - 3 months

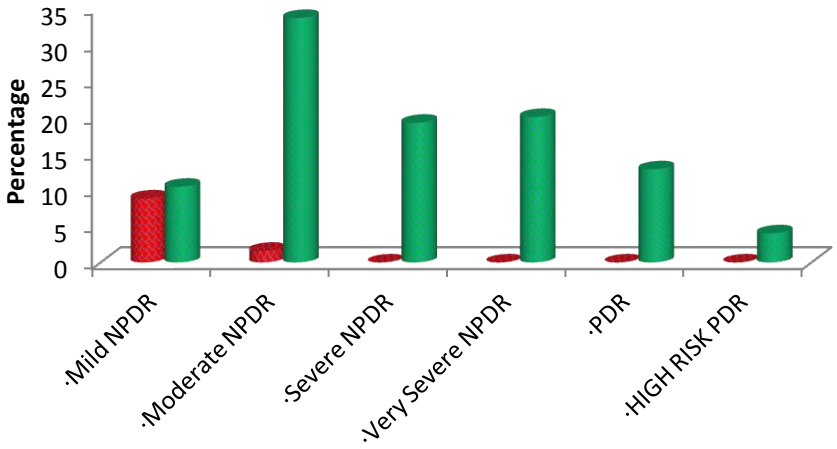

Figure no 6c: Diabetic Retinopathy Status- 9 months

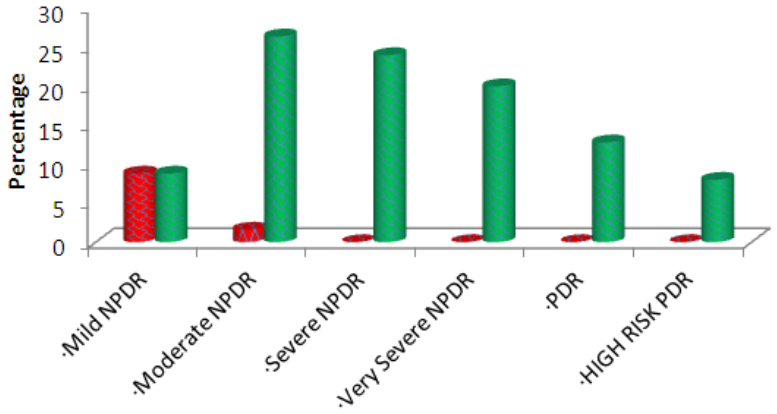

Figure no 6d: Diabetic Retinopathy Status- 12 months

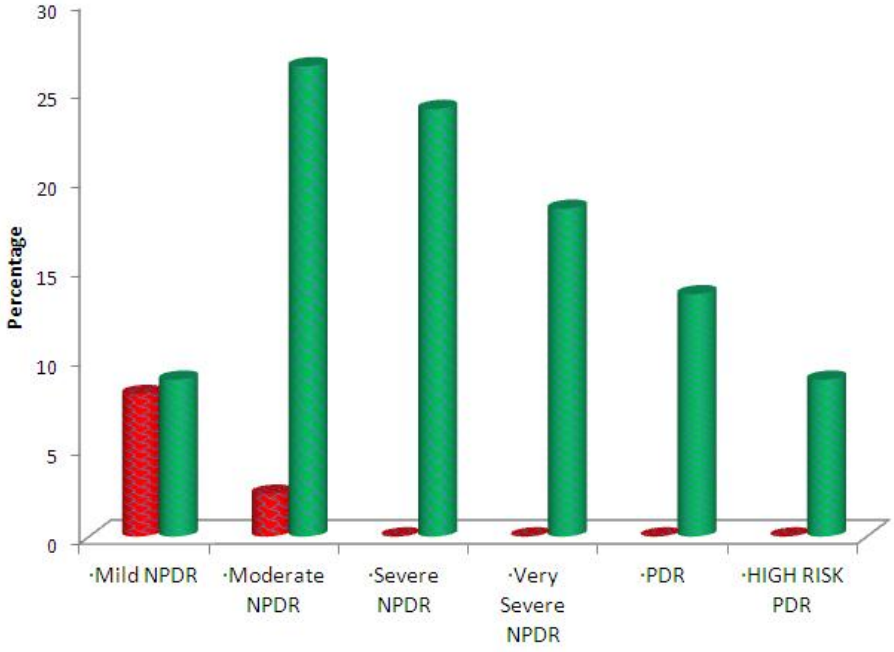

Figure no 6e: diabetic retinopathy status- 15 months

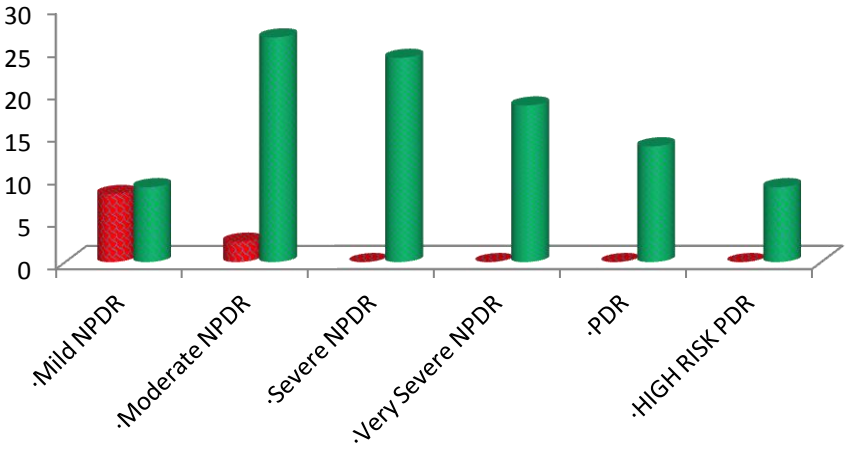

Figure no 6f: Diabetic Retinopathy Status- 18 months

At first follow i,e at 3months in group A, 8.8% had mild NPDR, 1.6% had moderate NPDR.
In group B, 12% had mild NPDR, 34.4% had moderate NPDR, 27.2% severe NPDR,12% had very severe NPDR, 14% had PDR and 3.2% had patients had progressed to high risk PDR.

At the end of 18months, in group A, 10% had mild NPDR, 2.4% had moderate NPDR.
Where as in group B , 8.8% had mild npdr,26.4% had moderate NPDR, 24% had severe NPDR,18.4% had very severe NPDR, 13.6% had PDR and 8.8% had high risk PDR.

Table 7: HbA1c% -Comparison in two groups of patients studied

HbA1c%	Group A (n=13)	Group B (n=125)	Total (n=138)	P value
3months	6.55±0.11	9.74±1.50	9.43±1.71	<0.001**
6months	6.48±0.14	9.86±1.58	9.54±1.80	<0.001**
9months	6.45±0.12	9.98±1.57	9.64±1.82	<0.001**
12months	6.53±0.11	10.02±1.60	9.69±1.84	<0.001**
15months	6.56±0.19	9.98±1.81	9.66±2.00	<0.001**
18months	6.59±0.33	10.11±1.64	9.78±1.87	<0.001**

