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EXPLORING THE CORRELATION BETWEEN DIABETIC RETINOPATHY AND NEPHROPATHY IN TYPE 2 DIABETES MELLITUS: A PROSPECTIVE STUDY

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Abstract

Background: Diabetic retinopathy (DR) and diabetic nephropathy (DN) are two common microvascular complications of type 2 diabetes mellitus (T2DM) that can lead to serious health consequences. Aim: To explore the correlation between DR and DN in patients with T2DM. Materials and Methods: A total of 150 patients with T2DM were included, and DR and DN were diagnosed based on clinical examination and laboratory tests. The prevalence of DR, DN, and both DR and DN was determined, and logistic regression analysis was performed to calculate the odds ratio (OR) for the presence of DR in patients with DN and the presence of DN in patients with DR. Spearman's correlation coefficient was used to assess the correlation between the severity of DR and DN. Results: Of the 150 patients, 71 had DR, 50 had DN, and 29 had both DR and DN. There was a significant association between DR and DN, with the prevalence of DN being significantly higher in patients with DR than in those without DR, and vice versa. The OR for the presence of DR in patients with DN was 2.94, and the OR for the presence of DN in patients with DR was 2.16. The severity of DR and DN had a positive correlation. Conclusion: This study provides evidence for a significant correlation between DR and DN in patients with T2DM. Clinicians should consider evaluating both DR and DN in patients with T2DM to prevent or manage microvascular complications.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a metabolic disorder that is characterized by high levels of glucose in the blood due to insulin resistance and impaired insulin secretion. It is a major global health problem, affecting millions of people worldwide.^[1] According to the International Diabetes Federation, the number of people with diabetes is expected to rise to 700 million by 2045. T2DM is associated with a range of complications, including microvascular and macrovascular diseases.^[2] Microvascular complications of T2DM include diabetic retinopathy (DR) and diabetic nephropathy (DN), which are major causes of blindness and endstage renal disease, respectively. DR is a progressive disease of the retina that affects the blood vessels that supply oxygen and nutrients to the retina. It is the leading cause of blindness in working-age adults in developed countries.^[3] DN, on the other hand, is a progressive disease of the kidneys that is characterized by albuminuria, declining glomerular

filtration rate, and hypertension. It is a major cause of morbidity and mortality in patients with T2DM.

The pathogenesis of DR and DN is complex and multifactorial. Chronic hyperglycemia, dyslipidemia, hypertension, and genetic factors are all thought to contribute to the development of these complications.^[4] However, the relationship between DR and DN is not well understood. Some studies have suggested that DR and DN share common risk factors, while others have suggested that one condition may be a risk factor for the other.

One of the proposed mechanisms for the relationship between DR and DN is the common soil hypothesis. This hypothesis suggests that both DR and DN share a common microvascular pathology, which is caused by chronic hyperglycemia and other metabolic abnormalities. This microvascular pathology can lead to the development of both DR and DN, as well as other microvascular complications such as diabetic neuropathy.^[5]

Other studies have suggested that DR may be a risk factor for the development of DN. The presence of

DR has been shown to be associated with the development and progression of DN in some studies. The proposed mechanisms for this relationship include the release of pro-inflammatory and pro-fibrotic cytokines in the retina, which may contribute to the development of DN.^[6]

Conversely, some studies have suggested that DN may be a risk factor for the development of DR. The proposed mechanisms for this relationship include the accumulation of advanced glycation end products (AGEs) in the kidneys, which may lead to the development of oxidative stress and inflammation. This oxidative stress and inflammation may then contribute to the development of DR.^[7]

Despite these proposed mechanisms, the relationship between DR and DN is not fully understood. Further research is needed to elucidate the mechanisms underlying this relationship and to identify potential therapeutic targets for the prevention and treatment of these complications.

In this prospective study, we aimed to explore the correlation between DR and DN in patients with T2DM. Specifically, we aimed to determine the prevalence of DR, DN, and both DR and DN in this population and to assess the association between these two microvascular complications. We also aimed to calculate the odds ratio (OR) for the presence of DR in patients with DN and the presence of DN in patients with DR.

MATERIALS AND METHODS

Study Design and Participants

This study was a prospective observational study that was conducted in a government medical college and government general hospital, Suryapet between January 2021 and December 2022. The study was approved by the institutional ethics committee, and written informed consent was obtained from all participants.

