Ethnic Differences in Pediatric Systemic Lupus Erythematosus

LINDA T. HIRAKI, SUSANNE M. BENSELER, PASCAL N. TYRRELL, ELIZABETH HARVEY, DIANE HEBERT, and EARL D. SILVERMAN

ABSTRACT. ***Objective.*** Prevalence and severity of systemic lupus erythematosus (SLE) in adults is suggested to be distinctly different between ethnic groups. The impact of ethnicity is not as well delineated in pediatric SLE (pSLE). We compared prevalence and extent of major organ involvement, disease activity, and damage in pSLE between different ethnic groups.

Methods. Ethnic demographic profiles of an inception cohort of 265 patients with pSLE followed at Sick Kids Hospital in Toronto were determined and compared to the Metropolitan Toronto at-risk population. Patients were categorized into ethnic subsets based on self-designated ethnic origins. Disease characteristics including major organ involvement, disease activity, and damage measures were longitudinally determined and compared among ethnic groups.

Results. Ethnicity data were available on 259/265 pSLE patients (99.6%); the majority were non-Caucasian (60%) compared to the Metropolitan Toronto at-risk population (40%) ($p < 0.0001$). Non-Caucasian patients were younger at diagnosis than Caucasian patients, Black patients being the youngest at diagnosis (12.6 vs 14.6 yrs; $p = 0.007$). Renal disease was significantly more common in non-Caucasian than in Caucasian pSLE patients (62% vs 45%; $p = 0.01$). There was a trend toward increased prevalence of central nervous system disease in Black patients compared to Asian patients ($p = 0.108$). There was no difference in gender ratio, SLE Disease Activity Index, or damage scores between ethnic groups.

Conclusion. Non-Caucasian ethnicity is associated with increased pSLE disease prevalence. Non-Caucasian pSLE patients were significantly younger and more likely to have nephritis. However, disease activity and damage were strongly associated with major organ disease independent of the patient's ethnicity. (J Rheumatol First Release Oct 15 2009; doi:10.3899/jrheum.081141)

Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS PEDIATRICS ETHNICITY
DISEASE ACTIVITY ORGAN DAMAGE OUTCOME

Ethnicity has been reported to be a predisposing factor as well as a prognostic factor of disease outcome in adults with systemic lupus erythematosus (SLE)[1]. The reported prevalence of SLE in Asian countries has ranged from 58.8 to 70.4 per 100,000 persons in China[2,3] and Hong Kong[4], 19.1 per 100,000 in Japan[1,5], and 40 per 100,000 in Singapore[6]. Studies in North America have shown prevalence rates of SLE in the Black and Hispanic populations 3 to 4 times higher than that of the Caucasian population[7,8]. Studies in England have shown that women of East Indian descent are 3 times more likely to develop SLE than Caucasian women[9]. Incidence rates of pediatric SLE (pSLE) have been reported to be 0.28–0.48/100,000 children, with prevalence rates of 6.3–24.0 per 100,000 depending on the ethnic background of the study population.

Non-Caucasian ethnicity has been identified as a risk factor for poor outcome in SLE[1,10]. To date there have been few comparisons of disease presentation and severity among pediatric SLE patients based on racial/ethnic background[11-15].

The purpose of our study was to determine if the frequency of pSLE differed among ethnic groups in a racially diverse population (Lupus Clinic at Sick Childrens Hospital, Toronto, Canada) and to compare disease presentation, major organ involvement, disease activity, and organ damage among ethnic groups.

MATERIALS AND METHODS

Patients. The study population consisted of an inception cohort of all 265 patients with pSLE diagnosed at Sick Childrens Hospital from June 1985 to July 2005. All patients met at least 4 of 11 American College of Rheumatology (ACR) classification criteria for SLE[16]. All patients were followed in the pediatric lupus clinic and since 1988, all data were prospectively collected and entered into a dedicated SLE database. Data obtained prior to 1988 were retrospectively obtained from chart review. Prior to the initiation of the study, Research Ethics approval was obtained (No. 1000004037).

From the Divisions of Rheumatology and Nephrology, Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada.

L.T. Hiraki, MD; S.M. Benseler, MD; P.N. Tyrrell, MSc, Division of Rheumatology; E. Harvey, MD; D. Hebert, MD, Division of Nephrology; E.D. Silverman, MD, Division of Rheumatology.

Address correspondence to Dr. E.D. Silverman, Hospital for Sick Children, 555 University Avenue, Elm Wing, Room 8253, Toronto, Ontario M5G 1X8.

Accepted for publication June 15, 2009.

Ethnicity. Self-designated ethnicity data were available on 259/265 patients. According to the guidelines of Statistics Canada, patients were categorized into subsets of Caucasian, Black, Asian, South Asian, Aboriginal, Latin American, and Arab ethnicity. The 18 patients of mixed ethnicity were excluded from further analysis, leaving a study cohort of 241 patients. For most analyses patients were divided into Caucasian and non-Caucasian ethnicity.

The Metropolitan Toronto at-risk population was calculated based on the 2001 Statistics Canada Census (the most up to date statistics available at the time of writing), which reports the visible minority population divided by age. The "at-risk" population in Metropolitan Toronto was defined as all children aged 7 to 18 years within each defined ethnic group.

