



Comparison of Hypertension, Macular Edema, and Non-Hypertension Patients with Diabetes Mellitus for Risk of Diabetic Retinopathy

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ABSTRACT

Diabetic retinopathy is a retinal disorder caused by changes in retinal blood vessels due to diabetes, resulting in nutritional disorders of the retina. Diabetic retinopathy can occur in most patients with long-standing diabetes mellitus (DM). Poor glycemic control, dependence on insulin, proteinuria, nephropathy, hyperlipidemia and hypertension are risk factors that influence it. This study compares the risk of developing diabetic retinopathy between hypertensive and non-hypertensive patients who suffer from diabetes mellitus at Guntur General Hospital (GGH), Guntur. This study's main objective was to determine whether there was a correlation between the amount of time after type 2 diabetes mellitus was diagnosed and the incidence of hypertension as well as the emergence of macular edema in diabetic retinopathy. Cross-sectional methodology was chosen in this study since it is analytical descriptive research. This study was carried out at Guntur General Hospital (GGH) in Guntur from January 28 to July 19, 2021. A thorough sampling process was used to choose the 90 participants who made up the study's sample size. The results of the study showed that patients with diabetes mellitus and hypertension had a statistically significant 11 times higher chance of developing retinopathy than those without hypertension (OR=12.2; 95% CI =3.6 to 57). The chi-square test was used in a bivariate study. The duration of type 2 diabetes mellitus diagnosis ($p = 0.001$), the prevalence of hypertension ($p = 0.000$), and the emergence of retinal edema in sufferers of diabetic retinopathy were all linked in the study. Diabetes-related retinopathy is more common in hypertensive people than in non-hypertensive patients.

Keywords: diabetic retinopathic, comparison of hypertension and non-hypertension, diabetic macular edema, diabetes mellitus

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INTRODUCTION

Diabetes is a metabolic disorder marked by hyperglycemia. Diabetes mellitus (DM) has been found to increase in incidence and prevalence in epidemiological studies, affecting a global health threat. According to World Health Organisation (WHO) data, Southeast Asian countries, including India, experienced the greatest increase in the number of people living with diabetes [1]. Diabetes prevalence in India was 7.1% in 2009 and increased to 10.9% in 2021 [2]. The increasing incidence of DM is also accompanied by an increase in the possibility of developing complications from DM. DM complications can include macroangiopathy and microangiopathy. Diabetic retinopathy is one of the microangiopathic complications of DM. Diabetic retinopathy is a disease that affects the retinal blood vessels, where damage and blockages occur in the retinal blood vessels [3]. Diabetic retinopathy is a disease that is the main cause of visual impairment in DM sufferers; in the last decade, it was discovered that macular edema is a complication of diabetic retinopathy, which is an important cause of blindness in people living with diabetes. Macular edema occurs due to damage to the blood vessel barrier in the retina, resulting in leakage and fluid accumulating in the intraretinal layer and causing macular thickening [4]. The prevalence of diabetic retinopathy varies by study population. In India, diabetic retinopathy has surpassed cataracts as the leading cause of blindness. Diabetic patients are 25 times more likely than non-diabetics to become blind. Diabetes patients are more likely to develop retinopathy as their diabetes progresses. According to WHO data, the prevalence of diabetic retinopathy ranges from 5.2 to 30.8% of the diabetes mellitus

