Association between Diabetic Nephropathy Grade and Quality of Life among Type II Diabetic Patients

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[4]*Department of Anatomy, Faculty of Medicine, Mansoura University, Mansoura, Egypt***Abstract**

Introduction: One of the most profound long-standing consequences of diabetes mellitus is diabetic nephropathy. In many countries, diabetes is proved to be the most frequent single cause of end-stage renal disease. ***Aim of the work***: analyze the association between diabetic nephropathy grade and quality of life among type II diabetic patients. ***Material and methods***: Quantitative descriptive study design applied on a purposive sample of 41 individuals with type II diabetes attended to the medical outpatient clinic in Menoufia University Hospital. ***Tools:*** Tool I- A structured interviewing questionnaire. Tool II- Assessment of the kidney function. Tool III- Kidney Disease Quality of Life. ***Results***: serum creatinine and blood urea nitrogen were increased, also the estimated glomerular filtration rate (eGFR) was decreased in individuals with type II diabetes as disease duration increase. The prevalence of diabetic nephropathy in the current work was high representing 56.1%. In addition increasing body mass index more than 25. Diabetic nephropathy was associated with all five HRQOL dimensions as patients in stage 3-kidney disease had lower scores than patients in stages 1 and 2. ***Conclusion***: The present data confirm that the most striking risk factors for diabetic nephropathy in the type II diabetes are BMI $\geq$ 25, diabetes duration, hypertension, age $\geq$ 50 years, and family history. ***Recommendation***: The current study recommended that urinalysis should be performed regularly as part of a screening program which is a preventive intervention to preserve the kidneys in diabetic patients and will detect individuals with nephropathy early.

*Key words***:** Diabetes mellitus, eGFR , diabetic nephropathy, kidney functions

Introduction

Diabetes mellitus (DM) and associated consequences have reached pandemic proportions, affecting the economy and health worldwide. Worldwide, the overall number of diabetic persons with is expected to rise from 415 million (8.8 %) in 2015 to 642 million (10.4 %) in 2040, with the most substantial changes likely to happen in the urban population of low- to middle-income countries (LMICs). Of these, type II diabetes accounts for over 90 % of individuals with diabetes. [1, 2]

DM and Diabetic Nephropathy (DN) are both global and public health problems, as Diabetic kidney disease (DKD) developed in 20–40%of diabetic patients. DN is a progressive renal disease that evolves over time, peaking after 10–20 years of diabetes. [3]   DM has progressively overtaken chronic glomerulonephritis as the leading reason of kidney function loss. This implies that more individuals will suffer kidney impairment throughout their lives. [4]

The incidence of Diabetic Nephropathy as a cause of ESKD is increasing each year. DKD is characterized by increased urine albumin excretion or decline of a glomerular filtration rate (GFR), or both. The United States National Kidney Foundation 2002 guidelines had pointed that chronic kidney disease is for individuals having a glomerular filtration rate less than 60 ml/min/1.73 m^2 for a period exceeding three months (stage 3 to 5), or GFR more than 60 ml/min/1.73m2 (stage 1 to 2) in case of there is a clue regarding kidney damage. [5]

Moderate albuminuria is more frequent in type II diabetes than type I diabetes. Its prevalence rate affects between 21 and 39 %. Severe albuminuria has been found to occur in 3.0-20.5 % . The frequency of albuminuria has not altered over time but definitely varies among ethnic groups. [6, 7]

Because individuals with type II diabetes mellitus often have several comorbidities, such as obesity and hypertension, renal damage may be evident before the initial visit to a doctor. As a result, chronic kidney disease may be present even when diabetes mellitus is diagnosed. [8]

The increasing identification of non-proteinuric diabetic chronic kidney disease may be attributed in part to improved glycaemic, lipid, and blood pressure management, the lower HbA1c levels are linked with lower albuminuria but not improved GFR. [9]

The stimulation of inflammatory promoters, suppression of antioxidant defense systems, and insulin resistance have all been related to the worsening of kidney disease in diabetic persons.

Furthermore, a prior research found that individuals with DN and DM had greater co-morbidities, as well as worse uremia and volume load tolerance. [7] As a consequence, these patients had to deal with greater limitations in their everyday lives and less social participation, and they needed dialysis sooner than non-diabetic patients. As a result of these variables, diabetic individuals with Diabetic Nephropathy have a greater number of unfavorable factors affecting their HRQOL. Detecting and treating early in diabetes can help to improve these patients' HRQOL, although the gradual loss of renal function and problems in other organs. [10]

One of the main objectives of modern medicine is health-related quality of life (HRQOL), which is suitable for Diabetic Nephropathy and patients with DM getting long-term therapy and care for their progressive and complicated diseases. Evaluating health-related quality of life and associated variables in patients with Diabetic Nephropathy and DM is critical for guiding health education and suitable personalized treatment. [11, 12]

At the level of disease prevention, increasing public awareness about diabetes and its associated risk factors as obesity and lack of exercise is essential and can support current institutional efforts. This can be achieved through collaborative work from all stakeholders such as the ministry of health (MOH) and universities in several ways such as including the publication of small Arabic booklets in plain language, Discussions, lectures, etc[13, 14]

Finally, to combat the increasing prevalence of diabetes, there is now an urgent need for a long-term national plan focusing on prevention, education, and a multidisciplinary approach. As well as monitoring the health services and evaluating them to ensure their influential role in reducing the burden of diabetes[10,13] CKD and DM interact, causing damage to the kidney as well as other organs such as the retina, cardiovascular, and neurological systems. [15] Furthermore, there was no reliable data in Egypt on the duration of DKD for patients with diabetes and its association to HRQOL. [13, 16] Therefore, the present research was intended to evaluate HRQOL in patients with Diabetic Nephropathy and DM, as well as to explore the relationship between DM and HRQOL in patients with CKD stages 1 to 4. Early detection and treatment of glucose metabolism disorders in Diabetic Nephropathy patients by health care professionals will help to their good quality of life.