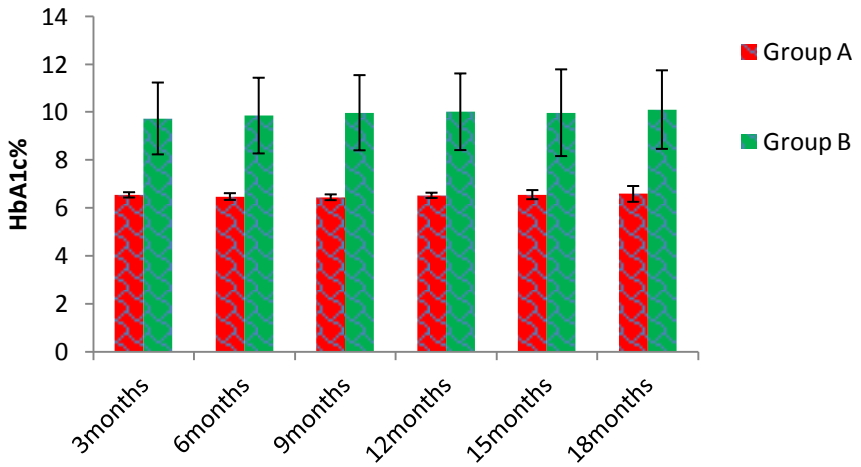

Figure no 7: HbA1c% -Comparison in two groups

At 3rd month follow up, the mean HbA1C levels in group A was 6.55±0.11 and in group B was 9.74±1.50. At the end of 18th month, it group A it was 6.59±0.33 and in group B was 10.11±1.64.

Table 8 : Association of Diabetic retinopathy in relation to HbA1c and hypertension of patients at baseline studied

DR at baseline	Group A (n=125)	Group B(n=125)			Total (n=138)
	Very Good Control (<7% hba1c	Good Control (7-8% hba1c)	Fair Control (8-10% hba1c)	Poor Control (>10% hba1c)	
	n=13	n=19	n=57	n= 49	
Mild NPDR	11(84.6%)	15(78.9%)	0(0%)	0(0%)	26(18.9%)
Moderate NPDR	2(15.4%)	4(21.1%)	38(66.7%)	0(0%)	44(32.1%)
Severe NPDR	0(0%)	0(0%)	18(31.6%)	19(38.8%)	37(26.3%)
Very Severe NPDR	0(0%)	0(0%)	1(1.8%)	12(24.5%)	13(9.4%)
PDR	0(0%)	0(0%)	0	18(36.7%)	18(13.1%)
High Risk PDR	0(0%)	0(0%)	0	0(0%)	0(0%)

P<0.001**, Significant, Fisher Exact test

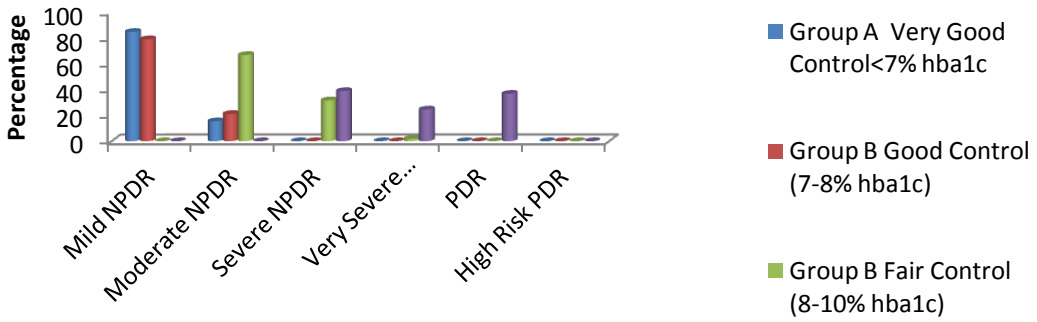

Figure no 8a: DR at baseline

At baseline

In group A- No HTN, very good control (<7% HbA1C) had 13 patients with diabetic retinopathy. Out of which 84.6% had mild NPDR and 15.4% had moderate NPDR.

In group B- HTN+

--**good control** (7-8% HbA1C) had 19 patients. Out of which 78.9% had mild NPDR and 21.1% had moderate NPDR.

--**fair control** (8-10% HbA1C) had 57 patients. Out of which 66.7% had moderate NPDR, 31.6% had severe NPDR and 1.8% had very severe NPDR.

--**poor control** (>10% HbA1C) had 49 patients. Out of which 38.8% had severe NPDR, 24.5% had very severe NPDR and 36.7% had PDR.