Data collection. Baseline data included demographic information such as gender and age at diagnosis, standardized assessment including clinical manifestations of pSLE, and laboratory features of pSLE over disease course. All patients with renal disease had an abnormal renal biopsy according to the World Health Organization classification[17]. Only 3 patients with clinically apparent renal disease did not have a renal biopsy due to patient refusal or contraindication (anticoagulation). These patients were not included in the analysis as having renal disease. Central nervous system (CNS) disease was defined using the 1999 ACR nomenclature and case definition for neuropsychiatric SLE[18]. Major organ involvement was defined as evidence of nephritis and/or CNS disease.

Disease activity was determined utilizing the previously validated Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) or the modified version SLEDAI-2K[19,20], and was completed at each visit, every 1 to 4 months. For those patients assessed prior to 1985 the SLEDAI was completed retrospectively. SLEDAI area under the curve (AUC) or average interval mean SLEDAI (AIMS) was derived from the sum of all SLEDAI scores over disease course, divided by the total number of days followed.

Organ damage was evaluated using the definitions of the Systemic Lupus International Collaborative Clinics–Damage Index (SLICC-DI), which has been validated for use in pSLE[21-23]. Organ damage is defined as SLICC score $\geq$ 1. Patient mortality was recorded.

Standardized laboratory investigations analyzed were complete blood count, white blood cell (WBC) differential, and autoantibodies that consisted of antinuclear antibody (ANA), and anti-dsDNA, anti-Ro, anti-La, anti-Sm, anti-RNP, and the antiphospholipid antibodies anticardiolipin and lupus anticoagulant. All autoantibody tests were performed in a single laboratory.

All medications were recorded at each visit.

Statistical analysis. Demographic data and clinical and laboratory features were analyzed using descriptive statistics. The ethnic demographic profile of the lupus cohort was compared to that of the Metropolitan Toronto population. The number of patients with respective laboratory and clinical manifestations of disease was compared between ethnic groups. Comparisons of means, medians, and frequencies between clinical and laboratory features were made using unpaired t test, Wilcoxon rank-sum test, and chi-square or Fisher's exact test, where appropriate. Kaplan-Meier damage-free survival curves were created to compare rates of accrual of damage by ethnic group and by major organ involvement (log-rank test). Statistical analyses were performed using SAS 9.1 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Patients and ethnicities. The study cohort consisted of 259 pSLE patients, 87 (34%) Caucasian, 61 (24%) Asian, 44 (17%) Black, 39 (15%) South Asian, 5 (2%) Latin American, 4 (1.5%) Aboriginal, 1 (0.4%) Arab, and 18 (7%) of mixed ethnicity (Figure 1). There was a greater proportion of non-Caucasians in our pSLE cohort as compared to the Metropolitan Toronto at-risk population (60% vs 40%, respectively; $p < 0.0001$).

The median age at diagnosis was 13.7 years (mean 13 ± 3.1, range 3–18 yrs) and the female to male ratio was 4.8 to 1. There was no difference in gender ratio among ethnic groups; however, the non-Caucasian group was diagnosed at a younger age than the Caucasian group (median 13.3 vs 14.6 yrs; $p = 0.007$), with Black patients composing the youngest group at diagnosis of 12.6 years versus 14.6 years in Caucasians ($p = 0.007$; Table 1).

Followup information was available for 247 patients. The mean duration of followup was 4.1 ± 2.5 yrs (range 0–15 yrs, median 3.8), with no difference in the mean followup time of Caucasian patients (mean 4.2 ± 2.7 yrs, median 3.7) and non-Caucasians (mean 3.9 ± 2.4 yrs, median 3.8) ($p = 0.39$).

Clinical manifestations. Malar rash and photosensitivity were more common disease manifestations over the course of disease among Caucasian compared to non-Caucasian patients ($p < 0.01$). However, other rashes, including discoid rash, and fever were more commonly found in non-Caucasian patients ($p < 0.01$). No other clinical manifestations were significantly different among the ethnic groups (Table 1).

Major organ involvement. Renal disease was more prevalent in the non-Caucasian population than the Caucasian population (63% vs 44%; $p = 0.01$), with Black and Asian patients having a higher prevalence of renal disease compared to Caucasian patients (68% and 66% vs 44%, respectively; $p = 0.04$ and $p = 0.01$, respectively; Table 2). The proportion of patients with proliferative renal disease (Classes III and IV nephritis) and membranous nephritis (WHO Class V) was not statistically significantly different across ethnic groups. There was a trend for a greater number of Black patients with CNS disease, particularly when compared to Asian patients ($p = 0.108$), although there was no significant difference between Caucasians compared to non-Caucasians regarding CNS disease (Table 2).

Laboratory manifestations. Anti-Sm and anti-Ro antibodies were found more commonly in non-Caucasian patients compared with Caucasian patients (56% vs 34%, $p = 0.001$, and 51% vs 28%, $p = 0.001$, respectively; Table 3). There was a trend toward significance for anti-RNP antibodies to be more commonly found in non-Caucasian patients (42% vs 30%; $p = 0.07$). There was no significant difference in the frequency of anti-dsDNA antibodies and antiphospholipid antibodies between ethnic groups. There were no significant differences in hematologic manifestations among the ethnic groups (Table 3).

