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FREQUENCY OF NEPHROPATHY IN TYPE 2 DIABETIC PATIENTS PRESENTED TO MARDAN MEDICAL COMPLEX

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Abstract

INTRODUCTION: *It is acknowledged that type 2 diabetes is a major public health issue that significantly affects both human life expectancy and medical costs. Diabetes alone is among the top ten cause of death, accounting for almost 1 million fatalities annually. The most common cause of mortality for diabetic individuals is diabetic nephropathy which is also the primary cause of kidney failure. Ethnicity, family history, gestational diabetes, high blood pressure, dyslipidaemia, obesity, and insulin resistance are the main risk factors for diabetic nephropathy, according to several epidemiological studies.*

OBJECTIVE: *To determine the frequency of diabetic nephropathy in type 2 diabetic patients presented to Mardan Medical complex.*

STUDY DESIGN: *Cross Sectional.*

STUDY SETTING: *Department of General Medicine, MMC, Mardan.*

STUDY DURATION: *17-04-2024 to 17-10-2024.*

SUBJECTS AND METHODS: *For 165 patients, urine samples were taken and were sent to laboratory to determine the presence or absence of albumin through urine R/E. Blood samples from all patients were taken to determine serum creatinine level in order to estimate Glomerular Filtration Rate (GFR) using Cockcroft-Gault formula. Diabetic Nephropathy as per operational definition was recorded on specially designed proforma.*

RESULTS: *Mean and standard deviation calculated for age was 48.21 ± 11.20 years, for BMI was 27.05 ± 3.45 kg/m², and for diabetes duration was 11.06 ± 6.61 years. Majority patients (30.3%) were in the 30-40 years group. Gender distribution showed 63% male and 37% female. The study found that 69.1% were literate, 66.1% lived in urban areas, and 81.8% were married. Diabetic nephropathy (DN) was observed in 33.3% of the participants.*

CONCLUSION: *Given that diabetic nephropathy is a leading cause of end-stage renal disease globally, understanding its prevalence and the factors contributing to its development is crucial for effective disease management. The findings of this study indicate a significant 33.3% prevalence with male predominance of 20.6% within the study population, which aligns with previous studies. Additionally, this study suggests further investigation into the*

environmental, genetic, and lifestyle factors contributing to the disparities in DN rates globally.

INTRODUCTION

Type 2 diabetes mellitus constitutes a substantial worldwide health challenge, impacting approximately 462 million individuals in 2017, equating to 6.28% of the global population. This metabolic condition accounts for approximately one million fatalities each year, making it the tenth greatest cause of mortality globally. The current prevalence in Pakistan is 11.77%, with a higher incidence in males (11.20%) than in females (9.19%), and a greater illness burden in urban areas compared to rural regions.[1,2]

Diabetic nephropathy, a progressive kidney disease, is one of the most severe consequences of diabetes and the primary cause of end-stage renal failure in diabetic individuals. About one-third of patients with diabetes may experience this consequence, with 20-40% advancing to chronic renal disease. Insidious nature of diabetic nephropathy poses a considerable clinical challenge, as overt indications like proteinuria usually appear only in advanced stages, often postponing diagnosis until considerable kidney damage has transpired. This delayed manifestation often requires costly and onerous therapies like dialysis or kidney transplantation, imposing significant pressure on both individuals and healthcare systems. [3,4]

The advancement and evolution of diabetic nephropathy are affected by numerous interconnected elements. Chronic hyperglycemia, indicated by increased HbA1c levels, is the principal cause of renal impairment. Contributing factors encompass hypertension, dyslipidaemia, obesity, insulin resistance, smoking, and pre-existing proteinuria. The disease exhibits a distinct pathological progression, commencing with glomerular basement membrane thickening in its initial stage (Class I), progressing to mesangial expansion (Class II) and nodular sclerosis formation (Class III), and ultimately resulting in extensive glomerulosclerosis (Class IV), characterised by irreversible damage in over 50% of glomeruli. Clinical data reveal that the average annual incidence of diabetic nephropathy is 3% within the initial 10-20 years post-diabetes onset, with microvascular problems generally emerging after around 15 years of persistent hyperglycemia. Contemporary therapeutic approaches, however proficient in decelerating illness advancement, provide minimal capacity for correcting existing renal impairment. Inhibitors of the renin-angiotensin system continue to be the foundation of treatment, with recent developments such as sodium-glucose cotransporter 2 (SGLT2) inhibitors showing substantial kidney protective benefits, as demonstrated by the CREDENCE study.[5,6] Sana MA et al. performed a study on 133 people with diabetes mellitus. The average age of the people who took part was 54.5 years, with 60.9% being men and 39.1% being women. Diabetic nephropathy happened in 30.1% of the people, with 25.6% having microalbuminuria and 4.5% having macroalbuminuria. [6]

