Original paper

Outcome of Idiopathic Steroid Resistant Nephrotic Syndrome of Children in Central Child Teaching Hospital

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Abstract

Background: Steroid resistant nephrotic syndrome accounts for 10%-20% of all cases of idiopathic nephrotic syndrome. These patients are at risk of developing end stage renal disease.
Aim of the study: to determine the outcome in pediatric patients with steroid resistant nephrotic syndrome, demographic characteristics, renal biopsy findings, and response to immunosuppressive treatment.
Materials and Methods: This retrospective study included 136 patients diagnosed as primary steroid resistant nephrotic syndrome followed by pediatric nephrology department in central child teaching hospital during the period from 2000 to December 2015 (by collecting files of patients). the study done from June 2016 to December 2016. Age at first episode, gender and family history of nephrotic syndrome were recorded. Demographic characteristics, clinical features at presentation, renal biopsy findings, response to immunosuppressive treatment and outcome were analyzed.
Results: one hundred thirty-six patients involved in the study, mean age at first episode of nephrotic syndrome was 7.18+_ 3.9 years (range: 1 - 16 years). renal biopsy was done for 83 patients and main histopathology was focal segmental glomerulosclerosis found in 54 patients represent (65.1%). Many items of drugs given to the patients and most commonly used and most effective drug is Cyclosporine A in which 34 from patients achieved complete remission. There were 21 patients (15.4%) get complete remission, 38 patients (27.9%) lost follow up, 6 patients (4.4%) died, 13 patients (9.6%) developed stage 3 chronic kidney disease 24 patients (17.6%) developed stage 4 chronic kidney disease and 34(25%) patients developed End stage renal disease. There is significant relationship between hypertension, hematuria, and impaired renal functions at presentation and response to immunotherapy and development of end stage renal disease, while there is no significant relationship between age of patient at presentation, gender, histopathology and development of end stage renal disease.
Conclusion: we found near half of the patients developed chronic renal failure and 25% developed end stage renal disease. Patients with atypical presentation, resistance to immunosuppressive are liable to develop End stage renal disease significantly. In addition, we found Cyclosporine A is more effective than other immunotherapy as the initial therapy for many patients.

Keywords: steroid resistant nephrotic syndrome, chronic kidney disease.

Introduction

Nephrotic syndrome is a common type of kidney disease seen in children. childhood nephrotic syndrome is classified into steroid-sensitive nephrotic syndrome (SSNS) and steroid-resistant nephrotic syndrome (SRNS), steroid resistance is the inability to achieve remission despite 4 to 8 weeks of high-dose daily corticosteroid therapy. (1) The majority of children with SRNS have minimal change disease (MCD), mesangioproliferative glomerulonephritis (MesPGN) or focal segmental glomerulosclerosis (FSGS). FSGS is a leading cause of end-stage kidney disease (ESKD) in children. In most children with steroid-resistant nephrotic syndrome (SRNS), the underlying cause is not known. However, advances in molecular genetics of glomerular diseases have shown single gene defects that affect glomerular podocyte differentiation and

function are responsible for a quarter to a third of all pediatric cases of isolated and syndromic SRNS in many parts of the world [1,2]. The majority of patients with steroid-resistant nephrotic syndrome (SRNS) will have focal segmental glomerulosclerosis (FSGS) found on biopsy. Historical studies examining SRNS, specifically caused by FSGS, provided evidence that >50% of children who do not respond to initial steroid therapy would progress to end-stage renal disease (ESRD) within 3 years. [3]

Outcome of SRNS: Reported rates of steroid resistance among the biopsy series vary from 10 to 20% in different studies. The underlying histopathology usually affects the course of the disease as well as the response to treatment. Results of studies by the International Study of Kidney Disease in Children (ISKDC) revealed focal and segmental glomerulosclerosis (FSGS), mesangial proliferative glomerulonephritis (MesPGN) and minimal change disease (MCD) as the respective morphologic lesions seen in 70%, 44% and 7% of children with SRNS. An entity is difficult to manage. Without treatment, progression to pre-terminal (CRF) or (ESRD), few years after diagnosis, is very high. Different aggressive and potentially toxic treatment regimens have been tried to forestall disease progression, with varied outcome. Partial remission of massive proteinuria is considered as better outcome than no remission.