Disease activity and organ damage. Disease activity was measured by SLEDAI scores, calculated prospectively in patients diagnosed in 1988 and later, and retrospectively in those diagnosed before 1988 (5%). Disease activity over time, as measured by mean AIMS, was found to be similar for Caucasians and non-Caucasians (2.9, SD 1.6, and 3.4, SD 2.8, respectively; $p = 0.11$). Mean SLEDAI scores of

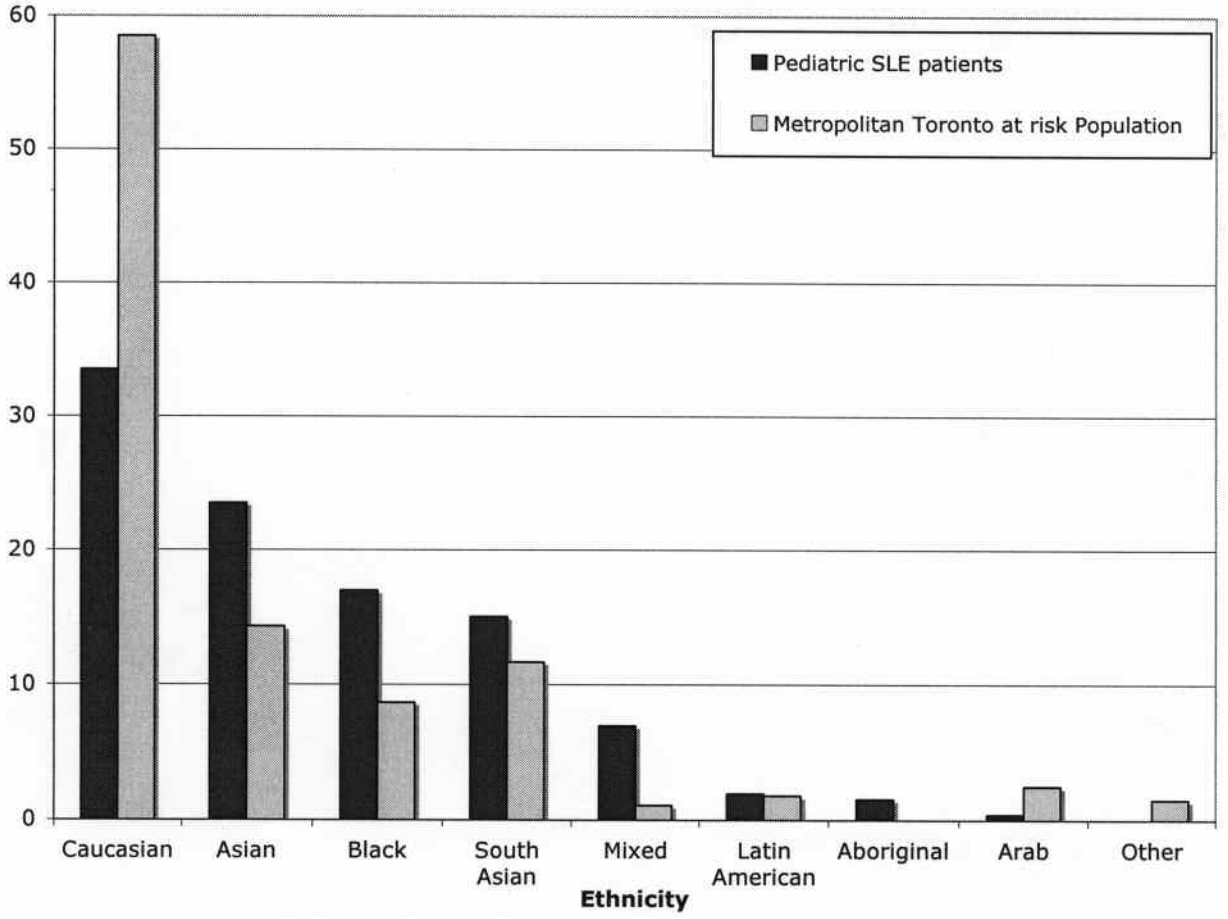

Figure 1. Ethnicity of patients and age-matched population of Metropolitan Toronto taken from 2001 Census statistics. On the x-axis are the ethnic categories and on the y-axis, the percentage of the total pSLE population and Metropolitan Toronto at-risk population.

disease activity at diagnosis were also similar between Caucasian and non-Caucasian patients (13.48, SD 9.15, and 12.6, SD 7.92, respectively; p = 0.45; median values, Table 1). There were 6 patient deaths during the time of this study: 5 non-Caucasian deaths (3 Black and 2 Asian), no Caucasian patient deaths (4% vs 0%; p = 0.1), and one death in a patient of mixed ethnicity. All the patients who died had major organ involvement: 3 with renal disease, one with CNS disease, and 2 with both renal and CNS disease. Five patients died during acute presentation; their cause of death was sepsis in 4 patients and acute cerebral hemorrhage in one patient. One patient died of complications of SLE more than 7 years after diagnosis.

