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Severe paediatric systemic lupus erythematosus nephritis—a single-centre experience

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Abstract

**Background.** Paediatric patients with systemic lupus erythematosus (SLE) often have severe presentations including lupus nephritis (LN). Few paediatric studies have evaluated the anticardiolipin antibody (aCL) and renal histology. The purpose of this study was to evaluate clinicopathologic features, including aCL, short-term clinical and renal histologic outcomes of paediatric patients with new-onset SLE nephritis.

**Methods.** We conducted a single centre, retrospective inception cohort study. Charts were reviewed at presentation (initial renal biopsy), 6-month (follow-up biopsy) and 12-month follow-up.

**Results.** The population consisted of 21 patients (median age, 14.5 years): 19/21 were female, 6/21 African American, 3/21 Asian, 9/21 Caucasian and 3/21 Hispanic. At presentation, 19/21 had elevated aCL, 15/21 hypertensive, 12/21 nephrotic and 7/21 required haemodialysis (HD)—2/7 HD patients had thrombotic microangiopathy, 1/7 crescentic glomerulonephritis. Two patients had thromboembolism: both had aCL, were taking oral contraceptives and required HD, one was nephrotic and the other had elevated lupus anticoagulant. Initial biopsies revealed 6/21 ISN/RPS class II nephritis, 3/21 class III, 7/21 class IV and 5/21 class V. Treatment consisted of methylprednisolone, corticosteroids, cyclophosphamide or mycophenolate mofetil. Follow-up biopsies revealed 12/13 to have improved histology. Indication for a follow-up biopsy was severe illness at presentation. At 12-month follow-up, no patients were nephrotic (P < 0.001) or required HD (P < 0.001), and 3/14 had elevated aCL (P < 0.001).

**Conclusion.** Elevated aCL, hypertension, nephrotic syndrome and need for HD were common presentations among our paediatric SLE nephritis population. Renal histology and aCL were helpful in the therapeutic management.

**Keywords:** anticardiolipin antibody; dialysis; paediatrics; systemic lupus erythematosus

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Introduction

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with multiorgan involvement. Paediatric patients with SLE often have severe disease presentations including renal involvement, which ranges from asymptomatic urinary findings to acute renal failure [1–4]. Lupus nephritis (LN) remains one of the most important factors influencing therapeutic management and long-term prognosis [5–8]. An early renal biopsy and, perhaps, follow-up renal biopsy are therefore essential to aid in the management of this difficult to treat the paediatric population [9].

SLE is characterized by the appearance of autoantibodies well before the clinical onset of symptoms [10,11]. The presence of antiphospholipid (aCL) antibodies at disease presentation negatively impacts renal outcomes and is predictive of a more severe disease course [11–13]. Paediatric patients with SLE and antiphospholipid antibodies, primarily lupus anticoagulants (LAC) and elevated aCL antibody, are also at risk of developing thromboembolic events [14–18]. This is of particular concern in paediatrics since children with SLE exhibit a higher prevalence of aCL antibody than adults [3]. Screening of aCL antibody in paediatric patients may therefore serve to identify paediatric patients at risk for poor renal outcomes, severe disease course and thromboembolism.

Since the inception of our paediatric nephrology program, we have routinely performed renal biopsies on paediatric patients presenting with SLE and evidence of LN. A follow-up renal biopsy is commonly performed on patients after 6 months of treatment to assess for therapeutic management. We routinely obtain laboratory studies, including aCL antibody, initial and follow-up renal biopsies, which has been reported in few paediatric studies. The purpose of this study was to evaluate the clinicopathologic features, including aCL antibody, as well as short-term clinical and renal histologic outcomes of paediatric patients with new-onset SLE nephritis.

