An audit study on the management of children with lupus nephritis admitted to Assiut University Children Hospital

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Background
Childhood-onset systemic lupus erythematosus (cSLE) is a severe multisystem autoimmune disease. Renal involvement occurs in the majority of cSLE patients and is often fatal. It occurs in 50–75% of all cSLE patients, mostly within the first 2 years after diagnosis. The aim of this study was to evaluate the management of children with lupus nephritis (LN) admitted to the Pediatric Nephrology and Rheumatology Units, Assiut University Children Hospital according to the guidelines of the American College of Rheumatology and the European League Against Rheumatism (2012), searching for defects, obstacles, or needs to improve the management of such cases.

Patients and methods
Medical records of children with LN admitted to the Nephrology and Rheumatology Units, Assiut University Children Hospital during the period from 1 July 2016 to 30 June 2017 were collected and reviewed to choose the cases which fulfilled the criteria of the study. A structured data collection form was designed to gather clinical, laboratory, and therapeutic data from the included records. This form was designed according to the published guidelines for LN by the American College of Rheumatology and the European League Against Rheumatism (2012).

Conclusion
Data of this study showed a severe defect in recording both the admission and the follow-up historical data of the studied cases. In addition, registered data about the clinical examination of such cases were also defective. Furthermore, the recorded data revealed neglection of important diagnostic investigations, for example, renal biopsy which was performed for only 50% of the studied cases and also evaluation of CH_{50} serum level which was not performed on any of the studied cases. The therapeutic regimens which were used for the treatment of the studied cases were random, and did not follow any well-known published guidelines for the treatment of such cases.

Keywords:
lupus nephritis, renal biopsy, systemic lupus erythematosus

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Introduction

Childhood-onset systemic lupus erythematosus (cSLE) is a severe multisystem autoimmune disease. Renal involvement occurs in the majority of cSLE patients and is often fatal [1]. It occurs in 50–75% of all cSLE patients, mostly within the first 2 years after diagnosis [2]. Initial manifestations of renal disease range from minimal proteinuria and microscopic hematuria to nephrotic-range proteinuria, urinary casts, severe hypertension, peripheral edema, and renal insufficiency or acute renal failure. It can also present with features of thrombotic microangiopathy including both atypical hemolytic uremic syndrome as well as thrombotic thrombocytopenic purpura [1]. Kidney biopsy and evaluation of renal histopathology remain the gold standard for establishing the diagnosis of systemic lupus erythematosus (SLE) nephritis and determining specific therapeutic regimens [3]. Treatment of childhood lupus nephritis (LN) using steroids is associated with poor outcome with excess side effects. The addition of cyclophosphamide to the treatment schedule has improved disease control. In view of treatment failure using these drugs, many newer agents such as immune modulators and monoclonal antibodies are being tried in patients with cSLE [1].

Aim

The aim of this study was to evaluate the management of children with LN admitted to the Pediatric Nephrology and Rheumatology Units, Assiut University Children Hospital according to the guidelines of the American College of Rheumatology and the European League Against Rheumatism (EULAR) (2012), searching for defects, obstacles, or needs to improve the management of such cases. We consider that this critical appraisal of our own performance is a crucial step before any

further correction or development of that performance could take place.

Patients and methods

Medical records of children with LN admitted to the Nephrology and Rheumatology Units, Assiut University Children Hospital during the period from 1 July 2016 to 30 June 2017 were collected and reviewed to choose the cases which fulfilled the criteria of the study.

We designed a structured data collection form to gather the clinical, laboratory and therapeutic data from the included records. This form was designed according to the published guidelines for LN by the American College of Rheumatology and the EULAR (2012).

Study participants

Inclusion criteria

All SLE patients admitted to the Pediatric Nephrology and Rheumatology Units with persistent proteinuria, that is, 0.5 g per day (a spot urine protein/creatinine ratio of 0.5 can be substituted) or greater than 3+ by dipstick; and/or cellular casts including red blood cells, granular, tubular, or mixed.

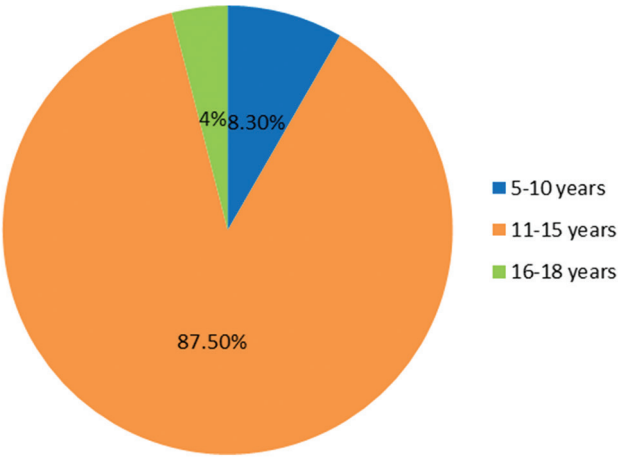
Exclusion criteria

(1) Patients with glomerulonephritis caused by other causes other than SLE
(2) SLE patients who did not fulfill the inclusion criteria.