SLICC scores of organ damage were available for 259 patients, with detailed information on organ damage available in 247 patients. There was no difference in the proportion of Caucasian and non-Caucasian patients with organ damage at last followup (33% vs 41%, respectively; p = 0.27; Table 4). Kaplan-Meier damage-free survival curves showed no significant difference in the rate of accrual of damage in Caucasian and non-Caucasian patients (Figure 2A; p = 0.17). However, comparisons of rates of damage accrual based on the presence of renal and/or CNS disease (Figure 2B) showed a significant difference between groups. Patients without renal or CNS disease had a slower rate of accrual of damage compared to those with renal/CNS disease or with renal and CNS disease (p < 0.0001).

DISCUSSION

To date there have been few reports on the effect of ethnicity on disease manifestations, severity, and outcome in pSLE[24]. In this study we report on disease manifestations, disease activity, and outcome in 259 patients with pSLE diagnosed and followed at a single center. Sick Childrens Hospital is the ideal center to complete this research as it is a major tertiary-care center serving a large catchment area in Southwestern Ontario and is located in a metropolitan area with multiple ethnic groups. Referrals to the lupus clinic are received from family physicians, pediatricians, and pediatric and adult rheumatologists. As such our lupus population may reflect the more severe spectrum of disease, but otherwise we do not anticipate other socioeconomic or ethnic bias in referral patterns.

Table 1. Clinical manifestations in Caucasian and non-Caucasian patients with pSLE.

	Caucasian, n = 87 (%)	Non-Caucasian, n = 154 (%)	Asian, n = 61 (%)	Black, n = 44 (%)	South Asian, n = 39 (%)
Median age at diagnosis, yrs (range)	14.6 (3–18)	13.3 (3–18)	13.6 (6–18)	12.6 (3–17)	13.2 (4–18)
Female:male	4.8:1	4.7:1	4.6:1	5.3:1	5.5:1
Median SLEDAI at diagnosis (range)	10 (2–40)	11 (0–39)	12 (0–39)	9 (3–30)	12 (0–31)
Arthritis	65 (75)	102 (66)	33 (54)	32 (73)	28 (72)
Renal disease	38 (44)*	94 (61)*	40 (66)	28 (64)	21 (54)
Proliferative	29 (76)	65 (69)	25 (63)	19 (68)	16 (76)
Membranous	7 (18)	13 (14)	6 (15)	4 (14)	3 (14)
CNS disease	21 (24)	39 (25)	11 (18)	14 (32)	10 (26)
Mucocutaneous					
Malar rash	75 (86)*	102 (66)*	48 (79)	21 (48)	26 (67)
Other rash	27 (31)*	76 (49)*	29 (48)	20 (45)	24 (62)
Oral ulcers	26 (30)	47 (31)	18 (30)	12 (27)	13 (33)
Alopecia	28 (32)	51 (33)	24 (39)	9 (20)	13 (33)
Photosensitivity	35 (40)*	27 (18)*	16 (26)	5 (11)	5 (13)
Nasal ulcers	11 (13)	18 (12)	9 (15)	4 (9)	4 (10)
Digital ulcers	2 (2)	9 (6)	5 (8)	3 (7)	1 (3)
Serositis					
Pericarditis	17 (20)	27 (18)	8 (13)	10 (23)	6 (15)
Pleuritis	15 (17)	27 (18)	7 (11)	11 (25)	6 (15)
Raynaud's phenomenon	25 (29)	25 (16)	13 (21)	6 (14)	4 (10)
Diffuse lymphadenopathy	14 (16)	35 (23)	12 (20)	13 (30)	4 (10)
Constitutional symptoms					
Fatigue	50 (57)	90 (58)	31 (51)	23 (52)	27 (69)
Fever	31 (36)*	78 (51)*	36 (59)	18 (41)	17 (44)
Weight loss	30 (34)	54 (35)	19 (31)	13 (30)	17 (44)
Anorexia	21 (24)	40 (26)	16 (26)	7 (16)	13 (33)
Headache	19 (22)	29 (19)	11 (18)	11 (25)	5 (13)

* $p < 0.01$.

Table 2. Prevalence of major organ involvement by ethnicity.

	No. of Patients with Nephritis	Percentage with Nephritis	Percentage with Proliferative Nephritis on Biopsy	Percentage with CNS Disease
Total (N = 241)	132*	55	66	26
Caucasian (N = 87)	38	44**	76	24
Non-Caucasian (N = 154)	94[a]	61**	69	25
Asian (61)	40	66	63	18***
Black (44)	28[b]	64	68	32***
South Asian (39)	21[c]	54	76	26

* Biopsy-proven nephritis in 132 patients and clinical renal disease in 135 patients. Biopsy declined/contraindicated in 3 patients: [a] all non-Caucasian; [b] 2 Black patients; and [c] 1 South Asian patient. ** Significant difference in percentage with renal disease ($p < 0.01$). *** Trend toward significance ($p = 0.108$).

Our patient population is uniquely different from reported North American cohorts primarily comprising Caucasian, African American, and Hispanic patients: our non-Caucasian population largely comprised Asian, Black, and South Asian patients.

We found an increased frequency of pSLE patients in non-Caucasians compared to what was predicted based on the Metropolitan Toronto population. This is consistent with incidence and prevalence reports in adult SLE, suggesting a higher frequency in North American Blacks, Hispanics, North American Natives, South Asians, and Asians[1,10,11,13,25,26].

