Disparities in Childhood-Onset Lupus

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KEYWORDS

• Pediatric • Lupus • Disparities • Race • Ethnicity • Socioeconomic • Geographic • Access

KEY POINTS

- There are known disparities in the prevalence of childhood-onset systemic lupus erythematosus (SLE), disease severity, physical and mental morbidity, and mortality across racial/ethnic groups.
- Although health care quality for pediatric patients with SLE varies by socioeconomic status and accessibility of pediatric rheumatologists, there are significant gaps in the literature regarding the impact of socioeconomic status on health outcomes.
- Further studies are needed to better understand specific drivers for disparate outcomes for patients with childhood-onset SLE, and to develop effective interventions for eliminating health inequity.

INTRODUCTION

Systemic lupus erythematosus (SLE) occurring in childhood, as in adults, is a chronic, autoimmune disease that has the potential to involve any organ system. In children and youth with childhood-onset SLE (cSLE), however, the most severe forms of SLE, namely life-threatening renal or central nervous system (CNS) disease, occur more frequently.[1] Individuals with cSLE are at risk of stroke, end-stage renal disease (ESRD), and early death.[2–4]

Similar to adult-onset disease, cSLE does not affect populations equally. Higher prevalence rates have been reported in several racial and ethnic minorities, most notably in Native American and First Nation Canadians, black, Latino, and Asian people.[5–8]

Furthermore, disparities have been observed in outcomes of cSLE, care delivery, and SLE-related comorbidities, including mental health disorders. These disparities may be along the lines of race/ethnicity, income, and geography. Despite this, the

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understanding of disparities affecting patients with cSLE is limited by a dearth of large studies with diverse demographics and a paucity of studies that examined differences across demographics.

In this review, the authors present the current knowledge regarding disparities in cSLE and related outcomes and the gaps in knowledge that require further investigation. In this review of the literature on disparities in cSLE, the authors used a broad definition of health disparities, consistent with Health People 2020, as "a particular type of health difference that is closely linked with social, economic, and/or environmental disadvantage."[9]

DISPARITIES IN PREVALENCE OF CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

Populations across the globe are not at equal risk of developing SLE. Studies that have been conducted looking at prevalence discrepancies across populations in cSLE show similar trends to what has been described in adult-onset SLE. Native American/American Indian children have the highest documented prevalence rates globally of cSLE. Among child Medicaid beneficiaries in the United States, Native American children are more than 3 times as likely to develop cSLE that other US race/ethnicities with prevalence rates of 13.4 per 100,000.[5] These prevalence rates have been corroborated in studies of prevalence rates among Native American children seen by Indian Health Services.[6] Children of First-Nation populations in Canada also appear to be at greater risk of developing cSLE than other Canadians. British Columbia First Nations children have a prevalence rate of 8.8 per 100,000 for SLE compared with 3.3 per 100,000 in the general population.[10]

Asian populations, both in Asia and across the globe, also exhibit higher prevalence rates of cSLE than the prevalence rates documented in European populations[11,12] and in general US[13] and Canadian populations.[14] Chinese children from Taiwan have a prevalence of 6.3 per 100,000.[7]

Although SLE prevalence rates in New Zealand and Australia are much lower than the United States and Canada, children of indigenous populations of New Zealand (Maori) are twice as likely to have SLE as their counterparts of European descent in New Zealand.[15] Rates of SLE in Aboriginal and Torres Strait Islander children of Australia are 4 times that of the general pediatric population of Australia.[16]

In the United States and Canada, single-center studies from large urban cities indicate that Asian, black, and Latino/Hispanic children have higher prevalence rates of SLE than white children,[14] similar to adult-onset SLE. In particular, black SLE patients are among the youngest diagnosed with SLE and disproportionately represent cSLE populations, even in comparison to what is expected from the increased rates of cSLE overall.[8]

Finally, for large populations in developing countries, the epidemiology of cSLE is largely unknown. In many lower- and middle-income countries in Africa and Asia, with large populations and very few pediatric rheumatologists, delays in diagnosis and delays in access to care have been described. Likely a large proportion of cases in these underserved countries are being missed. In South Africa, for instance, the large burden of infectious disease, including human immunodeficiency virus, and trauma is noted to overwhelm underresourced medical systems, challenging care for chronic pediatric disease.[17] Similar challenges have been described in India, with regard to the care of children with SLE.[18]