Study design

We conducted a single centre, retrospective inception cohort study of paediatric patients diagnosed with SLE and biopsy-proven LN at Helen DeVos Children’s Hospital from September 2003 to September 2008. This study was approved by the Spectrum Health Institutional Review Board. The population was predominantly female (20/21) and ethnically diverse—6/21 African American, 3/21 Asian, 9/21 Caucasian, and 3/21 Hispanic. Although the median serum

Definitions

Hypertension was defined as three or more diastolic or systolic blood pressures greater than or equal to the 95th percentile for age, gender, and height or the use of antihypertensive therapy [21]. Nephrotic Syndrome was defined as (1) 40 mg/m²/h of urinary protein or protein-to-creatinine ratio >3.0 on a random urine sample, (2) hypoalbuminaemia with serum albumin <2.5 g/dl, and (3) peripheral oedema. We did not include (4) hypercholesterolaemia in the definition of nephrotic syndrome due to lack of data.

Clinical data

Charts were reviewed at disease presentation—at the time of the initial renal biopsy and prior to treatment with cyclophosphamide (CYP) or mycophenolate mofetil (MMF), at the time of the repeat renal biopsy—during 6-month follow-up, and at 12-month follow-up. The following data were obtained: demographic data [age, gender, race/ethnicity], clinical data [nephrotic syndrome, hypertension, need for haemodialysis, thromboembolism, use of oral contraceptive pills (OCPs)], laboratory data [aCL antibody, double stranded DNA (dsDNA) antibody, lupus anticoagulant, C3, C4, serum creatinine, haemoglobin, platelet count, and white blood count], and renal histology evaluated according to the International Society of Nephropathy/Renal Pathology Society (ISN/RPS) classification [22].

Laboratory tests

C3 and C4 were measured by rate nephelometry in a Beckman Immage rate nephelometer (Beckman Coulter, Inc.; normal >80 mg/dl and >15 mg/dl, respectively). Anti-dsDNA antibodies were detected by ELISA (Varelisa, Pharmacia Diagnostics; normal <34 IU/ml). The presence of lupus anticoagulant was measured using a modified dilute Russell viper venom test (dRVVT) (Siemens, formerly Dade Behringer; normal value <45 s, normal ratio <1.2). Antiphospholipid antibodies were detected using the commercially available Varelisa Cardiolipin Antibody Screen test (Pharmacia Diagnostics, Freiburg, Germany). The assay is adjusted to internationally recognized standard sera established by Harris et al. and detects patient serum IgG, IgM and IgA antibodies to β2-Glycoprotein-1 (β2GP1) bound to immobilized cardiolipin [23]. Results are expressed as screening ratios: <1.0 (negative), 1.0–1.2 (low positive) and ≥1.2 (high positive). For the purposes of this study and others [24], a ratio ≥1.0 was considered ‘positive’.

Cardiolipin IgG and IgM titres were obtained using Varelisa Cardiolipin IgG and IgM tests, which express the results in anticardiolipin antibody concentrations calibrated to a standard curve (normal <10 GPL U/ml and <10 MPL U/ml, respectively). Estimated glomerular filtration rate (ml/min/1.73 m²) was calculated using the Schwartz formula [25]. A proportionality constant (k) of 0.55 was used to calculate eGFR in adolescent females, and a k of 0.70 was utilized in adolescent boys.

Treatment

In our institution, all patients with lupus nephritis initially receive three methylprednisolone pulses, hydroxychloroquine and oral prednisone (2 mg/kg/day). Class II patients receive MMF (300–600 mg/m²) [26,27]. Patients with class III, IV and V lupus nephritis receive 6-monthly pulses of CYP (first dose 500 mg/m² then 750 mg/m²) [28]. Patients typically undergo a follow-up renal biopsy after 6 months of treatment to assess for therapeutic management. At this time, patients either undergo continuation of CYP or transition to MMF.

Statistical analysis

Statistical analyses were conducted using SAS version 9.1 (SAS Institute Inc., Cary, North Carolina). To determine if there was significant difference among groups at disease presentation, we used the Fisher exact test for categorical variables or the Kruskal–Wallis test for ordinal or continuous variables. Statistical differences for the repeated measures (baseline, 6 months, and 12 months) of the clinical parameters were assessed with the Friedman test for continuous variables and Cochran’s Q test for dichotomous variables; each of these non-parametric tests was followed by multiple paired comparisons through the Conover test. Continuous data were expressed as median (range) and categorical data as number or percentage as appropriate to data. A P value of <0.05 was considered statistically significant.

