HISTOPATHOLOGICAL FINDINGS IN 60 PATIENTS WITH DIABETIC NEPHROPATHY

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ABSTRACT

Objective: Diabetes mellitus being a common disorder, having nephropathy as one of its major complication, was studied.

Material and Methods: Patients with hypertension, nephrotic syndrome, CRF and chronic NSAIDS intake were excluded. Renal biopsy was taken from all these cases and histopathological changes were recorded.

Results: The commonest picture found was Basement membrane thickening, followed by diffuse glomerulosclerosis and nodular glomerulosclerosis.

Conclusion: Early diagnosis, dietry modifications, meticulous glycemic control, regular exercise, weight reduction and control of hypertension early in the course of diabetes reduces the chances of diabetic nephropathy. Regarding the management of diabetic nephropathy until now no therapy has been shown to improve the clinical out come of these patients. Patients with diabetic nephropathy treated with intensive insulin therapy and with ACE inhibitors.

Key words: Diabetic Nephropathy, Diabetes mellitus, Renal biopsy.

INTRODUCTION

In the endocrine disorders, diabetes mellitus is by for the most common. It has affected about 30 millions people through out the world.[1] According to the available statistical data about 10 million people in United States of America are suffering from Diabetes mellitus.[2] While prevalence rate in UK is 1-2% of total population. The occurrence rate of this disease in Pakistan is not less than other countries.[3]

Diabetes mellitus is one of the most notorious endocrinopathy that ends up in many complications depending upon its duration and glycemic control. The most

dreaded complications are diabetic ketacidosis, neuropathy, retinopathy and nephropathy. In USA diabetic nephropathy accounts for 25% of patients on chronic renal dialysis. About 30-50% of patients with insulin dependent diabetes mellitus and some what less of those with non insulin dependent diabetes mellitus develop this complication.[4]

Patients developing diabetes before the age of 20 years, have a 50% chance of having diabetic nephropathy after 20 years of disease in contrast to those with diabetes occurring after the age of 40 years, who have only a 4% incidence of diabetic renal disease after 20 years.[5] Renal disease has become much more frequent among patients with diabetes since the introduction of insulin treatment. The reasons are not completely clear but it is apparent that the increased life span gives a longer time for the various structural changes to develop. There is also a possibility that the insulin used in the treatment of diabetes might be responsible for some of the changes and this will be considered along with other possible factors.[6]

The kidneys may be damaged by diabetes in three main ways, Glomeruler damage due to poor glycemic control, Ischemia due to hypertrophy of afferent and efferent arterioles, and Ascending infection due to stasis of urine in the bladder because of autonomic neuropathy. The earliest evidence of diabetic nephropathy is microalbuminuria which in turn progresses to frank proteinuria. Hypertension is a common development and may itself damage the kidneys further. Diabetic nephropathy ultimately ends in renal failure. On renal biopsy in diabetic kidney, the following findings usually occurs.

1. Glomeruler basement membrane thickening.
2. Kimmelstiel and Wilson nodules.
3. Mesangial sclerosis.
4. Exudative lesions.

The pathogenesis of diabetic nephropathy is still unknown clearly. Adequate insulin administration is the most important preventive measures. Hypertension if present should be aggressively treated to delay the progression of renal disease. Good nutrition, prompt treatment of UTI and caution in the use of radiocontrast agents are other preventive measures. Advancement are being made, however that promise a better future for diabetics with nephropathy.

MATERIALS AND METHODS

This study was conducted in the Medical 'C' Unit of Khyber Teaching Hospital Peshawar. It was completed in a period of 2½ years. The total number of cases finally included in this study were 60, 40% being males and 60% females. All of them were having established diabetic nephropathy. 45 were having non insulin dependent diabetes mellitus and the remaining 15 with insulin dependent diabetes mellitus. Those patients who along with diabetes were also having systemic hypertension, CRF and nephrotic syndrome were not included in this study. Also those diabetics who were taking drugs like NSAIDS, diuretics, alcohol etc. were excluded from this study.

Eligibility criteria included:

a. Every patient having established diabetes mellitus according to WHO criteria.
b. None of my selected cases were having proteinuria due to any other renal disease or due to hypertension, CCF, burns, blood transfusion, bee stings, alcohol abuse or orthostatic proteinuria
c. Proteinuria due to carcinoma, CLL and Hodgkin lymphoma were excluded.
d. None of these patients were taking drugs like penicillamine, gold, mercury, cadmium, very high doses of captopril, contaminated heroin and phenindione.

Detailed history of the patients was taken including drugs history particularly the dose of insulin therapy and oral hypoglycemic drugs. After examining the patients clinically the following investigations were done before deciding for renal biopsy.

1. Base line investigations
2. Fasting and 2 hours post prandial blood glucose level.
3. 24 hours urinary proteins and special importance was given towards microalbuminuria and albuminuria. Microalbuminuria indicates an albumin excretion rate of approximately 20-200 ug/ minute or 30-300 mg/24 hours.
4. Serum electrolytes, creatinine, uric acid, LFTs, TFTs, X-ray KUB, U/S abdomen. IVP if needed, coagulation profile, blood grouping were made. Apart from these investigations, contraindication of renal biopsy were kept in mind like, uncooperative patients, Haemorrhagic disorders, Gross obesity or oedeme, Uncontrolled hypertension, single kidney (with the exception of transplanted kidney, when biopsy is acceptable) and small kidneys.

