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Clinical Profile Of Renal Disorders In Diabetic Patients.

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Abstract

Background: The worldwide prevalence of Diabetes mellitus has risen dramatically over the past two decades. Long standing Diabetes mellitus (DM) due to improper glycemic control leads to multiple organs dysfunctions. Renal disorder in diabetic patients are a major cause of morbidity and mortality. ***Objective:*** to study the occurrence of renal diseases in diabetics due to diabetes per se and due to Non-diabetic causes. ***Methods:*** This study was conducted in a government general hospital from Oct 2015 to June 2017. A total of 100 patients diagnosed to have DM (according to predefined criteria- ADA Guidelines) and having proteindipstix positive albuminuria were randomly enrolled in the study. Most of the study patients were indoor patients (in medicine wards) and the rest were OPD patients ***Result:*** The median age of patients was 45.56 yr. Mean age of patients having DN (Diabetic Nephropathy) was 53.6 yr. Mean age of patients having NDRD (Non Diabetic Renal Disease) was 45.4 yr. Mean duration of DM in patients having NDRD was 6.7 year. Mean duration of DM in patients with DN was 12.18. Significant number of patients with DN were taking insulin, whereas, a significant number of patients with NDRD were taking OHA's. In DN patients, 8 (25%) patients gave history of hypertension and in NDRD patients, 24(35.3%) patients had hypertension in past. The DN group was more likely to have biochemical and metabolic abnormalities like anemia, hyperkalemia, hypocalcemia and hyperphophatemia. DN patients also had a lower fasting BSL than the NDRD group.
Conclusion: Since the prognosis and management of diabetic nephropathy and non-diabetic renal disease are different, high clinical suspicion of non-diabetic renal disease in diabetic patients will be helpful in early differentiation of both the condition and ultimately improved patient outcome.

Keywords: Diabetes Mellitus, Diabetic Nephropathy, Non Diabetic Renal Disease,

INTRODUCTION

Renal disease is a relatively common complication of type I and type II DM. the size of diabetic renal disease became clear in the 1950s as patient with type I DM began to survive for long periods, following discovery of insulin in 1921 by Banting and Best1.

Renal disorders in diabetics may range from asymptomatic microalbuminuria to overt nephropathy. Proteinuria is the hallmark of renal disease in diabetic patients. Excess mortality is seen in diabetic patients those who have proteinuria2. And it is not only due to end stage renal disease but also from cardiovascular disease. Diabetic retinopathy and glomerulopathy result from a relatively specific form of microvascular disease (microangiopathy). Diabetics are 17 times more prone to kidney disease and 25 times more prone to blindness.

Proteinuria ranging from microalbuminuria to persistent albuminuria in DM patient is either due to Diabetic Nephropathy or due to Non Diabetic Renal Disease (NDRD). Individuals with diabetic nephropathy almost always have diabetic retinopathy1,2. Thus, if patients with DM have persistent proteinuria without retinopathy, then that proteinuria is mostly due to Non Diabetic Renal Disease.

Although some physicians may consider renal biopsy to be unnecessary in diabetic patients with proteinuria, there may be the certain circumstances in which it is indicated because of increased likelihood of diagnosing NDRD2.

Diabetic Nephropathy: It is defined clinically as the presence of persistent proteinuria in a diabetic patient with retinopathy, elevated blood pressure and declining glomerular function in the absence of urinary tract infection, other renal disease, or heart failure.

Non Diabetic Renal Disease:
Certain factor raises the suspicion of a Non Diabetic Renal diagnosis and referral to a renal physician may then be required. Present study is an attempt to study the occurrence of renal diseases in diabetics due to diabetes per se and due to Non-diabetic causes.

MATERIALS AND METHODS

This study was conducted in diabetic OPD and indoor patients in medicine wards of government general hospital. A total of 100 diabetic patients with renal dysfunction (proteinuria/raised creatinine) were included in the study.

INCLUSION CRITERIA-
Diabetic patient having proteindipstix positive albuminuria.

Age > 12 years.

EXCLUSION CRITERIA-
Diabetic patient without proteinuria or those with microalbuminuria

The patients enrolled into the study were given a preformed standardized questionnaires and an informed written consent was taken for participation into the study. The patients were examined clinically and detailed history of duration and treatment of diabetes, past history of UTI or any other renal disease were taken. Their baseline blood, urine and other relevant investigation were done.

Patients were subjected to detailed fundoscopic examination in the ophthalmology OPD by consultant in ophthalmology. Diabetic retionopathy was diagnosed by fundoscopy by the pressure of background retinopathy (micro aneurysms, haemorrhages and soft or hard exudates) with or without proliferative changes. They were subjected to USG abdomen to see for kidney size, corticomedullary differentiation, renal echogenicity, and pre/post void residues.