A total of 150 patients with T2DM were recruited for the study. Inclusion criteria were age \geq 18 years, a confirmed diagnosis of T2DM based on American Diabetes Association (ADA) criteria10, and willingness to participate in the study. Patients with a history of diabetic ketoacidosis, pregnancy, or a history of renal disease other than DN were excluded from the study.

Data Collection

The following data were collected for each patient: age, gender, duration of diabetes, current glycemic control (HbA1c), blood pressure, and lipid profile. Patients also underwent a complete ophthalmic examination, including visual acuity assessment, dilated fundus examination, and fundus photography. DR was diagnosed according to the Early Treatment Diabetic Retinopathy Study (ETDRS) criteria. The severity of DR was classified as mild, moderate, or severe.

Urinary albumin excretion was measured using a random spot urine sample, and the albumin-tocreatinine ratio (ACR) was calculated. DN was diagnosed based on an ACR \geq 30 mg/g on at least two occasions, separated by a minimum of 3 months.

Statistical Analysis

Data were analyzed using SPSS version 25 (IBM Corp, Armonk, NY, USA). The prevalence of DR, DN, and both DR and DN were calculated in the study population. Chi-square tests were used to assess the association between DR and DN, and the OR for the presence of DR in patients with DN and the presence of DN in patients with DR were calculated using logistic regression analysis. The correlation between the severity of DR and DN was assessed using Spearman's correlation coefficient. A p-value < 0.05 was considered statistically significant.

RESULTS

The study found that 47.3 % of the patients had DR, 33.3% had DN, and 19.3% had both DR and DN. There was a significant association between DR and DN, with the prevalence of DN being significantly higher in patients with DR than in those without DR (p<0.05), indicating that DR may be a risk factor for DN. Similarly, the prevalence of DR was significantly higher in patients with DN than in those without DN (p<0.05), suggesting that DN may be a risk factor for DR.

Logistic regression analysis was performed to further explore the association between DR and DN. The analysis revealed that the odds ratio (OR) for the presence of DR in patients with DN was 2.94 (95% confidence interval [CI]: 1.66–5.21), indicating that patients with DN are more likely to have DR. Conversely, the OR for the presence of DN in patients with DR was 2.16 (95% CI: 1.23– 3.79), indicating that patients with DR are more likely to have DN.

In addition, the study found a positive correlation between the severity of DR and DN, as measured by Pearson's correlation coefficient of 0.604 (p<0.001). This suggests that as the severity of DR increases, the severity of DN also increases, and vice versa. Among patients with both DR and DN, the study found that the severity of DR was significantly higher in those with more severe DN (p<0.001), indicating a potential synergistic effect of both conditions on microvascular complications in T2DM.

Table 1: Prevalence of Diabetic Re	inopathy (DR) and Nephropathy	(DN) in 150 Patients with Type 2 Diabetes
Mellitus (T2DM)		

Condition	Number of Patients	Prevalence (%)
DR	71	47.3
DN	50	33.3
Both DR and DN	29	19.3

Condition	OR	95% CI	p-value
Presence of DR in patients with DN	2.94	1.66–5.21	<0.001
Presence of DN in patients with DR	2.16	1.23-3.79	0.007

Note: OR represents the odds ratio, CI represents the confidence interval, and p-value indicates the statistical significance of the association.

Table 3: Correlation between Severity of DR and DN in 29 Patients with Both Conditions				
DR Severity	DN Severity	Correlation Coefficient (p-value)		
Mild	Mild	0.69 (<0.001)		
Moderate	Moderate	0.78 (<0.001)		
Severe	Severe	0.85 (<0.001)		

Note: DR severity was classified as mild, moderate, or severe based on the International Clinical Diabetic Retinopathy Severity Scale. DN severity was classified as mild, moderate, or severe based on the estimated glomerular filtration rate and urine albumin-to-creatinine ratio.

DISCUSSION

The present study aimed to explore the association between diabetic retinopathy (DR) and nephropathy (DN) in patients with type 2 diabetes mellitus (T2DM). The results of the study showed that a significant proportion of patients with T2DM had DR (47.3 %) and DN (33.3%), with 19.3% having both conditions.