population. Meanwhile, according to another source, diabetic retinopathy blinds 5,000 people in the United States each year. Diabetic retinopathy is the fourth leading cause of blindness in the United Kingdom [5]. The prevalence of diabetic retinopathy in India is 21.7% [6] of the entire diabetes mellitus population. Several factors that influence the onset and progression of diabetic retinopathy include the length of time the patient has suffered from diabetes mellitus, glucose control, and blood pressure control. Intensive blood glucose control cannot completely prevent retinopathy, but it can reduce the risk of developing diabetic retinopathy and worsening existing diabetic retinopathy. Clinically, good glucose control can protect vision and reduce the risk of undergoing laser photocoagulation therapy. The duration of suffering from DM is related to the risk of developing diabetic retinopathy. According to WHO, more than 75% of patients with DM for 20 years or more will experience complications in the form of diabetic retinopathy [5]. With increasing life expectancy, the incidence of diabetic retinopathy will also increase. Other risk factors are poor glycemic control, dependence on insulin, proteinuria, nephropathy, hyperlipidemia and hypertension. Among the risk factors, hypertension can be up to twice as common in diabetes compared to non-diabetic sufferers; in DM type 1, hypertension is found in 10-30% of sufferers, while in DM type II, 30-50% of sufferers suffer from hypertension. Hypertension is a disease that is common in developed and developing countries [7]. In the United States, it is estimated that 20% of the population has a blood pressure of more than 160/90 mmHg. In India, the prevalence is not yet known with certainty but is estimated to be between 8.8-11.8%. Around 90% of DM cases are classified as type 2 DM. More than 50% of type 2 DM sufferers experience hypertension [8]. Hypertension and DM that occur simultaneously can increase the risk of microvascular and macrovascular complications. Therefore, efforts are needed to properly manage antihypertension in type DM type II patients as a strategic and very important treatment step, with the hope that these efforts can delay the development of complications or inhibit the progression of complications that have occurred. The emergence of hypertension in diabetes is caused by hyperglycemia in diabetes mellitus, which can increase angiotensin II, which can cause hypertension; with the emergence of hypertension, it can cause further complications such as coronary heart disease, diabetic nephropathy and diabetic retinopathy. Type 2 diabetes mellitus and hypertension are two chronic diseases that are often found in society and are often found simultaneously because both diseases are degenerative diseases, namely diseases caused by the function or structure of the body's tissues or organs progressively decreasing over time due to age or lifestyle choices [9]. Without adequate treatment, both will end in the same complications, namely death due to cardiocerebrovascular disease and kidney failure. Because the presence of complications like the above can cause Drug Related Problems (DRPs), it is possible that diabetes medication can worsen the condition of hypertension or hypertension medication can increase the patient's blood glucose levels. Hypertension in type 2 DM appears simultaneously with or may even precede the appearance of diabetes. This is because hypertension sufferers often find a group of other disorders such as central obesity, dyslipidemia, hyperuricemia and, hyperinsulinemia/insulin resistance or what is now called metabolic syndrome [10]. So, from this research, it can be concluded that in essential hypertension, there is a state of insulin resistance. In this study, people who had a history of hypertension were more at risk of developing type 2 DM compared to people who did not have a history of hypertension, although this was not statistically significant. This is in accordance with previous research in America, which showed that individuals with hypertension were 2.5 times more likely to experience type 2 DM than normotensives. The single type of antihypertensive most commonly used in type 2 DM patients complicated by hypertension is ACEI (54.17%) and a combination of ACEI-diuretic (37.49%). The blood pressure reduction target was achieved by 20.83% of DM patients with hypertension without other complications and 6.25% of patients with CKD complications [11]. People with greater blood pressure, who did not smoke, higher glycaemic levels at the outset, and higher glycaemic levels throughout six years all had worse retinopathy. In this example, the person had a history of diabetic retinopathy, which was connected to being old, male, having high blood sugar (as seen by a high HbA1c), and not smoking [12]. The findings highlight the need of controlling blood sugar levels and hypertension in order to avoid diabetic retinopathy. Based on the description of the background to the problem above, researchers are interested in finding out more about the comparison of the occurrence of diabetic retinopathy in hypertensive and non-hypertensive patients who suffer from diabetes mellitus at Guntur General Hospital (GGH), Guntur.

