RENAL BIOPSY ANALYSIS OF YOUNG PATIENTS WITH MEDICAL RENAL DISEASE IN A TERTIARY CARE CENTRE HOSPITAL

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ABSTRACT

BACKGROUND

Renal diseases are commonly diagnosed and managed as per syndromic approach depending on clinical and laboratory findings. But recent usefulness of USG-guided percutaneous renal biopsy has made it possible to diagnose exact pathology and treat these patients better.

The aim was to find out the effectiveness of such intervention in young medical renal disease patients.

MATERIALS AND METHODS

In this prospective study, 52 young adult patients with renal parenchymal disease were subjected to renal biopsy and their clinical profiles compared.

RESULTS

Clinical case scenario for all these patients was obtained and their renal biopsy findings were compared as per different age groups. Also, biopsy findings were analysed with respect to clinical symptoms, lab features and provisional diagnosis. It was found that during many occasions, diagnosing medical renal disease, just on clinical and lab features can mislead from original pathological process. Thus, wherever possible renal biopsy should be considered in young patients with medical renal disease early in diagnostic workup to achieve better treatment results without increasing any complications.

CONCLUSION

Obtaining renal biopsy at early stage can help patients more. It is better than waiting for it, as a last resort.

KEY WORDS

Medical Renal Disease, Percutaneous Renal Biopsy, USG-Guided Renal Biopsy.

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BACKGROUND

Normal kidney function helps to maintain body homeostasis through numerous cellular processes. Not only the excretory, but also the maintenance of body fluid composition including electrolyte and acid-base balance are functions of kidneys. Disturbance in any of these functions can lead to constellation of abnormalities that may be detrimental to survival. From the Hippocrates times, formation of urine and diseases related to it are a matter of much interest.[1] Mild renal disease is often clinically silent and patient may occasionally remain asymptomatic, until their renal disease is so advanced as to cause near total loss of kidney function. Sometimes kidney diseases can be incidentally detected during routine evaluation. Kidney disease is associated with high incidence of morbidity in the form of hospital admissions and prolonged stay, once renal involvement occurs in patients admitted for non-renal problems.[2]

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A major challenge in the investigation and management of Acute Kidney Injury is the timely recognition of the syndrome. Similarly, in patients with steady deterioration of renal function, interventions can slow the progression to End Stage Renal Disease (ESRD).

The routinely performed tests like serum creatinine and urea estimations can point out renal involvement in asymptomatic patients who are primarily screened for other reasons like health insurance, check-up for unrelated medical conditions. They can also be used as monitoring tools in patients with risk factors like diabetes and hypertension. Urine analysis is also many times done as a routine procedure that may reveal a renal pathology.

Microscopic haematuria[(6)] is a common clinical finding with reported prevalences of up to 22%. Ultrasound, the most evolved radiological tool without radiation hazards can sometimes overtly pick up renal abnormalities like raised cortical echogenicity in the absence of any obvious other abnormalities. At times patient may present with symptoms of uraemia or related to disease states like haematuria or facial puffiness or pedal oedema. And at instances admitted patient may develop abnormalities of renal function, acid base or electrolyte imbalance that brings renal problems to notice.

The renal biopsy has recently developed as important tool in diagnosing the exact pathological nature of renal disease. It is very useful as speculations can be converted into evidence. Though renal biopsies have been performed from way back in 1950,[(3)] the recent use of percutaneous real time ultrasound-guided biopsy was a major boon. Though the use

of this intervention is not that well developed in Indian settings, it appears to be used more frequently now in developed centres in major cities. A renal biopsy in the setting of glomerulonephritis quickly identifies the type of glomerular injury and often suggests a course of treatment. Each region of a renal biopsy is assessed separately. By light microscopy (at least 10 and ideally 20) are reviewed individually for discrete lesions; < 50% involvement is considered focal and > 50% involvement is diffuse. Injury in each glomerular tuft can be segmental involving a portion of the tuft or global involving most of the glomerulus.

This study was aimed at study of clinical profiles of young patients with medical renal disease (Renal parenchymal disease) and analysis of their renal biopsy findings for diagnosing the specific disease entities. It was useful in providing basis for planning better definitive management of these patients.

MATERIALS AND METHODS

This study was a prospective and descriptive study of patients admitted under Department of Medicine at a Tertiary Care Teaching Hospital. The primary diagnosis in these patients was renal diseases including cases of Acute Kidney Injury. The age group selected was of 13 yrs. to 40 yrs. Both males and females in this age group were included irrespective of place of residence. Patients were started on standard line of treatment on the basis of available relevant clinical and laboratory information.