Table 9: DR Status 3months distribution in relation to HbA1c of patients at baseline studied

DR at 3 months	Group A (n=125)	Group B(n=125)			Total (n=138)
	Very Good Control (<7% hba1c	Good Control (7-8% hba1c)	Fair Control (8-10% hba1c)	Poor Control (>10% hba1c)	
	n=13	n=18	n=59	n= 48	
Mild NPDR	11(84.6%)	14(77.8%)	1(1.7%)	0(0%)	26(18.8%)
Moderate NPDR	2(15.4%)	4(22.2%)	39(66.1%)	0(0%)	45(32.6%)
Severe NPDR	0(0%)	0(0%)	19(32.2%)	15(31.2%)	34(24.6%)
Very Severe NPDR	0(0%)	0(0%)	0(0%)	15(31.2%)	15(10.9%)
PDR	0(0%)	0(0%)	0(0%)	4(8.3%)	4(2.9%)
High Risk PDR	0(0%)	0(0%)	0(0%)	14(29.1%)	14(10.1%)

P<0.001**, Significant, Fisher Exact test

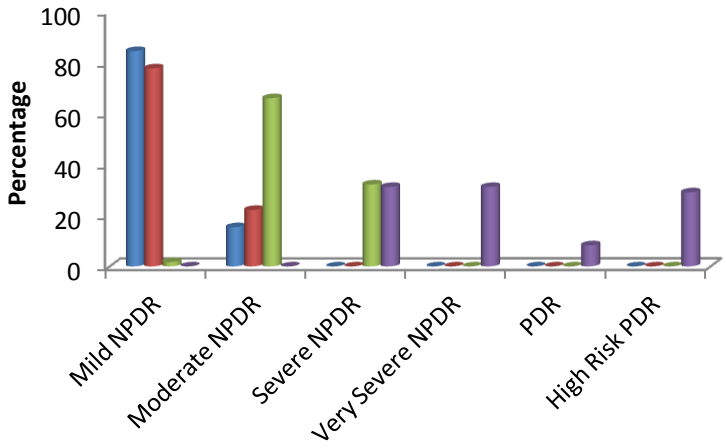

figure no 8b: DR at 3 months

At 3months

In group A-(No HTN) very good control(<7% HbA1C) had 13 patients with diabetic retinopathy. Out of which 84.6% had mild NPDR and 15.4% had moderate NPDR.

In group B- (HTN+)good control (7-8% HbA1C) had 18 patients. Out of which 77.8% had mild NPDR and 22.2% had moderate NPDR. **In fair control** (8-10% HbA1C) had 59 patients. Out of which 1.7% had mild NPDR, 66.1% had moderate NPDR and 32.2% had severe NPDR. **In poor control** (>10% HbA1C) had 48 patients. Out of which 31.2% had severe NPDR, 31.2% had very severe NPDR,8.3% had PDR and 29.1% had high risk PDR.

Table 10: DR Status 6months in relation to HbA1c of patients at baseline studied

DR at 6 months	Group A (n=125)	Group B(n=125)			Total (n=138)
	Very Good Control (<7% hba1c	Good Control (7-8% hba1c)	Fair Control (8-10% hba1c)	Poor Control (>10% hba1c)	
	n=13	n=17	n=53	n= 55	
Mild NPDR	11(84.6%)	13(76.5%)	2(3.8%)	0(0%)	26(18.8%)
Moderate NPDR	2(15.4%)	4(23.5%)	38(71.7%)	0(0%)	44(31.9%)
Severe NPDR	0(0%)	0(0%)	11(20.8%)	7(12.72%)	18(13.0%)
Very Severe NPDR	0(0%)	0(0%)	2(3.8%)	28(50.9%)	30(21.7%)
PDR	0(0%)	0(0%)	0(0%)	4(7.2%)	4(2.9%)
High Risk PDR	0(0%)	0(0%)	0(0%)	16(29.0%)	16(11.6%)