We also found that non-Caucasian patients were diagnosed at a younger age than Caucasian patients, with Black patients comprising the youngest group at diagnosis. This finding is consistent with previous reports in adult SLE showing African American patients in the United States were diagnosed at a younger age than Caucasian patients[7,8]. A recent study from the LUMINA cohort reported a larger

Table 3. Laboratory manifestations comparing Caucasian and non-Caucasian patients with pSLE.

	Caucasian, n = 87 (%)	Non-Caucasian, n = 154 (%)	Asian, n = 61 (%)	Black, n = 44 (%)	South Asian, n = 39 (%)
Autoantibodies					
Anti-dsDNA	75 (86)	129 (84)	54 (89)	34 (77)	33 (85)
Anti-Sm	30 (34)*	87 (56)*	29 (48)	29 (66)	22 (56)
Anti-RNP	26 (30)	65 (42)	26 (43)	23 (52)	10 (26)
Anti-Ro	24 (28)*	70 (45)*	35 (57)	18 (41)	13 (33)
Anti-La	11 (13)	27 (18)	15 (25)	7 (16)	5 (13)
Anti-cardiolipin	31 (36)	72 (47)	27 (44)	23 (52)	17 (44)
Lupus anticoagulant	15 (17)	24 (16)	13 (21)	5 (11)	6 (15)
Rheumatoid factor	15 (17)	20 (13)	9 (15)	4 (9)	6 (15)
Hematologic					
Thrombocytopenia	25 (29)	60 (39)	29 (48)	14 (32)	16 (41)
Lymphopenia	44 (51)	80 (52)	39 (64)	16 (36)	20 (51)
Coombs positive hemolytic anemia	23 (26)	46 (30)	13 (21)	15 (34)	15 (38)

* $p < 0.01$.

Table 4. Proportion of patients with organ damage documented by SLE International Collaborating Clinics Damage Index (SLICC) score.

SLICC Damage	Total†, n = 247 (%)	Caucasian, n = 80 (%)	Non-Caucasian, n = 150 (%)	Asian, n = 61 (%)	Black, n = 44 (%)	South Asian, n = 37 (%)
Damage, n = 259	102 (39)	29 (33)	63 (41)	23 (38)	17 (39)	20 (51)
Ocular	39 (38)	10 (34)	24 (38)	11 (48)	2 (12)	9 (45)
Cataracts	39	10	24	11	2	9
Retinal change	0	0	0	0	0	0
Optic atrophy	0	0	0	0	0	0
MSK	23 (23)	14 (48)	15 (24)	6 (26)	3 (18)	12 (60)
Avascular necrosis	23	14	15	6	3	12
Endocrine	8 (7)	3 (10)	4 (6)	0 (0)	4 (24)	0 (0)
Diabetes	6	2	3	0	3	0
Premature gonadal failure	2	1	1	0	1	0
Cardiopulmonary	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cardiac infarction	0	0	0	0	0	0
Skin	3 (3)	1 (3)	2 (3)	1 (4)	1 (6)	0 (0)
Tissue infarction	3	1	2	1	1	0
Significant soft tissue loss	0	0	0	0	0	0
Renal	6 (6)	0 (0)	6 (10)	2 (9)	2 (12)	0 (0)
Glomerular filtration rate < 50%	4	0	4	1	2	0
Proteinuria, > 3.5 g/24 h	2	0	1	0	1	0
Endstage renal disease	1	0	1	1	0	0
Neurologic	12 (12)	2 (7)	11 (17)	2 (9)	3 (18)	2 (10)
Cognitive impairment	5	0	5	1	2	2
Seizures	7	2	5	1	2	1
Cerebral vascular accident	9	1	8	1	3	1
Cranial neuropathy	0	0	0	0	0	0
Transverse myelitis	1	0	1	1	0	0
Malignancy	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

† Organ-specific damage data available on 247 of the 259 patients. Patients with mixed ethnicity (n = 17) are not included in the ethnic subgroups but are included in the total.

proportion of African Americans within the pediatric SLE group compared with the adult SLE group[27].

We found the same gender ratio across ethnic groups, consistent with reports in adults[10,28]. The effect of ethnicity on gender ratio has not been previously reported in pSLE; however, our observed gender ratio is consistent with other pSLE reports[13,25,26,29] and less than that reported for adults with SLE[30].

Renal disease was significantly more prevalent among non-Caucasian patients, with the highest prevalence in Black and Asian patients. However, in contrast to previous reports in adults with SLE, the percentage of patients with

