Clinical and Laboratory Profile of Diabetic-Hypertension, Kidney Disease Syndrome - A Hospital Based Study in South India

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ABSTRACT

BACKGROUND

Diabetes mellitus and hypertension remain one of the most common causes of chronic kidney disease. Diabetes hypertension, kidney disease syndrome is a new term introduced in medical terminology. The present study was conducted to examine clinical & laboratory profile of diabetes hypertension kidney disease syndrome – "DHKD syndrome" over a period of one year**.**

METHODS

A hospital-based observational cross-sectional study was done in the Department of General Medicine and Nephrology, outpatient department (OPD), among 120 patients with diabetes & hypertension in combination with kidney disease, with duration of diabetes > 2 years and duration of hypertension > 2 years after obtaining ethical clearance. The patients were then scored based on modified diet in renal disease (MDRD) formula and chronic kidney disease epidemiology collaboration equation (CKD EPI) formula to calculate the estimated glomerular function rate & placed into various stages of CKD.

RESULTS

A total of 120 subjects were included in the final analysis. The mean age was 63.64 ± 10.80. In study population of no albuminuria group, 50 % had glomerular filtration rate (GFR) of 30 - 44 (grade 3 CKD) and 50 % had GFR of < / = 15 (grade 5), among microalbuminuria group, 4.45 % had GFR of 60 - 89 (grade 2) and 1 had GFR of 45 - 59 (grade 3a), 13.64 % had GFR 30 - 44 (grade 3b), 40.91 % had GFR 15 - 29 (grade 4), 36.36 % had GFR < = 15 (grade 5), among macroalbuminuria group, 4.6 % had GFR 45 - 59 (grade 3a), 9.2 % had GFR 30 - 44 (grade 3b), 13.79 % had GFR 15 - 29 (grade 4) and 72.41 % had GFR < = 15 (grade 5). Majority had macro albuminuria. The proportion of the difference between systolic blood pressure (SBP) and macroalbuminuria was statistically significant. (P-value < 0.05) as well as proportion of the difference between insulin usage with macroalbuminuria was statistically significant. (P-value < 0.05).

CONCLUSIONS

Our study delivers sufficient evidence endorsing high relationship between diabetes, hypertension, and kidney disease.

KEYWORDS

Diabetic Nephropathy, Macroalbuminuria, Hypertension, DHKD Syndrome

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BACKGROUND

India accounts for 17 % of the world's population and is known as the diabetic capital. Due to factors like low socioeconomic status, low monetary allocation has led to suboptimal outcome specially in terms of non-communicable diseases.[1,2]

Diabetes and hypertension are the ever-mounting problem in a developing country like ours and there's a significant association of both with development of CKD (Chronic Kidney Disease).[3]

Since much of the focus is given to Diabetic kidney disease and impact of hypertension in diabetic kidney disease and chronic kidney disease, focus on DHKD as a syndrome is not yet studied in detail. Like diabetes, CKD is common, harmful, and treatable. If noticed early and coped suitably, DHKD progression may be prevented or delayed.[4,5]

"DHKD syndrome is defined with persistent severely elevated albuminuria of > 300 mg / 24 hour or urinary albumin to creatinine ratio [UACR] of > 300 mg / g, a relentless decline in 'Glomerular Filtration Rate', raised arterial blood pressure and enhanced cardiovascular morbidity." DHKD syndrome is not yet recognized globally.[6] The prevalence of CKD is about 800 per million population with incidence being 150 - 200 per million population and the leading cause for this is diabetic nephropathy.[7]

Ideal treatment of patients with diabetic hypertensive kidney disease (DHKD) needs right interpretation, markers use and designating phases of CKD, stratifying diabetics and hypertensive, speedy disease recognition and team work between nephrologists and primary care doctors.

METHODS

This was a hospital based cross sectional study carried at the Department of General Medicine and Nephrology at Dr KLE Prabhakar Kore hospital and MRC on 120 subjects from January 2019 to December 2019 after obtaining ethical clearance from institutional ethical committee and informed consent from the participants. All the participants who fit into inclusion criteria and gave consent were included in the study using the convenience sampling method.

Participants

Patients with diabetes and hypertension in combination with kidney disease with duration of diabetes > 2 years and any duration of hypertension > 2 years who attended to the Department of General Medicine and Nephrology at Dr KLE Prabhakar Kore hospital and MRC were included in the study.

Variables

Detailed history, physical examination, duration of diabetes and hypertension, prior records of renal function tests were analysed. Renal function tests include serum creatinine, blood urea nitrogen, serum electrolytes. Urinalysis includes urine protein and urine albumin to creatinine ratio which were calculated by taking the ratio between urinary albumin or urine protein and urinary creatinine in random spot urine. 'Serum creatinine ≥ of 1.2 mg / dl (as per our lab standard) and serum creatinine were measured on more than 3 occasions in 6 months (after correction of acute kidney injury factors if any). Proteinuria categorised into normal albuminuria (< 30 mg / g) or micro albuminuria (30 to 300 mg / g) or macro albuminuria (> 300 mg / g)'.