P<0.001**, Significant, Fisher Exact test

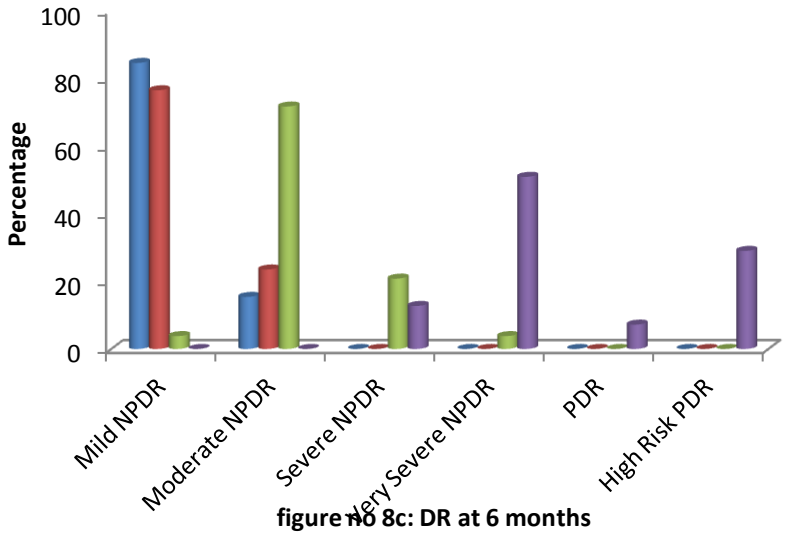

figure no 8c: DR at 6 months

Table 11: DR Status 9months in relation to HbA1c of patients at baseline studied

DR at 9 months	Group A (n=125)	Group B(n=125)			Total (n=138)
	Very Good Control (<7% hba1c	Good Control (7-8% hba1c)	Fair Control (8-10% hba1c)	Poor Control (>10% hba1c)	
	n=13	n=16	n=43	n= 66	
Mild NPDR	11(84.6%)	12(75%)	1(2.3%)	0(0%)	24(17.4%)
Moderate NPDR	2(15.4%)	4(25%)	38(88.4%)	0(0%)	44(31.9%)
Severe NPDR	0(0%)	0(0%)	2(4.7%)	22(33.3%)	24(17.4%)
Very Severe NPDR	0(0%)	0(0%)	2(4.7%)	23(34.8%)	25(18.1%)
PDR	0(0%)	0(0%)	0(0%)	5(7.5%)	5(3.6%)
High Risk PDR	0(0%)	0(0%)	0(0%)	16(24.2%)	16(11.6%)

P<0.001**, Significant, Fisher Exact test

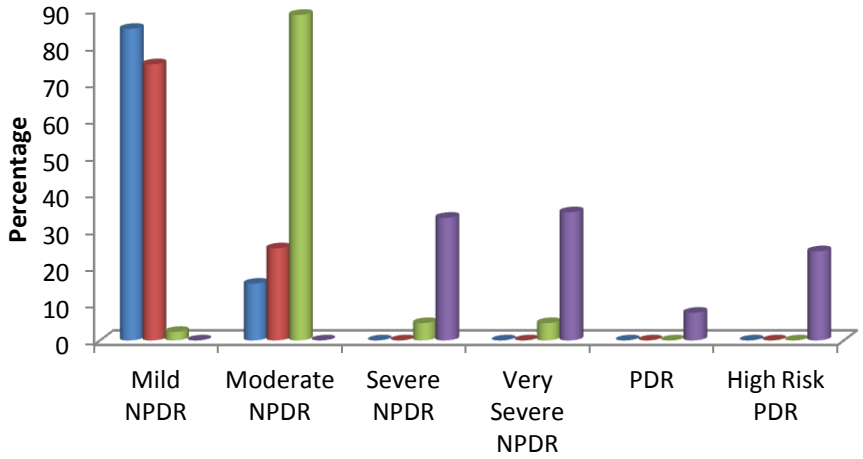

Figure no 8d: DR at 9 months

Table 12: DR Status 12months in relation to HbA1c of patients at baseline studied