Significance of the study

Diabetes prevalence and incidence are rising globally, with a fast progression observed in middle- and low-income nations. According to the latest version of the International Diabetes Federation (IDF) about 9.2 % aged 18–99 years (39.9 million people) in the Middle East and North Africa Region (MENA) had diabetes in 2017. The number of diabetics in the Middle East and North Africa area is predicted to be greater than double by 2045 (International Diabetes Federation, 2017). [17]

Egypt is an Arab country with a high incidence of microalbuminuria and one of the nations with the greatest prevalence of macroalbuminuria. The prevalence of diabetes 20% in urban Egypt. Diabetic albuminuria prevalence 21% in Egypt. According to an Egyptian cross-sectional research,42 % of diabetes patients had nephropathy, 22% had peripheral neuropathy, 0.8 % had foot ulcers, and 5% were blind. [18]

DM and its consequences have involved significantly to the burden of death and morbidity globally. [19] The Worldwide burden of disease study 2015 recognized DM as the 9th main reason for decreased life expectancy and revealed that high fasting blood glucose (FBG) level was the third most frequent worldwide risk hazard for morbidity-adjusted life years in 2015[20]

Quality of life (QoL) indices are strong determinants of person's ability to sustain long-term health, well-being, and productivity. Enhancing QoL has been identified as a key objective of all healthcare treatments, including diabetes control regimens. As a result, it is critical to understand the degree of health-related QoL (HRQoL) of diabetes patients in relation to the significant expenditure from the national budget. Identifying variables linked with poor HRQoL may aid policymakers in allocating funding and implementing initiatives to enhance QoL[21]

Diabetes affects patients' QoL, according to research from the Middle East and the rest of the globe, although the degree of impairment varies. All the studies advocated for enhancing diabetes patients' health and HRQoL in order to minimize the social and individual expenses associated with diabetes treatment [22-25]

Despite the fact that diabetes is currently the main cause of CKD, the HRQOL of Egyptian patients with CKD and diabetes is widely unclear. [16] Therefore, the current research was designed to investigate the relationship between DM and HRQOL in patients with CKD stages 1 to 4.

Aim of the study

This study was intended to analyze the association between diabetic nephropathy grade and quality of life among type II diabetic patients.

Research questions

The following research question was tested

- Is there an association between diabetic nephropathy grade and quality of life among type II diabetic patients?

Material and Methods

Study Design:

Quantitative descriptive study design applied on a purposive sample to achieve the aim of this study

Study setting

The study conducted at medical outpatient clinic at Menoufia University Hospital, Egypt.

Study period

The study conducted at a specific time (between the dates of 1 January to 30 April 2021).

The study population

Men and Women who have type II (DM) and visited/registered /attending medical outpatient clinic in Menoufia University Hospital at the specified time for the study.

Sampling

In this study a purposive sample was used. According to outlined several criteria for

inclusion and exclusion, it was selected to obtain a representative sample .

A total of 41 subjects with type II diabetes were eligible for the study and attended the medical outpatient clinic in Menoufia University Hospital during the period of study were screened.

Inclusion criteria: Ages $\geq$ 30 years old, Men and Women who have type II DM.

Exclusion criteria: Patients with evidence of kidney disease before onset of diabetes.

Data collection tool

The following tools were used to collect data:

Tool I- A structured interviewing questionnaire: It was developed by the researchers and contained socio-demographic and medical data sheet of the patients; it included characteristics of the study participants as gender, age, marital status, level of education, history of medical disease, type of diabetes, duration of diabetes, past history, and family history.

Tool II- Assessment of the kidney function: it was included the following lab investigations as kidney function tests that include (serum creatinine, blood urea nitrogen, and uric acid) were assessed by Cobas c 311 analyzer Operator's Manual from The clinical chemistry analyzer Cobas c 311 5th generation of routine and

dedicated chemistry experiences (cobas® 4000 analyzer series). [26]

Estimation of GFR:

By using The CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation which was developed by Levey et al., (2009) [27] The CKD-EPI equation, expressed as a single equation, is: $eGFR = 141 * min (Scr/\kappa,1)^{\alpha} * max(Scr/\kappa, 1)^{-1.209} * 0.993^{Age} * 1.018$ [if female] $* 1.159$ (if black) Scr is serum creatinine (mg/dL), κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1. The median estimated GFR was 94.5 mL/min per 1.73 m^2.