DISPARITIES IN DISEASE MANIFESTATIONS AND SEVERITY

Several early studies that examined differences in SLE disease manifestations and reported data on demographic groups of cSLE patients had either too few minority patients[19] or too few numbers overall to fully investigate differences across demographics. However, even among these, it is evident that some of the most severe SLE manifestations, such as lupus nephritis (LN) and CNS lupus, are more prevalent among black and Hispanic patients.[14,19]

Recent studies, including two from large academic centers in Canada[14] and the United Kingdom,[20] show more definitively increased rates of LN in nonwhite SLE children. Although the UK study only reported race/ethnicity dichotomously as white/nonwhite,[20] others reported race-specific rates of LN in black children with SLE between 36% and 64%[14,21,22] and 66% in Asian children.[14] The largest cohort to date representing black children in the United States is from the first iteration of the SLE registry of the Childhood Arthritis and Rheumatology Research Alliance (CARRA Legacy Registry), which includes approximately 1000 patients from 60 CARRA sites across the United States, 35% of whom are black.[21] The rate of biopsy-confirmed LN in black CARRA Registry patients is 42%,[21] similar to the overall rate of biopsy-proven LN in the total CARRA Legacy Registry (43%).[23] Lewandowski and colleagues[21] compared the CARRA Registry patients with a cohort of mainly nonwhite patients of African descent (92%) from South Africa and found that patients represented in the South African cohort had notably higher rates of biopsy-proven LN (61%). This cohort, the PULSE cohort, is a retrospective cohort of pediatric SLE patients developed from records at 3 hospital centers in Cape Town, South Africa who presented from 1988 to 2012.

A study from China found LN in 61% of children with cSLE.[7] In contrast, in a cohort from Singapore, which was largely of Chinese ethnicity, the rate of LN was 41%.[24] In a cohort of 33 children from Trinidad, the rate of renal disease (not biopsy proven) was 64%.[25] The highest rates of LN documented were in small cohorts of cSLE patients from Egypt (88%) and Turkey (86%), but these rates are likely biased based on the composition of these cohorts of patients referred to pediatric nephrology (despite potential absence of resources in pediatric rheumatology).[26,27]

Less is known about neuropsychiatric manifestations across demographics in cSLE. Rates of CNS disease in cSLE vary greatly between studies, and few studies reported rates across race/ethnicity. Rates reported range between 24% and 27% from cohorts from Canada, United States, and China, and up to 95% from 1 cohort from New Mexico with most being Hispanic patients.[28] These rates are likely due as much to the differences in definition and attribution (specifically for symptoms of lupus headache, cognitive dysfunction, and mood disorder) as they are to variance among prevalence rates in differing populations. Hiraki and colleagues[14] found that black children with cSLE had the highest proportion of CNS disease with 32% affected, compared with 24% in white patients and significantly higher than the 18% Asian children with SLE.

In the largest cohort to date to study cardiac manifestations of cSLE, from the United States, Chang and colleagues[29] found that black race was associated with an incident rate ratio of 6.6 compared with white race. Although cardiac manifestations were reported with a similar frequency in the PULSE cohort from South Africa, they had worse severity than the US cohort described by Chang and colleagues.[30]

DISPARITIES IN MORBIDITY AND MORTALITY

Among sources of organ damage from SLE in childhood and young adults, renal damage and specifically ESRD are best studied. In a large US study that looked across

ages, black SLE patients were at the highest risk for ESRD among young people with LN.[31] From 1995 to 2006, rates of ESRD among black LN patients have increased, as have rates of ESRD among LN patients ages 5 to 39.[32] Among pediatric LN patients with ESRD captured by the US Renal Data System, black children were half as likely to receive transplants as white children and almost twice as likely to die. Hispanic patients were also less likely to receive transplants than non-Hispanic patients. Regional disparities were also found, because children in the southern United States were less likely to receive transplants than children in the northwest and western United States.[31] Outside of the United States, high rates of ESRD from LN were described in the South African PULSE cohort (13%).[21]

Osteoporosis/osteopenia is another form of SLE-related damage. In a preliminarily study, disparities in osteoporosis/osteopenia by race/ethnicity were not evident.[33]