Patients were then scored based on MDRD formula to calculate estimated glomerular function rate and placed into various stages of CKD. Using serum creatinine levels, estimated glomerular filtration rate for each patient was computed according to the equation of MDRD formula and CKD EPI formula and average was taken.

Statistical Analysis

For normally distributed quantitative parameters mean values were compared between study groups, categorical outcomes were compared between study groups using chi square test / Fisher's Exact test (if the overall sample size was < 20 or if the expected number in any one of cells is < 5, Fisher's exact test was used). P-value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

RESULTS

The mean age was 63.64 ± 10.80 years in the study population, minimum and maximum was 40 and 89 in the study population. Among the study population, 87 (72.50 %) were males and 33 (27.50 %) were females.

Among study population, 94 (78.33 percent) had generalised weakness, 86 (71.67 percent) had peripheral oedema, 57 (47.50 percent) had decreased urine output, 58 (48.3 percent) had loss of appetite, 21 (17.5 percent) had nausea and vomiting, 71 (59.17 percent) had dyspnoea, 30 (25.00 percent) had weight loss and 13 (10.8 percent) had change in mental status.

Among study population, 72 (60 percent) had pallor, 89 (74.2 percent) had oedema, 38 (31.7 percent) had muscle wasting and 11 (9.2 percent) had altered mental status. mean systolic BP was 149 ± 28.5, diastolic BP was 84 ± 14.05, height was 168.3 ± 6.73, weight was 70.2 ± 11.33, BMI was 24.77 ± 3.88 mean haemoglobin was 10.43 ± 1.6, 193.9 ± 86.97, PPBS was 219.21 ± 86.77, Hba1C was 8.11 ± 2.13, creatinine was 6.11 ± 3.52, urea was 90.59 ± 42.66, sodium was 135.49 ± 5.32, potassium was 4.99 ± 0.79, calcium was 8.52 ± 0.94, phosphorous was 4.71 ± 1.71

Among A1 albuminuria, 1 patient (50 %) was in the range of 30 -44 in EGFR and 1 patient (50 %) was < = 15 in EGFR, among A2 albuminuria, 1 patient (4.45 %) was in the range of 60 - 89 and 45 -59 in EGFR, 3 patients (13.64 %) were in the range of 30 - 44 in EGFR, 9 patients (40.91 %) were in the range of 15 - 29 in EGFR, 8 patients (36.36 %) were < = 15 in EGFR, among A3 albuminuria, 4 patients (4.6 %) were in the range 45 - 59 in EGFR, 8 patients (9.2 %) were in the range of 30 - 44 in EGFR, 12 patients (13.79

%) were in the range of 15 - 29 in EGFR and 63 patients (72.41 %) were in the range of < = 15 in EGFR.

Among these patients, most of them had renal failure. Out of 120 patients, 80 patients had undergone renal replacement therapy, and the rest 40 were medically managed.

Various parameters were compared among patients with micro albuminuria and macro albuminuria. It was found that the systolic blood pressure was statistically significant among micro albuminuria patients.

Various parameters were compared among patients with macro albuminuria. It was found that the systolic blood pressure, fasting blood glucose levels, changes in renal parenchyma was statistically significant among macro albuminuria patients.

Parameter	Mean ± SD	Median	Minimum	Maximum	95 % C.I Lower	95 % C.I Upper
Haemoglobin (g / dl)	10.43 ± 1.6	10.25	7.40	14.10	10.14	10.72
FBS (mg / dl)	193.9 ± 86.97	180.50	70.00	542.00	178.18	209.62
PPBS (mg / dl)	219.21 ± 86.77	196.00	79.00	511.00	203.52	234.89
Hba1C	8.11 ± 2.13	7.60	5.20	15.60	7.73	8.50
Creatinine (mg / dl)	6.11 ± 3.52	5.75	1.20	16.36	5.47	6.74
Urea (mg / dl)	90.59 ± 42.66	92.00	27.00	209.00	82.88	98.30
Sodium (mEq / L)	135.49 ± 5.32	136.00	117.00	148.00	134.53	136.45
Potassium (mEq / L)	4.99 ± 0.79	4.95	3.35	7.20	4.84	5.13
Calcium (mg / dl)	8.52 ± 0.94	8.40	6.20	12.20	8.35	8.69
Phosphorous (mg / dl)	4.71 ± 1.71	4.25	1.70	10.10	4.40	5.02

Table 1. Descriptive Analysis of Lab Investigations in the Study Population

EGFR	Albuminuria A1 (N = 2) < 30	A2 (N = 22) 30 - 299	A3 (N = 87) > = 300
60 - 89	0 (0 %)	1 (4.55 %)	0 (0 %)
45 - 59	0 (0 %)	1 (4.55 %)	4 (4.6 %)
30 - 44	1 (50 %)	3 (13.64 %)	8 (9.2 %)
15 - 29	0 (0 %)	9 (40.91 %)	12 (13.79 %)
< = 15	1 (50 %)	8 (36.36 %)	63 (72.41 %)

