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Research Article

**RELATIONSHIP BETWEEN DIABETIC RETINOPATHY
AND DIABETIC NEPHROPATHY IN BAHAWALPUR
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Abstract:

The two most feared types of diabetes are probably diabetic nephropathy (DN) as well as diabetic retinopathy (DR), together they lead severe disease and mortality. If retinopathy is not present in diabetic patients, diabetic nephropathy is very difficult to distinguish from certain glomerular diseases; this can only be done if renal biopsies are conducted. Thus it is essential to distinguish the characteristics of diabetic nephropathy patients with and without diabetic retinopathy. Therefore, we conduct this study to explore if there is an association between Diabetic retinopathy and Diabetic nephropathy. It is a review paper that uses a screening, inclusive and exclusive process. For review of the article, we set an eligibility requirement, as years from 2003-2020 are considered. Google Scholar, NCBI and PubMed are the sources of information that provides the information. The findings suggest a close association between diabetic retinopathy and diabetic nephropathy. DR itself is correlated with accessible nephropathy and is a 20.0% occurrence in DM patients. The appearance of patients of DR may be an indication of DN involvement. No connection between diabetic nephropathy and diabetic retinopathy was found in few studies (Kotlarsky P, 2015) But, A number of other scholars, such as Rius Riu and Tzeng, supported our findings. J studies from Zhang may suggest that the renal results in patients with diabetic nephropathy may be expected by diabetic retinopathy. Diabetic nephropathy ($p=0.047$) is slightly higher in the diabetic nephropathical patients with retinopathy than diabetic nephropathy ($p<0.001$) and diabetic vascular disorders ($p=0.047$).

Key Words: Diabetic retinopathy, diabetic nephropathy, Nephropathy, retinopathy, Diabetes

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1. INTRODUCTION:

The chronic hyperglycemic condition of diabetes mellitus is marked by insulin production or insular action defects (Kerner W, 2014). Diabetes prevalence has been increased by nearly 10 times in the last 3 decades due to urbanization and industrialisation, excessive caloric intakes, poor diet, as well as fast development of the elderly population (Xu Y, 2013). Diabetic nephropathy is a chronic condition which is defined by continuous albuminuria, hypertension, an unceasing decline in GFR as well as high risk of heart morbidities and death. This life-threatening complication is most common, in approximately 20 percent to 40 percent of type 1 patients and much less than 20 percent of diabetic types (Skyler JS, 2001). Diabetic nephropathy has been a serious social and economic issue for about the majority of the world's end-stage renal diseases.

Eye disease called diabetic retinopathy can occur for diabetes patients. High blood sugar are responsible for the damage to the retina blood vessels. This may swell or leak blood vessels. Or they could close and stop the passage of blood. Sometimes even the retina is expanding to unusual new blood vessels. (Kierstan Boyd, 2019). The major source of blindness in individuals under 65 years of age is severe microvascular disorder of diabetes mellitus. An approximate 50 000 new blindness cases arise each year, of which 50% are attributed to diabetes and, in fact, much to the consequences of DR (Prevent Blindness America, 2003). About 5.5 million adult diabeting patientes have DR. In the majority of cases, a strong correlation between DNA and retinopathy is identified, and a further explanation for the disease in the absence of retinopathy can be discovered.

Rational of the study

The two most feared types of diabetes are probably diabetic nephropathy (DN) as well as diabetic retinopathy (DR), lead together through severe disease and mortality. When they move into end-stage renal diseases (ESRD) and blindness, patients and the healthcare system are exposed to severe medical, economic and social costs. In patients with type 2 diabetes mellitus or renal disease (Gonzalez SML, 2013) diabolic retinopathy can be helpful to determine type of kidney psychology. Even so, it is difficult to distinguish diabetic nephropathy from other glomerular diseases and that the only method of retinopathy when diabetic patients do not suffer. However, if retinopathy is not present in diabetic patients, diabetic nephropathy is very difficult to distinguish from certain glomerular diseases; this can only be done if renal biopsies are conducted (He F, 2013). Thus it is essential to distinguish the characteristics of diabetic nephropathy patients with and without diabetic retinopathy. even so, there

are limited studies on the relationship between DR and DN, and population-based studies have not yet been reviewed. Because in patient's association between diabetic retinopathy and diabetic nephropathy are frequently linked.

Purpose of the study

The purpose of this study is to explore if there is an association between Diabetic retinopathy and Diabetic nephropathy.