Results

As demonstrated in Fig. 1: 87.5% of cases were between 11 and 15 years of age and 87% of cases were women, as demonstrated in Fig. 2. As demonstrated in Table 1 we noticed that Malar rash, oral ulcer, seizure, and psychosis were asked in all studied cases. Discoid rash was not asked in 79% among the studied cases. Photosensitivity was not asked in 25% of the studied cases. Malar rash, arthritis, serositis, seizure, and psychosis were examined in all studied cases. Discoid rash was not examined in 79% of the cases while oral ulcer was not examined in 25% of cases. In Table 2 we noticed that renal biopsy was done for only 50% of the studied cases. Complements (C_3.C_4) were done for 91.7% of the studied cases; 24 h urine for protein excretion was done for 87.5% of the studied cases. Serum cholesterol was done for 41.7% of the studied cases. CH_{50} was not performed for all the studied cases. From Table 3 we found that focal LN (type III) and diffuse LN (type IV) or either of them represent 33.3% of the cases. From Table 4 we noticed that death

Figure 1

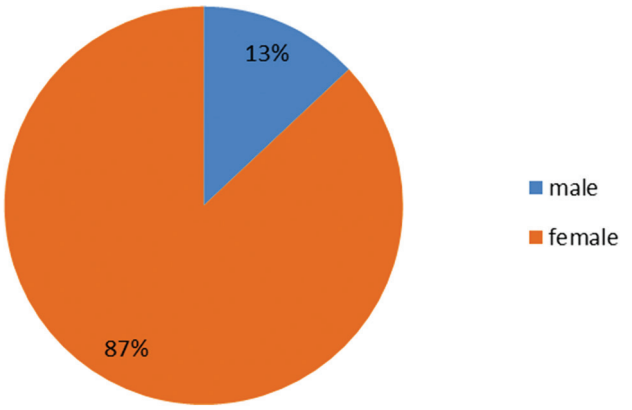


Age distribution among the studied cases, 87.5% of cases were between 11 and 15 years of age.

Table 1 Rates of registered clinical data of systemic lupus erythematosus activity among the studied cases

Data of the history	Frequency	Rate (%)
Malar rash		
Asked	24	100
Not asked	0	0
Discoid rash		
Asked	5	21
Not asked	19	79
Seizure and psychosis		
Asked	24	100
Not asked	0	0
Photosensitivity		
Asked	18	75
Not asked	6	25
Oral ulcer		
Asked	24	100
Not asked	0	0
Data of the examination		
Malar rash		
Examined	24	100
Not examined	0	0
Discoid rash		
Examined	5	21
Not examined	19	79
Oral ulcer		
Examined	18	75
Not examined	6	25
Seizure or psychosis		
Examined	24	100
Not examined	0	0
Arthritis		
Examined	24	100
Not examined	0	0
Serositis		
Examined	24	100
Not examined	0	0

Figure 2



Sex distribution among the studied cases, 87% of cases were women.

occurred in 20.8% of the cases. Remission and relapses occurred in 33.3% of the cases.

In all, 25% of the cases were missed; 12.5% of the cases were treated with inappropriate course, discharged on therapy, and did not enter in remission. One case was discharged on regular hemodialysis. In this study, 25% of the cases received induction therapy with steroid therapy and cyclophosphamide with incomplete course; 16.7% of the studied cases received induction with steroid therapy and MMF. On the other hand, 41.7% of the studied LN cases started induction therapy with steroid therapy alone; out of them 12.5% of cases were biopsied, who were of grades III, II and V. In this study, five (20.8%) cases received rituximab, three of them were of grade IV, one was of grade III, and the last one was of grade V.

Discussion

cSLE is a severe multisystem autoimmune disease. Renal involvement occurs in the majority of cSLE patients and is often fatal. It occurs in 50–75% of all cSLE patients, mostly within the first 2 years after the diagnosis [2]. Bakr [4] reported that a high rate of renal involvement (80.8%) among Egyptian children with SLE.

The present data showed that 87.5% of the studied cases were within the age group from 11 to 15 years; 87% of the cases were women while 13% were men. This is in agreement with Huang *et al.* [5] who reported that the median age of onset of SLE is between 11 and 12 years (rare below 5 years), and 80% of patients are women.