Selected patient with proteinuria > 2 gm/d in NDRD group were subjected to kidney biopsy after their due to informed written consent. Biopsy was done by spring loaded biopsy gun under all aseptic precautions under local anesthesia and with ultrasonographic guidance. The biopsy specimens were sent for routine histopathology examination (HE stain) as well as special stains and immune florescence if required.

Statistical analysis
Patients were divided into two groups for the purpose of statistical analysis. The patients with albuminuria and diabetic retinopathy were grouped into diabetic nephropathy group. Those with albuminuria but no diabetic retinopathy were classified as nondiabetic renal disease group (NDRD). These two groups were compared with each other for presence or absence of various risk factors. Chi – square test and t test were used to compare various characteristics between the two groups.

RESULTS

Patients were categorized into two categories depending on the presence or absence of diabetic retinopathy on fundoscopy. Diabetic nephopathy (DN) – Patients having diabetes and albuminuria with diabetic retinopathy on fundoscopy. (32 patiensts)

Non- diabetic renal disease (NDRD) – patients having diabetes and albuminuria without diabetic retinopathy on fundoscopy. (68 patients).

Out of 100 patients 57(57%) were men and 43 (43%) were women.The median age of patients was 45.56 yr. Mean age of patients having DN (Diabetic Nephropathy) was 53.62 yr. Mean age of patients having NDRD (Non Diabetic renal diease) was 45.44 yr. (* $p < 0.017$).

Thus patients with younger age were more likely to have NDRD and elder patients likely to have diabetic nephropathy. This could be due to longer duration of diabetes in patients with DN.

The sex wise occurrence of DN and NDRD was not significant. Mean duration of DM in patients having NDRD was 6.735 yr. Mean duration of DM in patients having DN was 12.187 yr. This difference in duration of DM was statistical significant (p value <0.0001).

TABLE – 1: Diabetic nephropathy Vs Non Diabetic renal Disease

Diabetes	Diabetic Nephropathy		Non Diabetic Renal Disease (NDRD)		Total
	Male	Female	Male	Female	
Type I	5	5	5	9	24
Type II	11	11	36	18	76
Total	16	16	41	27	100

Statistical, type of DM whether type I or type II was not significant in relation to occurrence of DN or NDRD.

TABLE – 2: Comaprison between two groups with respect to mean age of patients in years

	GROUP	N	Mean	Std. Deviation	t	P
MEAN AGE	DN	32	53.62	18.10	2.423	0.0172
	NDRD	68	45.44	14.58		

***p<0.05 : difference is significant**

TABLE 3: Comparison between two groups with respect to presence or absence of hypertension

HTN	GROUP		Total
	DN (%)	NDRD(%)	
PRESENT	8 (25)	24(35.3)	32
ABSENT	24(75)	44(64.7)	68
Total	32	68	100

X^2 = 1.059, P= 0.3032, NS

Out of 100, 68 patients had BP ≤ 140/90 and 32 patients had BP > 140/90. Postural hypertension (on standing, fall of systolic BP >20 mmHg and diastolic BP>10 mmHg) was seen in 1 patient. The patient was 75 yr. female with 20 yr. history of type II DM hap postural fall of BP, he also had diabetic peripheral neuropathy and Rt. Renal artery stenosis.

In DN patients, 8 (25%) patients gave history of hypertension and 24 (75%) did not give history of hypertension, but many of those who were not giving history of hypertension in the past, were found to have hypertension on examination.
In NDRD patients, 24(35.3%) patients had hypertension in past and 44(64.7%) were not hypertensive.

TABLE 4: Comparison between two groups with respect to OHA use

OHA	GROUP		Total
	DN (%)	NDRD(%)	
TAKING	17(53.1)	17(25)	34
NOT TAKING	15(46.9)	51(75)	66
Total	32	68	100

X^2 = 7.67, P<0.0056, HS

Out of 100 patients, 34 were taking OHA(Oral hypoglycemic agents) only. 52 patients were taking only insulin.
When the two groups were compared for the use of insulin and OHA, it was evident that, significant number of patients with DN were taking insulin, whereas, a significant number of patients with NDRD were taking OHA's.

Normocytic normochromic anemia in CKD is because of deficiency of erythropoietin. Amongst the study patients, the Hb value recorded was 3 gm % and highest one was 16 gm%. Median Hb of the study was 9.86 gm%.

It was found that statistically significant severe degrees (2 to 4) of albuminuria were found in the DN group as compared to other group. The median serum creatinine was 3.52 mg%. patients with diabetic nephropathy had mean serum creatinine of 5.74 and those with NDRD had mean creatinine of 2.48. This difference was statistically highly significant. Mean serum

calcium levels were significantly lower in patients with DN than in NDRD group. Mean serum phosphorus was significantly higher in patients with DN as compared to NDRD.