SLE-related damage, in general, measured by Systemic Lupus International Collaborating Clinics SLE Damage Index (SLICC SDI) also showed no race/ethnicity disparities in a study from British Columbia, largely of white and Asian patients, and with no black or Hispanic patients[34] and from a multinational study of cSLE, including centers from North America, Europe, and Asia.[35] In contrast, a significantly higher percentage of children from the South African PULSE cohort had evidence of damage on SLICC SDI compared with those from a US cohort (from the CARRA Legacy Registry), 63% versus 23%.[21] Within the CARRA Legacy Registry, poverty, and not race/ethnicity, was associated with worse disability.[36]

Although decreases in mortality in cSLE have been described over the past 20 years, mortality still remains significant, specifically because of ESRD. cSLE patients with ESRD have twice the risk of death compared with other pediatric ESRD patients.[2]

A recent large national study of US pediatric patients with SLE showed regional and racial disparities in mortality. Black children and children from the southern US region had twice the risk of death with inpatient hospitalizations, compared with white children and children from the northeastern US.[4]

In another study that was not designed or powered to find significant differences in mortality, the proportion of deaths seen in minority race/ethnicities, and most notably in black children with SLE, was outsized.[14] In a small Trinidadian cohort of cSLE, East Indian and mixed race children had the highest mortalities (higher than black children or children of African descent).[25]

DISPARITIES IN MENTAL HEALTH AND HEALTH-RELATED QUALITY OF LIFE

Although a cross-sectional study of depression and anxiety in US youth with cSLE found that youth of nonwhite race were more likely to have symptoms of depression,[37] a large study of Medicaid-enrolled cSLE youth found that black children with cSLE were significantly less likely to be diagnosed with anxiety or depression, and less likely to be treated with anxiolytics.[22]

Specific disparities around mental health diagnosis and treatment among lower-income US black children with cSLE may have long-lasting effects on not only the mental health but also on the physical health of this population, given observed associations between mental health symptoms and aspects of self-care, such as medication adherence.[38]

Studies of associations between health-related quality of life (HRQOL) and race/ethnicity in cSLE populations have been inconsistent. In studies including US populations, black race[39] and nonwhite race[40] were risk factors for lower HRQOL measures, although a Canadian study found the opposite, with children identifying as white more likely to report worse HRQOL.[41]

DISPARITIES IN HEALTH CARE QUALITY AND UTILIZATION

Disparities between younger and older adult SLE patients have been identified with regards to quality of care. Young adult patients aged 18 to 34 are less likely than older adults to receive care that meets quality metrics related to SLE care, including pneumococcal vaccination, medication toxicity monitoring, and cardiovascular monitoring.[42] However, few studies have examined quality metrics across demographics, specifically among cSLE patients.

Among Medicaid-enrolled US youth with SLE, black, Hispanic, and "other" nonwhite races have higher rates of glucocorticoid use,[22] although this may be a result of differences in disease severity or activity. Similarly, greater cost for inpatient hospitalization is associated with male gender and black race among US children hospitalized with SLE.[43]

Disparities During Transition to Adulthood

The transition period between pediatric and adult health care models is a time of particular vulnerability to poor outcomes and barriers to quality care and access to care. Thus, in cSLE, this is a period of special concern. Limited studies have investigated potential race/ethnicity disparities during transition. A recent study of a large administrative database of youth on private insurance found that there were no differences among SLE youth in the rates of successful transfer to adult rheumatology by race/ethnicity. Neither were there differences in health care utilization.[44] A smaller study of patients from Boston found that white race and low education were associated with missed appointments during transition.[45] In adolescents and young adults with chronic diseases, living in higher-income neighborhoods is associated with transition readiness.[46]

Causes and contributors to these disparities in cSLE in US populations have yet to be investigated. A qualitative study in South Africa of adult caregivers and medical providers caring for children with SLE explored barriers to seeking and receiving care for cSLE, and how they may contribute to poor outcomes observed in this population of SLE patients. Major barriers included severe financial difficulties for families (18% of families came from households without running water or electricity), social stigma related to a chronic diagnosis, lack of trained staff in pediatric rheumatology, and prior misdiagnosis.[17]

Access to pediatric rheumatologists may drive some disparities in US populations as well. A study of SLE patients enrolled in the CARRA Legacy Registry found that location in a state with a high density of pediatric rheumatologists was a predictor for being seen expeditiously (within the first month from symptom onset), whereas being from a low-income household was a predictor for severe delay (seen $\geq$1 year from symptom onset).[47]