MATERIAL AND METHODS

This study is an observational analytical study with a cross-sectional design. From January 28 to July 19, 2021, the chi-square test analytic approach was used at Guntur General Hospital (GGH), Guntur, employing the SPSS 20 For Windows programme. This study's population included all diabetes mellitus patients with hypertension at GGH, Guntur. This study included 90 participants with diabetes mellitus, both hypertensive and non-hypertensive. Total sampling was used, with inclusion criteria including patients diagnosed with diabetic retinopathy by an ophthalmologist at the GGH eye clinic and patients suffering from type 2 diabetes

mellitus, and exclusion criteria including patients who have had eye surgery in the last three months, patients with macular edema due to other eye diseases, patients with incomplete medical records, and patients who do not know when type 2 diabetes mellitus was diagnosed. Data on the length of type 2 diabetes mellitus diagnosis were gathered through patient interviews, while hypertension data was obtained through blood pressure measurements with a sphygmomanometer. The Chi-square statistical test is used in bivariate analysis. The instruments used in the research were Questionnaires, patient medical records and stationery. The variables in this study were divided into hypertension as the independent variable, diabetic retinopathy as the dependent variable and the length of time the patient suffered from diabetes mellitus, and glucose metabolic control as the external variable. Prior approval was obtained from the Research Committee of the Faculty of Human Medicine to proceed with the execution of the research project, approved with resolution No. 126-2021.

RESULTS

This research is a descriptive-analytical study using a cross-sectional approach. This research was carried out at GGH, Guntur, from January 28 to July 19, 2021. In this study, a sample of 90 hypertensive and non-hypertensive diabetes mellitus patients was obtained.

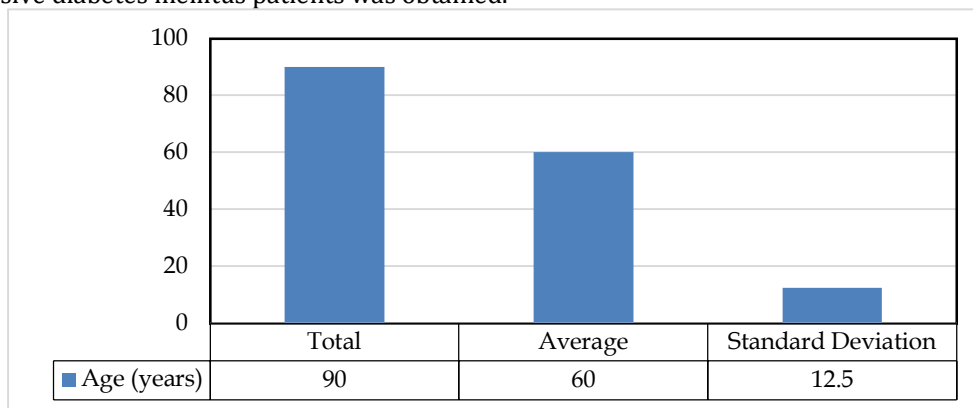


Figure 1. Sample characteristics by age

From figure 1 above, it can be seen that the number of samples in this study was 90 people with an average age of 60 years and a standard deviation of 12.5. Of the 90 respondents, the majority were aged 51-60 years, and 53 respondents (58.88%). 5 respondents (5.5%) aged 41-50, 26 respondents (28.88%) aged 51-60, 6 respondents (6.66%) aged 61-70, and at age 71-80 there were no respondents (0 %) who experienced macular edema. In this study, most respondents had a bachelor's degree, namely 32 respondents (35.55%). Macular Edema occurred in 1 respondent (1.11%) with no school education, 11 respondents (12.22%) with primary school education, 4 respondents (4.44%) with junior high school education or equivalent, 4 respondents (4.44%) with a high school education or equivalent and 14 respondents (15.55%) with a bachelor's degree. Of the 90 respondents, 54 respondents were female (60%), while 36 respondents were male (40%). Macular edema occurred more frequently in male respondents, namely 22 respondents (22.9%), while in female respondents, there were 18 respondents (18.8%)

