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STUDY OF OUTCOME OF CHRONIC KIDNEY DISEASE IN DIABETIC PATIENTS IN THANJAVUR MEDICAL COLLEGE HOSPITAL

General Medicine

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ABSTRACT

Background: Diabetes Mellitus is one of the common causes of Chronic Kidney Disease which usually leads to end-stage kidney disease. Thus this study was planned to find out the outcome of CKD in DM, disease progression, appropriate management and the complications.
Methods: A cross sectional study among Diabetes Mellitus patients with Chronic Kidney Disease attending the Department of Nephrology and Department of Medicine in Thanjavur Medical College Hospital during the period of July and August 2018. The duration of study period was 2 months. All patients who attended the outpatient department (OPD) and in-patients departments with Type I and Type II diabetes mellitus associated with chronic kidney disease, on any line of management were included in this study. A total of 101 patients were included. Statistical Package for Social Sciences (SPSS for Windows V20) was used for data analysis.
Results: Poor glycemic control, albuminuria, hypertriglyceridemia (greater than 150), increase in LDL levels (greater than 100), BMI (greater than or equal to 25), poor BP control and a longer duration of diabetes mellitus had a strong positive correlation with decrease in eGFR less than 60 ml/min. Glycemic control, weight reduction and adequate BP control retard the progression of CKD.
Conclusion: Albuminuria and decline in eGFR both are independent risk factors for diabetic CKD and are strong predictors of morbidity and mortality from a major vascular event, especially cardiovascular complications and stroke.

KEYWORDS

Chronic Kidney Disease, Diabetes mellitus, Albuminuria, eGFR

INTRODUCTION

Chronic kidney disease (CKD) is an important health problem and it increases health care expenditure, morbidity and mortality. Diabetes Mellitus is one of the common causes of CKD and it is already the leading cause of end-stage kidney disease (ESKD) in most of the developed countries, and the growth in the number of people with ESKD around the world parallels the increase in diabetes. The presence of kidney disease is associated with a markedly elevated risk of cardiovascular disease and death in people with diabetes[1].Chronic kidney disease (CKD) has become the new epidemic of the twentieth and twenty-first centuries.

Chronic kidney disease comprises a spectrum of pathophysiological processes associated with abnormal kidney functions and progressive decline in Glomerular Filtration Rate (GFR). Stages of chronic kidney diseases are stratified by both estimated glomerular filtration rate (eGFR) and degree of albuminuria to predict the progression of disease.

Over 70% of the population with diabetes live in low and middle income countries. This rise, in prevalence of diabetes, increases disease related mortality and morbidity. The raise in disease significantly enhances the burden on health care infrastructure. The mortality and morbidity due to DM is attributed to a range of complications, which includes both micro-vascular and macro-vascular complications. One such micro vascular complication is diabetic nephropathy, which is characterized by micro albuminuria, which over a long period turns into macro albuminuria, causing overt nephropathy[2]. The glomerular filtration rate (GFR) degrades gradually during the disease progression. If not treated, nephropathy progresses into end stage renal disease.

CKD in patients who have DM, is clinically defined as, elevated urinary albumin excretion ≥ 30 mg/g, a persistent reduction in the estimated GFR (eGFR) <60ml/min/1.73 m^2 of BSA, or both[3]. This association of DM and CKD complicates the treatment of DM both clinically as well as financially. CKD in T2DM patients decreases the efficacy of oral anti diabetic drugs[4]. This shows the need for adjusting the dose of anti-diabetic drugs in T2DM patients with CKD. DM complications range from cardiovascular diseases, heart failure, renal failure, infections, adverse drug reactions,to impaired quality of life and premature mortality.

The reported prevalence of CKD in different regions ranges from 1% to 13%, and recently, data from the International Society of Nephrology's Kidney Disease Data Center Study reported a prevalence of 17%[5]. The etiology of CKD varies considerably throughout India. Parts of the states of Andhra Pradesh, Odisha and Goa have high levels of CKD of unknown etiology, which is a chronic interstitial nephropathy with insidious onset and slow progression[6].

Henceforth this study was planned to find out the outcome of CKD in DM, disease progression, appropriate management and the complications. This study also helps to enlighten diabetic patients, about the importance of glycemic control and the importance of renal failure diet to prevent the progression of diabetic nephropathy to chronic kidney disease.