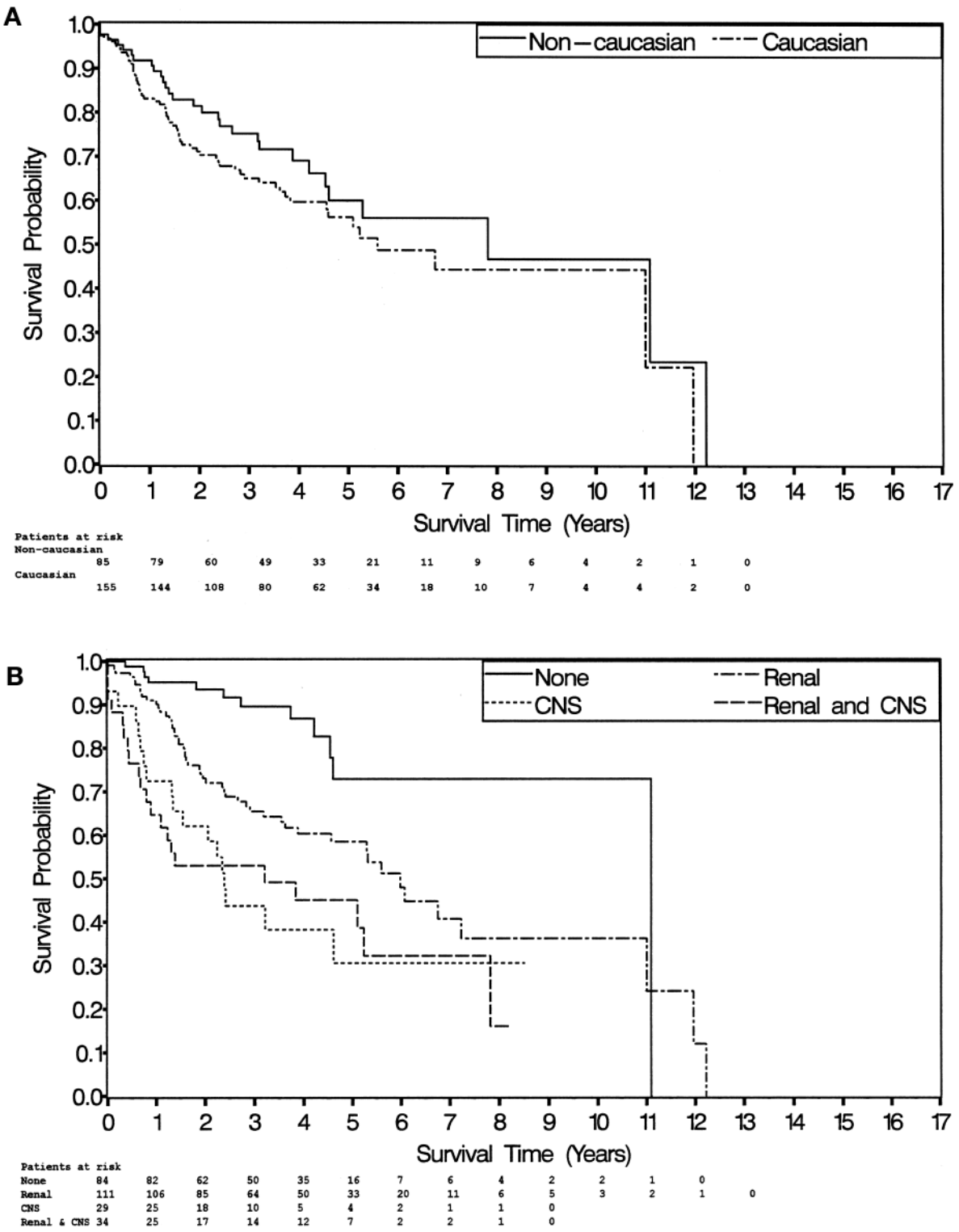

Figure 2. A. Kaplan-Meier damage-free survival comparing Caucasian and non-Caucasian patients. Time in years is shown on the x-axis and the probability of damage-free survival on the y-axis. No significant difference was found between the 2 groups ($p = 0.17$). B. Kaplan-Meier overall damage-free survival comparing patients without renal or central nervous system (CNS) disease to patients with renal disease only, CNS disease only, and patients with both renal and CNS disease. Time in years is shown on the x-axis and the probability of damage-free survival is shown on the y-axis. At least 1 group was found to be significantly different from the other 3 groups plotted on the graph ($p < 0.0001$).

each class of lupus nephritis did not differ between ethnic groups; similarly, we found a lower rate of endstage renal disease and renal SLICC damage than reported in adult cohorts with either Caucasian or non-Caucasian populations[13,24,26]. These low SLICC scores were present across ethnic groups.

In addition to renal disease, we found a trend for differences in the prevalence of CNS disease, as Black patients tended to have more CNS disease compared to Asian patients, although there was no difference between Caucasian and non-Caucasian patients. Previous studies in adults have also suggested that neuropsychiatric symptoms are more common among African American SLE patients compared to Caucasian patients[8]. No previous study has compared Black patients to Asian patients regarding the frequency of CNS disease.

Non-Caucasian ethnic background, particularly African American and Hispanic, has previously been associated with poor prognosis in both adult and pediatric SLE patients, although the majority of these studies were in adult patients[10,13,24,28,30]. Of note, the pediatric study, which was from an American inner city center, showed an ethnic difference in outcome, while the previous Canadian study of adults with SLE did not[13,24]. The LUMINA study of adults with SLE found predictors of early mortality included poverty, less than full-time employment, difficulty accessing healthcare, shorter disease duration, and cardiovascular and renal involvement[30]. The socioeconomic factors that were found in the LUMINA study may explain the differences between our findings and the inconsistent findings of the previous pediatric cohorts, or alternatively, the differences between pediatric studies and adult studies may reflect true differences between pediatric and adult patients with SLE. African American lupus patients made up 52% of their reported mortality. However, when they examined rates of damage accrual they found Hispanics accrued damage more rapidly than African American or Caucasian patients[31]. In contrast, a previous, smaller study of a pSLE cohort comprising Asian and South Asian patients found no association between ethnic origin and worse longterm outcome[13]. Again, these findings, taken together with our findings, may reflect differences in outcome between pediatric patients and adult patients, or may reflect the other important factors delineated by the LUMINA study[30]. We suggest that large prospective pediatric studies examining the role of socioeconomic status and the role of universal healthcare in overcoming potential discrepancies in access to healthcare are required to address these important issues.