Outcome of treatment is quite variable. In good number of patients outcome is guarded. Fifty percent of steroid resistant nephrotic syndrome may progress to end stage renal disease (ESRD) within 5 years of diagnosis. [4]

Aim of study: to determine the outcome in pediatric patients with idiopathic steroid resistant nephrotic syndrome, demographic characteristics, Clinical features, renal biopsy findings, and response to immunosuppressive treatment.

Patients and Methods

Study design: A retrostrospective study analyzed 136 patients with steroid resistant nephrotic syndrome followed by pediatric nephrology department of central child teaching hospital at Baghdad, Iraq from January 2000 to December 2015. The data collected from medical records of patient's clinical information. The analyses patients who met our criteria of childhood idiopathic steroid resistant nephrotic syndrome in which patient age between 1 year to 16 years with idiopathic nephrotic syndrome and minimum follow up of 1 year. Mean time follow up is 4.2 ± 0.2 years and the range (1 year – 8 years).

Study population and sample: A total of 136 patients,89 males and 47 females were attended the nephrology department of the central child teaching hospital during the period from January 2000 till December 2015 had been included in this study SRNS according to the inclusion criteria that will be explained later. four patients are excluded in our study, as the later diagnosis as a cases of secondary SRNS.

Study time: The data was collected and studied during the period from June 2016 until December 2016.

Inclusion criteria:

- Age at presentation of nephrotic syndrome (one year-16 years)
- Diagnosed and confirmed as idiopathic SRNS.
- Received immunotherapy
- Least follow up one year

Exclusion criteria:

- Patients with age < 1 year with nephrotic syndrome are excluded from our study.
- Patients with secondary SRNS with systemic diseases, hepatitis B infection, SLE, Henoch-Schonlein purpura, membranous nephropathy, IgA Nephropathy and rapidly progressive glomerulonephritis, or any other cause that might produce secondary SRNS were excluded.

The basic data about age of onset NS symptoms, gender, clinical manifestations and family history of similar condition of nephrotic syndrome are collected. Also, clinical manifestations of disease at presentation, blood pressure, response to steroid (dose and duration), laboratory data (urea, creatinine, estimated glomerular filtration rate (Schwartz's formula) for whom were calculated [5], dip stick for albumin shedding in urine, hematuria, infection, serum level of cholesterol and albumin and renal biopsy results). the data related to patients' treatment, duration and response are collected and evaluated.

Blood pressure was regularly monitored on each visit and data are compared centile charts for age, gender and height of patient. Blood pressure was measured according to the recommendations of the Task Force on Blood pressure in children [6]. **Steroid resistant** confirmed by data that all patient as failure to respond to 4 weeks of oral prednisolone at dose 2 mg/kg or 60 mg/m2, then 3 doses of every other day

of IV pulse methylpredinosolone [7,8]. patients who respond to steroids initially then developed late resistant to steroid are included in the study. **Urine analysis** results for patients evaluated for disease process, Standard urine dipstick tests are more sensitive in detecting albumin than in detecting low molecular weight proteins [9]. **UTI** diagnosis based on symptoms and findings on urinalysis; a urine culture is necessary for confirmation and appropriate therapy [10].

Renal biopsy was done for eighty-four patients with idiopathic nephrotic syndrome (INS) in the following situations [11]:

1- Steroid resistance
2- Age older than 10 years
3- Unusual presentation (such as long previous course of mild proteinuria, macroscopic hematuria, marked hypertension and renal insufficiency.