2. Literature Review

Ahmed MH (2017) explains in his paper that diabetic nephropathy is a serious social and economic problem for almost a third of the worldwide end stage renal disease. The purpose of his research was to investigate how retinopathy has been linked. Nearly one-third of diabetic patients have developed nephropathy, and a substantial correlation has been identified between nephropathy and retinopathy development.

In his paper, Jeng CJ (2016) attempt in a nationwide population cohort in Taiwan to investigate the development and progression of diabetic retinopathy (DR). They found that DN is an independent risk factor for development and growth in DR, but DN does not significantly affect the development of DME within this study and further research is required in order to make possible the association of these disorders.

Chandy A (2008) stated that the association of diabetic nephropathy with diabetic retinopathy as well as coronary artery disease has been considered to be good. In his paper he goes on to say that very few researches has shown that the diabetic nephropathy and neuropathy have also associated with peripheral vascular disease. The proliferative diabetic retinopathy, neuropathy and cardiovascular disease has been described as related to diabetic nephropathy through univariable study. Diabetic nephropathy also was greatly compromised with proliferative diabetic retinopathy as well as coronary artery disease through multivariate studies. They concluded that in Indian patients there is a close connection between diabetic nephropathy and other micro and macrovascular complications.

In a population-driven analysis of diabetes mellitus (DM) patients in Korea, Lee W (2004) established the risk factors as well as relationship between diabetic retinopathy (DR) and diabetic nephropathy (DN) in his research. Microalbuminuria is correlated with diabetic proliferation and DR in Korean DM patients is correlated with active nephropathy. Their results indicate that a prompt assessment of patient's renal condition will be conducted anytime an ophthalmologist discovers DR or PDR.

METHODOLOGY:

It is a review paper that uses a screening, inclusive and exclusive process. Screening is being used for eligibility determination, it has been used exclusively to remove documents which are not relevant to my research, to include papers for systematic review and, where applicable, to papers.

For review of the article, we set an eligibility requirement, as years from 2003-2020 are considered. Google Scholar, NCBI and PubMed are the sources of information that provides the information.

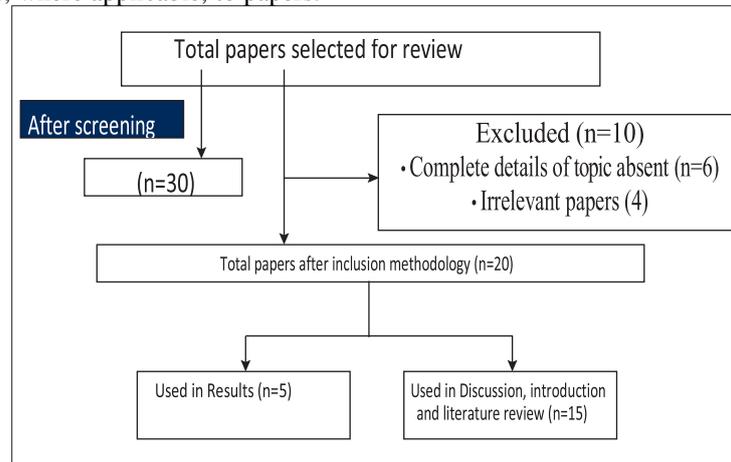


Figure 1: Process of selection of Papers

Relationship between Diabetic Retinopathy (DR) and Diabetic Nephropathy (DN):

Numbers of articles for this phase are reviewed and only 5 articles have been chosen to explain the connection between diabetic retinopathy (DR) and diabetic nephropathy (DN). (Table 1) offers a description of the findings presented in the following paper:

Table 1: Summary of the review papers

Sr. No	Authors	Year	Research type	Results
1.	Lee, W. J	2014	cross-sectional study	DR itself is associated with overt nephropathy
2.	Zhang, J	2018	cross-section study	DR may predict the renal prognosis of patients with DN.
3.	Cao, X	2019	Retrospective Study	Diabetic nephropathy patients with and without diabetic retinopathy have different clinical and laboratory profiles.
4.	Zachariah, S	2015	Review study	The Scottish Grading protocol grades the severity of retinopathy from R0 to R4 and of maculopathy as a separate grade from M0 to M2
5.	Mogensen, C. E.,	1983	Review study	Alterations in renal function and structure are found even at the onset of diabetes mellitus.

Grading of DR

The Scottish Grading Protocol measures the severity of the grade of R0-4 and M0-M2 retinopathy (Table 1). R6 is an additional classification for weak pictures that cannot be rated. If patients suffer mechanical photographic loss, they must be further tested by biomicroscopy with slit lamps (Zachariah, S. et al 2015).