TABLE 5: Comaprison between two groups with respect to presence or absence of metabolic acidosis

METABOLIC ACIDOSIS	GROUP		Total
	DN (%)	NDRD(%)	
PRESENT	18(56.25)	12(17.64)	30
ABSENT	14(43.25)	56(82.36)	70
Total	32	68	100

X^2 = 15.44, P= 0.00009, HS

TABLE 6: Comaprison between two groups with respect to presence or absence of hyperkalemia

SERUM K	GROUP		Total
	DN (%)	NDRD(%)	
K<=5.5	18(56.25)	59(86.76)	77
k>5.5	14(43.75)	9(13.24)	23
Total	32	68	100

X^2 = 11.44, P= 0.0007, HS

23 patients were found to be hyperkalemic. Of these, 14 patients (60.86%) belonged to the DN group. Thus, patients with DN were significantly likely to be hyperkalemic.

TABLE 7; Comaprison between two groups with respect to presence or absence of raised renal cortical echogenicity on abdominal ultrasonography

RAISED RENAL CORTICAL ECHOGENICITY	GROUP		Total
	DN (%)	NDRD(%)	
PRESENT	25(78.13)	27(39.70)	52
ABSENT	7(21.87)	41(60.30)	48
Total	32	68	100

X^2 = 12.86 , P= 0.0003, HS

DISCUSSION

Statistically there was no significant difference in the two groups as regards to history of hypertension. This finding is similar to two other studies by Eun Young Lee at all (1999) and S.K. Mak at all (1997)3,4.
In addition to hypertension, some patients in the study had other concurrent illnesses like RVHD, ischemic heart disease, hypothyroidism, hyperthyroidism, infectious disorders and malignancies, Methanol consumption, PGA, Homochromatosis, Leptospirosis.

Anemia was defined as a Hb level < 10gm% for the purpose of this study5. Out of study patients, 49 patients (49%) were anemic. In the DN group, 21(65.6%) patients were anemic, whereas in the NDRD group, 28(41.2%) patients were anemic. This difference was stastically significant.

23 patients were found to be hyperkalemic. Of these, 14 patients (60.86%) belonged to the DN group. Thus, patients with DN were significantly likely to be hyperkalemic. Type IV renal tubular acidosis (hyporeninemic hypoaldosteronism) occurs in DN. These individuals develop a propensity towards Hyperkalemia and it is frequently out of proportion to their degree of renal isufficiency.

Normal serum creatinine level is <1.5 mg/d1. of the study patients, the minimum recorded creatinine was 0.7 and the maximum was 17 mg%. The median serum creatinine was 3.52 mg%. patients with diabetic nephropathy had mean serum creatinine of 5.74 and those with NDRD had mean creatinine of 2.48. This difference was statistically highly significant. Thus a more deranged serum creatinine was more likely to be associated with DN than NDRD. These results are in cortradistinction with two other similar studies3,4. This can be partly explained due to a significantly longer duration of diabetes in population with DN as compared to NDRD. A longer duration of lead to rise in the serum creatinine levels.

Normal serum calcium and level is 9-10.5 mg/dl and normal serum phospphorus level is 3-4.5 mg/d1. Mean serum calcium levels were significantly lower in patients with DN than in NDRD group. Mean serum phosphorus was significantly higher in patients with DN as compared to NDRD. These changes in calcium and phosphorus levels can be explained by the more advanced state of renal insufficiency in patients with DN than NDRD group.

Mean fasting blood sugar level was significantly lower in patients with diabetic nephropathy as compared to the non diabetic renal diseases. (149 Vs. 171 mg%).

During the phase of declining renal function, insulin requirement may fall, as the kidney is a site of insulin degradation6. As the patients in the diabetic nephropathy group were in a state advanced renal insufficiency as compared to the NDRD group, this fact might partly explain the lower fasting BSL levels in this group.

Patients spot urine albumin was checked by proteindipstix . The proteinuria was graded into 5 categories as trace,1+,2+,3+ and 4+. Trace alminuria was found in 18 patients, where 4+ was found in 9 patients. When the degree of alminuria was compared between the DN and NDRD. group using Pearson's Chi square test, it was found that statistically significant severe degrees (2 to 4) of albuminuria were found in the DN group as compared to other group.

Because of wide fluctuations in AER, multiple collections or a single 24 Hr urine collection are better methods3.

Keeping in view, these facts, the study patients were asked to collect 24 HR urine in a clean container and 24 hr albumin excretion was thus measured. The mean 24 Hr urine protein in DN patients was 1.0456 gm whereas in NDRD group it was 0.8855 gm. It was evident that the DN patients had significantly higher 24 Hr urine albumin excretion rate as compared to the other group. Our results are in accordance with a study of Mak et al3 done in Hong Kong.