Twenty-three patients with INS have subsequent biopsies were performed to evaluate nephrotoxicity and in patients who presented unexpected clinical deterioration. For analysis purpose, we considered the result of the last biopsy. During follow-up, glomerular filtration rate (GFR) for each patient were estimated by the method of Schwartz et al. In addition, the stages of CRF are determined according to the recent national kidney foundation (NKF) report and (K/DOQI) guidelines classification:

Table I. stages of chronic kidney disease [1]

Stage	Description	GFR(ml/min/1.73 m2)
1	Kidney damage with normal or increased GFR	>90
2	Kidney damage with mild reduction of GFR	60-89
3	Moderate reduction of GFR	30-59
4	Severe reduction of GFR	15-29
5	Kidney failure	<15

Treatment

Prednisolone (PDN) was given at a dose of 2 mg/kg/day or 60 mg/m2/day (maximum daily dose: 80 mg) administered orally in divided doses for 4 weeks, then 3 doses of IV methylprednisolone every other day, if failed to enter remission, the term steroid resistant patients was given to them and renal biopsy was performed [12]. If response to steroid after 4 weeks of oral daily PDN or in addition to three successive IV methylprednisolone in dose of 20-30 mg/kg/day, then oral prednisolone to daily dose of 40 mg/m2 every other day, after that PDN was progressively tapered and the dose reduced by 15 mg/m2/2 weekly and continue on 5-10 mg/day [13]. Patients who did not respond to this initial regime were given other course of cyclophosphamide or cyclosporine A (Cs A), Mycophenolate Mofetile (MMF), or a high dose of methyl prednisolone I.V. plus oral administration of an alkylating agent, as proposed by Mendoza et al [14]. 10/ 136 patients were received course of tacrolimus (TAC); 15/ 136 patients were found received Rituximab IV doses. Due to its side effects, cyclophosphamide (CYC) was not administered for a period exceeding 12 weeks. Patients were administrated CYC mostly orally given at dose 2-3 mg single daily dose for 8-12 weeks, few patients were received iv doses. Cyclosporine A (Cs A) was prescribed as an initial dose of 3-6 mg/kg/day in two divided doses for three to six months and then tapering continued for more than one year. during follow up plasma creatinine was monitored every 3 months. After 6 months, patients that did not respond to cyclosporine (Cs A) were switched to other therapy. TAC was initiated with a dose of 0.1-0.15 mg/kg/day divided into two doses over 12 h intervals. MMF were given orally at daily doses 500-1000mg/m2/day for twice daily for (6-48 months). Rituximab was given in 14 patients admitted to the ward in the form of iv infusion over 10-12 hrs. in dose 375 mg/m2 with concurrent follow up blood pressure, allergy or anaphylaxis and infusion related complications. most of the cases received rituximab as trial therapy and given as one dose weekly and no more than six doses. refractory edema was treated with regular albumin infusions combined with furosemide in hemodynamically unstable patients while in hemodynamically stable patients it was controlled with frusemide alone or with spironolactone. blood pressure was regularly monitored on each visit and if there was increase in blood pressure from base line then patients were added captopril as antihypertensive. Other groups of antihypertensive medications were also added if blood pressure is not controlled with single drug having maximum dose. lipid-lowering drugs were not routinely prescribed for those patients. patients with chronic kidney disease (CKD) were given supportive treatment and appropriate renal replacement therapy was administered in those with end stage renal disease (ESRD).

Statistical Analysis

Variables distributed normally are represented as mean ± SD and the others as proportion (percentage)

and range. P value <0.05 was considered to be significant. Data were analyzed by SPSS 22th version using Chi-square test for comparison of proportions and Study test to compare means between two groups. Ethical consent is taken from the families of our patients.

Results

The mean age of the patients at diagnosis was 7.18+_ 3.9 years (range: 1 year - 16years). most of the patients aged 6-10 years, 53(39%), while there were 48(35.3%) patients aged 1-5 years and 35(25.7%) patients aged 11- 16 years, as shown in figure (1). There were 89(65.4%) males and 47(34.6%) females, as shown in figure (2).

Clinical features of the patient with SRNS at presentation:

Of the total patients 18(13.2%) had positive family history of Nephrotic syndrome. most of the patients presented with generalized edema 71(52.2%), while 65(47.8%) presented with local edema. there were 76(55.9%) patients had infection (urinary tract infections, pneumonia or skin infections) on presentation. on presentation 75 (55.1%) patients had hematuria, 94(69.1%) had hypertension and 40(29.4%) had impaired renal functions, as shown in table (1).