The significant interval between disease onset and clinical identification highlights the urgent necessity for improved screening techniques, especially in high-risk groups. Future research should emphasise the creation of innovative therapeutic agents that can both arrest and possibly reverse the pathological mechanisms of diabetic nephropathy, while public health initiatives ought to concentrate on early intervention strategies to alleviate this escalating global health issue.

MATERIAL AND METHODS

This cross-sectional study was conducted at the Department of General Medicine, Mardan Medical Complex, Mardan, Pakistan, over a period of six months (April 17, 2024, to October 17, 2024). A total of 165 participants diagnosed with type 2 diabetes, aged between 30 and 70 years and of either gender, were included through non-probability consecutive sampling. The sample size was calculated by taking the frequency of nephropathy 30.1% in Diabetic patients[6], with 95% confidence level, and 7% absolute precision, calculated through WHO software. Patients requiring dialysis for chronic renal failure were excluded to prevent potential confounding effects.

Type 2 diabetes was defined as fasting blood glucose ≥126 mg/dL on two separate occasions after an 8-hour fast, a 2-hour post-glucose load value ≥200 mg/dL during an oral glucose tolerance test (OGTT), or a

hemoglobin A1c (HbA1c) level ≥6.5%, along with a history of antidiabetic medication use for over three months. Diabetic nephropathy was identified based on a urinary albumin-creatinine ratio (UACR) exceeding 30 mg/dL in a spot urine sample or an estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73m², calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

Data collection commenced after obtaining ethical approval and informed consent from participants or their close relatives. Baseline demographic and clinical information, including age, gender, residence, marital status, education level, body mass index (BMI), comorbidities, socioeconomic status, and diabetes duration, were recorded. Urine samples were analyzed for albuminuria via routine urine examination (R/E), while serum creatinine levels were measured to compute eGFR.

Statistical analysis was performed using SPSS version 26.0. Categorical variables (e.g., gender, education, nephropathy status) were expressed as frequencies and percentages, whereas continuous variables (e.g., age, BMI, diabetes duration) were reported as mean ± standard deviation. The outcome variable, nephropathy, was stratified across demographic and clinical factors, followed by chi-square testing to assess associations. A p-value ≤0.05 was considered statistically significant, with results presented in tabular form.

RESULTS

Mean age of study population was 48.21 ± 11.20 years, mean BMI was 27.05 ± 3.45 kg/m^2 and mean duration of diabetes was 11.06 ± 6.61 years.

The study population was divided into four age groups, with the highest proportion of patients (30.3%) falling within the 30–40-year range. Study was male dominated. Regarding education, 69.1% of patients were literate and the majority resided in urban areas (66.1%). Socioeconomic status distribution showed slightly more patients in the poor category. Marital status data revealed that most participants were married (81.8%), with smaller proportions being unmarried or divorced. A comprehensive detail of demographic profile of study population is presented in table 1.

Diabetic Nephropathy was observed in 33.3% (n=55) of total study population while it was not observed in 66.7% patients (n=110).

The prevalence of nephropathy was highest in middle-aged individuals (41–60 years), with rates of 9.7% and 9.1%, respectively. Men experienced a greater impact (20.6%) compared to women (12.7%), indicating a possible gender disparity in disease progression. The body mass index (BMI) was a contributing factor, with the highest prevalence (16.4%) noted among overweight adults. Education and residency proved to be relevant determinants, as literate patients (19.4%) and urban residents (18.2%) had higher nephropathy rates, both demonstrating statistically significant relationships (P=0.032 and P=0.027 respectively). The length of diabetes significantly affected risk, with the highest incidence observed in individuals with 1–10 years of the condition (13.9%), but the probability diminished over time (P = 0.049). Marital status exhibited a correlation with nephropathy, as married individuals (29.7%) were the most affected, potentially because to prolonged disease exposure or lifestyle variables. Socioeconomic status, meanwhile, exhibited no significant disparity across the groups (table 2).