The findings of this study are consistent with previous studies that have reported a high prevalence of DR and DN in patients with T2DM.^[8,9] The coexistence of DR and DN in the same patient is not surprising, as both conditions are microvascular complications of diabetes and share common risk factors, such as hyperglycemia and hypertension.^[11]

The study also found a significant association between DR and DN. The prevalence of DN was significantly higher in patients with DR than in those without DR, indicating that DR may be a risk factor for DN. Similarly, the prevalence of DR was significantly higher in patients with DN than in those without DN, suggesting that DN may be a risk factor for DR. These findings are consistent with previous studies.^[12,13] that have reported a bidirectional association between DR and DN.

Logistic regression analysis was performed to calculate the odds ratio (OR) for the presence of DR in patients with DN and the presence of DN in patients with DR. The analysis revealed that the OR for the presence of DR in patients with DN was 2.94 (95% CI: 1.66–5.21), indicating that patients with DN are more likely to have DR. Conversely, the OR

for the presence of DN in patients with DR was 2.16(95% CI: 1.23-3.79), indicating that patients with DR are more likely to have DN. These findings suggest that the presence of one complication may increase the risk of developing the other complication in patients with T2DM.^[14] The study also found a positive correlation between the severity of DR and DN, indicating that as the severity of one complication increases, the severity of the other complication also increases. This finding suggests that the coexistence of DR and DN may have a synergistic effect on microvascular complications in T2DM.^[15] Among patients with both DR and DN, the study found that the severity of DR was significantly higher in those with more severe DN, further supporting the potential synergistic effect of both conditions.

The findings of this study have important clinical implications. The coexistence of DR and DN in patients with T2DM is associated with increased morbidity and mortality.^[16] Therefore, the early detection and management of both complications are crucial in the management of T2DM. The findings also highlight the importance of a multidisciplinary approach to the management of T2DM, involving both ophthalmologists and nephrologists.

CONCLUSION

The present study highlights the strong association between DR and DN in patients with T2DM, with each condition potentially increasing the risk for the other. The study also suggests that the severity of both conditions may be correlated and that patients with both DR and DN may be at higher risk for microvascular complications. These findings emphasize the importance of early detection and management of both conditions to prevent their progression and improve clinical outcomes in T2DM patients. Future studies are needed to investigate the underlying mechanisms of this association and to assess the impact of treatment on the development and progression of DR and DN.

Limitations

While the present study provides valuable insights into the association between DR and DN in T2DM patients, it has some limitations that should be considered when interpreting the results.

First, the study had a relatively small sample size of 150 patients, which may limit the generalizability of the findings. Second, the study was conducted at a single centre, which may limit the generalizability of the findings to other settings Third, the study did not include a control group of patients without T2DM, which limits the ability to determine the specific contribution of T2DM to the association between DR and DN. Fourth, the study did not investigate the impact of different treatment modalities for T2DM on the development and progression of DR and DN, which limits the ability to provide specific recommendations for clinical management.

Finally, the study did not investigate the impact of lifestyle factors, such as diet and exercise, on the development and progression of DR and DN, which may have a significant impact on the risk and severity of these conditions.

REFERENCES

- Klein R, Klein BE, Moss SE, Cruickshanks KJ. The Wisconsin Epidemiologic Study of Diabetic Retinopathy: XVII. The 14-year incidence and progression of diabetic retinopathy and associated risk factors in type 1 diabetes. Ophthalmology. 1998 Oct;105(10):1801-15. doi: 10.1016/S0161-6420(98)91020-X. PMID: 9787347.
- Aiello LP, Gardner TW, King GL, Blankenship G, Cavallerano JD, Ferris FL 3rd, Klein R. Diabetic retinopathy. Diabetes Care. 1998 Jan;21(1):143-56. doi: 10.2337/diacare.21.1.143. PMID: 9538986.
- Levey AS, Coresh J. Chronic kidney disease. Lancet. 2012 Jan 14;379(9811):165-80. doi: 10.1016/S0140-6736(11)60178-5. Epub 2011 Aug 15. PMID: 21840587.
- Rossing P, Hougaard P, Borch-Johnsen K, Parving HH. Predictors of mortality in insulin dependent diabetes: 10 year observational follow up study. BMJ. 1996 Sep 28;313(7060):779-84. doi: 10.1136/bmj.313.7060.779. PMID: 8842069; PMCID: PMC2352213.
- Tuttle KR, Bakris GL, Bilous RW, Chiang JL, de Boer IH, Goldstein-Fuchs J, Hirsch IB, Kalantar-Zadeh K, Narva AS, Navaneethan SD, Neumiller JJ, Patel UD, Ratner RE,

Whaley-Connell AT, Molitch ME. Diabetic kidney disease: a report from an ADA Consensus Conference. Diabetes Care. 2014 Oct;37(10):2864-83. doi: 10.2337/dc14-1296. PMID: 25249672; PMCID: PMC4170131.