Subjects and methods

For inclusion into the study, subjects were required to meet four or more of the American College of Rheumatology (ACR) classification criteria for SLE [19,20], and have histological evidence of LN by a renal biopsy at disease presentation.

Results

Clinicopathologic features at presentation

The population consisted of 21 paediatric patients diagnosed with new-onset SLE and biopsy-proven LN. The median age at presentation was 14.5 years (range, 1.6–20.2). The population was predominantly female (20/21) and ethnically diverse—6/21 African American, 3/21 Asian, 9/21 Caucasian, and 3/21 Hispanic. Although the median serum
creatinine was 0.8 mg/dl (range, 0.4–5.2) and the median eGFR was 98 ml/min/1.73 m² (range, 18–205) at disease presentation, 100% of patients had evidence of lupus nephritis by renal histology—6/21 ISN/RPS class II, 3/21 class III, 7/21 class IV and 5/21 class V. In addition, 12/21 had nephrotic syndrome, 15/21 were hypertensive and 7/21 required haemodialysis at disease presentation—of these, 5/7 had class IV lupus nephritis, 2/7 thrombotic microangiopathy and 1/7 crescentic glomerulonephritis. The median dsDNA antibody titre was 1000 IU/ml (range, 60–2000). Nineteen patients (90%) had elevated aCL antibody positivity rates. The median age of this population was 15.1 years (range, 4.4–16.7), 4/4 were Caucasian and 2/4 female. At presentation, 2/4 had aCL antibody screening ratios >1.2 (high positive) and 5/4 had screening ratios 1.0–1.2 (low positive). The remaining 2/21 patients had screening ratios <1.0 (negative).

We identified four patients diagnosed with new-onset SLE without nephritis from September 2003 to September 2008 to serve as an ad hoc comparison group for aCL antibody positivity rates. The median age of this population was 15.1 years (range, 4.4–16.7), 4/4 were Caucasian and 2/4 female. At presentation, 2/4 had aCL antibody screening ratios >1.2 (high positive) and 2/4 screening ratios <1.0 (negative), no patients had screening ratios 1.0–1.2 (low positive). Although the 50% aCL antibody positivity rate among SLE non-nephritis patients was lower than the 90% among SLE with nephritis patients, this comparison did not attain statistical significance (P = 0.11). Two patients were screened during follow-up: 2/2 had screening ratios <1.0 (negative).

The patients were stratified according to initial renal histologic classification to compare groups at disease presentation (Table 1). There was no difference in age among groups. Patients with class II lupus nephritis tended to have a mild presentation. Patients with class III, IV and V lupus nephritis tended to have low C4 (P = 0.01).

Table 1. Comparison of parameters among ISN/RPS renal histologic groups at disease presentation

| Class | ISN/RPS class II | ISN/RPS class III | ISN/RPS class IV | ISN/RPS class V |
|-------|-----------------|------------------|-----------------|----------------|
| Number (n) | 6 | 3 | 7 | 5 |
| Age (years) | 14.3 (13.4–18.5) | 11.5 (9.9–15.6) | 14.5 (5.7–20.2) | 16 (1.6–16.4) |
| Male:female | 0:6 | 1:2 | 0:7 | 0:5 |
| AA:As:C:H | 2:0:3:1 | 1:2:0:0 | 0:0:5:2 | 3:1:1:0 |
| Creatinine (g/dl)* | 0.6 (0.4–1.5) | 0.7 (0.6–0.9) | 2.7 (1.2–5.2) | 0.7 (0.4–2.8) |
| eGFR (ml/min/1.73 m²)† | 159 (61–205) | 125 (98–130) | 32 (18–83) | 102 (32–128) |
| Need for haemodialysis (n) | 1 | 0 | 5 | 1 |
| Nephrotic Syndrome (n) | 0 | 0 | 7 | 5 |
| Hypertension (n) | 3 | 1 | 6 | 5 |
| dsDNA antibody (IU/ml) | 765 (163–1998) | 1162 (483–2000) | 1000 (89–2000) | 179 (60–2000) |
| Positive aCL antibody screening ratio (n) | 5 | 3 | 6 | 5 |
| >1.2 (high positive) | 5 | 0 | 5 | 4 |
| 1.0–1.2 (low positive) | 0 | 3 | 1 | 1 |
| <1.0 (negative) | 1 | 0 | 1 | 0 |
| C3 (g/l) | 103 (38–200) | 57 (16–92) | 40 (28–86) | 37 (18–110) |
| C4 (g/l)† | 15 (4–24) | 3 (2–3) | 6 (3–10) | 4 (2–5) |
| Haemoglobin (g/l) | 10.9 (8.5–13.7) | 9.1 (6.7–10.3) | 10.2 (6.0–11.0) | 10.0 (8.8–12.2) |
| Platelet count (× 109/l) | 228 (95–543) | 280 (270–326) | 183 (103–281) | 137 (106–344) |
| White Blood Count (× 109/l) | 5.9 (2.7–16.4) | 5.4 (3.5–7.6) | 6.2 (2.5–12.6) | 5.4 (2.0–17.7) |

