Clinicopathological Correlation in Adult Nephrotic Syndrome

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ABSTRACT

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The main aim of this study was to elucidate a relationship between the clinical parameters and renal histology. The practice followed in pediatric NS and to a lesser extent in adolescent NS is to offer a trial of steroid therapy and deferring renal biopsy as per response. This practice is mainly based on the statistical fact that majority of NS patients in these age group were having MCNS and hence steroid responsive. Although in adult NS, this statistical prediction does not corroborate, there are well defined clinical parameters like age, onset, temporal profile, hypertension, urinary sediment, renal failure, degree of proteinuria etc., which can differentiate MCNS from others. An attempt has been made in this study to clarify such clinical parameters and then to confirm their relationship to the morphological picture by renal biopsy.

Adult patients with primary Nephrotic syndrome who came to Thrissur Medical College for treatment were selected for this study. The following features- age, gender, duration and degree of proteinuria, hematuria, oliguria, hypertension, edema, pleural effusion, ascites, hemoglobin, total and differential count, urine albumin, urine sediment, 24 hour urinary protein, renal function tests, serum cholesterol, serum albumin and ultrasound of the abdomen of these patients were studied. Prior to renal biopsy each patient was analyzed in detail and the possible histopathological lesion predicted. Renal biopsy was done with automated Tumour biopsy gun under ultrasonic guidance with all necessary precautions in these patients. The tissue was analyzed by light and immunofluorescence microscopy. The histopathological lesions were correlated with demographic, clinical and laboratory parameters. The predictive value of these clinical and laboratory parameters on the renal histology were sought. Results were analyzed using standard statistical methods.

We strongly recommend renal biopsy in all adult patients with NS prior to steroid treatment.

Keywords: Nephrotic syndrome, Renal biopsy, Histology

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INTRODUCTION

Nephrotic Syndrome is a leading cause of oedema due to renal disease in clinical practice. In paediatric patients the approach to nephrotic syndrome is empirical steroid therapy based on the presumption of Minimal Change Nephrotic Syndrome as the usual cause. In children renal biopsy is indicated only if there are atypical features, which are encountered in less than 10% of patients. This is an acceptable practice considering the difficulty to do renal biopsy which may necessitate even general anaesthesia. In adult patients the clinical scenario is entirely different. Here only a minority of patients are having minimal change disease. Even in this group the clinical response to empirical steroid therapy is rather unpredictable often needing as long as 4 months for remission. In addition the morbidity of empirical steroid therapy is substantial, especially in the elderly. On the other hand performance of renal biopsy is very easy in adults and has become virtually problem free after the advent of the automated tumour biopsy Gun based on the principle of Wim Silverman needle.

Still there is a substantial group of patients and physicians who avoid doing renal biopsy waiting for response to empirical steroid therapy. This may be justifiable in the adolescent age group which still behaves to a certain extent like the paediatric patients. On the other hand the only argument possible for such an approach among adult patients is based on a logical prediction of the histological diagnosis. There are salient features in the clinical data of the patient which can often guide the clinician to predict the histological type of nephrotic syndrome without doing the renal biopsy. These include epidemiologic, clinical and laboratory features which when judiciously applied to the individual scenario, an empirical histological prediction can be made. We designed a prospective study to look at the potential of such a design. The individual

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data in the patient is utilized to make a prediction of the histological type and then correlated with the actual status after renal biopsy. We are exploring for a model of clinical database in adult nephrotic syndrome patients to make an accurate histological prediction without renal biopsy.

MATERIAL AND METHOD

Design

This is an observational study on the clinicopathological correlation in nephrotic syndrome so as to assess the predictive value of clinical and laboratory parameters on the renal histology.

Setting

The study is conducted in the general medicine department and nephrology unit of Thrissur, Medical College.

Subjects

Adult Patients aged above 12 years with nephrotic range proteinuria, having no secondary causes for nephrotic syndrome is included in this study.

Inclusion Criteria

1. Age more than 12 years.
2. Nephrotic range proteinuria.
3. Performance of Renal biopsy.

Exclusion Criteria

1. Age less than 12 years.
2. Previously biopsied patients on follow up.
3. Secondary causes of Nephrotic syndrome.
4. Refused biopsy.