POTENTIAL CONTRIBUTORS TO DISPARITIES

Several potential contributors to disparities in cSLE have yet to be fully investigated. In **Fig. 1**, the authors describe different factors related to social disadvantage, health care systems and access, family environment and resources, and individual patient treatment that may lead to inequities in care for youth with cSLE. This conceptual framework is based on social-ecological models of health, such as Bronfenbrenner's, used in other disciplines to study health disparities.[48]

Although challenges of caring for patients with cSLE by a small pediatric rheumatology workforce have been well described, regarding areas of the globe and states within the United States that lack access to specialists, the impact of the limitations

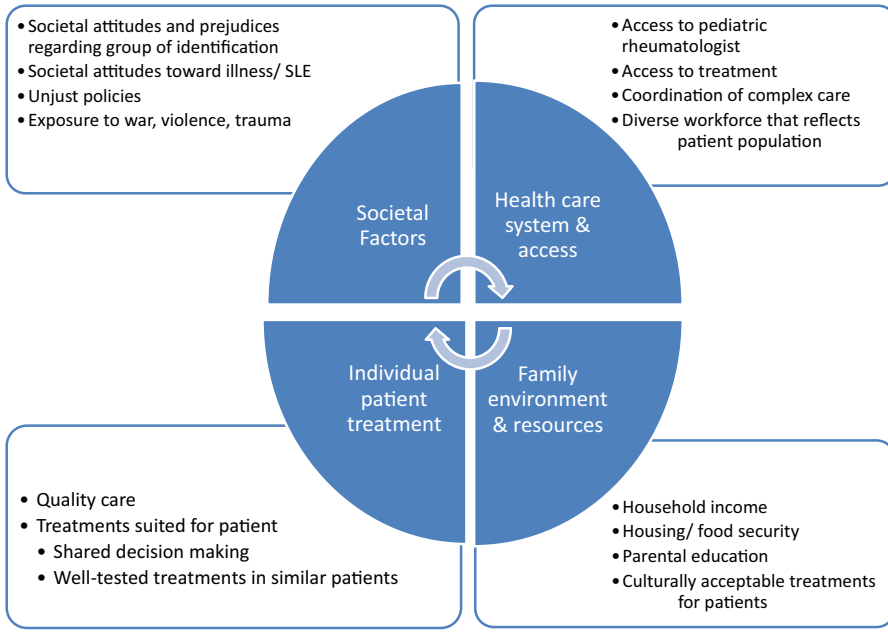

Fig. 1. Modified social-ecological model of contributors to health disparities and health equity in cSLE. Potential contributors to health disparities in cSLE related to societal, health system and health access, family, and individual patient factors. This conceptual framework is modeled after the modified social-ecological model by Reifsnider and colleagues,[48] based on Bronfenbrenner's social-ecological model.

of diversity in the workforce has not been investigated. A decade ago, the pediatric rheumatology workforce was made up of greater than 90% white providers.[49] A recent study of subspecialist trainees in internal medicine over the past 10 years showed that rheumatology lagged behind other subspecialties in recruiting residents from race/ethnicities that were underrepresented in medicine.[50] Changes in the pediatric rheumatology workforce over the past decade have yet to be described.

Building diverse provider workforces regarding gender, race/ethnicity, and other sociodemographics is essential to address health disparities.[51] Severe mismatches in provider/patient sociodemographics may challenge the ability to give culturally competent care. Patient comfort and language preferences are also influenced by the presence or lack of diversity within the workforce; barriers to these can impede quality of care.

ADDRESSING DISPARITIES

Evidence-based approaches to address disparities in cSLE will rely not only on research that defines disparities but also on studies that test interventions (a) for how effective they are in at-risk populations and (b) so that these interventions not only improve outcomes but also close gaps in heath inequity (**Fig. 2**). Developing effective and appropriate interventions for at-risk populations requires partnerships with community members and other stakeholders to lead to change and improved care.