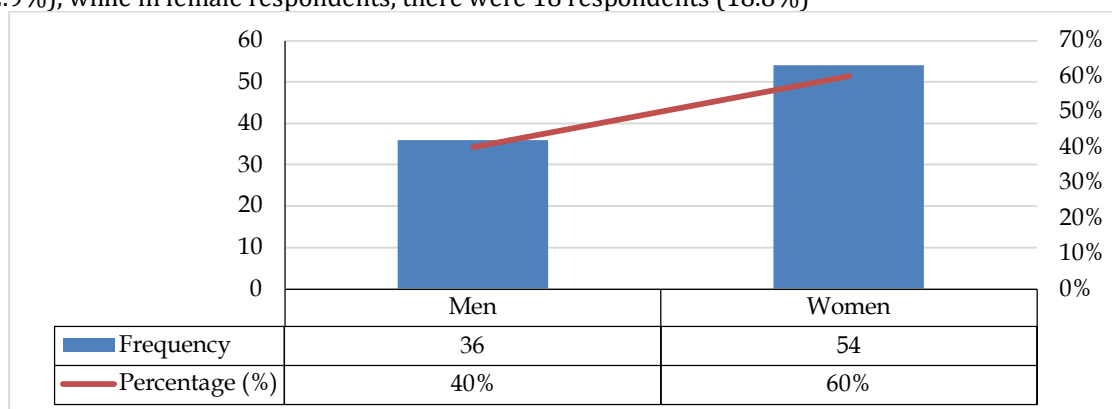


Figure 2. Sample Characteristics Based on Gender

According to figure 2, more women, 60% or 54 people, suffer from retinopathy, while men suffer from 40% or 36 people.

Table 1. Results of comparative analysis of the risk of retinopathy in hypertensive and non-hypertensive patients suffering from Diabetes Mellitus (n=90)

Hypertensive Status	Retinopathy	No retinopathy	Total (%)	OR	X ²	95% (CI)
	F(%)	F (%)				
Hypertensive	16(17.78%)	19(21.11%)	35(38.89%)	12.2	14.9	3.6 to 57
Non-Hipertense	8(8.89%)	49(54.44%)	57(63.33%)			

According to Table 1, diabetes mellitus patients with hypertension have a 12 times greater chance of developing retinopathy than non-hypertensive patients, and the increased risk is statistically significant (OR = 12.2; 95% CI = 3.6-57).

Table 2. Characteristics of Respondents Based on the Incident of Macular Edema

Macular Edema	Sum	Percentage (%)
Negative	50	55.56
Negative	40	44.44
Total	90	100

Of the 90 respondents with diabetic retinopathy who experienced macular edema, 40 patients (44.44%) and diabetic retinopathy respondents who did not experience macular edema were 50 patients (55.56%) (Table 2).

Bivariate Analysis

In this study, 51.4% of the participants with Type 2 Diabetes Mellitus had macular edema after 5 years, while 48.26% did not. In this study, one in every twelve people with Type 2 Diabetes Mellitus had macular edema, while 87% did not. The Chi-Square test demonstrated a statistically significant link between the period between type 2 diabetes mellitus diagnosis and the development of macular edema (p = 0.001) (Table 3). This investigation supports the findings of He et al. [13]. In this Chinese population, macular edema was found to be substantially linked with the length of time a patient had been diagnosed with type 2 diabetes mellitus. Although the cause of hyperglycemia is unknown, it has been linked to retinal damage. While chronic hyperglycemia has been linked to oxidative injury, microthrombi formation, cell adhesion molecule activation, leucocytosis, and cytokine activation (including vascular endothelial growth factor), there is still substantial evidence that these effects are caused by hyperglycemia. This combination of cytokines causes further retinal damage. Hyperglycemia is a cause of diabetic retinopathy, which can progress to macular edema. Diabetic retinopathy will cause increased capillary permeability or damage to retinal cells, which disrupts the fluid balance in the retina, resulting in fluid leakage and macular edema forming [14]. Continuous hyperglycemia will initially be compensated by the body. Still, over time, the body will become exhausted and cause damage to endothelial cells and dysfunction of the BRB, which leads to DME. An epidemiological study conducted by Klein et al. [15] stated that the duration of diabetes was related to macular edema, where there was an increased risk of developing macular edema with a diabetes duration of more than 5 years.