After doing these investigations, all the 60 biopsies were performed under ultrasound guidance, selecting the lower pole of the left kidney with true cut biopsy needle. The specimen was put in formalin bottle, sealed and labeled. All patients were observed for haematuria and other complications for at least 24 hours after the biopsy. There was no mortality. Biopsy specimen were sent to the pathology unit of KTH Peshawar.

RESULTS

Total number of patients included in the study were sixty, all having established diabetes mellitus. Male to female ratio was 3:2 and age range was 25 to 70 years. 80% were Pakistanis and 20% Afghan refugees. The least affected group was laborer and farmers. Regarding the duration of diabetes mellitus, majority were having this disease for the last 15-20 years. The diet in majority of cases was carbohydrate and fats. 80% were having poor glycemic control by measuring HBA^{Ic} . The diabetic retinopathy was found in 80% cases. 20% having abnormal renal functions test. 24 hours urinary proteins in all the 60 cases of both sexes with both types of diabetes mellitus were measured. All of them have some sort of diabetic nephropathy. Regarding the renal biopsy findings on histopathology in these 60 cases of both types of diabetes mellitus in both sexes of different duration of illness 66% having only basement membrane thickening, 17% having diffuse glomerulosclerosis and 17% noduler glomerulosclerosis.

24 HOURS URINARY PROTEINS IN BOTH TYPES OF DIABETES IN 60 DIABETIC CASES

24 hours urinary proteins (mg/24 hours)	Male	Female	Type I diabetes	Type II diabetes	Total % age
30 – 300	15(25%)	20 (33%)	10 (16%)	25 (41%)	35 (58%)
300 – 600	8 (13%)	10 (16%)	3 (5%)	15 (25%)	18 (30%)
More than 600	2 (4%)	5 (9%)	2 (4%)	5 (9%)	7 (12%)
Total	25 (42%)	35 (58%)	15 (25%)	45 (75%)	60 (100%)

TABLE – 1

RENAL BIOPSY FINDINGS IN 60 CASES OF DIABETES MELLITUS WITH DIABETIC NEPHROPATHY

Renal biopsy findings	Male	Female	Type I	Type II	Total % age
Capillary basement membrane thickening	16 (26%)	24 (40%)	10 (15%)	30 (51%)	40 (66%)
Diffuse glomerulosclerosis	4 (7%)	6 (10%)	3 (5%)	7 (12%)	10 (17%)
Nodular glomerular sclerosis	4 (7%)	6 (10%)	3 (5%)	7 (12%)	10 (17%)
Total	24 (40%)	36 (60%)	16 (25%)	44 (75%)	60 (100%)

TABLE – 2

DISCUSSION

Diabetic nephropathy is one of the most dreaded complications of diabetes mellitus and is one of the leading cause of end stage renal disease is diabetics. In USA about 10% are type 1 and 90% are type 2 diabetics . It is estimated that 30-40 % of type 1 and 20-30% of type 2 will develop diabetic nephropathy.[7]

In our study 20% were having type 1 diabetes mellitus while 80% were having type 2 diabetes mellitus. Although the association between hypertension and the advanced stages of diabetic nephropathy is well recognised,[8-9] the elevation in blood pressure has usually been considered secondary phenomenana as a result of renal damage. This study provides evidence for a different interpretation of this association. Patients with three stages of diabetic nephropathy (incipient nephropathy, overt protenuria and renal failure) were included to represent the range of renal damage during two decades of diabetes mellitus. Among these subgroups, elevation of systemic blood pressure, corresponded with the severity of renal damage (those with incipient nephropathy had little or no elevation). Where as markers of a predisposition to essential HTN were more common in all three subgroups than in patients with diabetes in whom renal disease did not develop. My study also correlates with the same.

In the different studies,[10-13] there is a genetic predisposition to hypertension and susceptibility to nephropathy in patients with diabetes. The genetic predisposition along with metabolic disturbances of diabetes may be the initial factors that led to the development of renal disease. We also made a similar.

It was found that patients with poorly controlled diabetes have substantially increased risk of diabetic nephropathy

Furthermore among the patients with poor glycemic control, diabetic nephropathy occurred mainly among those with genetic predisposition to hypertension. This predisposition was not associated with the few cases of diabetic nephropathy found among those with an index of hyperglycemia below the median. These findings suggest that uncontrolled diabetes mellitus should be considered the principal risk factor for renal disease whose effect is enhanced in a patient with a genetic predisposition to hypertension. Thus it is possible that in the presence of poorly controlled diabetes, any of the abnormalities in the renal haemodynamics may be magnified further and lead to rising intra glomeruler pressure. This could be the essential hemodynamic derangement responsible for the development of diabetic nephropathy.[14]

Another possibility is that poor glycemic control or the conditions associated with it could produce vasodilatation of pre-

glomeruler vessels,[15] this would allow the direct transmission into the glomeruli of systemic blood pressure, which have been found to be higher in persons predisposed to hypertension. The elevated intra glomeruler pressure would damage the glomeruli and initiate the development of diabetic nephropathy.

Regarding the renal biopsy findings in my study, there is female preponderance in favour of which no previous literature is available. Majority of our patients have capillary basement membranes thickening, followed by diffuse and noduler glomerulosclerosis. Most investigators believe that the morphology of diabetic nephropathy is similar in patients with type 1 and type 2 diabetes.[16,17] My study also favours the same.

CONCLUSION

Early diagnosis, dietry modifications, meticulous glycemic control, regular exercise, weight reduction and control of hypertension early in the course of diabetes reduces the chances of diabetic nephropathy. Regarding the management of diabetic nephropathy until now no therapy has been shown to improve the clinical out come of these patients. Patients with diabetic nephropathy treated with intensive insulin therapy and with ACE inhibitors.

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