Table 2. The different grades of diabetic retinopathy (DR) in the Scottish Grading Protocol: features and outcomes

Grade	Features	Outcome
R0	No disease	Rescreen in 12 months
R1	Mild background DR Including microaneurysms, flame exudates, >4 blot haemorrhages in one or both hemifields, and/or cotton wool spots	Rescreen in 12 months
R2	Moderate background DR >4 blot haemorrhages in one hemifield	Rescreen in 6 months
R3	Severe non-proliferative or pre-proliferative DR: >4 blot haemorrhages in both	Refer

	hemifields, intra-retinal microvascular anomalies (IRMA), venous beading	
R4	Proliferative retinopathy NVD, NVE, vitreous haemorrhage, retinal detachment	Refer
M0	No macular findings	12 month rescreening
M1	Hard exudates within 1–2 disc diameters of fovea	6 month rescreening
M2	Blot haemorrhage or hard exudates within 1 disc diameter of fovea	Refer

Stages of nephropathy

Changes in renal function and architecture arise right as diabetes mellitus starts. Studies in the last ten years now allow the production of renal diabetes changes to be described in a number of phases. This distinction may be useful for both clinical and study studies.

Early hyperfunction and hypertrophy are characterized by stage 1. These modifications are noticed before therapy with insulin. A further signature result is decreased urinary albumin excretion, exacerbated during exercise. Alterations in insulin treatment are at least partially reversible. Step 2 grows slowly for several years, with no clinical symptoms marked by morphological lesions. But examination and morphometry of the kidney system on biopsy specimens was seen to alter. A number of patients are still living in stage 2. Stage 3, the precursor for open-layer diabetic nephropathy is initial diabetic nephropathy. Its primary effect, assessed by radio-immune test, is the abnormally accelerated excretion of urinary albumin. The key characteristic of this phase, that in the base situation seemed to be approximately 15 and 300 $\mu\text{g} / \text{min}$, is a rate higher than the values in normal subjects and somehow lower in clinical disease. Here in this crucial phase of kidney disease,

when blood pressure increases, a slow gradual rise over the years is predominant. In patients with increased blood pressure, the increased rate of albumin excretion is higher. GFR is also being tested in this process of supranormal and antihypertensive treatment using a physical activity method.

Step 4 is the primary agent of chronic proteinuria-active diabetic nephropathy ($> 0,5 \text{ g}/24 \text{ h}$). The mean decrease in renal function is about 1 ml / min / MB when linked high blood pressure is left unchecked. The long-term treatment reduces the rate of decline by approximately 7 and therefore substantially postpones uremia.

Stage 5 is renal endstage total failure to diabetic nephropathy with uremia. The biggest medical concern today in culture is diabetic nephropathy and diabetic vasculopathy (Mogensen, C. E., 1983).

Diabetic retinopathy may predict the renal outcomes of patients with diabetic nephropathy:

Zhang j in his paper pointed to DR as well as DR as the independent risk for renal results in DN patients, where DR was able to accurately predict the renal prognosis in patients with DN. Zhang J also pointed out that DR had significantly been linked to DR.

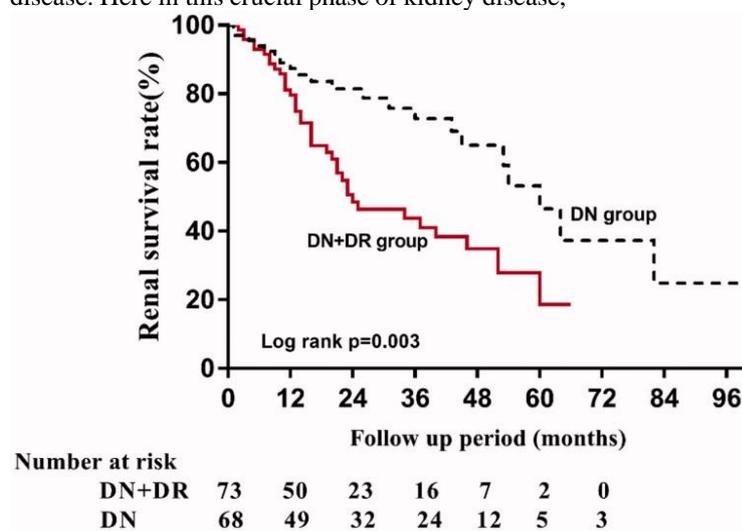


Figure 2: The renal rate of survival of Kaplan – Meier curves for DN patients with or without DR.