Continuous variable values expressed as median (range). AA, African American; As, Asian; C, Caucasian; H, Hispanic. *P = 0.01 for difference among different race-ethnic groups. †P < 0.001 for difference among different race-ethnic groups.
Table 2. Comparison of parameters at presentation (initial renal biopsy), 6-month follow-up (repeat renal biopsy), and 12-month follow-up for all patients

| Parameters                          | Initial Renal Biopsy | 6 Months Follow-up | 12 Months Follow-up | P value |
|-------------------------------------|----------------------|--------------------|---------------------|---------|
| Creatinine (mg/dl)                  | 0.9 (0.4–5.2)        | 0.8 (0.3–3.6)      | 0.7 (0.2–1.2)       | 0.035   |
| eGFR (ml/min/1.73 m²)               | 98 (18–205)          | 110 (19–164)       | 122 (72–217)        | 0.034   |
| 60–90 (n)                           | 3                    | 2                  | 3                   |         |
| 30–60                               | 1                    | 3                  | 0                   |         |
| <30                                 | 7                    | 1                  | 0                   |         |
| Need for haemodialysis (n)          | 7                    | 0                  | 0                   |         |
| Nephrotic syndrome (n)              | 12                   | 0                  | 0                   | <0.001  |
| Hypertension (n)                    | 15                   | 15                 | 14                  | 0.819   |
| Anti-dsDNA (IU/ml)                  | 814 (60–2000)        | 46 (15–431)        | 47 (12–302)         | <0.001  |
| Positive aCL antibody screening ratio (n) | 19                    | 1                  | 3                   | <0.001  |
| >1.2 (high positive)                | 14                   | 1                  | 0                   |         |
| 1.0–1.2 (low positive)              | 5                    | 0                  | 0                   |         |
| <1.0 (negative)                     | 2                    | 2                  | 11                  |         |
| C3 (g/l)                            | 62 (16–200)          | 96 (44–160)        | 108 (66–161)        | 0.012   |
| C4 (g/l)                            | 5 (2–24)             | 15 (5–32)          | 18 (6–30)           | <0.001  |
| Haemoglobin (g/l)                   | 10.2 (6–13.7)        | 11.5 (7.8–14.8)    | 12.9 (9.8–15.3)     | 0.038   |
| Platelet (× 10⁹/l)                  | 195 (95–543)         | 304 (140–479)      | 289 (177–396)       | 0.022   |
| WBC (× 10⁹/l)                       | 5.6 (2–17.7)         | 7.1 (1.4–22.6)     | 5.5 (2.8–24.1)      | 0.047   |

Continuous variable values expressed as median (range).
Repeated measures (presentation, 6 months, 12 months) of clinical parameters were assessed for significance (P value).
The repeated measures analysis was followed by multiple paired comparisons.
*P < 0.05 for comparison versus presentation; †P < 0.01 for comparison versus presentation; ‡P < 0.001 for comparison versus presentation; §P < 0.05 for comparison versus 6 months; ¶7/21 patients were not screened for aCL antibody at 12 months.