Histopathological result of renal biopsy:

Biopsy was taken from 83(61%) children, the biopsy of 54(65.1%) children revealed FSGS, and the biopsy of 21(25.3%) children revealed MCD, while just 8(9.6%) children had MPGN in their biopsy, as shown in figure (3).

Immunosuppressive treatment:

There were 54 patients treated by Methylprednisolone (Mendoza protocol) of them 39(72.2%) patients received this drug as a first choice, 4(7.4%) received the drug as a second choice, 9(16.6%) received this drug as a third choice and two (3.7%) received this drug as a fourth choice and as shown in table (2).

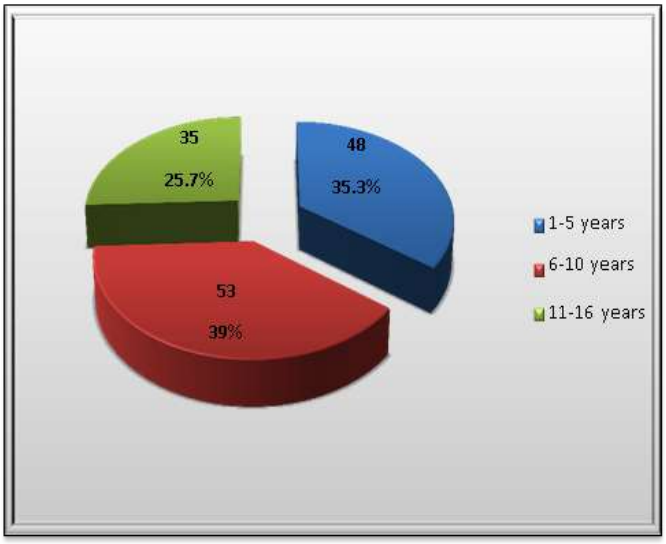

Figure1. Distribution of the patients with SRNS according age groups

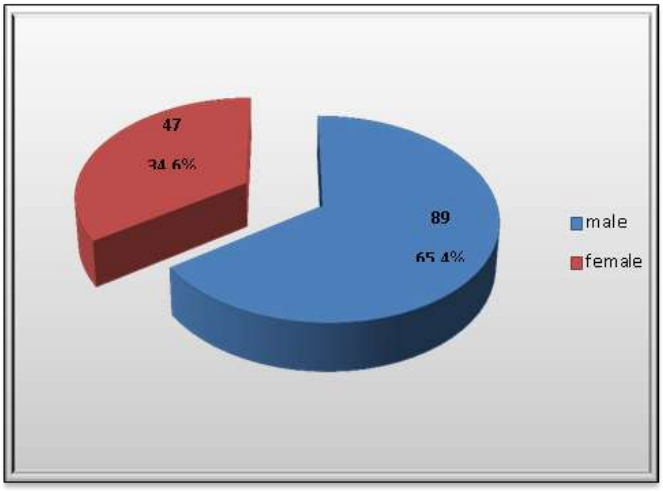

Figure 2. Distribution of the patients with SRNS according to the gender

Table 1. Distribution of the patients with SRNS according to the clinical and demographic characteristics at presentation.

Clinical and demographic characteristics	No.	%
Positive Family history	18	13.2
Generalized edema	71	52.2
Infection	76	55.9
Hematuria	75	55.1
Hypertension	94	69.1
Normal Renal function	96	70.6

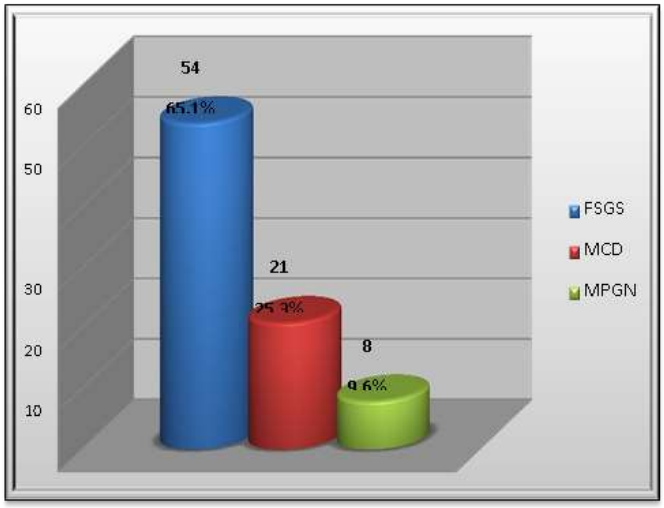

Figure 3. Distribution of the patients according to the histopathological results of renal biopsy