Therapeutic Targets are

HbA1C <7% (estimated average glucose, 154 mg/dl)
BP <130/80 mmHg for CKD without proteinuria
LDL-C <100 mg/dL
BMI 18.5–24.9 kg/m2

AIMS AND OBJECTIVES

- To study the time of onset of Chronic Kidney Disease in diabetic patients, correlating – Chronic Kidney Disease with glycemic control, HbA1c values, lipid profile, albuminuria, eGFR and BMI values.
- To assess the percentage of diabetic chronic kidney disease patients requiring peritoneal dialysis, hemodialysis and renal transplant.

MATERIALS AND METHODS

This study was done as a cross sectional study among Diabetes Mellitus patients with Chronic Kidney Disease attending the Department of Nephrology and Department of Medicine in Thanjavur Medical College Hospital. The duration of study period was 2 months (July and August 2018).

INCLUSION CRITERIA

All patients who attended the outpatient department (OPD) and all in-patients with Type I and Type II diabetes mellitus associated with chronic kidney disease on any line of management (conservative and renal replacement therapy) and both the sexes above 25 years of age

were included in this study after obtaining written informed consent.

EXCLUSION CRITERIA

Patients who have not consented for the study and patients with other causes of chronic kidney disease like systemic hypertension, connective tissue disorders, autosomal dominant polycystic kidney disease, tubular interstitial nephropathy and glomerular nephritis and the patients less than 25 years were excluded from the study.

Table 1: Background Characteristics of the Participants

Characteristics	Frequency	Percentage
Age group		
<40 years	12	11.9
41-50 years	27	26.7
51-60 years	31	30.7
61-70 years	22	21.8
>70 years	9	8.9
Sex		
Female	46	45.5
Male	55	54.5
Type of diabetes		
Type 1 DM	2	2.0
Type 2 DM	99	98.0
Duration of diabetes		
≤5 years	57	56.6
>5 years	44	43.7
Monitoring of Blood Sugar		
Bad	82	81.2
Fair	19	18.8

After obtaining Institutional Ethics Committee approval, written informed consent was gathered from the participants who satisfied the inclusion criteria. There were 100 patients with DM with CKD during the period. Details of the participants regarding Diabetes status, clinical history, general examination, systemic examination were recorded using a pre formed questionnaire by an interview schedule. All 100 participants were subjected to clinical and laboratory parameters like Blood sugar, urea, HbA1C, creatinine, albumin in urine, urine protein- creatinine ratio, lipid profile and eGFR.

Statistical Package for Social Sciences (SPSS for Windows V20) was used for data analysis. All descriptive data were described as frequency and percentage. p value less than 0.05 was considered, for statistical significance.

RESULTS

- This study included 101 patients with DM and nephropathy. It was observed that
- 30.7 % of the participants were in the age of 51 to 60 years of age and 8.9% were above 70 years of age.
- Sex distribution was slightly higher in males. 54.5% of patients were males and 45.5% of patients were females.
- Most of the patients had T2DM accounting for 98% and 2% had T1DM(Table 1).
- Prevalence of CKD stage 1, 2, 3, 4 and 5 was 1.98%, 15.84%, 21.78%, 9.9% and 50.49% respectively.
- For 56.6% of the participants the duration of DM was less than 5 years and 43.7% of the participants had DM more than 5 years duration.
- Among the 101 participants in this study 57.4% were having normal BMI, 18.8% were overweight, 13.9% were underweight and 9.9% participants were found to be obese. BMI positively correlates with decrease in eGFR less than 60 ml/min, the patients with increase in BMI had progression to decrease in eGFR less than 60 ml/min.

Among all the diabetic kidney disease patients (100%) all presented with proteinuria and albuminuria. Complications of DM like diabetic retinopathy and neuropathy was found in 17.8% and 27.7% of the patients respectively. Diabetic foot was seen in 12.9% of the individuals and half and half nail among 29.7% patients. Other conditions like follicular dermatosis, pallor and pedal edema was observed in 7.9%, 97.0% and 64.4% patients respectively. No cases of uremic frost were found in this study. Uremic pericarditis was seen in 10.9% of the patients. Hyperkalemia was observed in 9.9% patients and metabolic acidosis in 40.6% patients. 4% of the individuals presented with uremic encephalopathy.

Among the 101 participants 65.5% of the study subjects had hypertension and congestive cardiac failure (CCF) was present in 13% of individuals. In 5.9% of patients with diabetes, stroke was found to be present.