(Table 2). Serum creatinine decreased from 0.9 mg/dl (range, 0.4–5.2) at presentation to 0.8 mg/dl (range, 0.3–3.6) at 6 months and 0.7 mg/dl (range, 0.2–1.2; P < 0.05) at 12 months and eGFR increased from 98 ml/min/1.73 m² (range, 18–205) at presentation to 110 ml/min/1.73 m² (range, 19–164) at 6 months and 122 ml/min/1.73 m² (range, 72–217; P < 0.05) at 12 months. The patients also demonstrated significant improvement from 6 months to 12 months (P < 0.05). No patients were nephrotic or required haemodialysis at 6 months. Anti-dsDNA titres significantly decreased from 814 IU/ml (range, 60–2000) at presentation to 46 IU/ml (range, 15–431; P < 0.001) at 6 months and 47 IU/ml (range, 12–302; P < 0.001) at 12 months. The number of patients with aCL antibody screening ratios ≥1.0 (low and high positive) decreased from 19/21 at presentation to 1/21 at 6 months (P < 0.001) and 3/14 at 12 months (P < 0.001). Patients also demonstrated significant improvements in C3, platelet count and WBCs at 6 months, followed by significant improvements in C3 and haemoglobin at 12 months. Five patients had a total of 7 flares within 12 months of presentation. The flares consisted of a drop in complement and a rise in the dsDNA antibody without significant changes in urinary protein excretion, renal function or blood pressure. All flares were related to non-compliance, and reconstitution of prescribed therapy resulted in a normalization of complement and dsDNA abnormalities.

Because class IV lupus nephritis patients (n = 7) presented with a more severe disease presentation, we performed an ad hoc analysis comparing repeated laboratory measurements of class IV lupus nephritis patients. Class IV patients demonstrated significant improvements in serum creatinine and eGFR—serum creatinine decreased from 2.7 mg/dl (range, 1.2–5.2) at presentation to 1.1 mg/dl (range, 0.7–3.6; P < 0.05) at 6 months and 0.8 mg/dl (range, 0.4–1.2; P < 0.001) at 12 months, and eGFR increased from 32 ml/min/1.73 m² (range, 18–83) at presentation to 72 ml/min/1.73 m² (range, 19–143; P < 0.05) at 6 months and 125 ml/min/1.73 m² (range, 72–217; P < 0.001) at 12 months. Patients demonstrated significant improvements in eGFR and serum creatinine from 6 months to 12 months. Anti-dsDNA titres significantly decreased from 810 IU/ml (range, 89–2000) at presentation to 43 IU/ml (range, 15–145; P < 0.001) at 6 months and 39 IU/mL (range, 13–120; P < 0.001) at 12 months. The number of Class IV patients with aCL antibody screening ratios ≥1.0 (low and high positive) at presentation decreased from 6/7 at presentation to 1/7 at 6 months (P < 0.05) and 1/6 at 12 months (P < 0.05). Class IV patients also demonstrated significant improvements in C3, C4 and platelet count at 6 months, followed by significant improvement in haemoglobin at 12 months.

Renal histologic outcomes

Follow-up renal biopsies were performed on 13/21 patients at 6-month follow-up (Table 3). The indication for a follow-up biopsy included severity of clinical illness at presentation (nephrotic syndrome, haemodialysis), and this consisted of the majority of patients with initial renal histology significant for class III, IV and V lupus nephritis. All patients that underwent a second renal biopsy demonstrated an improvement in ISN/RPS classification, with the exception of a single patient with global class IV lupus nephritis and...
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Table 3. Renal histologic ISN/RPS lupus nephritis classification pre/post treatment