Detailed evaluation of the patients admitted with renal disease was done considering demographical characteristics, medical history, physical examination, ultrasound of abdomen and laboratory tests. Those suspected for medical renal disease were screened and cases to be considered were evaluated on inclusion and exclusion criteria.

The age, sex and address of each patient were recorded. The residence was primarily classified as urban and rural. Then patient's presenting complaints were noted. History of pre-existing risk factors and family history of renal diseases was also documented. We also recorded any use of renal replacement therapy in the form of haemodialysis and peritoneal dialysis in past or current admission.

Patients were then examined especially for presence of hypertension, pallor and oedema which are traditionally mentioned to be associated with renal diseases. Other physical examination was also carried out and any abnormalities if found were recorded.

Laboratory evaluation considered in the study included serum creatinine, urea, blood urea nitrogen, plasma albumin concentration, abnormalities of blood sugar and lipid profiles. BUN: Creatinine ratio for all patients was calculated. Urine analysis was done with consideration of dysmorphic RBCs with or without casts. 24 Hrs. urinary sampling was done meticulously to document proteinuria.

Patients were also screened for HIV, HBsAg and anti-HCV as these three are known independent causes of renal parenchymal disease and glomerular involvement.

All the patients who had consented for biopsy were explained the procedure in detail.

Coagulation parameters (prothrombin time, partial thromboplastin time) were measured using standard methods in all patients prior to biopsy. If there were any abnormalities in coagulation tests that could not be explained by reversible causes, renal biopsy was not performed. All patients were asked to abstain from aspirin or NSAIDs for at least 5 days before biopsy. Bleeding time was routinely measured in all patients on the morning of the scheduled renal biopsy to rule out platelet dysfunction due to intrinsic causes (e.g. uraemic coagulopathy, von Willebrand's disease) or extrinsic causes (Aspirin or NSAIDs). In all patients, blood pressure was measured before procedure. Atropine 0.6 mg was administered intramuscularly before the procedure.

A 20-cm needle was used for biopsies of kidneys. The diameter of the needle was 1.2 mm (18 gauge). In all cases, the caudal pole of the kidney was used for biopsy. Usually, the biopsy was performed on the left kidney. In cases with cysts, small cortex or medium-sized arteries at the caudal pole of the left kidney, the right kidney was biopsied. Single kidney (Anatomically or functionally) was not biopsied.

An adequate assessment of native renal biopsies includes Light Microscopy (LM), Immunofluorescence Microscopy (IF), and Electron Microscopy (EM). For transplant biopsy, LM and IF are considered the standard with repeat to biopsies only needing LM in many cases.

So all samples were divided into two sections, one for light microscopy in formalin and for fluorescence microscopy on autoclaved gauze or blotting paper soaked in normal saline. Samples were transferred to pathologist immediately. In cases where it was possible, one sample in formaldehyde was preserved for electron microscopy.

Patients were continued on treatment as per the clinical diagnosis and renal biopsy reports awaited. Once the biopsy reports were available, comparison with pre-biopsy diagnosis was done and any required changes in the ongoing treatment modalities were done.

RESULTS

After a period of 18 months, the data obtained from clinical proforma and laboratory details was analysed in accordance with renal biopsy findings and then findings of different subgroups were statistically compared.

The age group under consideration was from age of 13 yrs. to 40 yrs. 24 patients were in the age group of 13 yrs. to 25 yrs. and 28 in the age group of 26 yrs. to 40 yrs.

Diagnosis	13-25 Years	25-40 Years	
GN	11	6	P = 0.079
NS	9	11	P = 1.000
VD	2	0	P = 0.208
TID	1	5	P = 0.199
UD	1	6	P = 0.107
Total	**24**	**28**	

Table 1. Glomerular Disease cases in both Age Groups

In the first age group, there were 11 cases of Glomerulonephritis (GN) and 9 had Nephrotic Syndrome (NS) and in second group 11 had NS and 6 had GN and 5 had tubulointerstitial diseases. But statistically, the difference was compared by Fisher test and found not significant.

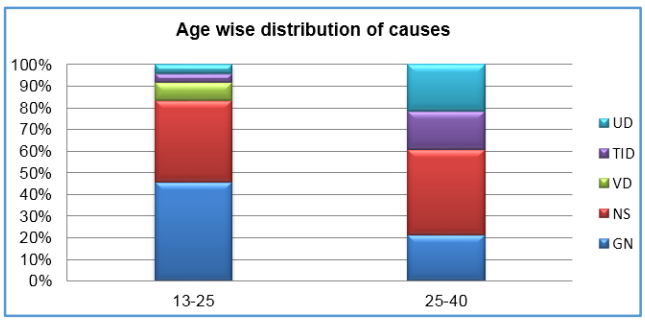

Figure 1. Age Wise proportion of Renal Pathologies

Out of 9 cases of haematuria 7 had glomerulonephritis (association significant, P < 0.01) and 2 had HSP, while out of 19 patients with oedema 17 had nephrotic syndrome (association significant, P < 0.001), 1 had glomerulonephritis and 1 had tubulointerstitial disease.