Among 65.5% hypertensive patients 65.3% were on anti-hypertensive medication. Systolic blood pressure was found to be more than 140 mm Hg. In 27.7% of patients the diastolic blood pressure was more than 90 mm Hg. Hypertension was prevalent with eGFR less than 60 ml/min requiring the need for anti-hypertensive therapy. (Figure 1)

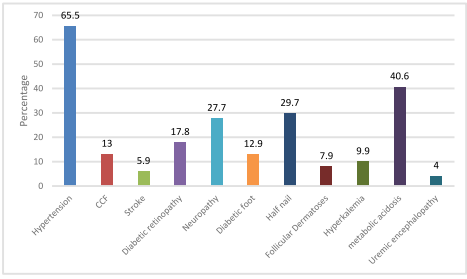

Figure 1: Clinical manifestations of the study participants

In this present study all the 101 participants were on restricted salt diet which is less than 2gms/day. Fluid restriction was calculated based on the severity of disease and 56.4% of the study subjects were on less than 1 liter/ day of fluids, 32.7% were on 1.5litre/day, 9.9% were on less than half liter/day and 1% of patient were on less than 2 liters/day fluid restriction. 96% of the study population was on statins and all the study participants were on insulin therapy for their diabetic management. 14.9% of the patients had undergone peritoneal dialysis. Likewise, 19.9% of the patients had undergone hemodialysis in this study, among them the frequency of hemodialysis was more than 10, in two individuals. All the patients who had complications like anemia, metabolic acidosis, uremic encephalopathy, uremic pericarditis, uremic gastritis, hyperkalemia required dialysis (34.65%). (Table 2)

Table 2: Modalities of Diabetic Nephropathy Management

Variables	Frequency	Percent
Salt restriction		
<5g/day	101	100.0
Fluid restriction		
0.5 liters/day	10	9.9
1.0 liters/day	57	56.4
1.5 liters/day	33	32.7
2.0 liters/day	1	1.0
Anti-hypertensive therapy		
Nil	35	34.7
Taking	66	65.3
Medications		
On Statins	97	96.0
On Insulin	101	100.0
Peritoneal dialysis		
Never done	86	85.1
No of times done		
1	12	11.9
2	2	2.0
3	1	1.0
Hemodialysis		
Never done	81	80.2
No. of times done		
Once	10	9.9
Twice	5	5.0
Thrice	2	2.0
More than thrice	3	3.0

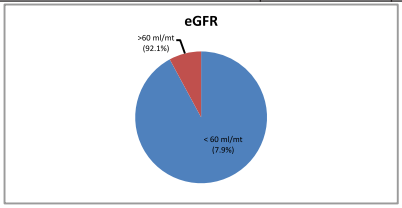

Figure 2: eGFR findings among the study participants

As shown in figure 2, eGFR was found to be reduced < 60ml/min/m^2in 92.1% of the study population, in this current study, whereas 7.9% of the patients had eGFR> 60 ml/min/m^2 of BSA. Laboratory findings of the study participants are shown in figure 3 and association of various parameters and eGFR is shown in table 3.

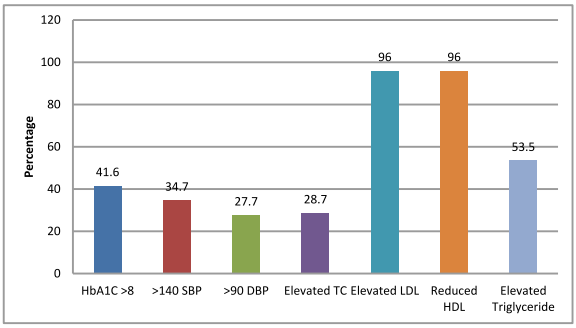

Figure 3: Laboratory findings among the study participants

Statistical significance was established between duration and decline in eGFR less than 60 ml/min showing that, the longer the duration of diabetes mellitus greater is the risk for decline in eGFR (p value =0.00000318) which is statistically significant.

Table 3 : comparison of variables with eGFR

VARIABLE	eGFR less than 60ml/min(92%)	Percentage (101)
UACR > 2	54	53%
Duration > 5 years	54	53.4%
BMI > 25	28	27.7%
Poor Glycemic Control	75	74.25%
TGL >150	52	51.48%
LDL > 100	26	25.74%
High Blood Pressure	72	71.76%
Complications	65	64.3%

DISCUSSION

Microvascular disease is much more prevalent in type 1 DKD than in type 2 DKD. In Diabetes Mellitus, the annual rate of GFR decline accelerates during the proteinuric phases. Due to hyperglycemia-induced accumulation of matrix, diabetic kidneys are frequently normally sized when examined by ultrasound. Hypertension (HTN) occurs in ~80% of adult diabetics, and a lack of nocturnal BP dipping may precede the micro-albuminuric phase, with clear-cut HTN developing during the macro-albuminuric phase. Importantly, HTN may be present in ~70% of patients initiated dialysis for ESRD due to DKD[7].