Cyclosporine A is the most used drug as first and choice and total patients who received the drug is 100 and 71(71%) as first choice and 26(26%) as second choice. Mycophenolate is used for 52 patients and mostly used as 2nd choice in 21(41.4%) and 3rd choice 19(36.5%) and 1st choice 12(23%). And the least used drugs according to their availability are the tacrolimus in 10 cases 4(40%) as 1st choice,4(40%) as 3rd choice and 2(20%) as 4th choice. And the Rituximab in 14 cases used as 3rd in 6cases (42.9%) and 4th choice in 6 cases (42.9%) and 2 cases (14.3 %) received drug as 2nd choice.

Regarding the response of the patients to immunosuppressive treatments, There were 54 patients treated by Methylprednisolone (Mendoza protocol) of them 10(18.5%) patients complete remission to this treatment, 14(25.9%) partial remission to it and 30(55.5%) not remission to treatment by this drug and as shown in table(3). While, the most drug used and achieved complete remission is the Cyclosporine A in 34 patients (34%) and 40 patients (40%) achieved partial remission. In addition, we found good response was obtained in patients received Mycophenolate, 16 (30.7%) patients achieved complete remission and 18(34.6%) patients obtained partial remission.

Outcome of patients with SRNS:

There were 21(15.4%) patients get complete remission,38(27.9%) patients lost follow up, 6(4.4%) patients died, 13(9.6%) patients developed stage 3 CKD, 24 (17.6%) patients developed stage 4 CKD and 34 (25%) patients developed ESRD, table (4). From the entire patient who developed CKD (71 patients) there were 34(47.9%) children had ESRD, 24 (33.8%) children had stage 4 and 13(18.3%) children had stage 3, as shown in figure (4).

Table 2. Distribution of the children according to the drugs of choice.

Drugs	1st choice	2nd choice	3rd choice	4th choice	Total No.
Methylprednisolone (Mendoza protocol)	39(72.2%)	4(7.4%)	9(16.6%)	2(3.7%)	54
Cyclosporine A	71(71%)	26(26%)	1(1%)	4(4%)	100
Cyclophosphamide	10(31.3%)	15(46.8%)	3(9.4%)	4(12.5%)	32
Mycophenolate	12(23%)	21(40.4%)	19(36.5%)	0	52
Tacrolimus	4(40%)	0	4(40%)	2(20%)	10
Rituximab	0	2(14.3%)	6(42.9%)	6(42.9%)	14

Table 3. Distribution of patients with SRNS according to their immunosuppressive drugs

Drugs	Complete remission	Partial remission	No remission	Total N0.
Methypredinosolone (Mendoza Protocol)	10(18.5%)	14(25.9%)	30(55.5%)	54
Cyclosporin A	34(34%)	40(40%)	26(26%)	100
Cyclophosphamide	6(18.8%)	12(37.5%)	14(43.8%)	32
Mycophenolate	16(30.7%)	18(34.6%)	18(34.6%)	52
Tacrolimus	0	4(40%)	6(60%)	10
Rituximab	0	4(28.6%)	10(71.4%)	14

Table 4. Distribution of the children according to the outcome

Outcome	No.	%
Complete response	21	15.4
Lost follow up	38	27.9
Death	6	4.4
CKD Stage 3	13	9.6
CKD Stage 4	24	17.6
ESRD	34	25
Total	136	100