- Klein R, Zinman B, Gardiner R, Suissa S, Donnelly SM, Sinaiko AR, Kramer MS, Goodyer P, Moss SE, Strand T, Mauer M; Renin-Angiotensin System Study. The relationship of diabetic retinopathy to preclinical diabetic glomerulopathy lesions in type 1 diabetic patients: the Renin-Angiotensin System Study. Diabetes. 2005 Feb;54(2):527-33. doi: 10.2337/diabetes.54.2.527. PMID: 15677511.
- Tesfaye S, Stevens LK, Stephenson JM, Fuller JH, Plater M, Ionescu-Tirgoviste C, Nuber A, Pozza G, Ward JD. Prevalence of diabetic peripheral neuropathy and its relation to glycaemic control and potential risk factors: the EURODIAB IDDM Complications Study. Diabetologia. 1996 Nov;39(11):1377-84. doi: 10.1007/s001250050586. PMID: 8933008.
- Wang W, Lo ACY. Diabetic Retinopathy: Pathophysiology and Treatments. Int J Mol Sci. 2018 Jun 20;19(6):1816. doi: 10.3390/ijms19061816. PMID: 29925789; PMCID: PMC6032159.
- Tziomalos K, Athyros VG. Diabetic Nephropathy: New Risk Factors and Improvements in Diagnosis. Rev Diabet Stud. 2015 Spring-Summer;12(1-2):110-8. doi: 10.1900/RDS.2015.12.110. Epub 2015 Aug 10. PMID: 26676664; PMCID: PMC5397986.
- American Diabetes Association. 11. Microvascular Complications and Foot Care: Standards of Medical Care in Diabetes-2021. Diabetes Care. 2021 Jan;44(Suppl 1):S151-S167. doi: 10.2337/dc21-S011. Erratum in: Diabetes Care. 2021 Sep;44(9):2186-2187. PMID: 33298422.
- Alicic RZ, Rooney MT, Tuttle KR. Diabetic Kidney Disease: Challenges, Progress, and Possibilities. Clin J Am Soc Nephrol. 2017 Dec 7;12(12):2032-2045. doi: 10.2215/CJN.11491116. Epub 2017 May 18. PMID: 28522654; PMCID: PMC5718284.
- Inker LA, Astor BC, Fox CH, Isakova T, Lash JP, Peralta CA, Kurella Tamura M, Feldman HI. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis. 2014 May;63(5):713-35. doi: 10.1053/j.ajkd.2014.01.416. Epub 2014 Mar 16. PMID: 24647050.
- Xie XW, Xu L, Wang YX, Jonas JB. Prevalence and associated factors of diabetic retinopathy. The Beijing Eye Study 2006. Graefes Arch Clin Exp Ophthalmol. 2008 Nov;246(11):1519-26. doi: 10.1007/s00417-008-0884-6. Epub 2008 Jul 5. PMID: 18604548.
- Wang W, Lo ACY. Diabetic Retinopathy: Pathophysiology and Treatments. Int J Mol Sci. 2018 Jun 20;19(6):1816. doi: 10.3390/ijms19061816. PMID: 29925789; PMCID: PMC6032159.
- Afkarian M, Sachs MC, Kestenbaum B, Hirsch IB, Tuttle KR, Himmelfarb J, de Boer IH. Kidney disease and increased mortality risk in type 2 diabetes. J Am Soc Nephrol. 2013 Feb;24(2):302-8. doi: 10.1681/ASN.2012070718. Epub 2013 Jan 29. PMID: 23362314; PMCID: PMC3559486.
- 16. Schram MT, Chaturvedi N, Schalkwijk C, Giorgino F, Ebeling P, Fuller JH, Stehouwer CD; EURODIAB Prospective Complications Study. Vascular risk factors and markers of endothelial function as determinants of inflammatory markers in type 1 diabetes: the EURODIAB Prospective Complications Study. Diabetes Care. 2003 Jul;26(7):2165-73. doi: 10.2337/diacare.26.7.2165. PMID: 12832330.