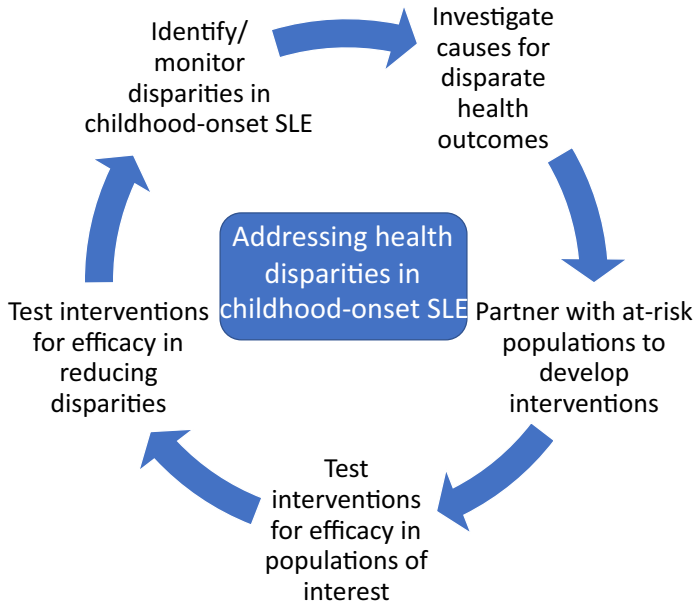

Fig. 2. Addressing health disparities in cSLE. A proposed iterative framework to address health disparities through evidence-based methods. This is modified from a conceptual framework developed by Rashid and colleagues.[56]

Some of this community-partnership work is underway. For example, to address presumed disparities in resources, access, and care to black and Latino communities, an educational intervention was developed to improve knowledge of SLE in reproductive health care providers from minority communities in New York with large black and Latino populations. A pilot of the intervention among reproductive health care providers showed improvement in self-reported knowledge and comfort in counseling adolescents and young women with SLE.[52]

SUMMARY

In this review of the literature on health disparities in cSLE, the authors found that there were disparities in prevalence, disease severity, morbidity, and mortality across race/ethnicity. Health care quality is adversely impacted by poverty and inaccessibility to pediatric rheumatologists on a regional level. Because of significant gaps in the literature, less is known about the contribution of income and other socioeconomic markers of disadvantage to outcomes of care.

Paralleling observations that have been noted in adult SLE literature,[53,54] black children with cSLE are at particularly high risk of poor outcomes and high morbidity. These disparities have been most well defined with regards to the risk of ESRD from LN, disparities in transplant rates, and mortality. The presence of these disparities in the pediatric population indicates that implementations only in older SLE patients may be missing the mark to effect change in adult patients with cSLE; earlier interventions in children with cSLE may bring about more equitable health outcomes among the black SLE patient population.

Few studies in cSLE have examined poverty and its impact on care and outcomes. Fewer studies have examined interactions between income and race/ethnicity. Some populations remain largely invisible in the literature. In literature from US centers, characterization of disease severity, care, and outcomes among Native American children with cSLE is largely absent, despite evidence that this may be a population at particular risk for both developing SLE and for being underserved specifically with regards to resources in pediatric rheumatologists and socially disadvantaged.

Authors of the reviewed studies have called for examining disparities in access to health care in youth with cSLE and the role that universal health care coverage may have to ameliorate health disparities for children with cSLE.[14] Although these are certainly warranted, the large studies of US Medicaid children[22,30] point to a problem that is more nuanced than simple health coverage.

Studies of health care quality and health care utilization among youth with cSLE are sparse. Work needs to be done with data that include at-risk youth from low-income backgrounds to understand and define potential disparities that have been observed in adult SLE populations.

Across the globe, observations, although preliminary, that youth with cSLE are more likely to come from socially disadvantaged and marginalized populations and that these populations are at particular risk for lower levels of care and worse outcomes, raise difficult questions about how damaging social structures, including systematic racism, may be affecting children at risk and with cSLE. Although these questions require further investigation, studies into understanding disparities need to be coupled with interventional studies looking at ways to ameliorate health inequities for children with cSLE.

This review was limited by the authors' very broad definition of health disparities, encompassing differences that are complex and multifactorial and that may include factors related to a wide variety of mechanisms of disease, system, and access differences in health care. More specific definitions of health disparities have been introduced to pinpoint inequities in care that are not accounted for by differences in access, preference, and need, including the definition used by the Institute of Medicine.[55] Few studies were designed to examine disparities in race/ethnicity while accounting for health care access and/or disease severity.

To better understand specific drivers for disparate outcomes among youth with SLE and adults with cSLE, future studies will have to leverage large disease registries that can account for multiple measures of access to care, race/ethnicity, income, and other measures of socioeconomic disadvantage.

DISCLOSURE

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