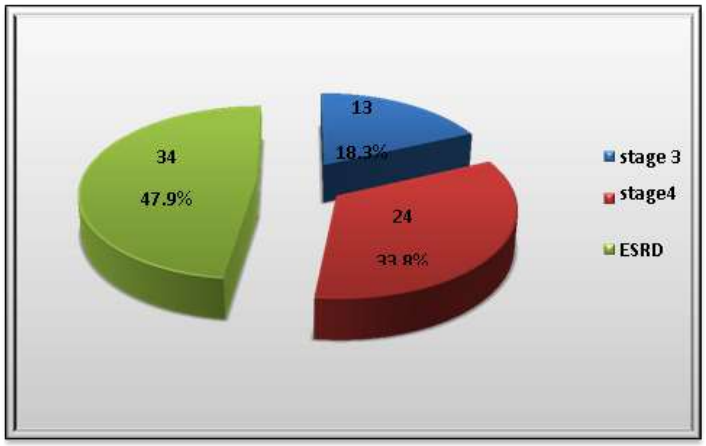

Figure 4. distribution of patients with SRNS according to the stages of CKD.

Relationship between patients with SRNS characteristics and development of ESRD:

Table 5 shows Pearson Chi square test that test the significance of association between children characteristics and development of ESRD, there was no association between age groups, gender, result of histopathology and the development of ESRD. there was significant association between the presentations with hypertension, hematuria, renal function, response to immunosuppressive drugs and the development of ESRD. patients who presented with hypertension 31(33%) tend to develop ESRD more frequently (p= 0.001). patients who presented with hematuria 29(38.7%) tend to develop ESRD more frequently (p=<0.001). patients who presented with impaired renal function 15(37.5%) tend to develop ESRD more frequently (p=0.030). no one of the patient who responded to immunosuppressive drugs developed ESRD (p=0.004).

Discussion

This is A retrospective study of children and adolescents with primary SRNS followed by department of nephrology of central teaching hospital of pediatrics. mean time follow up is 4.2 ± 0.2 years range (1 year-8 years). in this study, there were 89(65.4%) males and 47(34.6%) females with ratio 1.9:1, which is, near result obtained by Roy RR et al. [4] which was M: F=1.4. In a study in turkey was done by Renda et al. [15]

Table 5. Relationship between patient's characteristics and development of ESRD

Patient characteristics		ESRD				P value
		Developed		Not developed		
		No.	%	No.	%	
Age group	1-5 years	15	31.3	33	68.8	0.202^{NS}
	6-10 years	14	26.4	39	73.6	
	11-16 Years	5	14.3	30	85.8	
Gender	Males	19	21.3	70	78.7	0.176^{NS}
	Females	15	31.9	32	68.1	
Hypertension at presentation	Yes	31	33	63	67	0.001*
	No	3	7.1	39	92.9	
Hematuria at presentation	Yes	29	38.7	46	61.3	<0.001*
	No	5	8.2	56	91.3	
Renal function test	Normal	19	19.8	77	80.2	0.030*
	Impaired	15	37.5	25	62.5	
Histopathology	MCD	5	23.8	16	76.2	0.982^{NS}
	FSGS	14	25.9	40	74.1	
	MPGN	2	25	6	75	
Response to immunosuppressive drugs	Yes	0	0	21	100	0.004*
	No	34	29.6	81	70.4	

*Significant association (p< 0.05), NS=non-significant association.