In our study there were 6 patient deaths, all non-Caucasian patients, 3 of whom were Black. Although we found a trend toward higher mortality in our non-Caucasian patients with pSLE, there was no significant difference in rates of accrual of damage or in the proportion of patients with organ damage among ethnic groups, and our cohort's low mortality rate precludes any conclusions regarding any associations between ethnicity and mortality. We observed that there was a more rapid rate of accrual of damage in the presence of renal and/or CNS disease as compared to those patients without renal or CNS disease; however, we did not find any racial/ethnic difference in the accrual of damage as was reported[24].

Anti-Sm and anti-Ro antibodies were found more commonly in non-Caucasian patients compared to Caucasian patients. However, there was no difference in the frequency of other autoantibodies or laboratory variables between ethnic groups. Previous studies in adult SLE have shown a higher frequency of anti-Sm and anti-RNP antibodies in African American patients and also showed that anti-Ro antibodies clustered in patients of Asian origin[32]. Our findings in pediatric SLE are consistent with these findings in adult SLE. Previous studies have demonstrated leukopenia as a more common manifestation among African American patients[32,33]; however, this difference was not always statistically significant[8]. We did not observe a statistically significant difference in the frequency of lymphopenia between ethnic groups, possibly due to the higher relative frequency in our comparator groups of Asian and South Asian patients.

One limitation of our study is that the ethnic groupings were based on patient self-designation, and in a number of patients there were multiple designations. We did not undertake patient genetic testing. A second important limitation, which arose as a result of the study design, was that we did not collect data on socioeconomic status or on patient adherence, variables previously reported to be important predictors of disease outcome. However, as a result of universal access to healthcare in the Canadian system, we eliminated at least one barrier to care that has been previously associated with socioeconomic status. In addition, government subsidies are provided to low-income families to cover medications and long distance travel. However, we recognize the critical impact of social-economic status on health, and the potential interactions of these factors with ethnicity were not addressed. Future studies are essential to further clarify the nature of these interactions and determine how much of the effect is due to the genetic-immunologic factors, distinct from environmental, socioeconomic, and adherence factors. Our study observed differences among ethnic groups that may provide clues to environmental and genetic factors interacting and influencing disease development and outcome.

We found that childhood onset SLE was more commonly observed in non-Caucasian children compared with Caucasian children. Non-Caucasian children tended to be diagnosed at a younger age and have higher frequencies of renal disease and anti-Sm and anti-Ro antibodies versus Caucasian patients. There was no observed difference in disease activity and organ damage across ethnic groups.

Our study of the largest pSLE cohort in a single center

enabled comparison of disease presentation and disease course across multiple ethnic groups and eliminated the potential confounding effect of treatment variation. It would be important to validate our findings in other ethnically diverse populations.