DR at 12 months	Group A (n=125)	Group B(n=125)			Total (n=138)
	Very Good Control (<7% hba1c	Good Control (7-8% hba1c)	Fair Control (8-10% hba1c)	Poor Control (>10% hba1c)	
	n=13	n=15	n=38	n= 72	
Mild NPDR	11(84.6%)	11(73.3%)	0(0%)	0(0%)	22(15.9%)
Moderate NPDR	2(15.4%)	4(26.7%)	29(76.3%)	0(0%)	35(25.4%)
Severe NPDR	0(0%)	0(0%)	7(18.4%)	23(31.9%)	30(21.7%)
Very Severe NPDR	0(0%)	0(0%)	2(5.3%)	23(31.9%)	25(18.1%)
PDR	0(0%)	0(0%)	0(0%)	10(13.9%)	10(7.2%)
High Risk PDR	0(0%)	0(0%)	0(0%)	16(22.2%)	16(11.5%)

P<0.001**, Significant, Fisher Exact test

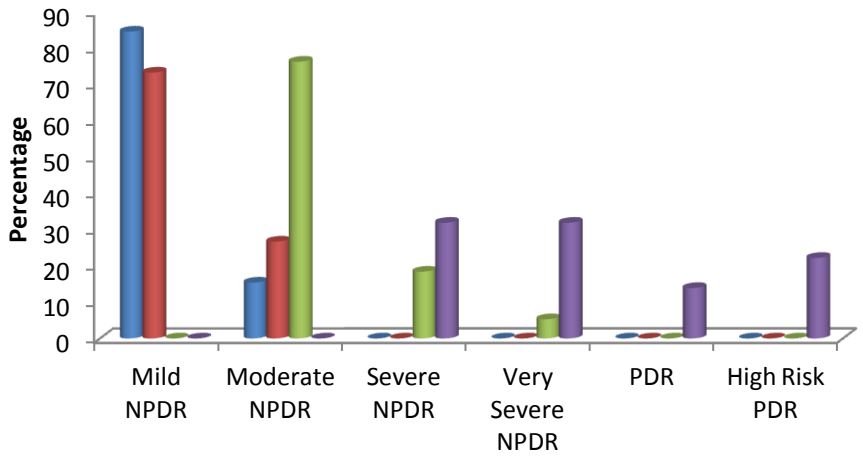

Figure no 8e: DR at 12 months

Table 13: DR Status 15months in relation to HbA1c of patients at baseline studied

DR at 15 months	Group A (n=125)	Group B(n=125)			Total (n=138)
	Very Good Control (<7% hba1c	Good Control (7-8% hba1c)	Fair Control 8-10% hba1c)	Poor Control (>10% hba1c)	
	n=13	n=16	n=52	n= 57	
Mild NPDR	10(76.9%)	11(68.8%)	0(0%)	0(0%)	21(15.2%)
Moderate NPDR	3(23.1%)	4(25%)	29(55.8%)	0(0%)	36(26.1%)
Severe NPDR	0(0%)	0(0%)	16(30.8%)	14(24.5%)	30(21.7%)
Very Severe NPDR	0(0%)	1(6.3%)	7(13.5%)	15(26.3%)	23(16.7%)
PDR	0(0%)	0(0%)	0(0%)	11(19.2%)	11(7.9%)
High Risk PDR	0(0%)	0(0%)	0(0%)	17(29.8%)	17(12.3%)