A number of observations can be made based on the data that have been collected, as regards history taking, clinical examination, investigation, and treatment among the studied cases:

Table 2 Rates of registered investigations of lupus nephritis among the studied cases

Investigations	Frequency (*n*=24)	Rate (100%)
Complete blood count		
Done	24	100
Not done	0	0
Antidouble stranded DNA		
Done	24	100
Not done	0	0
Serum urea and creatinine		
Done	24	100
Not done	0	0
ESR		
Done	24	100
Not done	0	0
CRP		
Done	24	100
Not done	0	0
Complement (C_3.C_4)		
Done	22	91.7
Not done	2	8.3
Serum cholesterol		
Done	10	41.7
Not done	14	58.3
CH_{50}		
Done	0	0
Not done	24	100
24 h urine for protein excretion		
Done	21	87.5
Not done	3	12.5
Urine analysis		
Done	24	100
Not done	0	0
Renal biopsy		
Done	12	50
Not done	12	50

ESR: erythrocyte sedimentation rate, CRP: c-reactive protein

Table 3 The histopathologic classification of the 12 biopsied cases studied

Class	Histopathology	Frequency	Rate (%)
Class I	Minimal mesangial	0	0
Class II	Mesangial proliferative	1	8.3
Class III	Focal lupus nephritis	4	33.3
Class IV	Diffuse lupus nephritis	4	33.3
Class V	Membranous lupus nephritis	3	25
Class VI	Advanced sclerosis lupus nephritis	0	0

As regards recording of historical data, this study showed a defective history taking about discoid rash which was not asked in 79% of the studied cases. Fabbri *et al.* [6] reported that discoid lupus is the most common form of chronic SLE and may be the initial presentation of SLE in up to 10% of cases. Photosensitivity was not asked in 25% of the studied cases. Oral ulcer was not examined in 25% of cases.

On the other hand, asking about fever and peripheral edema was registered in all studied files. Wallace [7] reported that many people with SLE get frequent fevers when their disease flares.

Table 4 Rates of the recorded outcomes and occurrence of remission among the studied cases

Outcome	Biopsied lupus nephritis (*n*=12)		Unbiopsied lupus nephritis (*n*=12)	
	Frequency	Rate (%)	Frequency	Rate (%)
Remission with relapses	4	33.3	5	41.7
Inappropriate course, no remission, and discharged on therapy	2	16.7	1	8.3
Dialysis (regular)	1	8.3	-	-
Missed cases + died	2	16.7	3	25
Missed cases	3	25	3	25

Fortunately, blood pressure measurement was registered in all the studied files. Faurschou *et al*. [8] reported that proteinuria and hypertension were the most prominent features of LN in their study. They added that renal injury is the most important predictor of mortality in patients with SLE. So careful evaluation of patients with SLE for hypertension and proteinuria carry specific prognostic value.

Morita *et al*. [9] found that assay of C4 and C3 levels alone may not alert the practitioner to the presence of complement deficiency. Indeed in the case of C1 deficiency, C4 and C3 levels may be high because of reduced consumption of classical pathway proteins. For this reason, a functional assay of the pathway, such as CH_{50}, should be considered in all patients with suspected SLE.

It should be mentioned here that any defect in history taking or incomplete clinical examination may lead to a delay in treatment decision according to the grade of LN.

The present data showed that renal biopsy was done only for 50% of cases. Renal biopsy is the gold standard for the diagnosis of LN and all guidelines recommend performing renal biopsy in suspected cases of LN. Kidney disease: Improving Global Outcomes recommends that LN should be suspected in SLE patients with proteinuria, renal dysfunction, active sediments, or hypertension and further all suspected LN cases should be confirmed by renal biopsy [10]. The EULAR and European Renal Association and European Dialysis and Transplant Association recommends to do renal biopsy if there is reproducible proteinuria of more than 0.5 g per day [11], whereas the American College of Rheumatology recommends to do renal biopsy in SLE cases if they have one of the following: 24 h proteinuria of more than 1 g, or abnormal renal function, or 24 h proteinuria of more than 0.5 g along with either active sediments or cellular casts [12]. The importance of renal biopsy is further stressed by the Systemic Lupus International Collaborative Clinics criteria, according to which renal biopsy finding characteristic of LN in the presence of either positive antinuclear antibody or antidouble stranded DNA antibody is sufficient to classify the patient as SLE [11].

In this study, the mesangial proliferative LN (type II) represents 8.3% of the cases, either focal LN (type III) or diffuse LN (type IV) represents 33.3%, while membranous LN (type V) represents 25% of the cases.

Lee *et al*. [13] in his study found that class IV LN was the most common type. So renal biopsy should be performed in all patients with SLE, as the evaluation of renal histopathology remains the gold standard for establishing the diagnosis of LN and determining specific therapeutic regimens [14].

Weidenbusch *et al*. [15] in a systematic analysis found that rituximab was able to induce complete or partial remission in 74% of the patients who were refractory to current first-line drugs in severe LN. One patient was managed by incorrect regimen (sandimmune) and he did go into remission.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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