

## A STUDY ON THE IMPACT OF HYPERTENSION IN PATIENTS WITH DIABETIC RETINOPATHY

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### ABSTRACT

#### BACKGROUND

Diabetes is one of the leading causes of morbidity and mortality all over the world. Diabetic Retinopathy is influenced by various systemic risk factors, one of them being hypertension. Blood pressure control has been shown to reduce the risk for both retinopathy and nephropathy. This study shows the link between hypertension and diabetic retinopathy and the benefit of good blood pressure control over diabetic retinopathy.

The aim of this study is to determine the impact of hypertension in patients with diabetic retinopathy.

#### MATERIAL AND METHODS

This study was conducted on 250 subjects in the Department of Ophthalmology and inpatient wards of CMC, Ludhiana, who were diagnosed to have diabetes mellitus type 2 for a minimum duration of 5 years, which included 125 subjects with hypertension and 125 subjects without hypertension.

#### RESULTS

In the diabetes only group, there were 119 patients (95%) with various degrees of Nonproliferative Diabetic Retinopathy (NPDR) and 6 patients (5%) with Proliferative Diabetic Retinopathy (PDR), whereas in diabetes and hypertension group, 98 patients (78%) had various degrees of NPDR and 27 patients (22%) had PDR. The distribution of patients with both diabetes and hypertension group is skewed more towards severe forms of NPDR and PDR (NPDR p-value: 0.007 and PDR p-value: 0.006).

#### CONCLUSION

Patients in Diabetes and Hypertension group have more severe forms of Diabetic Retinopathy as compared to diabetes only group, so we can infer that hypertension has a greater impact on the severity of Diabetic Retinopathy in patients with Diabetes Mellitus type 2.

#### KEYWORDS

Hypertension, Diabetes Mellitus, Diabetic Retinopathy.

**HOW TO CITE THIS ARTICLE:** Sinha A, Batra N, Bhatti A, et al. A study on the impact of hypertension in patients with diabetic retinopathy. J. Evid. Based Med. Healthc. 2016; 3(78), 4210-4214. DOI: 10.18410/jebmh/2016/897

**INTRODUCTION:** Diabetes is one of the leading causes of morbidity and mortality all over the world. The current burden of diabetes in India is more than 62 million and it may soon gain the status of a potential epidemic.<sup>(1,2)</sup> The prevalence of diabetes in 2013 in India was 9.1%, which is slightly higher than the world average 8.3%.<sup>(3)</sup> An estimated 65.1 million people were affected by DM in 2013 in India between 20 and 79 years of age, which was predicted to rise to 109 million by 2035.<sup>(4-7)</sup> The prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030. It is predicted that diabetes mellitus may

affect up to 79.4 million individuals in India followed by China (42.3 million) and the United States (30.3 million) by 2030.<sup>(8,9)</sup> The prevalence of DM has been shown to be lower in rural areas (3.1%) as compared to urban areas (7.3%).<sup>(10)</sup>

The prevalence of diabetic retinopathy in type 2 DM ten years after diagnosis is 40-50% and after 20 years, it is 90%.<sup>(11)</sup>

The retinovascular complications of diabetes are collectively known as Diabetic Retinopathy. It is the fourth major cause of blindness worldwide.<sup>(12)</sup> It is a microangiopathy, which primarily affects the precapillary arterioles, capillaries and postcapillary venules.<sup>(13)</sup> Microaneurysms are the first ophthalmoscopically detectable changes in Nonproliferative Diabetic Retinopathy.

Various risk factors have been identified for the development and progression of Diabetic Retinopathy. The best predictor of DR is the duration of the disease.<sup>(14)</sup>

Blood pressure control has been shown to reduce the risk for both retinopathy and nephropathy. In the Hypertensive and Diabetes Study, which was part of The

*Financial or Other, Competing Interest: None.  
Submission 06-09-2016, Peer Review 15-09-2016,  
Acceptance 25-09-2016, Published 27-09-2016.*

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DOI: 10.18410/jebmh/2016/897*



United Kingdom Prospective Diabetic Study Group (UKPDS)<sup>(15)</sup> and in the Wisconsin Epidemiologic Study of Diabetic Retinopathy,<sup>(16)</sup> it was shown that diabetic retinopathy progression was slow with more tightly controlled blood pressure. Risks of progressive nephropathy and neuropathy are also reduced with good blood pressure control. Klein and Klein did a study, which showed that elevated systolic blood pressure is a moderate risk factor for DR<sup>(14)</sup> while others have found blood pressure levels to be associated with severity of diabetic retinopathy. There are some other studies that have found that blood pressure is not a very strong risk factor for the progression of DR.<sup>(17)</sup> Studies have shown that the relative risk of diabetic retinopathy for diabetics also having hypertension is 1.7.<sup>(18-20)</sup> One study found that for every 10 mmHg increase in systolic blood pressure, there was a 1.23 times increased risk of diabetic retinopathy and 1.19 times increased risk of vision-threatening retinopathy.<sup>(21)</sup>