METHODS

Adult patients with primary Nephrotic syndrome who came to Thrissur Medical College for treatment were selected for this study. The following features- age, gender, duration and degree of proteinuria, hematuria, oliguria, hypertension, edema, pleural effusion, ascites, hemoglobin, total and differential count, urine albumin, urine sediment,

24 hour urinary protein, renal function tests, serum cholesterol, serum albumin and ultrasound of the abdomen of these patients were studied. Prior to renal biopsy each patient was analyzed in detail and the possible histopathological lesion predicted. Renal biopsy was done with automated Tumour biopsy gun under ultrasonic guidance with all necessary precautions in these patients. The tissue was analyzed by light and immunofluorescence microscopy. The histopathological lesions were correlated with demographic, clinical and laboratory parameters. The predictive value of these clinical and laboratory parameters on the renal histology were sought. Results were analyzed using standard statistical methods.

RESULTS

During the study period eighty six patients underwent renal biopsy in the nephrology unit of our hospital. Among them sixty five were found to have NS. Of these sixty five, fifty met the selection criteria of this study. They were included in this study, which was designed and conducted as a prospective study. A clinicomorphological correlation is sought.

The mean age of the patients in this study was34 years; with a standard deviation of 14.74 . The range was 14-71 years. Majority of the patients were in the age group 30-39 years 30%

The majority of the patients were males (70%). Of the total fifty patients thirty five were males. The predominance in male frequency was seen in all age groups. The combined age and sex distribution pattern is shown in Table.1 and Figure 1.

Four types of renal lesions constitute the majority of patients having adult primary NS. There is an overall reduction in the number of patients belonging to MPGN subtype in the western hemisphere. The same trend is noticed here also. There are no patients with MPGN in this study. The histological subtypes obtained in this study were minimal change disease (MCNS), focal segmental glomerulosclerosis (FSGS)

Table 1. The age sex distribution of the patients is given in the table below.

Age group	Female	Male	TOTAL
10 to 19	2	8	10
20 to 29	5	7	12
30 to 39	5	10	15
40 to 49	2	3	5
50 to 59	1	4	5
60 to 69	0	2	2
70 to 79	0	1	1
TOTAL	15	35	50
6/2004	260	19.7	800

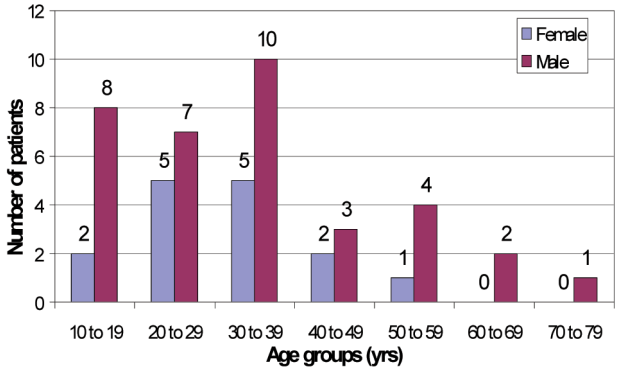

Figure 1. **Age Sex Distribution**

and membranous glomerulonephritis (MN). Of the 50 patients 11 belonged to MCNS constituting (22%), 16 belonged to MN (46%), and 23 belonged to FSGS(46%). The distribution pattern has been shown in Table 2 and Figure 2.

Table 2. Histological subtypes of NS patients

Histological Subtypes	Number of patients	%	95 % conf Limits	
			Lower	Higher
FSGS	23	46	31.80 %	60.70 %
MCNS	11	22	11.50%	36.00 %
MN	16	32	19.50 %	36.00 %
Total	50			

Majority of the patients were in the younger age group 30-40 years, 15 out of 50.There were 12 patients in the age group of 20-30 years, while only 3 patients were in the age group of more than 60 years. Of the 3 elderly patients 2 had FSGS and 1 had MN.