Table 3. Analysis of the Relationship between Duration of Diagnosis of Type 2 Diabetes Mellitus and the Occurrence of Macular Edema in Diabetic Retinopathy

Duration Diagnosed	Macular Edema						p
	Positive		Negative		Total		
	n	%	n	%	n	%	
< 5 Years	3	12.5	21	87.5	24	100	0.00
≥ 5 Years	37	51.4	35	48.6	72	100	

Table 4. Analysis of the relationship between the incidence of hypertension and the occurrence of macular edema in diabetic retinopathy

Hypertension	Macular Edema						p
	Positive		Negative		Total		
	n	%	n	%	n	%	
Hypertensive	37	60.7	24	39.3	61	100	0.00
Normal	3	8.6	32	91.4	35	100	

In patients who had hypertension in this study, 60.7% were positive for macular edema, and 39.3% had no macular edema. Of the patients who did not have a history of hypertension in this study, 8.6% had macular

edema, and 91.4% had no macular edema. The Chi-Square statistical test revealed a significant association between hypertension variables and the occurrence of macular edema, with a p-value of 0.000 (Table 4)

DISCUSSION

The study was carried out at Guntur General Hospital (GGH), Guntur, between January 28 and July 19, 2021. Using the chi-square test analytic approach in SPSS 20, 90 individuals with diabetes mellitus were surveyed, including both hypertensive and non-hypertensive patients. The results of the study were consistent with the hypothesis that hypertension is a risk factor for diabetic retinopathy. Compared to people without hypertension, those with hypertension have an 11-fold increased risk of developing retinopathy. In addition, UKPDS has looked into the relationship between hypertension and the development of diabetic retinopathy as a risk factor for the condition. The study included 19 hospitals from the United Kingdom, Scotland, and Ireland. The results of this study, based on Figure 1, show that the number of diabetes mellitus samples with hypertension and non-hypertension in this study was 90 people with an average age of 60 years and a standard deviation of 12.2. These results are also no different from the results of previous research conducted by Thapa [16], which found that the highest number of diabetic retinopathy patients aged 60-69 years was 33.33%. According to several theories, diabetic retinopathy occurs due to a long history of diabetes mellitus. Those aged 45-64 years are more likely to experience diabetic retinopathy because as age increases, glucose intolerance also increases, so people with a long history of diabetes mellitus at the age of >45 are more likely to experience diabetic retinopathy. It is also supported by several existing theories that at the age of >40 years, the metabolism and cell structures have more difficulty adapting and working. According to Figure 2 from this study, more patients had retinopathy in women, 60% or as many as 54 persons, compared to 40% or as many as 36 people in men. These findings are consistent with earlier research, which found that women made up 42 of the diabetic retinopathy patients (66%), while men made up only 22 of the patients (34%), representing a 32% disparity between the two genders [17]. Based on Table 1, it is known that patients with diabetes mellitus and hypertension have a statistically significant 12-fold increased risk of developing retinopathy compared to those without hypertension (OR=12.2; CI=96%; 3.6 to 57). These findings are also consistent with earlier research, which found that UKPDS had examined hypertension as a risk factor for diabetic retinopathy with a focus on the impact of hypertension on the development of diabetic retinopathy. 19 hospitals in England, Scotland, and Ireland participated in the study. 1148 individuals with type 2 diabetes mellitus, with an average duration of 2.6 years with the disease, an average age of 56, and an average blood pressure of <160/94 mmHg, were allocated into two groups at random. With beta-blocker or angiotensin-converting enzyme (ACE) inhibitor medication, 758 patients had stringent blood pressure control monitoring (<150/85) and 390 patients did not (<180/105). The Early Treatment of Diabetic Retinopathy Study (ETDRS) scale was used to assess the degree of retinopathy [18]. Patients with type 2 diabetes mellitus were the subject of several research that looked at hypertension. It is unknown if decreased blood pressure in patients with normotension (BP <140/90 mmHg) benefits vascular problems. In 480 type 2 diabetes mellitus patients with normal blood pressure, Schrier *et al.* [25]. examined the impact of intensive and moderate blood pressure treatment on vascular diabetic sequelae. With a randomised controlled trial, this study is prospective. The subjects were split into two groups: intensive (10 mmHg below diastolic blood pressure, or DBP) groups and moderate (80-89 mmHg below diastolic blood pressure, or DBP) groups. Patients in the intense therapy group received antihypertensive medications, while those in the moderate therapy group received a placebo. The progression of retinopathy and neuropathy was then evaluated, along with the prevalence of cardiovascular disease. The patients' average blood pressure was observed after 5.3 years. The average blood pressure in the intense group was $75 \pm 0.3/128 \pm 0.8$ mmHg. The average blood pressure in the moderate group was $81 \pm 0.3/137 \pm 0.7$ mmHg. A decreased incidence of stroke and a slower progression of diabetic retinopathy were also seen in the intensive group. Regarding the outcomes, there are several points of view. According to the study's findings, lowering blood pressure had no bearing on how quickly diabetic retinopathy developed. There was no difference in the progression of diabetic retinopathy between the group with tight blood pressure control (diastole 75 mmHg) and the group with loose blood pressure control (diastole between 80-89 mmHg) for 5.3 years, according to the Appropriate Blood Pressure Control in Diabetes (ABCD) study results from 2000 with a sample size of 470 [18]. The discrepancy in research findings is likely to be caused by people with diabetes mellitus and hypertension having a higher risk of developing diabetic retinopathy, albeit the exact process is yet unknown. This is probably due to a twofold stimulation of vascular endothelium-related biochemical activity, particularly VEGFs. This result (Table 2) is higher than research conducted by Luxmi *et al.*, (2018), which showed 14.5% of patients suffering from macular edema in urban India [24]. In analytical research conducted by Lee *et al.* [19], it was found that the prevalence of diabetic macular edema (DME) ranged from 1.4% to 33.3% in various studies, and this could be influenced by several factors such as type of diabetes, place of study and