Table 2. Comparison of EGFR (Average of MDRD and CKD EPI Formulas) across Albuminuria

*No statistical test was applied due to 0 subjects in the cells

	Parameters	Micro Albuminuria Yes (N = 22)	No (N = 89)	Chi Square	P Value
SBP	< 130	9 (40.91 %)	12 (13.48 %)	8.650	0.006
	> = 130	13 (59.09 %)	77 (86.52 %)		
	Parameters	Macro Albuminuria Yes (N = 85)	No (N = 26)	Chi Square	P Value
FBS	< 126	14 (16.47 %)	10 (38.46 %)	5.682	0.017
	> = 126	71 (83.53 %)	16 (61.54 %)		
SBP	< 130	12 (14.12 %)	9 (34.62 %)	5.453	0.041
	> = 130	73 (85.88 %)	17 (65.38 %)		
Insulin	Yes	55 (64.71 %)	10 (38.46 %)	7.952	0.019
	No	27 (31.76 %)	12 (46.15 %)		
	Not taking now	3 (3.53 %)	4 (15.38 %)		
USG Abdomen	Normal	20 (23.53 %)	13 (50 %)	7.607	0.055
	Grade 1 Rpc	35 (41.18 %)	9 (34.62 %)		
	Grade 2 Rpc	19 (22.35 %)	3 (11.54 %)		
	Grade 3 Rpc	11 (12.94 %)	1 (3.85 %)		

Table 3. Demographic and Laboratory Parameters Significantly Associated between Micro and Macro Albuminuria

Symptoms	Patients	Percentage
Headache	45	37.5
Epistaxis	29	24.16
Tinnitus	24	20
Dizziness	12	10
Fainting	10	8.33

Table 4. Clinical Profile of Patients with DHKD Syndrome

DISCUSSION

Among study population, patients with DHKD present mainly with vague complaints such as generalised weakness, breathlessness, peripheral oedema and decreased urine output as the chief presenting complaints. Most of the patients with DHKD were found to have pallor and their mean haemoglobin was found to be 10.43 mg / dl.

In this study correlation between systolic blood pressure and macroalbuminuria was statistically significant showing that strict control of blood pressure is required to prevent DHKD. DHKD patients show uncontrolled fasting blood glucose levels and this is detrimental in leading to worsening albuminuria as showed by our study. This portrays the importance of strict glycaemic control.

The above study shows that DHKD patients have electrolyte imbalance mainly of potassium, calcium and phosphorous levels and they need to be corrected to prevent electrolyte disorders. Study shows that there was no much correlation between number of years of diabetes or hypertension on progression to DHKD instead strict glycaemic control and BP control are essential.[8,9] Similar studies showed that nephropathy and albuminuria preceded among diabetic and hypertensive patients.[10] The other risk factors associated with DHKD were diabetes, hypertension, albuminuria, hyperglycaemia, dyslipidaemia, obesity and smoking.[11] Data shows that Sub-Saharan diabetic patients have high diabetic nephropathy accounting to more than 30 %.[12]

The study also projects the awareness among patients about complication of diabetes and hypertension as most patients commonly think IHD, nephropathy, and retinopathy are the main complications and very few are aware of neuropathy, peripheral vascular diseases (PVD) and cardiovascular diseases (CVA). A hospital-based study carried at Delhi revealed that diabetes was a major cause of CKD and was undiagnosed among various patients.[6,9] Studies also reveal that diabetes was significantly associated with diabetic nephropathy.[12]

Majority of DHKD population had macro albuminuria and high urine albumin creatinine ratio. This needs early detection. Drugs which help in decreasing albuminuria like angiotensin-converting-enzyme (ACE) inhibitors or ARBS should be used in younger age groups.[10,11] A hospital based study carried by Agarwal et al. found that hypertension was cause for kidney diseases and an incidence of nephropathy was about 17.5 %.[13,14] The cause of rise in hypertension among DHKD syndrome can be attributed to increase in sodium retention and peripheral vascular resistance.[13,14] In a study carried out in tertiary care hospital in South India among CKD patients showed that early screening and detection of chronic kidney disease individuals helps in slowing down the complications leading to end stage renal disease.[15]

Study shows that calculation of estimated GFR in every patient of diabetes and hypertension is important. In our study we found that more than half of patients were in kidney failure stage requiring renal replacement therapy. And rest were having high risk of progression to end stage renal failure. Out of 120 patients, 117 patients were in very

high risk category with 80 of them requiring renal replacement therapy.

CONCLUSIONS

Diabetes, hypertension and kidney diseases are more common among geriatric population. Hence, we recommend syndromic approach for early diagnosis and effective treatment of patients with diabetes and hypertension.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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