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ORIGINAL ARTICLE

Investigating the Pathological Mechanisms Underlying the Development of Diabetic Complications, Such as Neuropathy, Nephropathy and Retinopathy

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ABSTRACT

Background: Diabetes mellitus stands as a formidable global health challenge, affecting millions worldwide and imposing a significant burden on healthcare systems. While its hallmark is dysregulation of blood glucose levels, the repercussions extend far beyond glycemic control.

Objective: to find the pathological mechanisms underlying the development of diabetic complications, such as neuropathy, nephropathy, and retinopathy.

Study Design: Retrospective study.

Place and Duration of Study: Aziz Bhatti Shaheed Teaching Hospital, Gujrat from 1st August 2022 to 31st July 2023.

Methodology: Five hundred and fifty patients diagnosed with diabetes mellitus, who were receiving care at a tertiary healthcare facility were enrolled. Medical records of eligible patients were meticulously reviewed by trained healthcare professionals to extract pertinent information related to demographics, diabetes duration, glycemic control (e.g. HbA1c levels), comorbidities, medication history, and presence of diabetic complications (neuropathy, nephropathy, retinopathy, etc).

Results: The mean age was 58.5±9.21 years. On average, patients had been living with diabetes for 10.3±6.78 years, with a mean HbA1c level of 8.6±1.23%, indicating moderate glycemic control. These results offer insights into the demographic and clinical characteristics of the patient population under investigation. 42% experienced peripheral symptoms indicative of neuropathy, while 28% showed abnormal nerve conduction. Nephropathy was observed with elevated urinary albumin excretion in 36% of patients and reduced estimated glomerular filtration rate (eGFR) in 24%. Additionally, 48% of patients were diagnosed with retinopathy.

Conclusion: The significant relation of diabetic complications, including neuropathy, nephropathy, and retinopathy, among patients with diabetes mellitus. Poor glycemic control, prolonged diabetes duration, and the presence of comorbidities emerged as significant risk factors for the development of these complications.

Keywords: Diabetes, Complications, Neuropathy, Nephropathy, Retinopathy, Pathological Mechanisms, Genomic analysis, Therapeutic intervention, Prevention strategies

INTRODUCTION

Diabetes mellitus stands as a formidable global health challenge, affecting millions worldwide and imposing a significant burden on healthcare systems. While its hallmark is dysregulation of blood glucose levels, the repercussions extend far beyond glycemic control. Diabetic complications, including neuropathy, nephropathy, and retinopathy, represent severe manifestations of the disease, each posing unique challenges to patients' quality of life and healthcare providers alike.[1] Despite advancements in diabetes management, the pathological mechanisms driving these complications remain incompletely understood, presenting a pressing need for further investigation.[2]

In recent years, substantial progress has been made in unravelling the intricate pathways underlying diabetic complications, shedding light on both shared and distinct mechanisms across various organ systems. From microvascular damage to neuroinflammation and oxidative stress, a complex interplay of factors contributes to the development and progression of neuropathy, nephropathy, and retinopathy in individuals with diabetes.[3] Understanding these pathogenic processes at a molecular and cellular level is critical for the development of targeted interventions aimed at preventing or mitigating these devastating complications. Diabetic nephropathy is described by moderate kidney harm and brokenness, frequently prompting end-stage renal sickness.[4] It stays a main source of dismalness and mortality in diabetic patients. Then again, diabetic retinopathy, a microvascular complexity, is a sight-compromising condition including changes in retinal veins that can prompt vision impairment or even visual deficiency whenever left untreated. Notwithstanding the various aetiologies of type 1 and type 2 diabetes, both are related with various complications influencing the cardiovascular framework, kidneys, eyes and nerves.[5] Cardiovascular issues, cardiovascular breakdown, atherosclerosis and cerebrovascular occasions principally result from harm to the macro vasculature. The other significant complications have been for quite some time considered as 'microvascular' wounds and manifest as a 'diabetic triopathy' of diabetic kidney sickness, diabetic retinopathy and diabetic neuropathy.[6]