there was male to female ratio 1:2. the most common age group in this study is (6-10 years) which represents 53 (39%) patients, and then the age group (1-5 years) which represent 48(35.3 %) patients and the least age group was (11-16 years) which represents 35 (25.7%). this is different from Renda et al. [15] study were the most common age group was (1-5 years) which represents (65%). family history of patients with SRNS in our study was 18 case from 136 represent 13.2 % while Renda et al. study was 5 from 31 represent (16%). Roy RR et al. study [4] of patients with SRNS which include 32 cases with SRNS at Bangladesh: clinical presentation was 100% with massive edema, hematuria was 20 (62.5%), hypertension 13 (46.3%) and infection 70 %: while in our study generalized edema were 71 (52.2 %), hematuria 75 (55.1%), hypertension 94 (69.1), infection 76 (55.9%). renal biopsy is recommended for histological diagnosis of children with SRNS and for determining treatment options and prognosis [15]. Several recent studies reported that as the FSGS rate increases, the steroid response rate decreases. The best of this was shown in a study by Balanszak et al. [15] renal biopsy was done for 83, and most prevalent pathology was FSGS in 54 (65.1%), second most pathology was MCD 21(25.3%) and lastly MPGN in 8 (9.6%).while Renda et al. study [15] shows study mesangial proliferation and FSGS were found to be significantly high while MCD is lower pathology, on other study done by A. Kari in Saudi Arabia [16]; The renal histopathology was compatible with FSGS in 17 (55%) children, IgM nephropathy in 7 (23%) children, MCD in 2 (6%) children, MesPGN in 2 (6%) children, and C1q nephropathy in 3 (9%) children. Other study done by Roy RR [4], histopathology was MesGN (40.63%), MCD (18.75%) and FSGN 12.5% of his patients included in the study [4]. Other Histological findings included MCD, FSGS, diffuse MPGN, and global sclerosis in 19 (27.1%), 26 (37.1%), 21 (30.0%), and 4 (5.7%) of the patients, respectively in Otukesh study [17]. the best treatment of SRNS in children is not clear. treatment has been directed against immunological abnormalities in SRNS. Children with MCD or late resistant to steroid respond better to immunosuppressive therapy than children with FSGS or with initial resistant to steroid [17]. in our study, we found most common drugs used as first and second option after diagnosis of SRNS were Cyclosporine A, 100 patients used CSA and 34 (34%) achieved complete remission ,40(40%) partial remission and 26 (26%). no remission while in Renda et al. study [15]; Cs A was administered to 24 patients; 10 achieved complete remission (41.7 %), 4 had partial remission (16.6%), and 10 had no remission (41.7%). In other study done by Zagury et al. [18], Eighty patients were treated with Cs A and 52 (65%) of these were sensitive to the drug [18]. Otukesh et al. study [17] about Cyclosporine was used in the initial therapy of 17 children with newly diagnosed primary SRNS, Recovery more frequently occurred in the patients who received cyclosporine (41%) [17]. in general, MMF is very well tolerated with few serious adverse effects. In patients with idiopathic SRNS, it represents a suitable alternative to calcineurin inhibitors as a treatment for many patients, especially those with renal impairment [19]. in this study we found that Mycophenolate was used for 52 patients, mostly used as 2nd choice in 21 (41.4%) and 3rd choice 19 (36.5%) and 1st choice 12 (23%); we found good response was obtained in patients received Mycophenolate, 16 (30.7%) patients achieved complete remission and 18(34.6%) patients obtained partial remission while 18(34.6%) no remission. These results, complete remission near similar to result obtained by Renda et al. study [15] in which in 9 patients were treated with MMF, with a remission rate of 33.3%. while in Seyd Sajid Hussein et al. study [20], 21 cases received MMF with complete remission occurred in 18 (85.7%), partial remission in 2 (9.5%). In our study, we divided outcome of patients into 4 entities, (complete remission, death, CKD and patients lost follow up) and we found 21 (15.4%) patient achieved complete remission,6 cases were died (4.4 %) due to complications of NS,71 cases developed CKD (52.2%). patients developed CKD were (stage 3=13(9.6%), stage 4=24 (17.6%) and ESRD=34(25%). in A. Kari et al. study [16] 3 from 31 patients developed ESRD which represents 9.7% while in our study was more frequent 25 %. in Renda et al.study [15] , which include 31 cases; Among the 11 patients with CRF, 5 developed ESRD (16.1 %). in Otukesh study [17], 26% of the patients developed ESRD (near to our study), while complete