P<0.001**, Significant, Fisher Exact test

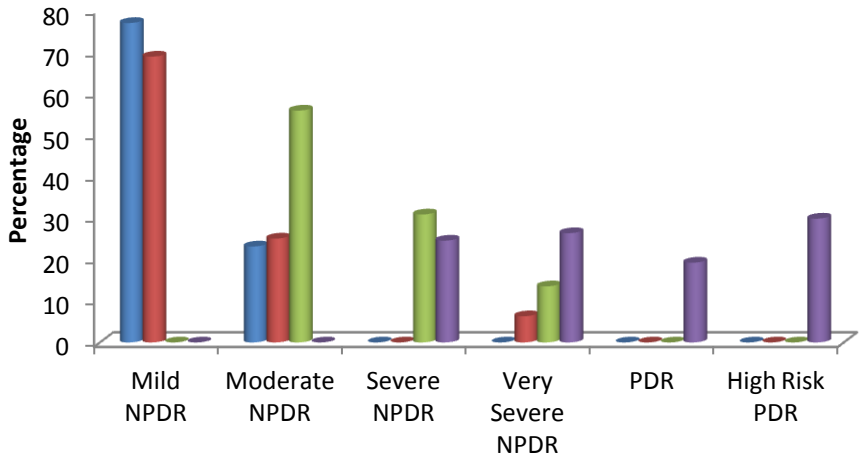

Figure no 8f: DR at 15 months

Table 14: DR Status 18months in relation to HbA1c of patients at baseline

DR at 18 months	Group A (n=125)	Group B(n=125)			Total (n=138)
	Very Good Control (<7% hba1c	Good Control (7-8% hba1c)	Fair Control (8-10% hba1c)	Poor Control (>10% hba1c)	
	n=13	n=15	n=52	n= 58	
Mild NPDR	10(76.9%)	11(73.3%)	0(0%)	0(0%)	21(15.2%)
Moderate NPDR	3(23.1%)	4(26.7%)	29(55.8%)	0(0%)	36(26.1%)
Severe NPDR	0(0%)	0(0%)	16(30.8%)	14(24.1%)	30(21.7%)
Very Severe NPDR	0(0%)	0(0%)	7(13.5%)	16(27.6%)	23(16.7%)
PDR	0(0%)	0(0%)	0(0%)	11(18.9%)	11(7.9%)
High Risk PDR	0(0%)	0(0%)	0(0%)	17(29.3%)	17(12.3%)

P<0.001**, Significant, Fisher Exact test

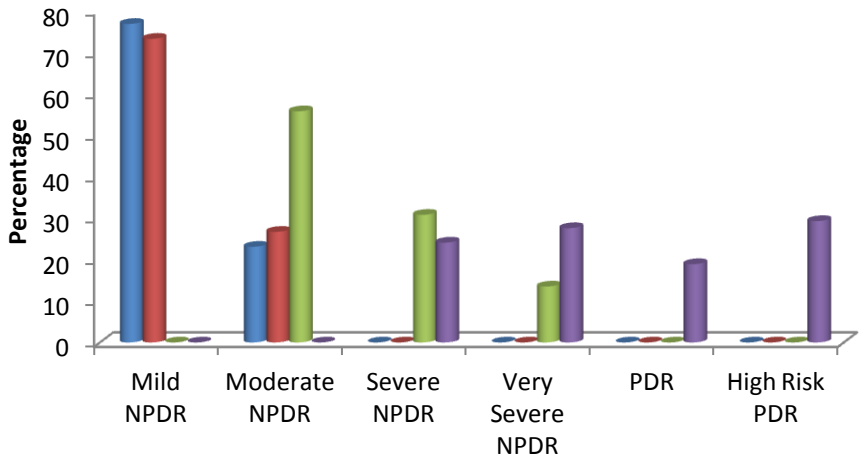

Figure no 8g: DR at 18 months

At 18months , In group A- (No HTN)very good control(<7% HbA1C) had 13 patients with diabetic retinopathy. Out of which 76.9% had mild NPDR and 23.1% had moderate NPDR.
In group B- (HTN+) good control (7-8% HbA1C) had 15 patients. Out of which 73.3% had mild NPDR and 26.7% had moderate NPDR. **In fair control** (8-10% HbA1C) had 52 patients. Out of which 55.8% had moderate NPDR, 30.8% had severe NPDR and 13.5% had very severe NPDR**. In poor control** (>10% HbA1C) had 58 patients. Out of which 24.1% had severe NPDR, 27.6% had very severe NPDR and 18.9% had PDR and 29.3% had high risk PDR.

IV. 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.

Relation between patient's age and diabetic retinopathy

The Mean age in each group was 51.17±5.69 and 63.70±9.57 respectively. The relationship of retinopathy with age was in accordance to that found in many other studies. Like several other epidemiologic studies, this study also showed an increased prevalence of DR with increasing age. APED Study[13], CURES Eye Study[14], Dondana et al[15] also have found remarkable correlation between the patient age and diabetic retinopathy.