| Initial renal biopsy (presentation) | Treatment                          | Follow-up renal biopsy (6-month follow-up) |
|------------------------------------|------------------------------------|--------------------------------------------|
| II                                 | MP, hydroxychloroquine, prednisone, MMF | I                                          |
| III (A)                            | MP, hydroxychloroquine, prednisone, CYP (MMF) | II                                         |
| III (A)                            | MP, hydroxychloroquine, prednisone, CYP (MMF) | II                                         |
| IV-S (A/Cr)                        | MP, hydroxychloroquine, prednisone, CYP (MMF) | I                                          |
| IV-S (A)                           | HD, MP, hydroxychloroquine, prednisone, CYP (MMF) | III (C)                                    |
| IV-G (A/TMA)                       | HD, MP, hydroxychloroquine, prednisone, CYP (MMF) | III (C)                                    |
| IV-G (A/TMA)                       | HD, MP, hydroxychloroquine, prednisone, CYP (MMF) | III (C)                                    |
| IV-G (A)                           | HD, MP, hydroxychloroquine, prednisone, CYP (MMF) | V                                          |
| IV-G (A/Cr)                        | HD, MP, hydroxychloroquine, prednisone, CYP (MMF) | IV-G (C)                                   |
| V                                  | MP, hydroxychloroquine, prednisone, CYP (MMF) | III (C)                                    |
| V                                  | HD, MP, hydroxychloroquine, prednisone, CYP (MMF) | III (C)                                    |
| V                                  | MP, hydroxychloroquine, prednisone, CYP (MMF) | III (C)                                    |
| V                                  | MP, hydroxychloroquine, prednisone, CYP (MMF) | II                                          |

A, active lesions; C, chronic inactive lesions; S, segmental; G, global; Cr, crescentic glomerulonephritis; TMA, thrombotic microangiopathy; HD, haemodialysis; MP, methylprednisolone; CYP, cyclophosphamide; MMF, mycophenolate mofetil; (MMF) mycophenolate mofetil administered after 6 months of treatment with CYP.

crescentic glomerulonephritis (Table 3). No patients had crescentic glomerulonephritis or TMA after 6 months of treatment, and only chronic inactive lesions were observed.

Discussion

SLE is an autoimmune disease that commonly involves renal damage in paediatrics. We retrospectively studied a paediatric inception cohort with new onset SLE and biopsy-proven LN. Patients had a severe disease presentation including a high prevalence of aCL antibody, nephrotic syndrome, and need for haemodialysis. We found initial and follow-up renal histology as well as aCL antibody studies to be useful in the therapeutic management of this patient population.

Paediatric patients with SLE commonly have severe disease presentations, which is consistent with this study. One third of patients required dialysis at presentation, which is likely accounted for by acute on chronic renal failure, thrombotic microangiopathy, and/or crescentic glomerulonephritis. While previous studies report a frequency of hypertension and nephrotic syndrome at presentation ranging from 40–55% and 18–40%, respectively [8,29–31]; in this study 71% were hypertensive and 57% nephrotic. Two patients (10%) presented with a thromboembolism, which is consistent with the paediatric literature [14,15]. Both of these patients had elevated aCL antibodies, were taking oral contraceptives and required haemodialysis, one had elevated LAC and the other was nephrotic. Elevated aCL antibodies and lupus anticoagulant are predictive of thrombosis in paediatric patients with SLE [15–18]. Both of these patients were treated with LMWH until normalization of aCL antibody and lupus anticoagulant as well as other risk factors such as nephrotic syndrome and haemodialysis. Taken together, paediatric patients with new-onset lupus nephritis may have a more severe disease presentation than is represented in the literature.

Despite the severity of SLE at disease presentation, the therapy utilized herein yielded a successful treatment response. Excluding a single case, all patients that underwent a repeat renal biopsy demonstrated an improvement in their histology (Table 3). Nephrotic syndrome, and need for haemodialysis did not persist beyond 6 months of immunosuppression (Table 2). This implies that the aggressive and prompt use of corticosteroids and cytotoxic agents are not only effective in reducing SLE activity, but also in decreasing aCL and anti-dsDNA antibody titres (Table 2). Massengill et al. [14] similarly found immunosuppressive therapy to be effective in this regard, but this remains controversial [32].