comorbidities. According to Holekamp [20], the incidence of DME is higher in people with type 1 diabetes mellitus (DM) compared to type 2 DM [13]. The location of research conducted in various countries will also influence the incidence of DME due to ethnic differences. Apart from the type of diabetes and place of study, comorbidities are also factors that influence the incidence of DME. In a study by Kiss et al. [22], it was found that the prevalence of DME with comorbidities was greater than that of DME without comorbidities. This study supports the findings of Jin et al., [23], who discovered a link between hypertension and the prevalence of macular edema in a Beijing, China population. In hypertension, the retinal blood vessels will experience several changes in response to increased blood pressure. A persistent increase in blood pressure will cause thickening of the intima of blood vessels, hyperplasia of the tunica media wall and hyaline degeneration. These changes can cause BRB damage. If the BRB is damaged, there is no regulation of fluid balance in the retina. This imbalance between the inflow and outflow of fluid in the retina ultimately causes macular edema.

CONCLUSIONS

According to this study, hypertension raises the risk of retinopathy in type II diabetes mellitus patients. Patients with type II diabetes mellitus who have hypertension are 11 times more likely to develop diabetic retinopathy than those who do not have hypertension (OR = 12.2; 95% CI 3.6 to 57). The length of type 2 diabetes mellitus diagnosis and the occurrence of macular edema in diabetic retinopathy at the GGH eye clinic are related. At the GGH eye clinic, there is a link between the prevalence of hypertension and the occurrence of macular edema in diabetic retinopathy.

RECOMMENDATIONS

In diabetes mellitus patients, it is necessary to pay attention to blood glucose control so that blood glucose is stable so that further complications can be avoided. Diabetes mellitus patients with hypertension need more attention, especially in terms of blood pressure control, so that retinopathy complications can be avoided. In patients with diabetes mellitus with hypertension and who have experienced diabetic retinopathy, blood pressure needs to be carefully monitored and controlled so that the progression of diabetic retinopathy can be suppressed. For further research, it can be further investigated to what extent hypertension treatment and blood pressure control in diabetes mellitus patients with hypertension can influence the onset and progression of diabetic retinopathy.

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AUTHOR'S CONTRIBUTIONS

Srikanth Medimpudi is a private medical practitioner and research scholar at department of Chemistry Acharya Nagarjuna University. He actively participated in the overall research work under the supervision of Subbarao Mannam, professor of chemistry, and drafted and analyzed the data for this manuscript.

ETHICAL CONSIDERATIONS

Prior approval was obtained from the Research Committee of the Faculty of Human Medicine to proceed with the execution of the research project, approved with resolution No. 126-2021.

CONFLICTS OF INTEREST

There are no conflicts to declare

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