Staging of kidney disease

Staging of chronic kidney disease was applied according to the National Kidney Foundation's Kidney Disease Quality Outcome Initiative (KDOQI) guidelines for the classification and evaluation of CKD. [28]

Stage 1 kidney disease: eGFR ≥ 90 mL/min/1.73m^2

Stage 2 kidney disease: eGFR= 60-89 mL/min/1.73m^2

Stage 3 kidney disease: eGFR = 30-59 mL/min/1.73m^2

Stage 4 kidney disease: eGFR= 15-29 mL/min/1.73m2

Stage 5 kidney disease (kidney failure): eGFR < 15 mL/min/1.73m^2)

Estimation of BMI according to Nuttall, 2015 [29]

-BMI: Weight (kg)

       Height (m2)

- Normal weight = 18.5–24.9   Overweight = 25–29.9   Obesity = 30 or greater

Tool III- Kidney Disease Quality of Life Instrument (KDQOL)

The KDQOL™-36 questionnaire version was applied to evaluate HRQOL in CKD patients; it was found to be a straightforward, effective, and trustworthy tool [30, 31] The scale has five dimensions: symptoms and complaints (S), kidney disease effects (E), renal disease burden (B), SF-12 physical function (PCS), and SF-12 mental function (M) (MCS). PCS is a flexible measure for assessing HRQOL in both patients and healthy people. [32] The original scores were linearly transformed to a 0–100 scale. A higher score indicates greater HRQOL. Scoring System of Kidney Disease Quality of Life Instrument (KDQOL) 5 scores ranging from 0 to 4 are given for Standardized answer options of none, mild, moderate, severe, and extreme, where none equal zero that, meant there was no difficulty to the extreme which meant the worst condition equal 4.

Validity of the tools:

All tools were tested for their content validity by three experts in the field of Medical-Surgical Nursing, Faculty of Nursing, Menoufia University, and two experts in the field of medical laboratories. Modifications were done accordingly.

Validity of Kidney Disease Quality of Life Instrument (KDQOL)

The questionnaire was reviewed for content validity by a five of experts in the field of medical-surgical nursing.

Reliability of tools:

Reliability was estimated among 10 participants by using the test-retest method with two weeks apart between them. Then Cronbach alpha reliability test was done through the SPSS computer package. It was 0.80 for interviewing questionnaire with the following Cronbach alpha reliability values for its parts.

Reliability of Kidney Disease Quality of Life Instrument (KDQOL):

The instruments' internal consistency was verified by the researchers. It is the administration of the same instruments to the same individuals under identical circumstances on one or more times. The Cronbach's alpha for the questionnaire was 0.9. The accuracy of all instruments shows excellent reliability.

Pilot Study:

To assess the stability of the responses, a pilot research was performed on 10% (5 patients) of the study sample that was not included in the sample. It was carried out to evaluate the readability of the questionnaire. It also assisted in estimating the time required to finish the surveys**.**

Ethical considerations:

This study was approved by the Ethical Committee for scientific research review in Menoufia University- faculty of nursing. Official permission was obtained from the hospital manager and head nurse of outpatient clinics.

All participants were given written and verbal information about the research. Participants completed a written permission form and were assured of confidentiality prior to the interviews. They were told that their participation in this research was entirely voluntary and that they may withdraw at any moment without cause. The research's objective was explained to them, and they were reassured that any information collected would be kept private and utilized solely for the purposes of the study.

Data Collection procedure: -

Preparation of data collection tools was carried out over a period of one month after extensive literature of review.

The tools were translated into Arabic format.

An official permission was obtained from the director of Menoufia University Hospital to take the agreement to collect the data.

- Data was collected in every Saturday according the hospital director who detected this day for data collection.

- All the participants were interviewed and assessed individually in the outpatients' clinics.

- The researchers collected all the interviewed participants who existed in this day of interview in groups.

The group was ranged from 3 to 5 participants.

The researchers explained the purpose of the study to the sample at the start of the interview and informed them that participation in the study was voluntary, any data given was confidential and used only for research purposes, and any participant could withdraw from the study at any time without giving a reason.

The interview lasted 15 minutes to fill the first part of the questionnaire (demographic characteristics and assessment them for BMI and Kidney Disease Quality of Life Instrument (KDQOL).

 Thereafter, blood samples were taken for the kidney function tests by cobas c 311 and Estimation of GFR.

Other medical data were taken from patient file.

Statistical Analysis: -

The numerical data were collected and computerized using the SPSS program (Statistical Package of Social Science) program, version 22.

The association between (renal function tests) and (duration of diabetes mellitus) were analyzed using the chi-square to detect the significances between variables of the study.

Descriptive analyses and frequency tables were carried out using this program for all variables. The data description was done in the form of mean ± standard deviation (SD) for normally distributed quantitative data.

 -Significance difference was considered when the P-value was ≤ 0.05 at a confidence interval of 95.%

- Odds ratio (with 95% confidence interval) and p-value of 0.05 or less were used as a level of significance for evaluating the risk factors of diabetic nephropathy. The association between different variables and the dimensions of HRQOL was assessed by univariate linear analysis. Multivariable regression analysis was carried out to determine factors associated with HRQOL.

Results

A total of 41 subjects with type II diabetes who presented at the outpatient clinic throughout the study period were screened. None of the subjects included had evidence of kidney disease.