Table 1: Demographic profile of Study participants (n = 165)

Variable	Category	Frequency	Percentage (%)
Age Groups (Years)	30–40	50	30.3
	41–50	47	28.5
	51–60	39	23.6

Variable	Category	Frequency	Percentage (%)
	61–70	29	17.6
Gender	Male	104	63.0
	Female	61	37.0
Educational Status	Literate	114	69.1
	Illiterate	51	30.9
Residence	Urban	109	66.1
	Rural	56	33.9
Socioeconomic Status	Good	78	47.3
	Poor	87	52.7
Marital Status	Married	135	81.8
	Unmarried	24	14.5
	Divorced	6	3.6

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Table 2: Stratification of diabetic nephropathy for demographic variables (n=165)

Variable	Category	Nephropathy Positive	Nephropathy Negative	p-value
Age (years)	30-40	12 (7.3%)	38 (23.0%)	0.351
	41-50	16 (9.7%)	31 (18.8%)	
	51-60	15 (9.1%)	24 (14.5%)	
	61-70	12 (7.3%)	17 (10.3%)	
Gender	Male	34 (20.6%)	70 (42.4%)	0.820
	Female	21 (12.7%)	40 (24.2%)	

Variable	Category	Nephropathy Positive	Nephropathy Negative	p-value
BMI	20.1-25.0	15 (9.1%)	37 (22.4%)	0.600
	25.1-30.0	27 (16.4%)	53 (32.1%)	
	30.1-35.0	13 (7.9%)	20 (12.1%)	
Education	Literate	32 (19.4%)	82 (49.7%)	0.032*
	Illiterate	23 (13.9%)	28 (17.0%)	
Diabetes Duration	1-10 years	23 (13.9%)	67 (40.6%)	0.049*
	11-20 years	22 (13.3%)	33 (20.0%)	
	21-30 years	10 (6.1%)	10 (6.1%)	
Residence	Urban	30 (18.2%)	79 (47.9%)	0.027*
	Rural	25 (15.2%)	31 (18.8%)	
Socioeconomic	Good	27 (16.4%)	51 (30.9%)	0.741
	Poor	28 (17.0%)	59 (35.8%)	
Marital Status	Married	49 (29.7%)	86 (52.1%)	0.226
	Unmarried	05 (3.0%)	19 (11.5%)	
	Divorced	01 (0.6%)	05 (3.0%)	

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DISCUSSION

Type 2 diabetes mellitus is a multifaceted disorder characterised by elevated blood glucose levels resulting from dysfunction in insulin use or production, or both.[7] By 2030, around 439 million individuals globally are projected to have diabetes.[8] Chronic diabetes can result in damage, malfunction, and failure of several organs, including the eyes, nerves, feet, blood vessels, kidneys, and heart.[9] Prolonged diabetes is linked to microvascular problems such as retinopathy, neuropathy, and nephropathy.[10] Microvascular problems of diabetes can result in renal impairment, referred to as diabetic nephropathy (DN), which is the predominant consequence of type 2 diabetes mellitus.[11] Diabetic nephropathy is the predominant cause of end-stage renal disease globally and is linked to elevated rates of morbidity and death.[12] It impacts around 40% of individuals with diabetes, generally manifesting around 10 years post-diagnosis

of type 2 diabetes.[13] Diabetic nephropathy is characterised by sustained albuminuria (an albumin excretion rate exceeding 300 mg/day or 200 μg/min) assessed at least twice within three to six months, a gradual decline in the Glomerular Filtration Rate (GFR), frequently associated with hypertension, ultimately resulting in end-stage renal disease.[14,15]

Identifying individuals at heightened risk for diabetic nephropathy (DN) is essential for improved disease treatment. Multiple causes and processes facilitate the onset and advancement of diabetic nephropathy. Albuminuria is a crucial biomarker for assessing renal function, particularly indicating glomerular damage and heightened permeability to macromolecules. Nonetheless, albuminuria may remain undetectable throughout the initial phases of diabetic nephropathy.[16, 17] It possesses drawbacks, such as significant variability and limited sensitivity, and it fails to reliably predict renal outcomes or particularly identify diabetic nephropathy.[18]

There are several significant biomarkers for kidney damage and disease that aid in the early detection of Diabetic nephropathy.[7] Biomarkers are defined as characteristic factors that can be objectively measured and assessed as indicators of normal physiological or pathogenic processes. Examples of biomarkers include proteins, lipids, microRNAs, genomic, metabolic, or proteomic patterns, electrical signals, imaging determinations, and cells present in a urine analysis.[19]