Studies done in India show that the frequency of hypertension in the diabetic population is almost twice as compared to nondiabetic general population.<sup>(22)</sup> About 50% of diabetics in India are hypertensives as well and studies have shown hypertension as a risk factor for the development and progression of diabetic retinopathy.<sup>(23,24)</sup> This study was undertaken to evaluate the severity of diabetic retinopathy in patients of DM-2 with hypertension.

**MATERIAL AND METHODS:** This study was conducted in the Department of Ophthalmology and in the inpatient wards of Christian Medical College and Hospital, Ludhiana. The study was conducted on 250 subjects who were diagnosed with diabetes mellitus type 2 for a minimum duration of 5 years, which included 125 subjects with hypertension and 125 subjects without hypertension. A written consent was obtained from all subjects.

All the subjects were diagnosed with type 2 diabetes mellitus as per the American Diabetes Association (2000).<sup>(25)</sup>

**Exclusion Criteria:** The following subjects were excluded from the study;

1. Subjects in whom dilatation of pupils was contraindicated, e.g. angle closure glaucoma, anterior chamber intraocular lens implant.
2. Subjects with hazy media, e.g. corneal opacities, healed or active anterior uveitis, cataract, vitreous opacities.
3. Subjects with type 1 diabetes mellitus.
4. Subjects with hyperlipidaemia.
5. Subjects with microalbuminuria.
6. Subjects with other conditions that affect retina, e.g. anaemia.

Subjects with a clear media in one eye and a hazy media in the other eye and one-eyed subjects were considered for the study. The findings of the eye with the clear media was taken for the data analysis. In subjects with asymmetrical fundus findings, the eye with the more severe disease was considered for the analysis.

Blood Pressure was measured using a sphygmomanometer in the sitting posture, also in the supine posture if need be. A comprehensive ophthalmological examination including visual acuity using Snellen’s chart and a thorough anterior segment examination using slit lamp microscope was carried out. Intraocular pressure was recorded using non-contact tonometer. Applanation tonometer was used wherever indicated.

The pupil of both eyes were dilated with 1% tropicamide and/or 5-10% phenylephrine eye drops to achieve maximum pupillary dilatation. Phenylephrine was avoided in hypertensive patients. A detailed fundus examination of both eyes was done using direct ophthalmoscope and indirect ophthalmoscope (Heine’s) using +20D lens (wherever applicable). Examination of the macula was done with +90 D Volk’s lens wherever indicated.

Retinopathy was classified as mild, moderate and severe NPDR and PDR according to Modified Airlie House Classification of Retinopathy.<sup>(26)</sup>

Hypertension was classified as mild (HTN I), moderate (HTN II) and severe (HTN III) according to the guidelines given by the Guidelines Committee of the European Society of Hypertension.<sup>(27)</sup>

Patient’s blood and urine samples were collected for the various investigations (FBS, 2 hours PPBS, HbA1C, Lipid profile).

**RESULTS AND ANALYSIS:** The following observations were made in our study.

Age group (in years)	Diabetes without hypertension	Diabetes with hypertension
20-30	1	0
30-40	13	2
40-50	26	18
50-60	37	41
60-70	36	43
70-80	9	15
>80	3	6
Average age	54	60
SD±	11.03	10.82

**Table 1**

Table 1 shows that average age of patients with diabetes mellitus was 54 years versus 60 years for patients with both diabetes mellitus and hypertension (p value: 0.0006). The male:female ratio of patients with diabetes mellitus is 70:55 versus 72:53 patients with both diabetes mellitus and hypertension. The difference is not statistically relevant (p value: 0.215).

A total of 84% of patients with diabetes mellitus were from an urban background versus 80% of patients with both diabetes mellitus and hypertension.