Table (1) showed the relation between fasting blood glucose (FBG), socio-demographic data, and risk factors. About 56.1% of patients were female, with no significant difference between males and females in the level of FBG. About 75.6% of patients were more than 50 years old while 24.4% less than 50years with no significant difference in the level of FBG between the two groups. About 87.8% of patients had a body mass index (BMI)more than or equal to 25 while 12.2% had BMI less than25, those with high BMI had a significant increase in FBG more than other groups. About 58.8% of patients were hypertensive and had FBG higher than normotensive patients, representing 41.5% of patients. About 73.2% of patients had a positive family history with a higher level of FBG than other groups with negative family history, representing 26.8% of the study group.

Table (2) showed Kidney function tests in diabetic patients based on the duration of diabetes. It was observed that mean serum creatinine was increased with the duration of diabetes in both males and females, but it still within the normal reference range.

Mean serum creatinine showed a significant increase in male more than female in diabetic patients less than 5 years of diabetes (0.83±0.02 and 0.67±0.12) respectively. Also, there was a significant increase in males more than females in patients with 5-10 years of diabetes (0.99±0.22 and 0.69 ± 0.13) respectively.

Mean serum blood urea was increased with the duration of diabetes in both males and females, but it still within the normal reference range. It showed a significant increase in males more than females in diabetic patients more than 10 years of diabetes (6.30 ±1.02 and 5.30 ± 0.90) respectively.

Mean serum uric acid was increased with the duration of diabetes in both males and females, but it still within the normal reference range. It showed a significant increase in males more than females in diabetic patients less than 5 years diabetes (4.16±1.27 and 3.31±1.11) respectively.

Table (3) showed a negative correlation between estimated glomerular filtration rate (eGFR) and duration of diabetes as eGFR is decreased with increased duration of diabetes. Also, eGFR is decreased with an increase in age in diabetic patients. It was (104.90 ± 11.88) and (103.85 ± 14.07) in patients < 50 years with duration of

diabetes <5years and >10years respectively. In patients ≥ 50 years, it was (92.25 ± 12.90) and (89.51 ± 10.89) with a duration of diabetes <5years and >10years respectively. It was also observed a significant decrease in eGFR in patients of ≥ 50 years compared with patients < 50 years with duration of diabetes less than 5 years and more than 10 years.

Table (4) showed a high rate of diabetic nephropathy (proteinuria) as the calculated prevalence was 56.1%. This study demonstrated staging of kidney disease in diabetic patients with proteinuria based on eGFR according to National Kidney Foundation's Kidney Disease Quality Outcome Initiative (KDOQI) guideline. It was observed that there was a positive correlation between the stage of kidney damage and the duration of diabetes. Diabetic patients with less than 5 years duration were stratified into 50% had stage 1 kidney damage, about one third had stage 2, and 16.7 had stage 3 kidney damage. Those with a duration of 5-10 years of diabetes were stratified into33.33% had stage 1 kidney damage, 33.33% had stage 2, and 33.34%.7 had stage 3 kidney damage. Finally, Diabetic patients with more than 10 years duration had the worst prognosis, being stratified into 20% with stage 1 kidney damage, 20% with stage 2, and 60 with stage 3 kidney damage.

Table (5) showed the presence or absence of proteinuria in diabetic patients based on the duration of diabetes as a risk factor. It was observed a significant positive correlation between the presence of proteinuria and the duration of diabetes. In patients with duration < 5 years, the frequency was 55.6% have no proteinuria while 44.4% had proteinuria. In patients with duration 5-10 years, the frequency was 25% have no proteinuria while 75% had proteinuria. In patients with duration > 10 years, the frequency was 16.7% have no proteinuria while 83.3% had proteinuria.

Table (6): showed the number and frequency of subjects with proteinuria concerning other risk factors. It was observed that proteinuria was highest in diabetic patients with age ≥ 50 years presenting (43.90%) of all diabetic patients. Proteinuria was highest in female diabetic patients presenting (29.30%) of all diabetic patients. It was observed that there was a significant correlation between proteinuria and BMI with increasing frequency in patients with BMI ≥ 25 reaching (56.1%) of all patients. Also, hypertension affected greatly on diabetic patients with a significant correlation between proteinuria and hypertension reaching a frequency of (34%) in diabetic patients. Family history of diabetes had a significant impact on proteinuria as

patients with positive family history presenting (43.9%) had proteinuria of all diabetic patients.

Table (7): demonstrates relative risk (RR) and odds ratio (OR) for risk factors of diabetic nephropathy based on proteinuria.

Figure (1): is the forest plot for odds ratio (OR) and relative risk (RR) for DN in the sample of the study. Patients with BMI $\geq$ 25 was the most significant risk with OR being 7.08 (0.93-14.33). Duration of diabetes was the second significant risk factor with OR of 6.48 (3.26 – 12.2) and 3.75(2.08 – 6.80) for the duration >10 years and 5-10 years respectively. Patients with a positive family history had an OR (95%CI) of 1.8 (0.51 – 7.22) followed by hypertension and Age $\geq$ 50 years with OR (95%CI) of 1.56(0.46 – 5.50) and 1.39 (0.3309 – 5.804), respectively. The female gender showed the lowest risk for proteinuria, with OR (95%CI) of 0.69 (0.19 – 2.30).

Table   (8) indicates that diabetic nephropathy was associated with all five HRQOL dimensions (P < 0.05). For patients in Stage 3-kidney disease, their scores in the "symptoms and problems," "effects of kidney disease," and Burden of kidney disease had higher than patients in the other two stages, indicating more problems and a higher level of symptoms. However, for physical function and Mental Function dimensions, patients in Stage 3-kidney disease had lower scores than patients in the other 2 stages, representing a lower level of functioning and health.