The connection between DR and DN can be defined from the following chart. Here DR factors in a renal DN prediction. Figure CI shows the interval of confidence; HR is the risk ratio. Model 1 relates to the period of T2DM at renal biopsy, the age, class, hypertension as well as the cigarette smoking. For-covariate plus HbA1c, hematuria and Serum Creatinine, Model 2 is adapted. Model 3 fixed in model 2 to the clinical variables and other renal pathology results, like glomerular and inflammation score interstitial (Zhang, J 2018).

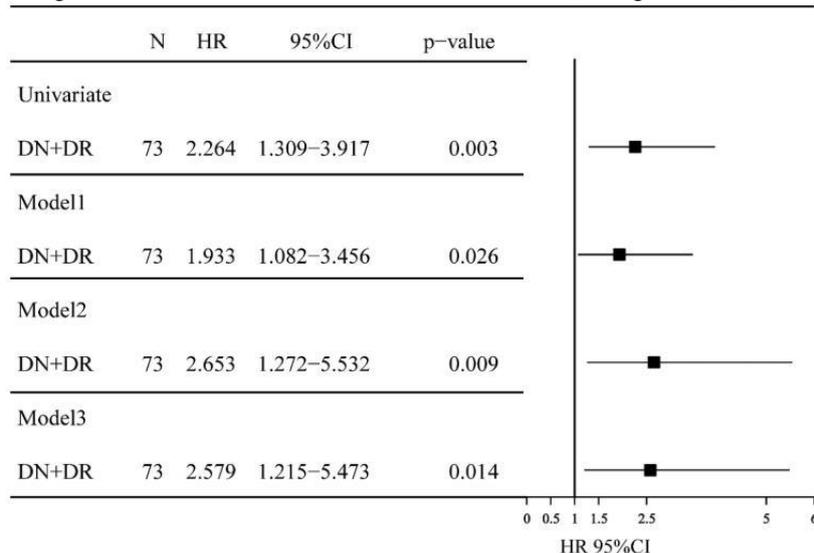


Figure 3: ESRD advancement hRrs for patients with the use of univariate / multivariate COX hazard analysis only for the cohort study DN + DR versus DN.

Characteristics of No-DN group in DM Patients

This was a cross - sectional design based on the population. DR itself is correlated with severe nephropathy, and in patients with DM, a incidence with 20.0 percent was observed in either DR. The appearance of patients of DR may be an indication of DN involvement. If an eye surgeon considers the involvement of DR, it will recommend speaking with an inner and / or referral to a nephrologist. The features of DN in DM patients are described in the following (table no 2). Written as mean (SD) are the values.

Table 3: DN unit characteristics in DM patients

Characteristics	DN, n = 731
Men, %	51.3
Age, y	61.91 (10.97)
HTN, %	57.7
Duration of HTN, y	8.00 (7.90)
Duration of DM, y	6.2 (7.5)
Total cholesterol, mg/dL	185.2 (42.1)
DR, %	16.3
PDR, %	2.3
CSME, %	0.5
ACR, µg/mg	7.37)

Comparisons between diabetic nephropathy patients without diabetic retinopathy

Table 3 compares the numerical properties of patients with or without diabetic retinopathy with diabetes nephropathy (pure diabetic nephropathy and diabetes nephropathy with coexisted non-diabetes renal disease). Diabetic nephropathy (p=0.047) is slightly higher in the diabetic nephropathical patients with retinopathy than diabetic nephropathy (p<0.001) and diabetic vascular disorders (p=0.047). In diabetic nephropathic patients without retinopathy, the length of hypertension was substantially longer (p=0.041). Diabetic nephropathy patients with and without diabetic retinopathy have similarly distributed the various population resources.