Severity	Diabetes without hypertension	Diabetes with hypertension
NPDR 1	91	48
NPDR 2	24	38
NPDR 3	4	12
Total NPDR	119	98
PDR	6	27

**Table 2**

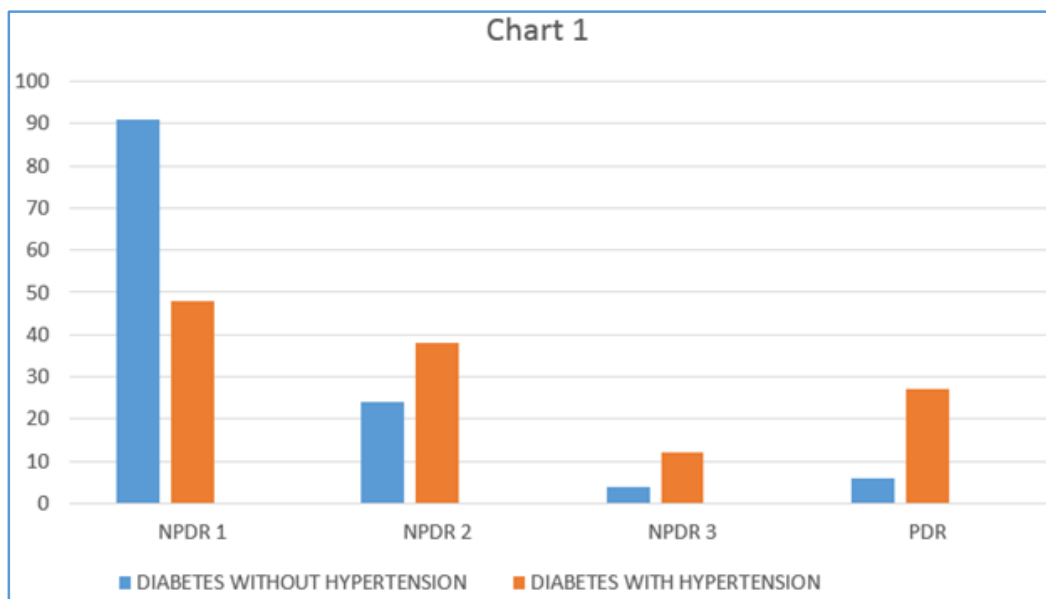


Table 2 and Chart 1 show the severity distribution according to diabetes status of all the subjects across both the groups. In the diabetes only group, there were 119 patients with various degrees of NPDR and 6 patients with PDR, whereas in the diabetes and hypertension group, 98 patients had various degrees of NPDR and 27 patients had PDR.

The distribution of patients with both diabetes mellitus and hypertension is skewed towards more severe forms of NPDR and PDR. The results are statistically relevant (NPDR: p value: 0.007; PDR: p value: 0.006).

Grades	NPDR1	NPDR2	NPDR3	PDR
HTN I	44(51%)	29(33%)	4(5%)	10(11%)
HTN II	2(6%)	6(19%)	8(25%)	16(50%)
HTN III	2(40%)	2(40%)	0(0%)	1(20%)

**Table 3**

Table 3 shows the correlation between the grades of hypertension and diabetes. There was no strong correlation found.

Group	No. of patients	Avg. duration of diabetes (years)	Std. deviation of duration of diabetes
Mild NPDR	139	9.0	5.1
Moderate NPDR	62	12.4	5.0
Severe NPDR	16	18.4	8.3
PDR	33	12.1	6.5
Total	250	10.9	6.0

**Table 4**

The average duration of diabetes rises from 9.1 years to 12.1 years along with standard deviation going from 5.1 to 8.3 from the mild NPDR category to severe NPDR category, which shows a mild correlation between severity of NPDR and duration. The average duration of diabetes for PDR patients is 12.1 years with a standard deviation of 6.5.

The mean HbA1C levels of patients with diabetes mellitus only is 7.7 versus 8.35 for patients with both diabetes mellitus and hypertension. The results are not statistically significant.

**DISCUSSION:** Unlike numerous other studies on Diabetic Retinopathy, the sample sets chosen for this study exclude nondiabetics. This has the benefit of being able to carry out detailed risk factor analysis for the isolated factor of Hypertension.

The average age in DM with HTN group was 54 years and in the DM without HTN group was 60 thus making the difference statistically significant (p value 0.006). Therefore, from this, we can infer that if a patient has both diabetes and hypertension, then he/she would develop diabetic retinopathy changes much earlier than the patients with diabetes alone.

In the population-based Wisconsin Epidemiological Study of Diabetic Retinopathy conducted on insulin taking, younger onset diabetic persons, retinopathy occurred in only one person in the first decade of life out of a total of 996 participants. Retinopathy of moderate severity or worse was present in 10% of persons aged 15 to 19 years, 41% of

persons aged 20 to 29 years, 58% of persons aged 30 to 44 years and 70% of persons 45 years or older.<sup>(16)</sup>

There was no statistically significant difference as far as the gender distribution of the patients was concerned across both the groups (p value 0.215).