Table   (9) indicates that, diabetic nephropathy was   related   to   with dimensions of Effects of kidney disease and Physical Function in the subgroup of CKD stages 1 to 2, whereas associated with symptoms problems and Physical Function in CKD stage 3. Although multivariable adjustments attenuated the magnitude of the relation, the statistical significance was essentially unchanged. The magnitude of the relation for the dimension of Physical Function was a slightly weaker in CKD stages 1 to 2 than that in CKD stage 3 with the regression coefficients of − 1.80 and − 2. 39, respectively.

Table (1): Relation between fasting blood glucose (FBG), socio-demographic data and risk factors.

Variabeles		Type II Diabetes Patients (41)		P-value
		Fasting Blood Glucose (mg/dl)		
		Reference range (70-99mg/dl)		
Sex		**Male**	**Female**	0.719
	Count (%)	18 (43.9%)	23 (56.1%)	
	Mean FBG	177.95±60.66	185.77±75.79	
Age		**< 50 years**	**≥ 50years**	0.754
	Count (%)	10 (24.4%)	31 (75.6%)	
	Mean FBG	187.33±69.80	179.46±68.22	
BMI		**< 25**	**≥ 25**	0.020*
	Count (%)	5(12.2%)	36(87.8%)	
	Mean FBG	177.31±68.59	210.71±47.43	
Hypertension		**Normotensive**	**Hypertensive**	0.548
	Count (%)	17 (41.5%)	24 (58.5%)	
	Mean FBG	173.70 ± 47.32	186.83±79.8	
Family History		**-ve Family Hx**	**+ve Family Hx**	0.291
	Count (%)	11 (26.8%)	30 (73.2%)	
	Mean FBG	162.69 ± 59.20	188.24± 70.83	

*P value <0.05 (Significant)

Table (2): Kidney function tests in diabetic patients based on duration of diabetes.

Variables		Reference range	< 5 years	5-10 years	> 10 years	Significance between groups (P value)
Mean Serum Creatinine (mg/dl)	**Male**	0.20 – 1.50	0.83±0.02*	0.99±0.22*	1 ± 0.88	0.4
	Female		0.67±0.12	0.69 ± 0.13	0.73±0.30	0.8
Mean Blood Urea Nitrogen (BUN)	**Male**	2.76 – 8.07	4.37 ± 1.07	4.80±1.03	6.30 ±1.02*	0.2
	Female		4.35±1.02	4.48 ± 0.83	5.30 ±0.90	0.1
Mean Uric acid (mg/dl)	**Male**	2.4 – 7.0	4.16±1.27*	4.43±1.07	4.99±1.09	0.2
	Female		3.31±1.11	4.19 ±0.62	4.23±1.24	0.9

*P value <0.05 (Significant)

Table (3): Relation between estimated glomerular filtration rate (eGFR) and duration of diabetes mellitus in different age groups.

Variables	Reference range	< 5 years	5-10 years	> 10 years	Pearson correlation	Significance between groups (P value)
eGFR in patients < 50 years (mL/min/1.73m^2)	99-116	104.90 ± 11.88*	104.45 ±18.60	103.85 ± 14.07*	- 0.037	0.9
eGFR in patients ≥ 50 years (mL/min/1.73m^2)	75-93	92.25 ± 12.90	91.43 ± 8.32	89.51 ± 10.89	- 0.123	0.5

*P value <0.05 (significant between age groups)

Table (4):Prevalence of different stages of diabetic nephropathy according to duration of diabetes based on presence of proteinuria

Variables	Total number of patients with proteinuria (23 , (56.1%))					
	Stage 1 kidney disease eGFR ≥ 90 mL/min/1.73m^2	Stage 2 kidney disease eGFR= 60-89 mL/min/1.73m^2	Stage 3 kidney disease eGFR = 30-59 mL/min/1.73m^2	Stage 4 kidney disease eGFR= 15-29 mL/min/1.73m^2	Stage 5 kidney disease (kidney failure) eGFR < 15 mL/min/1.73m^2	Pearson correlation, P value
< 5 years (12) No (%)	6 (50%)	4 (33.33%)	2 (16.67%)	0	0	0.351 0.1
5-10 years (6) No (%)	2 (33.33%)	2 (33.33%)	2 (33.34%)	0	0	
> 10 years (5) No (%)	1(20%)	1 (20%)	3 (60%)	0	0	

Table (5): Number and frequency of subjects with proteinuria according to duration of diabetes

Variable	< 5 years No (%)	5-10 years No (%)	> 10 years No (%)	X^2, P-value
No Proteinuria	15 (55.6%)	2 (25%)	1 (16.7%)	4.08*
Proteinuria	12 (44.4 %)	6 (75%)	5 (83.3%)	< 0.05
Total number	27 (100%)	8 (100%)	6 (100%)	(0.217)

*P value <0.05 (Significant)

Table (6): Number and frequency of subjects with proteinuria in relation to risk factors.

| Variable		No Proteinuria 18 (43.9%)	Proteinuria 23 (56.1%)	Pearson correlation	P-value
Age	< 50	5 (12.20%)	5 (12.20%)	0.217	0.66
	≥ 50 years	13 (31.71%)	18 (43.90%)		
Sex	Male	7(17.1%)	11 (26.8%)	0.089	0.58
	Female	11 (26.8%)	12 (29.3%)		
BMI	< 25	4(9.8%)	1 (2.4%)	0.421	0.006 *
	≥ 25	13 (31.7 %)	23 (56.1%)		
Hypertension	Normotensive	9 (22%)	9 (22%)	0.130	0.04 *
	Hypertensive	9 (22%)	14 (34%)		
Family History	-ve family Hx	6 (14.6%)	5 (12.2%)	0.135	0.34
	+ve family Hx	12 (29.3%)	18 (43.9%)		

*P value <0.05 (Significant)

Table (7): Relative risk, odd ratio & 95% interval for diabetic nephropathy risk based on proteinuria.

