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Trends in the epidemiology of childhood nephrotic syndrome in Africa: A systematic review

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SUMMARY

Background: Childhood nephrotic syndrome, if left untreated, leads to progressive kidney disease or death. We quantified the prevalence of steroid-sensitive nephrotic syndrome, steroid-resistant nephrotic syndrome, and histological types as the epidemiology of nephrotic syndrome in Africa remains unknown, yet impacts outcomes.

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Methods: We searched MEDLINE, Embase, African Journals Online, and WHO Global Health Library for articles in any language reporting on childhood nephrotic syndrome in Africa from January 1, 1946 to July 1, 2020. Primary outcomes included steroid response, biopsy defined minimal change disease, and focal segmental glomerulosclerosis (FSGS) by both pooled and individual proportions across regions and overall.

Findings: There were 81 papers from 17 countries included. Majority of 8131 children were steroid-sensitive (64% [95% CI: 63–66%]) and the remaining were steroid-resistant (34% [95% CI: 33–35%]). Of children biopsied, pathological findings were 38% [95% CI: 36–40%] minimal change, 24% [95% CI: 22–25%] FSGS, and 38% [95% CI: 36–40%] secondary causes of nephrotic syndrome.

Interpretation: Few African countries reported on the prevalence of childhood nephrotic syndrome. Steroid-sensitive disease is more common than steroid-resistant disease although prevalence of steroid-resistant nephrotic syndrome is higher than reported globally. Pathology findings suggest minimal change and secondary causes are common. Scarcity of data in Africa prevents appropriate healthcare resource allocation to diagnose and treat this treatable childhood kidney disease to prevent poor health outcomes.

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Introduction

Childhood nephrotic syndrome is a glomerular disorder with expected good clinical outcomes [1,2]. If left untreated, it may affect kidney function, or in children who have frequent relapses or are non-responsive to treatment, it may progress to chronic kidney disease, end stage kidney disease, or lead to early mortality [1]. While the cause of idiopathic childhood nephrotic syndrome remains unknown, treatment with corticosteroids (steroids) has greatly reduced the morbidity and mortality. Less than 5% of children who are non-responsive to steroid treatment progress to end-stage kidney disease in high-resource countries [1]. Response to steroid treatment, however, is variable depending on ethnicities and geographic regions [3]. Steroid-resistant nephrotic syndrome is associated with a worse prognosis and is a known risk factor for progression to end-stage kidney disease [1]. In the United States, African Americans have three times the prevalence of steroid-resistant nephrotic syndrome compared to European American children [3,4].

Among Africans, steroid resistance in children ranges from 16% to 73·5% [2,3]. In tropical Africa, incidence of nephrotic syndrome is 0·35–1·34% of hospital admissions, though studies from northern and southern African countries are not available [2]. Most studies are cross-sectional with few longitudinal studies, limited to single centers. As the cohort size is typically small, a pooled analysis is needed to understand the epidemiology and trends across the African continent. Recent reports suggest a changing epidemiology with more children responding to steroid treatment and lower rates of focal segmental glomerulosclerosis (FSGS), presumably due to the decline in quartan malaria infections and improved access to healthcare [5]. In tropical Africa, pre-1989, when quartan malaria nephropathy was the most common glomerular lesion reported among children, rates of steroid resistance were 73·5% and after 1989, declined to 27·4%, likely due to improved and affordable malaria treatment [2,5].

Rising rates of noncommunicable diseases in Africa, especially chronic kidney disease among children and young adults, makes understanding the epidemiology of childhood nephrotic syndrome in Africa crucial. If left unrecognized or untreated nephrotic syndrome can lead to chronic kidney disease/end-stage kidney disease which confers significant morbidity and mortality. Moreover, prevention of progression towards end-stage kidney disease is paramount, as renal replacement therapy is prohibitive to many health systems as well as the individuals and families. Updated information on the epidemiology and trends of nephrotic syndrome in children will ensure informed decisions on recognition, diagnosis and appropriate management of potentially treatable forms of childhood kidney disease. This systematic review was conducted to determine the proportions of steroid-sensitive nephrotic syndrome, steroid-resistant nephrotic syndrome, and its histological types among African children to understand how they impact outcomes.

Methods

We followed the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. Our search strategy involved a MEDLINE search from 1946 to July 1st 2020 and an Embase search from 1947 to July 1st 2020. Search terms included "nephrotic syndrome", or "edema hypertension proteinuria syndrome", or "oedema hypertension proteinuria syndrome" as well as "pediatric", "adolescent", and every country within the African continent (Supplementary File). African Journals Online and WHO Global Health Library were also searched using key terms "nephrotic syndrome", and "childhood" to find additional studies. References of any review articles were cross referenced to supplement additional relevant articles.

Eligibility criteria included studies in any language that contained primary data on children with nephrotic syndrome ages 0–18 years in any African country. Studies were excluded if the study population included only adult participants, were from outside of Africa and if the diagnosis was not nephrotic syndrome or only systemic diseases associated with nephrotic syndrome were reported. Single case reports were also excluded. Published studies were screened based on the title and abstract and if they met the inclusion criteria, the full text was reviewed if accessible.

Papers were assessed, screened, and abstracted (RW) with additional review by co-authors (investigators in the H3 Africa Kidney Disease Research Network). Any discrepancies were reviewed and adjudicated by two authors (JVR, RSP). Data collected included the country of study, age at diagnosis, sex, number of overall study participants, number with nephrotic syndrome, proportion of children treated with steroids, number of children with steroid-resistant or steroid-sensitive nephrotic syndrome, number of children biopsied, outcome of biopsies, and study period. For studies with overlapping patient populations, the single study with the larger patient cohort was included, or if more data were available on steroid response and biopsy results. Authors were contacted to avoid counting the same population twice. Six included studies were in French and translated into English. Studies in other languages did not meet inclusion criteria.

Risk of bias predominantly arose from lack of follow-up data. Quality of the papers were assessed using an adapted model [6], and all but two papers were found to be of reduced quality (Supplementary File). The model to assess quality was chosen for comparison to a similar study evaluating the epidemiology of chronic kidney disease in sub-Saharan Africa [6]. In total, 608 relevant published articles were found plus an additional 24 were added from review of references (Fig. 1). After excluding duplicates and all studies that did not meet the inclusion criteria, 81 records were included for analysis. Out of the 81 papers, 61 reported on steroid response and 63 on histology. One study had two separate study periods and was split into two studies [7]. A sensitivity analysis was performed by calendar year to assess temporal trends