Relation between gender and diabetic retinopathy

In this study, there was no relationship between gender and DR (p=0.570). in confirmation of the findings of Nakagami et al.,[16] Tapp et al.[17] However, Santos et al [18] showed that there was a trend toward a higher frequency of DR in men than in women.

Relation between duration of diabetes and diabetic retinopathy

In our study, the duration since diagnosis of diabetes (diabetic age) ranged from. There may be bias in estimating the exact duration of diabetes in these patients, as the discovery of diabetes could have been delayed due to lack of symptoms and the insidious onset of type 2 diabetes. The mean duration of diabetes in group A and group B was 5.10±3.15and 12.20±6.18years respectively. The association of longer duration with a higher the risk of DR(p=0.000) was in accordance with previously published reports(DCCT[19]; WESDR/Klein et al[20]; UKPDS[21]; Larsson et al[22]; Wong et al[23]; Varma[24]). Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) also found that risk of retinopathy is directly related to the duration of diabetes[20]. In India, nearly all studies have shown an increased prevalence of DR as the duration of diabetes increased[25](Gupta et al[26] APEDS study[27]). The CURES Eye study has found that for every five year increase in duration of diabetes, the risk for DR increased by 1.89times[14]

Relation between hypertension and diabetic retinopathy

Hypertension has been consistently demonstrated to have a positive association with the development of diabetic retinopathy.[28]

In our study hypertension had an additive effect in promoting development and progression of diabetic retinopathy. In group A with no hypertension , patients had very less incidence of diabetic retinopathy(13 patients out of 125) compared group B with hypertension where all 125 patients had diabetic retinopathy and progressed more when compared to group A. the association with hypertension with the elevated risk of DR was in conformity with other studies.

The LALES study found an OR of 1.26 (P=0.002) for every 20 mm Hg increase in blood pressure.[29] The Hoorn study estimated that patients with hypertension had more than double the risk of developing retinopathy after 10 years when compared with diabetic patients with normal blood pressure.[30] Stratton et al[31] found that the incidence of developing new retinopathy increased from 17% to 32% when comparing the lowest tertile with the top third mean blood pressure in patients with diabetic retinopathy (P<0.0001)

The landmark UKPDS 69 study has showed the importance of blood pressure control in patients with diabetic retinopathy.[32] 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).

Relation between HbA1C levels(glycemic control) and diabetic retinopathy

The glycemic status of the patient was evaluated using HbA1C values which showed a rise in HbA1C levels with the increasing severity of diabetic retinopathy in a statistically significant manner. Reduction in blood glucose levels or HbA1C levels through tight blood glucose control in diabetics reduces the development of microvascular complications like DR, diabetic nephropathy and neuropathy.

In the present study most of the subject in the group B had poor glycemic control suggested by high levels of HbA1C. The mean values HbA1C group B was higher than in group A. HbA1C levels in group A was constantly between 6-7%(very good control) and in group B it was between 8-12%(poor control) throughout the study period. In group A, patients had only mild to moderate NPDR changes whereas in group B, patients had both NPDR and PDR changes and they progressed more and had got high risk PDR changes also. 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.

Intensive glycemic control was effective in substantially reducing the incidence and progression of retinopathy in the Diabetes Control and Complication Trial (DCCT) group.[25] 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.[21,25] WESDR also found that risk of retinopathy is related to the control of blood glucose levels[33]. The CURES Eye Study observed a linear trend between prevalence of DR and poor glycemic control[14]

LIMITATIONS

- Information regarding the blood glucose levels in the patients, the psychosocial factors including health care access and utilisation were not incorporated. These might modify the relationship between the known risk factors and risk of developing DR.
- The study did not evaluate other risk factors for the development of retinopathy in diabetes like hyperlipidemia or dyslipidemia, smoking, obesity, antidiabetic drugs, anemia etc.

V. Conclusion

- The present study demonstrated statistically significant correlation between diabetic retinopathy, HbA1C levels and hypertension. Increased blood glucose levels was significantly associated with the occurrence of all grades of retinopathy especially severe NPDR, very severe NPDR and PDR. It also showed that 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.

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