Variable	Odds Ratio	Relative Risk	P-value, Fisher's exact test
Age ≥ 50 years	1.39 (0.33 – 5.80)	1.61 (0.65 – 2.57)	0.66
Female sex	0.69 (0.19 – 2.30)	0.85 (0.49 -1.50)	0.75
BMI ≥ 25	7.08 (0.93-14.33)	0.80 (0.54 -1.75)	0.0001*
Hypertension	1.56(0.46 – 5.50)	1.22(0.70 – 2.24)	0.53
+ve family Hx	1.8 (0.51 – 7.22)	1.32 (0.73 – 2.94)	0.34
DM Duration:5-10 yrs**	3.75(2.08 – 6.80)	1.69(1.33 – 2.19)	<0.0001*
DM Duration >10 yrs**	6.48 (3.26 – 12.2)	1.89 (1.51 – 2.42)	<0.0001*

*P value <0.05 (Significant)

** Related to diabetes duration < 5 years.
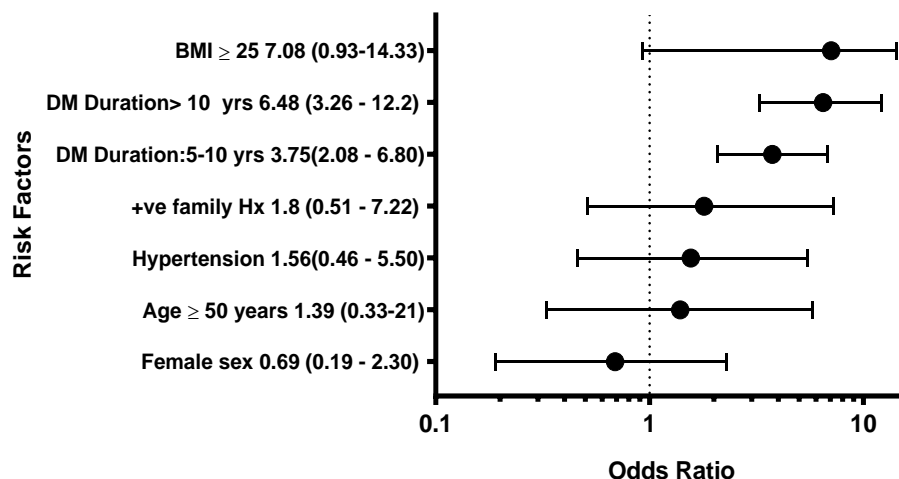
Fig. (1) :Forest plot for odds ratio & 95% confidence interval for diabetic nephropathy risk.

Table (8): Differences of health-related quality of life based on stages of diabetic nephropathy.

Variables	health-related quality of life					
	Stage 1 kidney disease eGFR ≥ 90 mL/min/1.73m^2	Stage 2 kidney disease eGFR= 60-89 mL/min/1.73m^2	Stage 3 kidney disease eGFR = 30-59 mL/min/1.73m^2	Stage 4 kidney disease eGFR= 15-29 mL/min/1.73m^2	Stage 5 kidney disease (kidney failure) eGFR < 15 mL/min/1.73m^2	Pearson correlation, P value
Symptoms and problems [#]	85.86± 13.71	88.72 ± 11.53	90.50 ± 10.71	0	0	< 0.001[**]
Effects of kidney disease[*]	83.77 ± 14.81	85.70 ± 13.04	87.29 ± 12.49	0	0	< 0·001[**]
Burden of kidney disease [*]	48.85 ± 27.40	50.30 ± 28.20	51.72 ± 28.40	0	0	0·149
SF-12 Physical Function (PCS) *	44.39 ± 8.82	43.50 ± 9.19	40.40 ± 9.77	0	0	< 0·001[**]
SF-12 Mental Function (MCS) [*]	50.50 ± 9.07	50.12 ± 9.82	50.60 ± 8.85	0	0	0.269

Note 1: [*] The variables are numerical and statistics are Mean (Standard deviation), *P*-value calculated based on *one-way Anova* test.

Note 2: [#] The variables are numerical and statistics are Median (Interquartile range), *P*-value calculated based on Wilcoxon test. Note 3: [**] Statistically significant at 0.05.

Table (9) The linear regression between diabetic nephropathy and KDQOL[TM]-36 scales stratified by CKD stages

KDQOL[TM]-36 scales	CKD stage 1-2		CKD stage 3	
	univariate regression	multivariable regression[**]	univariate regression	multivariable regression[**]
Log transformed symptoms and problems (S)[†]	0.014	-0.0026	0.028[*]	0.015[*]
Effects of kidney disease (E)	-1.94[*]	-2.10[*]	-0.70	-0.52
Burden of kidney disease (B)	-4.63	-4.36	0.070	-0.35
SF-12 Physical Function (PCS)	-3.38[*]	-1.80[*]	-3.52[*]	-2.39[*]
SF-12 Mental Function (MCS)	-1.07	-1.14	0.32	0.42

Abbreviations: CKD=chronic kidney disease.