MCNS is a disease of children while MN occurs mostly in adults. In this study also this pattern was seen as

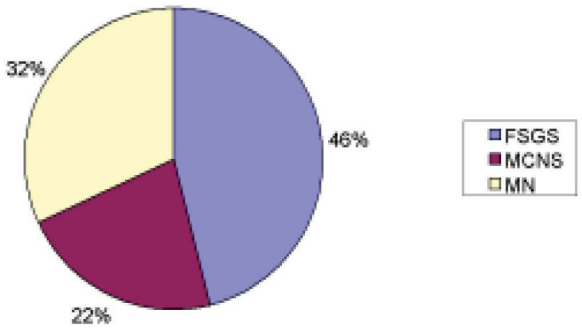

Figure 2. **Histological subtypes**

demonstrated in the Table3 and the figure 3. Of the 11 patients who had MCNS majority were in the age group less than 34 years. Of the 3 elderly patients 2 had FSGS and 1 had MN. It was observed that the largest histological group was FSGS and the dominance held in all age sub groups. This result is an agreement with the world wide tendency for an increase in the number of FSGS among NS patients.

Table 3. Age distribution of various histological subtypes

Age of Patients	Number of patient with each histological type			
	FSGS	MCNS	MN	TOTAL
10 to 19	3	4	3	10
20 to 29	6	3	3	12
30 to 39	8	0	7	15
40 to 49	2	2	1	5
50 to 59	2	2	1	5
60 to 69	1	0	1	2
70 to 79	1	0	0	1
TOTAL	23	11	16	50

The main objective of this study was to seek a clinicopathological correlation between the clinical features and the histological picture. Although the clinical prediction was in reasonable agreement with the pathological picture in all the three histological subtypes, there were still significant differences. This was worrisome enough to make prediction unviable. Of the 20 cases clinically predicted as FSGS, only14

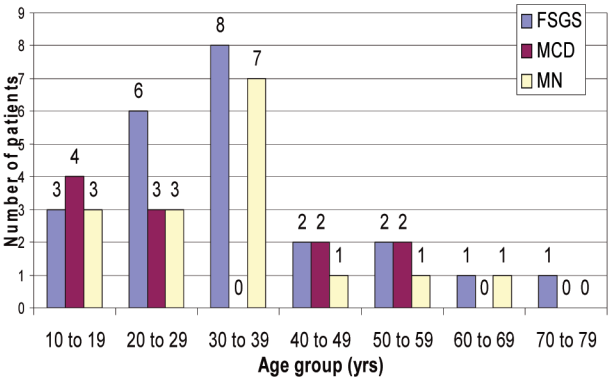

Figure 3. **Age distribution of various histological subtypes**

turned out to be true. Similarly predictions held good only in 5 / 9 of MCNS and 11 / 21 0f MN. The margin of error would be 30% in FSGS, 44%in MCNS and 48% in MN. These are unacceptable when we consider the ease with which a renal biopsy can be done and the hazards of inappropriate immunosuppressive therapy. (Table 4 and Figure 4)

Table 4. Clinicomorphological correlation of renal biopsy in NS patients

Histological Subtype	Clinical diagnosis			
	FSGS	MCNS	MN	TOTAL
FSGS	14	2	7	23
MCNS	3	5	3	11
MN	3	2	11	16
TOTAL	20	9	21	50

DISCUSSION

The main purpose of the present study is to seek a clinic morphological correlation of adult Nephrotic Syndrome. Clinicomorphological Correlation.

It has been an accepted practice in pediatric nephrology to defer renal biopsy in NS patients; till one course of glucocorticoids is given or obvious atypical features