Table 4: Diabetic nephropathic patient characteristics

Numbers of patients	217	106	111	p-Value	
Age	51.74±8.41	49.73±11.31	53.12±8.86**	0.058	
Hight (cm)	156.15±9.01	155.85±8.99	155.81±8.71	0.974	
Weight (kg)	58.41±8.22	58.11±8.01	57.99±7.91	0.912	
Body mass index (kg/m2)	24.45±2.01	24.41±1.95	24.46±1.81	0.845	
Gender	Male	145 (67)	72 (68)	73 (66)	0.211
	Female	72 (33)	34 (32)	38 (34)	0.062
Waist circumference (cm)	86.45±9.41	85.88±9.21	85.71±9.01	0.891	
Hip circumference (cm)	93.31±9.45	93.22±9.31	93.18±9.21	0.975	
Waist to hip ratio	0.91±0.09	0.90±0.08	0.91±0.08	0.358	
Waist to height ratio	0.56±0.02	0.55±0.02	0.56±0.05	0.057	
Diabetic complications					
Diabetic neuropathy	34 (16)	24 (23)*	10 (9)	<0.001	
Diabetic vascular diseases	68 (31)	35 (33)*	33 (30)	0.047	
Duration of diabetes (years)	9.74±7.48	10.33±6.77	9.14±8.19	0.241	
Duration of hypertension (years)	7.42±7.48	6.21±6.77	8.54±8.19**	0.041	
Area of residence	Urban	99 (46)	43 (41)	46 (41)	0.999
	Rural	118 (54)	63 (59)	65 (59)	
	Han Chinese	199 (92)	98 (92)	101 (91)	
Ethnicity	Tibetan	3 (1)	3 (3)	0 (0)	0.1
	Mongolian	15 (7)	5 (5)	10 (9)	
	Inactive	49 (23)	24 (23)	25 (22)	
Physical activity	Moderately active	101 (47)	49 (46)	52 (47)	0.995
	Active	67 (30)	33 (31)	34 (31)	

This study shows that diabetic nephropathy patients with different clinical and laboratory profiles without diabetes retinopathy. Diabetic nephropathy patients without DR tend to be less damaged by the kidneys, fewer diabetic complications and a better prognosis than diabetic nephropathy patients with DR.

DISCUSSION:

No connection between diabetic nephropathy and diabetic retinopathy was found in few studies (Kotlarsky P, 2015). However, several research studies have shown that diabetes retinopathy has been associated with diabetes mellitus in patients with type 2 diabetes mellitus. These findings reveal the presence of diabetic retinopathy with DNA but are sometimes inconsistent with diabetic retinopathy and DNA as separate diseases in Han in China (Jeng CJ, 2016). We explored the correlation between diabetic retinopathy and diabetic nephropathy and concentrated on parameters distinguishing between diabetic

nephropathy with retinopathy and diabetic nephropathy without retinopathy. Though this pathological mechanism for diabetic nephropathy and diabetic retinopathy were very well documented, research suggests distinctions among diabetic nephropathy and diabetic retinopathy. We also found that the renal outcomes of patients with diabetes nephropathy can be forecast by diabetic retinopathy.

In his report Cao X, 2019 concluded that patients who are diabetic nephropathic have various clinical and laboratory statuses in and without diabetic retinopathy. However, in 2017 Ahmed, M. H et al

conducted an experiment to prove that nephropathy and retinopathy develop significantly. A cross-sectional hospital dependent research was performed in Makkah 's complicated retina center, which included a total of 316 individuals with diabetes. Standard questionnaire was used for demographic information, medical history and the characteristics of life style. They concluded that about a third of diabetic patients have developed nephropathy, a major link between nephropathy and retinopathic development.

In a population-based study of diabetes mellitus (DM) patients in Korea, Lee has also carried out an experiment in 2014 to determine the relation between diabetes retinopathy (DR) and diabetes nephropathy (DN), including microalbuminuria and open nephropathy. This was a cross-sectional study based on the population. It was determined the prevalence of DR and DN. Multivariate logistical regression was carried out to determine risk factors in Korea, including DR.

In DM patients a 20.0% frequency for every DR and 3.8% for proliferative diabetic retinopathy (PDR) have been reported. Overt nephropathy risk factors included long duration of DM and the existence of DR. Overt DM is linked with proliferative diabetic retinopathy and DR is correlated with overt nephropathy. Their findings suggested that a timely assessment of the renal status of the patient must be suggested when the eye surgeon finds the presence of DR or PDR (Lee WJ, 2014).

A number of other scholars, such as Rius Riu and Tzeng, supported our findings. In Spanish clinics, Rius Riu and others developed a significant association between CAD incidents and the current ap pain or worsening of diabetic retinopathy and nephropathy (Rius RF, 2003). In contrast, Tzeng et al. found an association of a sign leniency with advanced nephropathy, often in dialytic patients (Tzeng TF, 2001).

CONCLUSION:

The findings suggest a close association between diabetic retinopathy and diabetic nephropathy. DR itself is correlated with accessible nephropathy and there is a 20.0% occurrence in DM patients. The appearance of patients of DR may be an indication of DN involvement. Jeng and Zhang studies may suggest that the renal results in patients with diabetic nephropathy may be expected by diabetic retinopathy. Diabetic nephropathy ($p=0.047$) is slightly higher in the diabetic nephropathical patients with retinopathy than diabetic nephropathy ($p<0.001$) and diabetic vascular disorders ($p=0.047$).

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