In the Wisconsin Epidemiological Study of Diabetic Retinopathy,<sup>(16)</sup> younger male patients with 10 or more years of diabetes were one-third times more likely to have PDR than younger onset female patients with similar disease duration. However, no association was found between gender and prevalence or severity of diabetic retinopathy in the older onset individuals in the Wisconsin Epidemiological Study of Diabetic Retinopathy.

There was no statistically significant difference as far as the geographical distribution (urban or rural) of the patients was concerned across both the groups (p value 0.112).

In the diabetes without hypertension group, 80% of patients were non-smokers versus 81% for patients with both diabetes mellitus and hypertension. There was no statistically significant difference.

There was no statistically significant difference in the HbA1C levels across both the groups. These findings were in agreement with the Action in Diabetes and Vascular Disease (ADVANCE) trial,<sup>(28)</sup> which showed that aggressive glycaemic control (HbA1c <6.5%) had no significant benefit in terms of onset or progression of retinopathy in patients with type 2 diabetes. A recent meta-analysis involving patients with type 2 diabetes from seven trials showed that intensive glycaemic control reduced the risk of DR by 20%.<sup>(29)</sup>

The average duration of diabetes in both the groups was 9.9±5.5 years for DM patients and 11.8±6.4 years for DM with HTN patients.

The three subsamples that our study population was divided into were: between 5 and 10 years duration; 10-20 years duration and greater than 20 years of duration. It was clear that 10 years and more of diabetes duration is a clear risk factor. However, it is difficult to conclude from our study that the duration continues to be a proportional risk factor. The results across both the groups were not statistically significant (p value: 0.038).

West et al conducted a multinational study based on the interrelationship of microangiopathy, plasma glucose and other risk factors and observed that the most important risk factor for development of diabetic retinopathy was the duration of the disease.<sup>(30)</sup>

Klein et al showed that the best predictor of diabetic retinopathy is the duration of the disease.<sup>(16)</sup>

In another study, Klein et al reported that the overall 10-year incidence of diabetic retinopathy was 74%, the rate of progression of retinopathy 64% and progression to proliferative retinopathy 17%.<sup>(31)</sup>

In India, Mohan et al in their study on vascular complications in South Indians with NIDDM found that as the duration of diabetes increased, the prevalence of diabetic retinopathy also increased. After 25 years of diabetes, the prevalence of diabetic retinopathy was found to be 52%.<sup>(32)</sup>

Well-controlled BP was associated with decreased incidence and progression of DR, but more studies are required to establish a clear BP cut-off before BP targets are incorporated into clinical practice.<sup>(33)</sup>

Blood pressure control has been shown to reduce the risk for both retinopathy and nephropathy. In the Hypertension and Diabetes Study, which was part of The United Kingdom Prospective Diabetic Study Group (UKPDS)<sup>(15)</sup> and in the Wisconsin Epidemiologic Study of Diabetic Retinopathy,<sup>(16)</sup> it was shown that diabetic retinopathy progressed significantly more slowly with more tightly-controlled blood pressure. The United Kingdom Prospective Diabetic Study Group<sup>(15)</sup> in a randomised controlled trial observed a 34% reduction in risk of deterioration of retinopathy and 47% reduction in risk of deterioration of visual acuity by three lines of the Early Treatment Diabetic Retinopathy Study<sup>(17)</sup> scale in the group assigned to tight blood pressure control as compared to the group assigned less tight control. Among the 1,148 hypertensive type 2 diabetic patients studied in the U.K. Prospective Diabetes Study (UKPDS),<sup>(15)</sup> significantly fewer diabetic micro- and macrovasculature complications and diabetic-related deaths occurred in the group with a mean blood pressure of 144/82 mmHg compared with the group with a mean blood pressure of 154/87 mmHg.

Studies done in India show that the frequency of hypertension in the diabetic population is almost twice as compared to nondiabetic general population.<sup>(25)</sup> In India, about 50% of diabetics have hypertension and studies have shown hypertension as a risk factor for the development and progression of diabetic retinopathy.<sup>(26,27)</sup>

The distribution of patients with both diabetes mellitus and hypertension is skewed towards more severe forms of NPDR and PDR. The results were statistically significant. According to these findings from our study, we can infer that hypertension has a greater impact on severity of diabetic retinopathy patients with type 2 diabetes mellitus.

**CONCLUSION:** Patients in Diabetes and Hypertension group have more severe forms of Diabetic Retinopathy as compared to diabetes only group, so we can infer that hypertension has a compounding effect on the severity of diabetic retinopathy. However, increasing grades of hypertension did not correlate with increasing severity of diabetic retinopathy.

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