Hypertension was found in 15 patients on examination with 4 having Glomerulonephritis, 1 with Nephrotic syndrome and 3 having Tubulointerstitial disease. Rest of the patients had diagnoses in non-specific categories like End Stage Renal Disease (ESRD) in 4 patients, interstitial nephritis with granuloma in 2 patients and 1 had findings of malignant nephrosclerosis. Oedema was present in majority of cases, 42 of 52. Pallor was also observed in 30 out of 52 patients.

Urine analysis has developed over centuries as a powerful tool and provides a sound base in diagnosis of all renal problems. Renal analysis was normal in 14 subjects including 12 having nephrotic syndrome. Abnormal urinalysis was an indication of renal biopsies in 24 patients.

Abnormal Urinalysis	Patients
Haematuria	16
Haematuria with casts	18
Casts	4
Total	**34**

Table 2. Number of Cases with Abnormal Urinalysis

Of the 17 cases of nephritis 8 had haematuria, 8 had haematuria with casts and 1 had normal urinalysis. Though haematuria with dysmorphic RBCs or casts is indicative of glomerular involvement with nephritis (P= 0.002), it gives no information as to specific disease pathologies.

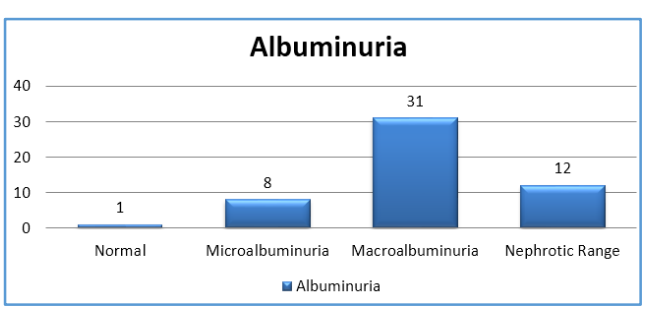

Figure 2. Number of Cases with Albuminuria

While considering as an indication of renal biopsy, macroalbuminuria was seen with nephritis in 12 cases and nephrotic syndrome in 10 cases. Proteinuria more than 3.5 gm/day, hallmark of nephrotic syndrome was also strongly associated in our study (P < 0.001). It is not helpful in diagnosing specific disease patterns. Moreover, macroalbuminuria with wide range from 300 mg to 3500 mg involves various entities of both tubular and glomerular pathologies. So, 24 hrs. urinary protein excretion was very much helpful.

As patients with small scarred kidneys and obstructive lesions were not part of our study, only cortical echogenicity and corticomedullary differentiation was considered. USG was suggestive of renal parenchymal disease in 45 of 52 patients.

As per classification prevalent in literature, renal biopsy diagnoses were classified. A comparison of histopathological diagnosis was done with pre-biopsy diagnosis. Because only diagnosing broad syndromic category is not advisable clinically, because it cannot give possible aetiological cause or guide management. Thus, pre-biopsy diagnosis was compared with post-biopsy histopathological diagnosis. Considering renal biopsy as the gold standard, it was found that pre-biopsy diagnosis was correct in only 17 cases out of 52. In 35 cases some alternate diagnosis, sometimes one of the unexpected diagnosis was noted. Percutaneous renal biopsy provided additional information than clinical diagnosis. In cases like Lupus Nephritis where renal biopsy confirmed diagnosis, it also gave important information like staging of renal disease. It provided evidence of ESRD in two unexpected cases of young adults.

DISCUSSION

It is indeed necessary to find out the exact pathology of renal affection in patients with medical renal disease, so that timely correct treatment can be initiated. Over the years syndromic approach is being followed and we overtly rely on laboratory values for diagnosis of kidney disease. For time and again, it was found that the gold standard way to histopathologically prove the diagnosis is to kidney biopsy. With advances in technology and tools now, we can do percutaneous USG-guided renal biopsy with ease and without complications. When tested in patients with young medical renal disease patients at a tertiary care centre, it proved very useful as it changed the direction of treatment significantly compared to syndromic approach. In the current study, 52 patients were selected as per inclusion criterion and they were subjected to percutaneous USG-guided renal biopsy and their data analysed. It was found that this differs significantly compared to syndromic approach and using demographic epidemiology into consideration.

Percutaneous Renal Biopsy (PRB) is an integral part of the clinical practice of nephrology. It is essential in the diagnosis of glomerular, vascular and tubulointerstitial diseases of the kidney, providing information that is invaluable in prognosis and patient management.[4] In our study, almost all biopsies and their histopathological examination provided sound base to judgement regarding patient evaluation and management. Many times, this information was used to diagnose more important systemic diseases.