Table 4: Comparison of different variables with eGFR

Variables (Mean±SD)	Decreased eGFR < 60 ml/mt	Normal eGFR >60 ml/mt	P value
Age (in yrs)	56.17±12.90	56.50±8.30	0.944
Duration of CCF (in yrs)	3.65±19.58	7.50±21.21	0.597
Systolic BP (mmHg)	142.45±28.08	127.50±40.97	0.168
Diastolic BP (mmHg)	86.63±16.40	83.75±33.35	0.668
BMI (Kg/m^2)	23.52±5.70	20.06±4.87	0.100
Urine albumin	1.00±0	1.00±0	-
FBS (mg/dl)	170.77±75.05	193.63±91.73	0.419
PPBS (mg/dl)	249.54±85.32	280.00±127.73	0.356
HbA1C (%)	8.22±2.30	7.09±2.64	0.188
LDL (mg/dl)	105.14±29.94	106.00±33.23	0.939
HDL(mg/dl)	30.83±6.08	27.25±10.10	0.136
Triglycerides(mg/dl)	163.14±48.39	143.63±33.82	0.268
Total cholesterol(mg/dl)	182.34±41.49	174.38±39.41	0.603

In our study, prevalence of CKD stage 1, 2, 3, 4 and 5 was 1.98%, 15.84%, 21.78%, 9.9% and 50.49% respectively. TS Ferguson et al[8] estimated the prevalence of CKD and found prevalence to be 86.3% based on KDIGO risk categories. Antonio Rodriguez-Poncelas et al[9] concluded in their study the prevalence for any type of CKD as 27.9%. This shows the prevalence of CKD has a wide range.

Hyperglycemia is a well-known risk factor for DKD, for in addition to other risk factors like male sex, obesity, hypertension, chronic inflammation, resistance to insulin, hypovitaminosis D, and dyslipidemia and some genetic loci and polymorphisms in specific genes. Diabetic kidney disease is not an uncommon complication of diabetes (type 1 and 2) all over the world and among geriatric population.[10]

In our study there was male predominance in DKD similar to study done by Osama Gheith et al[10] in 2016. Their study also assessed the prevalence of diabetic nephropathy and reported that one-third of diabetic patients showed microalbuminuria after 15 years of disease duration and less than half developed renal nephropathy.

Progressive kidney disease is more frequent in Caucasians patients with type 1 than type 2 diabetes mellitus (DM), although its overall prevalence in the diabetic population is higher in patients with type 2 Dm[10].

Men in particular provided the strongest evidence for a change in the trend of DKD that migration to high income countries results in a dramatic increase in risk for cardio-metabolic diseases[11].Another study shows CKD more in female diabetic patients with older age and with higher SBP bear the brunt of CKD[12].

eGFR is an important predictor of CKD. eGFR is reduced to ≤ 60 ml/minute in most of the patients in our study. In this group of study population with eGFR less than 60 ml/min/m^2 (92%) showed that atherogenic lipid profile was observed which warranted the use of statins.

A cross sectional study done in India among 6120 Indians by Ajay K Singh et al[13] between 2005 to 2007 found the mean eGFR of 84.27 ± 76.46 versus 116.94 ± 44.65 mL/min/1.73 m2 in non-CKD group while 79.5% in the CKD group had proteinuria, in our study all the participants had proteinuria.

A study conducted by Suchi et al among south Asians living in America found the prevalence of CKD among Indians living in Indian and U.S. cities is similar. Persons with CKD living in Indian cities face higher likelihood of experiencing end-stage renal disease since they have more severe kidney disease and little evidence of risk factor management[11].Another review study done in India by Leenasequira et al assessed that diabetes and hypertension are the commonest causes of CKD.[14]

A recent study done by Khanam et al[12] in Bangladesh found that that the prevalence of CKD among the newly registered diabetic patients is quite high in Bangladesh, which is similar to the current study. Duration of diabetes at the long term has a positive co-relation to the decline in eGFR. The longer the duration of diabetes; more severe is the decline in eGFR (< 60ml/min/m^2).

eGFR decline was highly prevalent in 1 to 5 years duration explaining many patients would have noticed the disease, later in its course once complication had set in and it also emphasizes that a tight-glycemic control in the initial years after detection of DM would serve the metabolic memory well to prevent and retard the onset and progression of diabetic kidney disease[12].