We observed a high prevalence of aCL antibodies in our patient population, which identifies patients at an increased risk for poor renal outcomes and a severe disease course [11,12]. The prevalence of aCL antibodies in lupus nephritis ranges from 33–67% in children and 30–77% in adults [13,14,33]. In this study, 90% were positive for aCL antibodies at presentation—after initial treatment with methylprednisolone but prior to treatment with CYP and/or MMF. Loizou et al. [13] screened adult lupus nephritis patients for aCL antibodies during an active disease state and reported the highest rate of aCL antibody positivity (77%). Massengill et al. [14] reported a prevalence of 67% in a cross section of paediatric patients with lupus nephritis, but the prevalence was higher at 73% in patients presenting with new-onset lupus nephritis. Children with active SLE and lupus nephritis are therefore more likely to test positive for aCL antibodies—especially when antibody titres are obtained at disease presentation. The presence of aCL antibodies at disease presentation or early in the disease course correlates with poor renal prognosis, renal relapse, central nervous system disease, and thromboembolism [11,12,17,18,33–35]. Children with SLE have a higher prevalence of aCL antibody at presentation than adults [3], which identifies aCL antibody as a potential biomarker for identifying paediatric patients at an increased risk for poor outcomes.

An important aspect of this report is the use of a follow-up renal biopsy after 6 months of treatment to assess for therapeutic management. In reviewing the literature, this appears to be an accepted style of practice among paediatric nephrologists [9,29,36,37]. After patients completed 6-monthly courses of MMF or CYP, we used a follow-up renal biopsy to identify patients with disease progression or lesion activity. This was useful in the therapeutic management of these patients, as 87% of those that underwent a follow-up biopsy were transitioned from treatment with CYP to MMF.
The limitations of this study include a retrospective study design, which is common in paediatrics. Study parameters were obtained via electronic records, which we believe reduced bias in data collection and strengthened our study methodology. The aCL anticardiolipin screening ratios with Cardiolipin IgG and IgM titres for all patients may have been helpful for analysis. Anticardiolipin antibody assays are difficult to standardize and are limited by poor reproducibility. We used a commercial assay commonly used in clinical practice which detects aCL antibodies to β2-GP-1 immobilized on cardiolipin, which are more reproducible and better correlated with venous thrombosis and lupus nephritis [13,34,35]. The estimated GFR reported herein was calculated using the Schwartz formula, which may misrepresent the actual renal function in this population. The small sample size herein is similar to previous paediatric reports of SLE/LN [35,38–41], yet it reports on a very interesting population of biopsy-proven lupus nephritis patients with aCL antibody screening at disease presentation.

Conclusions

In summary, we report on an ethnically diverse paediatric population with severe SLE and biopsy-proven nephritis. We observed a 90% prevalence of aCL antibody at initial presentation with associated hypertension, nephrotic syndrome and need for haemodialysis. Despite the severity of SLE disease at presentation, resolution of these clinical parameters was attainable 6 months or 12 months after presentation. The anticardiolipin antibody, in addition to renal histology, represents another helpful biomarker of disease severity and treatment response in paediatric patients with severe SLE nephritis.

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Age and cystatin C in healthy adults: a collaborative study

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Abstract

\textbf{Background.} Kidney function declines with age, but a substantial portion of this decline has been attributed to the higher prevalence of risk factors for kidney disease at older ages. The effect of age on kidney function has not been well described in a healthy population across a wide age spectrum.

\textbf{Methods.} The authors pooled individual-level cross-sectional data from 18 253 persons aged 28–100 years in four studies: the Cardiovascular Health Study; the Health, Aging and Body Composition Study; the Multi-Ethnic Study of Atherosclerosis and the Prevention of Renal and Vascular End-Stage Disease cohort. Kidney function was measured by cystatin C. Clinical risk factors for kidney disease included diabetes, hypertension, obesity, smoking, coronary heart disease, cerebrovascular disease, peripheral arterial disease and heart failure.

\textbf{Results.} Across the age range, there was a strong, non-linear association of age with cystatin C concentration. This association was substantial, even among participants free of clinical risk factors for kidney disease; mean cystatin C levels were 46\% higher in participants 80 and older compared with those <40 years (1.06 versus 0.72 mg/L, \(P<0.001\)). Participants with one or more risk factors had higher...