Note 1: [*]Statistically significant at 0.05.

Note 3: [†] The log transformation was performed by the formula: ln (175-score of symptoms and problems).

Discussion

Nephropathy is the most frequent reason for end-stage renal disease in type II diabetes, although the decrease in renal function varies greatly across people, and the predictors of kidney function loss early in the course of renal disease have not been recognized. Therefore, early identification of patients vulnerable for diabetic nephropathy (DN) is essential to intensify the treatment and modify associated risk factors. [33]

In the current study, It was noticed that female patients constituted a higher percentage than males, with no significant difference between males and females in FBG. Chukwu, Ezebuiro, Samue, and Nwachukwu (2013) [34] documented that females showed a higher incidence of DM than males. Females are more influenced by type II diabetes owing to less muscle, which prevents absorption of a given glucose load, and because they have high estrogen and progesterone levels, which are implicated in the decrease of whole-body insulin sensitivity. [35] In the present study, about 87.8% of patients had body mass index (BMI) ≥ 25 while 12.2% had BMI < 25, those with high BMI had a significant increase in FBG more than other groups. According to a research conducted by Zunt et al. (2018) [36] BMI was one of the causes that increased the

frequency of diabetes in nearly all nations. In the current study, about 41.5% of patients were hypertensive and had FBG higher than normotensive patients, representing 58.8% of patients. About 73.2% of patients had a positive family history with a higher level of FBG than other groups with a negative family history, representing 26.8% of the study group. According to Ein, Armstrong, and Vickers (2019) [37] diabetes individuals received the illness from either of their parents. Bommer et al. (2018) [38] discovered that type II diabetes was induced by a hereditary factor from a close family member and was linked to gene mutations passed down via the family's genetic line.

Results in the present study revealed a positive correlation between renal function tests in diabetics and duration of diabetes as serum creatinine and blood urea levels were increasing with the duration of diabetes. Inassi and Vijayalakshmy (2013) [39] reported similar results.

In the present study, there was a negative correlation between eGFR and duration of diabetes as eGFR is decreased with increased duration of diabetes. Differences in the rate of GFR decrease in individuals with type II diabetes and nephropathy have previously been reported in prior research, ranging from 0.36 mL/min/1.73m /year to

4.7 mL/min/1.73m /year in the Japanese population (Leehey, Kramer, Daoud, Chatha and Isreb, 2005). If hyperglycemia is not adequately managed, a higher baseline GFR is observed in the early stages of diabetes. [40] Furthermore, the majority of observational studies and meta-analyses have shown a substantial association between greater baseline GFR and subsequent accelerated GFR decrease in diabetic individuals. [41] In our study, we showed a decline in eGFR in patients with age more than 50 years compared with those less than 50 years. Lin et al., (2021) [42] found that elderly showed a substantially negative correlation with baseline eGFR; the average baseline eGFR declines by 0.50 ml/min/1.73 m2 when a patient's age increased by 1 year.

The current study presented a high rate of diabetic nephropathy (proteinuria) as the prevalence was 56.1%. Similar results were reported in a research that included participants from three Gulf countries: Bahrain, the United Arab Emirates, and Oman found that the total prevalence of albuminuria was 36%. In Bahrain, the prevalence was 42.5 %, 34.5 % in the UAE, and 29 percent in Oman. [43]

The current study showed a positive correlation between stage of kidney damage and duration of diabetes in which diabetic subjects over 10 years duration had the worst prognosis being stratified into 20% with stage 1 kidney damage, 20% with stage 2, and 60% with stage 3 kidney damage. The role of diabetes duration has been proven by the United Kingdom Prospective Diabetes Study (UKPDS), where about 25% of patients exhibiting microalbuminuria or deteriorating nephropathy after 10 years. [44] Our study revealed a significant positive correlation between proteinuria and the duration of diabetes. Inassi and Vijayalakshmy (2013) [39] stated that the development of low but abnormal proportions of albumin in the urine is the first clinical sign of nephropathy. They also verified that microproteinuria became more common as the duration of diabetes increased.

In the current work, It was noticed that proteinuria was highest in diabetic patients with age group $\geq$ 50 years presenting (43.90%) of all diabetic patients. Jitraknatee, Ruengorn, and Nochaiwong (2020) [45] observed that type II diabetic patients aged 56–65, 66–75, and >75 years had more than 2.8-fold, 5.4-fold, and 27.4fold higher adjusted ORs for CKD, respectively. Previous research found that older age was accompanying with a greater incidence of CKD in type II diabetic patients. [46]

The present study revealed that proteinuria was highest in female diabetic patients

presenting (29.30%) of all diabetic patients. This was in accordance with Yang et al.(2018) [46] who stated that males had a lesser rate of CKD than females. This could be clarified by the fact that female patients in our study were older. This was contradictory with Al-Rubeaan et al.(2014) [47] who claimed that Saudi males with type II diabetes had a greater prevalence of diabetic nephropathy, as has been found in other populations in comparable research. This may be explained by the fact that the estrogen hormone is essential for protection.