Amongst these patients having albuminuria, those patients having > 5 pus cells/hpf on light microscopy of urine, were considered to have urinary tract infection and their urine samples were sent for urine culture and for urinary AFB detection in some suspected patients. Out of 100 patients, 30 patients had urinary tract infection. 15 patients had positive urine culture, showing positive bacterial growth. Most of the patients with U.T.I. with culture negative had already received antibiotics elsewhere prior to their enrolment into our study. Various bacteria grown in urine cultures were E.Coil (10/15), proteus (2), Klebasiella(1) etc. Two patients had urine AFB positive.

Out of 30 patients with pus cells in urine, 25 patients were in NDRD group and 5 patients were in DN group. This difference was statistically significant. 5 patients had cystitis, 2 of which had urinary AFB. 2 patients had acute pyelonephrities. 6 patients had caculi either in kidney or in the ureter.

Metabolic acidosis is a common feature of advanced renal insufficiency. The acidosis results from inability of the compared kindney to produce ammonia1. Hyperkalemia further depresses urinary ammonium xecretion. The combination of hyperkalemia and hyperchloremic metabolic acidious (known as type IV renal tubular acidosis or hyporchloremic hypoaldosteronism) is most characeristic of patients with diabetic or tubulointerstitial renal disorder. Treatment of hyperkalemia in this case frequently improves the acidosis.

With advancing renal failure, the total urinary net dialy acid excreation is usually limited to 30-40 mmol and an anion gap of 20 mmol/L with a reciprocal fall in plasma bicarbonate may develop. In most patients, the acidosis is mild and can usually be corrected by oral soda bicarbonate supplementation or sodium citrate supplementation.

In this study, patients with an ABG analysis showing a pH of less than 7.35 with a normal or reduced pCO2 level were considered to have metabolic acidosis. A total of 30 patients werefound to be acidotic.18 Patients belonging to the DN group were significantly more likely to be acidotic than NDRD group.One of the possible reasons of this could be the fairly advanced degree of renal insufficiency in the DN group of this study.

When there is a sufficiently advanced degree of renal insufficiency, it will be frequently seen on the abdominal ultrasonography as diminished coticomedullary differentiation or raised renal cortical echogenicity.

Renal ultrasound is the most useful imaging study for the evaluation of renal insufficiency2. An ultrasound examination can verify the presence of two symmetric kidneys, provided an estimate of renal sizes and rule out obstructive uropathy. The documentation of small symmetric kidneys, though supports the diagnosis of progressive chronic renal size1. This fact was also confirmed in our study because most of the patients had normal sized and bilaterally symmetric kidneys. Other chronic renal disease associated with normal renal size include amyloidosis, ADPKD and HIVAN.

The ultrasonography findings evaluated under this study were renal ecogenicity, corticomedullaery differentiation . A poor renal corticomedullary differentiation and raised renal cortical echogenicity were factors found statistically more significant in DN than NDRD group.

Thus in this study, we have compared various parameters in diabetic patients having diabetic and non-diabetic renal disease. The present study however has some limitations. Most of the patients enrolled in this study were indoor patients, the prevalence of DN and NDRD in diabetic patients in this study may not be done in all patients in study as was done in above studies3,4.

Even though the most sensitivity technique of diagnosis of diabetic retinopathy is flouroscein angiography, because of the cost, invasive nature and limited access to this investigation we used Fundoscopy for the diagnosis of diabetic retinopathy. Since the prognosis and management of diabetic nephropathy and non-diabetic renal disease are different7, high clinical suspicion of non-diabetic renal disease in diabetic patients will be helpful in early differentiation of both the conditions and ultimately improved patient outcome.

CONCLUSION

Majority of diabetic patients with albuminuria in this study, have non-diabetic renal disease. (NDRD). Patients with diabetic nephropathy have more sever degrees of albuminuria as compared to non-diabetic renal disease. Patients with diabetic nephropathy have a longer duration of diabetes mellitus, are likely to be older and have more advanced renal insufficiency than non-diabetic renal disease. Patients with diabetic nephropathy more likely to have anemia, metabolic acidosis, hyperkalemia and hyperphosphatemia than patients with non-diabetic renal disease.

Diabetic nephropathy patients are more likely to have raised cortical echogenicity and reduced corticomedullary differentiation on renal ultrasonography. Since the prognosis and management of diabetic nephropathy and non-diabetic renal disease are different, high clinical suspicion of non-diabetic renal disease in diabetic patients will be helpful in early differentiation of both the condition and ultimately improved patient outcome.

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