REFERENCES

1. Lau CS, Yin G, Mok MY. Ethnic and geographical differences in systemic lupus erythematosus: an overview. Lupus 2006;15:715-9.
2. Chen SL, Xu YH, Shi SY. Diagnostic criteria for systemic lupus erythematosus in Chinese patients [Chinese]. Zhonghua Nei Ke Za Zhi 1987;26:533-6, 65.
3. Huang JL, Yao TC, See LC. Prevalence of pediatric systemic lupus erythematosus and juvenile chronic arthritis in a Chinese population: a nation-wide prospective population-based study in Taiwan. Clin Exp Rheumatol 2004;22:776-80.
4. Mok CC, Lau CS. Lupus in Hong Kong Chinese. Lupus 2003;12:717-22.
5. Fujikawa S, Okuni M. A nationwide surveillance study of rheumatic diseases among Japanese children. Acta Paediatr Jpn 1997;39:242-4.
6. Edwards CJ. Lupus in Singapore. Lupus 2001;10:889-91.
7. McCarty DJ, Manzi S, Medsger TA Jr, Ramsey-Goldman R, LaPorte RE, Kwoh CK. Incidence of systemic lupus erythematosus. Race and gender differences. Arthritis Rheum 1995;38:1260-70.
8. Cooper GS, Parks CG, Treadwell EL, St. Clair EW, Gilkeson GS, Cohen PL, et al. Differences by race, sex and age in the clinical and immunologic features of recently diagnosed systemic lupus erythematosus patients in the southeastern United States. Lupus 2002;11:161-7.
9. Samanta A, Roy S, Feehally J, Symmons DP. The prevalence of diagnosed systemic lupus erythematosus in whites and Indian Asian immigrants in Leicester city, UK. Br J Rheumatol 1992;31:679-82.
10. Fernandez M, Alarcon GS, Calvo-Alen J, Andrade R, McGwin G Jr, Vila LM, et al. A multiethnic, multicenter cohort of patients with systemic lupus erythematosus (SLE) as a model for the study of ethnic disparities in SLE. Arthritis Rheum 2007;57:576-84.
11. Kurahara DK, Grandinetti A, Fujii LL, Tokuda AA, Galario JA, Han MJ, et al. Visiting consultant clinics to study prevalence rates of juvenile rheumatoid arthritis and childhood systemic lupus erythematosus across dispersed geographic areas. J Rheumatol 2007;34:425-9.
12. Malleson PN, Fung MY, Rosenberg AM. The incidence of pediatric rheumatic diseases: results from the Canadian Pediatric Rheumatology Association Disease Registry. J Rheumatol 1996;23:1981-7.
13. Miettunen PM, Ortiz-Alvarez O, Petty RE, Cimaz R, Malleson PN, Cabral DA, et al. Gender and ethnic origin have no effect on longterm outcome of childhood-onset systemic lupus erythematosus. J Rheumatol 2004;31:1650-4.
14. Denardo BA, Tucker LB, Miller LC, Szer IS, Schaller JG. Demography of a regional pediatric rheumatology patient population. Affiliated Children's Arthritis Centers of New England. J Rheumatol 1994;21:1553-61.
15. Huemer C, Huemer M, Dorner T, Falger J, Schacherl H, Bernecker M, et al. Incidence of pediatric rheumatic diseases in a regional population in Austria. J Rheumatol 2001;28:2116-9.
16. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271-7.
17. Weening JJ, D'Agati VD, Schwartz MM, Seshan SV, Alpers CE, Appel GB, et al. The classification of glomerulonephritis in systemic lupus erythematosus revisited. J Am Soc Nephrol 2004;15:241-50.
18. Many Z. The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. Arthritis Rheum 1999;42:599-608.
19. Brunner HI, Silverman ED, Bombardier C, Feldman BM. European Consensus Lupus Activity Measurement is sensitive to change in disease activity in childhood-onset systemic lupus erythematosus. Arthritis Rheum 2003;49:335-41.
20. Gladman DD, Ibanez D, Urowitz MB. Systemic Lupus Erythematosus Disease Activity Index 2000. J Rheumatol 2002;29:288-91.
21. Brunner HI, Silverman ED, To T, Bombardier C, Feldman BM. Risk factors for damage in childhood-onset systemic lupus erythematosus: cumulative disease activity and medication use predict disease damage. Arthritis Rheum 2002;46:436-44.
22. Gladman DD, Goldsmith CH, Urowitz MB, Bacon P, Fortin P, Ginzler E, et al. The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index for systemic lupus erythematosus international comparison. J Rheumatol 2000;27:373-6.
23. Thumboo J, Lee HY, Fong KY, Chan SP, Chapman CA, Leong KH, et al. Accuracy of medical record scoring of the SLICC/ACR damage index for systemic lupus erythematosus. Lupus 2000;9:358-62.
24. Vyas S, Hidalgo G, Baqi N, Von Gizyki H, Singh A. Outcome in African-American children of neuropsychiatric lupus and lupus nephritis. Pediatr Nephrol 2002;17:45-9.
25. Houghton KM, Page J, Cabral DA, Petty RE, Tucker LB. Systemic lupus erythematosus in the pediatric North American Native population of British Columbia. J Rheumatol 2006;33:161-3.
26. Kurahara D, Tokuda A, Grandinetti A, Najita J, Ho C, Yamamoto K, et al. Ethnic differences in risk for pediatric rheumatic illness in a culturally diverse population. J Rheumatol 2002;29:379-83.
27. Tucker LB, Uribe AG, Fernandez M, Vila LM, McGwin G, Apte M, et al. Adolescent onset of lupus results in more aggressive disease and worse outcomes: results of a nested matched case-control study within LUMINA, a multiethnic US cohort (LUMINA LVII). Lupus 2008;17:314-22.
28. Reveille JD, Bartolucci A, Alarcon GS. Prognosis in systemic lupus erythematosus. Negative impact of increasing age at onset, black race, and thrombocytopenia, as well as causes of death. Arthritis Rheum 1990;33:37-48.
29. Singh S, Devidayal, Kumar L, Joshi K. Mortality patterns in childhood lupus — 10 years' experience in a developing country. Clin Rheumatol 2002;21:462-5.
30. Alarcon GS, McGwin G Jr, Bastian HM, Roseman J, Lisse J, Fessler BJ, et al. Systemic lupus erythematosus in three ethnic groups. VII [correction of VIII]. Predictors of early mortality in the LUMINA cohort. LUMINA Study Group. Arthritis Rheum 2001;45:191-202.
31. Alarcon GS, McGwin G Jr, Bartolucci AA, Roseman J, Lisse J, Fessler BJ, et al. Systemic lupus erythematosus in three ethnic groups. IX. Differences in damage accrual. Arthritis Rheum 2001;44:2797-806.
32. To CH, Petri M. Is antibody clustering predictive of clinical subsets and damage in systemic lupus erythematosus? Arthritis Rheum 2005;52:4003-10.
33. Quintero-Del-Rio AI, Bacino D, Kelly J, Aberle T, Harley JB. Familial systemic lupus erythematosus: a comparison of clinical manifestations and antibody presentation in three ethnic groups. Cell Mol Biol (Noisy-le-grand) 2001;47:1223-7.