It was noticed that there was a significant correlation between proteinuria and BMI with increasing frequency in patients with BMI $\geq$ 25 reaching (56.1%) of all patients. Obesity was identified as a risk factor in the progress of nephropathy in a Chinese study of 264 individuals with confirmed DKD based on renal biopsy. [48]

Our results demonstrated that hypertension greatly affected diabetic patients, with a significant correlation between proteinuria and hypertension reaching a frequency of (34%) in diabetic patients. A previous meta-analysis shown that hypertension is strongly linked with the development of diabetic nephropathy. [49] Inassi and Vijayalakshmy (2013) [39] documented that the microvascular consequences of diabetes mellitus are responsible for a

significant percentage of the related morbidity and death.

Family history of diabetes had a significant impact on the presence of proteinuria as patients with positive family history presenting (43.9%) had proteinuria of all diabetic patients. Chen, Li, Yang, Zhong, and Zhuang, (2016) [50] highlighted the importance of genetic susceptibility to DN through the substantial relationship between positive family history of DN and diabetic nephropathy development. Previous research has shown a link between the genes on the chromosome and type II diabetes-related kidney disease. Furthermore, diabetes family history is polymorphic and strongly associated with NOS3 rs11771443 in DN, which has never been observed previously.

The forest plot showed BMI $\geq$ 25 to be the most crucial risk factor followed by the duration of diabetes. Al-Rubeaan et al., (2014) [47] showed that diabetes duration to be the most critical hazard factor, particularly more than15 years. This was the same result across ethnic groupings, as shown by research in Korea, India, and Taiwan. [51, 52, 53]

The study findings indicated that diabetic nephropathy was associated with all five HRQOL dimensions (P < 0.05). For patients in Stage 3-kidney disease, their scores in the "symptoms and problems,"

"effects of kidney disease," and Burden of kidney disease had higher than patients in the other two stages, indicating more problems and a higher level of symptoms. However, for physical function and Mental Function dimensions, patients in Stage 3- kidney disease had lower scores than patients in the other 2 stages, representing a lower level of functioning and health. which suggested that diabetic nephropathy patients with CKD suffered a more impaired HRQOL. Also DM was ascertained to be negatively correlated with HRQOL in CKD patients in this study. [11]

According to univariate linear analysis, DM was associated with the "symptoms and problems," "effects of kidney disease," and "SF-12 physical function" dimensions. DM was significantly related to the dimensions of "symptoms and problems" and "SF-12 physical function". The results were consistent with the results of other countries that indicated that DM was related to low HRQOL in North America (P < 0.05). [12] In the study conducted in North America in 2016, their results were similar to our results, regarding the differences in demographic and clinical characteristics between the diabetic and non-diabetic groups. Another study in Japan found that HRQOL was impaired by the presence of DM. [54]

In the stratified analysis, diabetic nephropathy was associated with the effects of kidney disease and Physical Function in the subgroup of CKD stages 1 to 2, while associated with symptoms problems and Physical Function in CKD stage 3. Although multivariable adjustments attenuated the magnitude of association, the statistical significance was largely unchanged. The magnitude of association for the dimension of Physical Function was a little weaker in CKD stages 1 to 2 than that in CKD stage 3 with the regression coefficients of − 1.80 and − 2. 39, respectively.

Inconsistent with these results,(Chen et al., 2020) [11] recorded that DM was negatively correlated with HRQOL scores in both categories, but the magnitude and dimensions and of correlation were diverse. In impaired kidney function stage associated with increased co-morbidities (stages 3 to 4), the association between DM and the quality of life was enhanced in 2 dimensions of "symptoms and problems" and "SF-12 physical Function". In contrast, the association between DM and the quality of life was declining in 1 dimension, "effects of kidney disease," which may attributed to the increasing unfavorable impacts of low eGFR and enhanced or worsened consequences of CKD on the quality of life.

Another research in North America found that HRQOL was lesser in diabetic individuals with CKD stages 3 to 5. Regardless of renal disease stage, DM permanently results in a poor quality of life to this category of patients. As a result, healthcare workers should pay greater attention to the treatment of diabetes to maximize the long-term HRQOL in the course of treatment of patients with CKD. Diabetes control should not be neglected particularly when eGFR decreases substantially. [55]

Conclusion

Diabetic nephropathy manifests clinically in a predictable manner, beginning with proteinuria and progressing to end-stage renal failure. Diabetic nephropathy prevalence in this study was high representing 56.1%, raising concerns among the health professionals and decision-makers to deal with this problem. The current data confirm that the most striking risk factors for diabetic nephropathy in type II diabetes are body mass index BMI $\geq$ 25, diabetes duration, hypertension, age $\geq$ 50 years, and family history. Diabetic nephropathy was associated with all five HRQOL dimensions; patients in Stage 3-kidney disease had lower scores than patients in the other 2 stages, representing a lower level of functioning and health.

Recommendations

The current study recommended that urinalysis should be performed regularly as part of a screening program which is a preventive intervention to preserve the kidneys in diabetic patients and will detect individuals with nephropathy early.

We hope that our findings will raise awareness among health care workers about the relationship between diabetes and the quality of life in individuals with nephropathy in an attempt to enhance their quality of life by appropriate DM management.

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