In our study prevalence of CCF was 13% and stroke 5.9%.Karthikeyan et al in Tamil Nadu estimated the prevalence of diabetic complications, other than retinopathy and peripheral vascular disease, among known diabetic and found prevalence of Ischemic heart disease and stroke were 7.8% and 0.5% respectively1[5].

HbA1C management and control is also a risk factor for the disease. In our study 74.25% of patients had a poor glycemic control in eGFR group <60 ml/min, which showed that a poor glycemic control will progression on to CKD. In a study the results on analysis of HbA1c goal achievement showed that the patients without CKD had a better success rate to achieve the target <7% goal of HbA1c compared to those who had CKD (29.6% vs. 23.4%). Study reported higher prevalence of CKD which was driven by the ACR levels and majority of the patients had reasonable eGFR.[16]

The prevalence of CKD is increasing in India and studies done in India show that diabetes and hypertension are the commonest causes of CKD[14].Hypertension was reported in 65.5% of the population in the current study. Hypertension is an important risk factor for progression

of diabetic kidney disease. Rahim et al from Bangladesh in their study found than half of T2DM patients had CKD stages 3-5. Duration of diabetes and hypertension were significant risk factors and should be emphasized for the prevention of CKD in T2DM. Glycemic control will retard the progression of CKD in diabetes.[17]

Management of modifiable risk factors might help in reducing the incidence of CKD in future. Monitoring of sugars has a great impact. A proper glycemic control will retard and prevent the progression of diabetic kidney disease.

It must be stressed to all primary care physicians taking care of hypertensive and diabetic patients to screen for early kidney damage. Planning for the preventive health policies and allocation of more resources for the treatment of CKD/ESRD patients are obligatory in India. Identification of CKD in early stages is important to delay the progression which in turn decreases the economic burden on our nation. In this study though a strong association was made out. But statistical significance could not be established (except for duration and decline in eGFR) due to a shorter duration of study (2 months) in established CKD in diabetes.

CONCLUSION

From this study, it is concluded that albuminuria and decline in eGFR both are independent risk factors for diabetic CKD and are strong predictors of morbidity and mortality from a major vascular event, especially cardiovascular complications and stroke.

UACR has a positive and direct correlation to the cardiovascular outcome and BMI, TGL, LDL-C are independently related to decline in eGFR (due to less than 60 ml/min) and decrease in eGFR is associated with an atherogenic lipid profile, poor glycemic control and need for intensive HT regulation. Renal end point is positively associated with TGL.

Considering the higher prevalence of CKD with lifelong complications, it is of paramount importance for screening, early detection and treatment at the primary health care (PHC) level itself. India has become the capital of diabetes and lack of awareness among the people is still prevailing. Henceforth from this study we conclude that emphasize should be put on the importance of frequent blood sugar monitoring / Self-Monitoring of Blood Glucose, regular physician visits, glycemic control, diet plan and hypertension control. Physicians should have knowledge about diabetic complications and educate their patients regarding self-care and periodic screening for micro and macro vascular complications. The fact that, glycemic control and meal plan in diabetes works out wonders, by delaying onset and progression of complications like Diabetic Nephropathy / Chronic Kidney Disease, should be stressed to the community. If patients are properly health educated regarding diabetes, the need for resources in terms of money, manpower which is utilized for non-communicable diseases can utmost be reduced. National programmes like National programme for prevention and control of cancer, diabetes, cardiovascular diseases and stroke (NPCDCS) can be much more made stronger and followed in India like countries where the Government plays a crucial role in protecting its population

SUMMARY

Poor glycemic control, albuminuria, hypertriglyceridemia (greater than 150), increase in LDL levels (greater than 100), BMI (greater than or equal to 25), poor BP control and a longer duration of diabetes mellitus had a strong positive correlation to decrease in eGFR less than 60 ml/min.

Glycemic control, weight reduction and BP control retard the progression of CKD.

Since poor and a worst glycemic control correlates positively to albuminuria, community based awareness programmes are must for easy reduction of micro albuminuria / because albumin is an independent predictor of CKD progression and it is a strong predictor of morbidity and mortality from cardiovascular complication and stroke

DECLARATIONS

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Ethical approval: This study is registered with Institutional Human Ethical Committee, Thanjavur Medical College.

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