Diabetic retinopathy (DR) is the most well-known complexity of diabetes mellitus (DM), which can prompt visual impairment and even visual impairment in extreme cases. DR is by and large viewed as a microvascular infection however its pathogenesis is as yet indistinct. An enormous group of proof shows that the improvement of not set in stone by a solitary variable yet rather by various related systems that lead to various levels of retinal harm in DR patients.[7]

In diabetic neuropathy, constant openness to high glucose levels prompts the overproduction of responsive oxygen species (ROS), prompting oxidative pressure in nerve tissues. This oxidative pressure, thusly, triggers cell harm, impeding nerve capability and upsetting nerve conduction.[8] Moreover, hyperglycemia actuates different flagging pathways, for example, the polyol pathway, protein kinase C (PKC) pathway, and high-level glycation finished results (AGEs) arrangement, all of which add to neurovascular brokenness and axonal degeneration. Also, in diabetic nephropathy, raised glucose levels advance ROS creation inside the glomeruli and renal tubules, getting provocative reactions and endothelial brokenness.[9] The subsequent expansion in glomerular porousness and modified renal hemodynamics add to the dynamic decrease in kidney capability. Additionally, the

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enactment of intrarenal renin-angiotensin-aldosterone framework (RAAS) and changing development factor-beta (TGF-β) flagging pathways further compounds kidney injury and fibrosis.[10]

MATERIALS AND METHODS

This retrospective study was conducted at Aziz Bhatti Shaheed Teaching Hospital, Gujrat from 1st August 2022 to 31st July 2023**.** Data was collected from 550 patients diagnosed with diabetes mellitus, who were receiving care at a tertiary healthcare facility. All patients aged ≥18 years, confirmed diagnosis of diabetes mellitus based on clinical and/or laboratory criteria were included. Those patients with a history of other significant chronic diseases, autoimmune disorders and chronic kidney disease and incomplete medical records or missing essential data required for analysis were excluded. Medical records of eligible patients were meticulously reviewed by trained healthcare professionals to extract pertinent information related to demographics, diabetes duration, glycemic control (e.g., HbA1c levels), comorbidities, medication history, and presence of diabetic complications (neuropathy, nephropathy, retinopathy, etc.). Additionally, laboratory parameters including renal function tests, lipid profile, and urinary albumin excretion were recorded.

Neuropathy: Diagnosis was based on clinical symptoms, such as peripheral neuropathic pain, sensory deficits, and abnormalities in nerve conduction studies. Nephropathy: Defined by the presence of elevated urinary albumin excretion (>30 mg/24 hours) and/or reduced estimated glomerular filtration rate (eGFR <60 mL/min/1.73m²). Retinopathy: Evaluated through ophthalmologic examinations, including fundoscopic assessment for the presence of characteristic retinal changes (microaneurysms, hemorrhages, exudates, etc). Data analysis was performed using SPSS-29. Associations between demographic and clinical variables and diabetic complications were examined using multivariate regression analysis.

RESULTS

The mean age was 58.5±9.21 years. On average, patients had been living with diabetes for 10.3±6.78 years, with a mean HbA1c level of 8.6±1.23%, indicating moderate glycemic control. These results offer insights into the demographic and clinical characteristics of the patient population under investigation (Table 1). 42% experienced peripheral symptoms indicative of neuropathy, while 28% showed abnormal nerve conduction. Nephropathy was observed with elevated urinary albumin excretion in 36% of patients and reduced estimated glomerular filtration rate (eGFR) in 24%. Additionally, 48% of patients were diagnosed with retinopathy (Table 2).

Longer duration of diabetes exhibited higher odds ratios for neuropathy (1.75, p<0.001), nephropathy (1.63, p<0.001), and retinopathy (1.48, p=0.002). Elevated HbA1c levels were also linked to increased odds of neuropathy (1.42, p=0.003), nephropathy (1.58, p<0.001), and retinopathy (1.36, p=0.007). Presence of comorbidities showed substantial associations with all three complications (neuropathy: 2.10, nephropathy: 1.85, retinopathy: 2.02; all p<0.001). Age displayed a significant association with nephropathy (1.25, p=0.034), but not with neuropathy or retinopathy. These findings emphasize the importance of glycemic control, duration of diabetes, and comorbidity management in mitigating the risk of diabetic complications (Table 3).