improvement of nephrotic syndrome was achieved in 45% of them. SRNS is responsible for an increased risk of ESRD, leading to a 34-64% of probability of developing ESRD in 10 years. Various factors have been reported to influence the outcome in SRINS. Age, hematuria, hypertension, decreased creatinine clearance at initial clinical presentation, histopathological pattern as well as early versus late steroid resistance have been described as risk factors for ESRD [18] . in our study, we study Relationship between patients with SRNS characteristics and development of ESRD between children characteristics and development of ESRD. there is no signifance of age about those patients whom developed ESRD, also most of the patients belong to less than 6 years represents 31.3 %. while zagury et al. study [18], showed that the age at NS onset was significantly higher in the ESRD +ve group than in ESRD -ve group. Otukesh et al. study [17], there was no significant between age and development of ESRD. also, there is no significant of gender to the development of ESRD, same result obtained by outkesh et al. [17] and zaguryet al. [18] studies. hematuria at presentation was found in 29 (38.7%) patients in ESRD +ve versus in the ESRD –ve 46 (61.3%) patients and p value was significant, while outkesh study [17] there is no significant. the presence of hematuria and hypertension at onset were risk factors for ESRD by univariate analysis, and this fact could be explained by the higher incidence of hematuria and hypertension in patients with FSGS than those with MCD [18]. in our study, Patients who presented with hypertension 31 (33%) patients tend to develop ESRD more frequently (p= 0.001). same results in Zagury et al. study [18]; Hypertension at presentation was found in 26.5% in ESRD+ group versus 7% in ESRD-, p = 0.007, also outkesh study [17] was significant relationship between hypertension and development ESRD. Renal impairment at presentation, were considered risk factors for chronic kidney disease and ESRD. in our study, Patients who presented with impaired renal function 15 (37.5%) tend to develop ESRD more frequently. also, there was significant in zaguryet al. [18] and outkeshet al. [17] studies. the achievement of a complete or partial remission is one of most important factors related to a better outcome on SRINS [18]. we found No one of the patient who responded to immunosuppressive drugs developed ESRD (p value=0.004)., in outkesh study [17] , he found none of the patients with either complete response or partial response or relapse with cyclophosphamide, cyclosporine or mycophenolate reached ESRD. also in Zagury study [18], he found resistant to cyclosporine therapy , in which responsiveness to cyclosporine, no case progress to ESRD [18] . FSGS is the most prevalent histological pattern in SRINS and the major cause of ESRD. instead, few reports in literature have shown that the initial histological lesion has no influence on the development of ESRD. In a European multicenter study10 involving children with SRINS, the initial histopathological pattern was not a significant predictor for ESRD. Niaudet et al. [21] also found that in patients with SRNS the progression to ESRD was similar in patients with MCD or FSGS on initial biopsy; however, patients with MCD who progressed to ESRD and had a subsequent renal biopsy always developed FSGS [18]. as we mentioned before, we depend on last renal biopsy result, in our study, 14 case with FSGS developed ESRD, so no significant between FSGN and development of ESRD. while in Zagury A et al study [18], ESRD occurred in 51/87 (58.6%) patients with FSGS, so significant relationship of patients who have SRNS with histopathology FSGN and development of SRNS. in outkesh study [17], Histopathology's were not associated with the progression of ESRD in the patients is similar to our study. many factors suggest our result about relationship of FSGS and development of ESRD; because there is a limitation associated with this study; some patients did not do renal biopsy, also many patients only one sample was done for them, as many families refuse to do renal biopsy or multiple sampling, other did not continue follow up after received some treatment.

Conclusion

Near half of the patients developed CKD and the ESRD was 25 % of them. the patients with atypical presentation (hematuria, hypertension, and renal impairment) in patients with SRNS are liable to develop ESRD significantly. the histopathology FSGS is the most relevant pathology in our patient with SRNS. resistance to immunosuppressive drugs can lead to progression to ESRD. we found that

cyclosporine A is more effective than other immunotherapy as the initial therapy for patients with SRNS. Mycophenolate Mofetil had good response in many cases.

Recommendation

genetic study of SRNS to be done when facilities are available to choose better treatment protocol and prognosis. it is better to avoid aggressive treatment to patients with SRNS especially those who are liable to develop ESRD according to their clinical features and response to treatment because of the patient will be sever immunocompromised without any benefit. further prospective study needs to select proper drug for the treatment of SRNS.

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