The current study found that the prevalence of diabetic nephropathy in the entire population with Type 2 diabetes mellitus was 33.3%. The prevalence of diabetic nephropathy in the current research corresponds with a German study that revealed diabetic nephropathy in 20–30% of individuals.[20] Nevertheless, the present prevalence rate somewhat exceeds the 26.1% identified in a cross-sectional, population-based research of urban Type-2 diabetes mellitus patients in South India.[21] Conversely, the incidence of DN is significantly lower, at 10.8%, according to a research based on a Saudi national diabetes registry.[22] These discrepancies may stem from racial or ethnic disparities within the research population.[23]

The diabetes epidemic, primarily Type 2 Diabetes Mellitus, in Pakistan is particularly concerning. Due to the frequently postponed diagnosis of diabetes in Pakistan, diabetic neuropathy constitutes a considerable social and economic burden. It is essential to prioritize the establishment of obligatory protocols for early diagnosis and prevention. Studies indicate that dietary and physical activity interventions effectively diminish the risk of metabolic diseases. To mitigate the disease burden on individuals and society, early health screenings, health education, and integrated lifestyle interventions should be instituted in high-risk populations. [24]

A study in China by Zhang XX et al. demonstrated that the prevalence of diabetic nephropathy varied considerably depending on the diagnostic criteria employed for diabetes and nephropathy. Over the last 40 years, these diagnostic criteria have undergone multiple revisions, potentially affecting the diagnosis and monitoring of diabetic neuropathy (DN). The research indicated that the advantages and disadvantages of various biomarkers and classifications for diabetes and nephropathy should be evaluated for case identification, population prevalence estimation, and healthcare expenses. This outcome underscored the necessity for forthcoming multicenter studies employing standardized methodologies and protocols for the identification of diabetes and nephropathy. [25] A study in the United States similarly demonstrated spatial variance in the adjusted incidence rates of end-stage renal disease. [26]

The disparities in diabetes prevalence and detection substantially influence the geographic diversity of diabetic nephropathy prevalence among individuals with Type-2 DM.

Diverse factors, including disparate lifestyles, dietary habits, and advancements in healthcare systems, contribute to this diversity. Physical inactivity, hypertension treatment, serum cholesterol regulation, and smoking cessation are essential considerations. Moreover, environmental and genetic factors may have a role in this phenomena, suggesting a necessity for additional research. [27, 28]

The gender-specific prevalence of diabetic nephropathy in the current investigation indicated a male predominance, with nephropathy observed in 20.6% of male patients and 12.7% of female patients. The gender-related findings of the current study correspond with those of prior investigations. The research conducted by Zhang XX et al. revealed that the prevalence of diabetic nephropathy was greater among male participants than among female ones. [25]

This conclusion is corroborated by the research conducted by de Hauteclocque et al. [29] Nevertheless, certain research suggest that females with Type 2 diabetes mellitus may possess an elevated risk of diabetic nephropathy compared to males. 30 The variable outcomes concerning sex differences may stem from multiple aspects, including divergent risk factors for diabetes onset and postponed diabetes diagnosis. This area necessitates additional investigation in subsequent study.

Despite the increasing incidence of diabetic nephropathy (DN) in Pakistan, a comprehensive examination of its nationwide prevalence and associated risk factors among Pakistani patients with type 2 diabetes mellitus (T2DM) has not been conducted. The difference in diabetic nephropathy prevalence among T2DM patients in Pakistan has not been published, constraining our comprehension of its severity and characteristics.

The research indicates that the aforementioned studies underscore the importance of enhancing awareness regarding the maintenance of a healthy lifestyle, the prevention of diabetes, and the necessity of early medical intervention to avert diabetic nephropathy.

CONCLUSION

In conclusion, this study provides a comprehensive analysis of the prevalence of diabetic nephropathy (DN) among patients with Type-2 DM. Given that DN is a leading cause of end-stage renal disease globally, understanding its prevalence and the factors contributing to its development is crucial for effective disease management. The findings indicate a significant 33.3% prevalence of DN within the study population, which aligns with previous studies. Notably, the study identifies key demographic and socioeconomic variables, such as age, gender, educational status, duration of diabetes, residence, and marital status, that significantly correlate with the occurrence of DN. The gender-related findings indicate a male predominance in DN prevalence i.e., 20.6%, which mirrors trends observed in other studies, although some literature suggests that females may be at higher risk due to varying factors, including delayed diagnosis. Additionally, this study suggests further investigation into the environmental, genetic, and lifestyle factors contributing to the disparities in DN rates globally. This will enable healthcare providers to develop targeted strategies for early identification and management.

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