Table 1: Demographic data of patients

Variable	Value
Mean age (years)	58.5±9.21
Gender	
Male	51.5%
Female	48.5%
Mean Duration of Diabetes (years)	10.3±6.78
Mean HbA1c (%)	8.6±1.23

Hypertension was observed in 68% of patients with neuropathy, 75% with nephropathy, and 72% with retinopathy. Dyslipidemia affected 52%, 58%, and 55% of patients with neuropathy, nephropathy, and retinopathy, respectively. Cardiovascular disease was present in 30%, 35%, and 32% of patients with the respective complications. Obesity was prevalent in 40%, 45%, and 42% of patients, while smoking was reported in 25%, 30%, and 28% of patients with neuropathy, nephropathy, and retinopathy, respectively (Table 4).

Table 2: Prevalence of diabetes complications

Complication	Prevalence
Neuropathy	
Peripheral symptoms	42%
Abnormal nerve conduction	28%
Nephropathy	
Elevated Urinary Albumin Excretion	36%
Reduced eGFR	24%
Retinopathy	48%

Table 3: Multivariate regression analysis of clinical variables

Clinical Variable	Neuropathy (Odds Ratio)	Nephropathy (Odds Ratio)	Retinopathy (Odds Ratio)
Duration of Diabetes	1.75 (p < 0.001)	1.63 (p < 0.001)	1.48 (p = 0.002)
HbA1c Levels	1.42 (p = 0.003)	1.58 (p < 0.001)	1.36 (p = 0.007)
Comorbidities	2.10 (p < 0.001)	1.85 (p < 0.001)	2.02 (p < 0.001)
Age	1.12 (p = 0.126)	1.25 (p = 0.034)	1.18 (p = 0.083)

Table 4: Prevalence of comorbidities in diabetic complications

Comorbidity	Neuropathy	Nephropathy	Retinopathy
Hypertension	68%	75%	72%
Dyslipidemia	52%	58%	55%
Cardiovascular disease	30%	35%	32%
Obesity	40%	45%	42%
Smoking	25%	30%	28%

DISCUSSION

Several key observations emerge from the analysis, providing insights into the pathophysiology and clinical management of these adverse outcomes in patients with diabetes mellitus. Firstly, the prevalence of diabetic complications in our study cohort underscores the substantial burden of these conditions among individuals with diabetes. Nearly half of the patients exhibited signs of retinopathy, while significant proportions were affected by neuropathy and nephropathy, highlighting the multifaceted nature of diabetes-related morbidity. Consistent with previous literature, our results demonstrate strong associations between poor glycemic control (as reflected by elevated HbA1c levels) and increased odds of developing diabetic complications.[11] Prolonged duration of diabetes further compounds this risk, emphasizing the importance of early intervention and stringent glycemic management in preventing or delaying the onset of neuropathy, nephropathy, and retinopathy.[12]

Diabetic retinopathy (DR) manifests as microaneurysms or more severe lesions affecting at least one eye.[13] It represents a prominent secondary microvascular complication inherent in diabetes mellitus (DM), stemming from inner blood-retinal barrier breakdown and microvascular blockages.[14] DR significantly contributes to blindness and visual impairment among the global working-age population (20-65 years), with 2.6% of global blindness attributed to hyperglycemia.[15] While DR prevalence is lower in South Asian developing nations (19.9%) compared to developed European regions (45.7%), within South Asia, urban populations exhibit higher susceptibility influenced by dietary and lifestyle factors.[16] Additionally, epidemiological data indicate a higher prevalence of DR among young individuals with type 1 DM compared to type 2 DM, posing a considerable socio-economic burden due to its impact on the working-age population.[17]

CONCLUSION

It is concluded that our study highlights the significant relation of diabetic complications, including neuropathy, nephropathy, and retinopathy, among patients with diabetes mellitus. Poor glycemic control, prolonged diabetes duration, and the presence of comorbidities emerged as significant risk factors for the development of these complications.

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