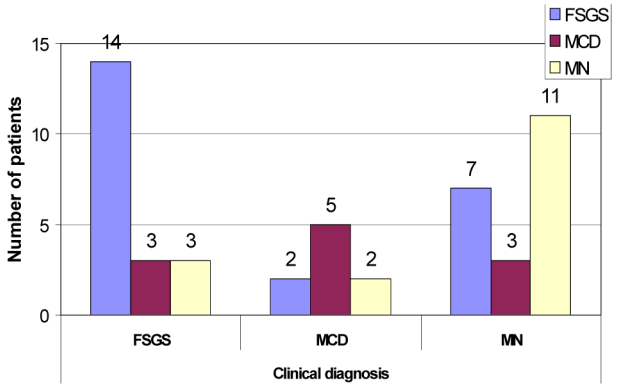

Figure 4. **Clinicomorphological correlation**

are present. This is based on the surmise that majority of these children have MCNS and hence will respond promptly to steroids. The obvious reluctance of the child and the parents to undergo an invasive procedure augment the above reasoning. Several studies[1,2,3,4,5] have attempted to extend this practice to adult nephrology. The main limitation for this approach is the fact that most of the adult NS patients do not have MCNS. To overcome this limitation several schemes have been proposed whereby the histology can be reasonably predicted so that steroids are started without a renal biopsy.[6,7,8] These include various demographic, clinical and laboratory parameters of adult NS patients. A study from Thiruvananthapuram was able to achieve reasonable correlation of age, renal function, hypertension and urinary sediment with the histological type so that empirical steroid therapy can be offered to a selected group of adult NS patients before renal biopsy. A retrospective analysis of adult NS patients from Kottayam Medical College[9] found that renal histology can be reliably inferred in adolescent children (13 to 18 years) so the need for biopsy is obviated. Another study attempting clinicomorphological correlation in adult NS from Rajasthan involving 30 patients revealed successful prediction in 77% cases. In our study the average Clinicopathological correlation across all groups were 60%, which is comparable to similar studies elsewhere. Although such a substantial correlation appears impressive, it is still not sufficient to justify blind steroid therapy. The reasons for this can be summarized as lack of a predictable response to steroids in adult patients, considerable toxicity for steroids in adults and the relative ease with which renal biopsy can be done in adults.

Role of Renal Biopsy in Nephrotic Syndrome

The main aim of this study was to elucidate a relationship between the clinical parameters and renal histology. The practice followed in pediatric NS and to a lesser extent in adolescent NS is to offer a trial of steroid therapy and deferring renal biopsy as per response. This practice is mainly based on the statistical fact that majority of NS patients in these age group were having MCNS and hence steroid responsive. Although in adult NS, this statistical prediction does not corroborate, there are well defined clinical parameters like age, onset, temporal profile, hypertension, urinary sediment, renal failure, degree of proteinuria etc., which can differentiate MCNS from others. An attempt has been made in this study to clarify such clinical parameters and then to confirm their relationship to the morphological picture by renal biopsy. Although there is some degree of accuracy in predicting the histological picture from the clinical data, the margin for error is too big to be acceptable. This is especially true when we consider the wide variation in response to steroid therapy even among adult patients with MCNS. Hence blind steroid therapy has little role even in adult MCNS not to mention FSGS, MN or MPGN. Over and above, the advent of the automated biopsy gun has made renal biopsy almost an outpatient procedure. In the past few years there has been a change in the frequency of histological picture in adult NS. Several studies have stressed the need for renal biopsy in older children and adults with NS. Retrospective meta analyses have shown that complications of indiscriminate steroid therapy were12 times greater than that of selective biopsy. It is now recommended that the cause of NS must always be established before embarking on therapy. In this study also the need for renal biopsy for establishing a correct diagnosis is emphasized.

CONCLUSION

Nephrotic Syndrome implies a different connotation in pediatric and adult scenario. In children empirical steroid therapy is the rule considering the prevalence of Minimal change disease and its near perfect response to steroids. On the other hand the situation is entirely different in adults with MCNS as a minority component, its steroid response unpredictable and the vulnerability of the target population to steroid toxicity

substantial. We have a sought a clinicomorphological correlation in adult NS patients in this study to create a model for clinical prediction of renal histology. Although there is a substantial clinicomorphological correlation (60%) in our study, considering the ease of renal biopsy in adults, the unpredictability of steroid therapy in the designated patients and its toxicity, a model for histological prediction does not appear to be viable. We strongly recommend renal biopsy in all adult patients with NS prior to steroid treatment.

END NOTE

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Conflict of Interest: None declared

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