The common clinical situations where biopsy is needed are Nephrotic Syndrome (NS), prolonged Acute Renal Failure, Rapidly Progressive Renal Failure (RPRF), non-nephrotic proteinuria, isolated microscopic haematuria, chronic glomerulonephritis, unexplained Chronic Renal Failure (CRF) with normal kidney size and familial renal disease.[5]

For comparing the disease patterns, the study group was divided in those with age 25 or less and age group of 26 to 40 yrs. The first group had more glomerular diseases and second had lesser proportion of them. Glomerulonephritis was proportionately more in first group, but nephrotic syndrome was showing similar rates in both groups. But these differences were statistically insignificant. Cases of PSGN were limited to first group, while amyloidosis was exclusively to second group. FSGS and MPGN were more common in first, with ESRD being more common in later group. In our study of 52 BPRD, proportion of nephrotic syndrome was more in males and proportion of GN was more in females. Two cases of IgA nephropathy/ HSP were both in males. And all 4 cases of LN were in females. Another finding was both cases of PSGN which were in females and only case of Mesangioproliferative GN was in males.

In our findings, haematuria was the presenting complaint in 17% of patients and almost 65% had on urine analysis haematuria with dysmorphic RBCs. The differential pathologic diagnosis of glomerular haematuria without proteinuria, renal insufficiency or red blood cell casts is IgA nephropathy, thin basement membrane nephropathy, hereditary nephritis or histologically normal glomeruli.[6] Out of these 9 patients with haematuria as presenting complaint and indication for biopsy, 7 had glomerulonephritis and 2 had IgA nephropathy which was slightly different than the current literature view of most common cause.[7] Our result showed that 6 patients presented with decreased urine output which on strict measurement was < 400 mL per day, one patient was anuric, most of them had tubulointerstitial disease. 19 patients had oedema as presenting complaint, but on examination oedema was present in 42 of 52 patients (in 80%). Out of these 42 were having oedema and 79% patients (33) had glomerular disease. Almost all of them had 24 hrs. urinary albumin excretion > 300 mg/ day. Majority (20) had nephrotic syndrome and 13 had GN.

Increase in Blood Urea Nitrogen (BUN) and Serum Creatinine (Cr) levels are hallmarks of kidney failure. The rate of rise in BUN and Cr levels varies considerably from patient to patient. As commonly observed, the normal BUN/Cr ratio of 10: 1 is usually maintained in cases of intrinsic AKI. The ratio is usually elevated (> 20: 1) in prerenal conditions and in some patients with obstructive uropathy, also in patients with significant upper gastrointestinal bleeding.[8] In contrast, the BUN/Cr ratio may be reduced in liver failure, malnutrition and rhabdomyolysis. Individuals with mild-to-moderate reductions in kidney function are at increased risk for cardiovascular disease.[9] F8 or most patient's diagnosis was made from the clinical findings and laboratory findings and treatment started. But after renal biopsy findings of correct pathological diagnosis was established, treatment and management plan of many patients had to be altered. This study gave us an insight that in many cases we may actually miss the exact diagnosis without renal biopsy. Syndromic approach is appropriate in the initial management of the patient, but eventually percutaneous renal biopsy would add significant information about the disease and prognosis.

CONCLUSION

Patients with age between 13 - 40 years are without many important risk factors that are prevalent in older populations. Worldwide data shows that glomerulonephritis is the most important cause of chronic kidney disease after diabetes and hypertension. The exact prevalence of these diseases is not clear and in regions where use of renal biopsy is common, the proportion of these diseases is more than expected. Proteinuria is an important marker and 24 hrs. urinary protein estimation is more useful in these patients. Hypoalbuminaemia of severe type with significant proteinuria is seen commonly in nephrotic syndrome. Renal function tests do not indicate the severity of glomerular involvement in diseases. USG is very useful to rule out post renal causes and also to pick up changes in cortical echotexture in medical renal diseases. Percutaneous renal biopsy is easy, and risks associated are small with proper patient selection. Clinical diagnosis differs from PRB proven pathological diagnosis in 2/3 cases. In many, known renal biopsy is still useful to stage disease like in case of lupus nephritis. Clinically, only syndromes can be identified, but renal biopsy is very useful in delineating the disease processes and suggesting causes. Many times, kidneys could be the only organs involved in systemic diseases and renal biopsy confirms the presence of disease. Maintaining proper computer-generated registry of renal biopsies can also generate potentially useful information about epidemiology of glomerular disease. Thus, obtaining renal biopsy at early stage can help patients more than waiting for it as a last resort.

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