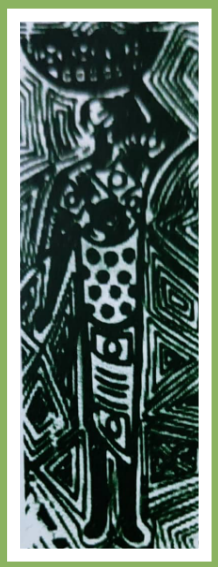
NIGERIAN JOURNAL OF PAEDIATRICS

https://www.njpaediatrics.com

PRINT: ISSN 0302-4660

ONLINE: ISSN 2814-2985

OFFICIAL JOURNAL
OF THE PAEDIATRIC
ASSOCIATION OF
NIGERIA



VOLUME 52
NUMBER 1
JANUARY – MARCH 2025

RESEARCH PROTOCOL

Nigerian Journal of Paediatrics 2025; Volume 52(1): 7-11.
https://dx.doi.org/10.63270/njp.2025.v52.i1.2000002

Prevalence of Sickle Cell and Sickle Cell Trait Among Children and Adolescents in Nigeria: A Protocol for Systematic Review and Meta-Analysis (Prospero ID: CRD42024556354)

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Abstract

Background

Sickle cell disease (SCD) is one of the most common genetic disorders globally, with Nigeria believed to have the highest burden in the whole world. Despite the high burden in the country, the true prevalence of SCD, as well as its main driver- sickle cell trait (SCT) is unknown. These parameters are important for planning and resource allocation.

Objective: To review the prevalence of SCD, SCT and associated factors in Nigerian children and adolescents.

Methods: The search strategy will include MeSH terms, keywords, and entry words from the following databases: AJOL, Google Scholar, Research Gate, PubMed, EMBASE, Cochrane Library, Scopus and Web of Science collections. Studies among children and adolescents in Nigeria that report the prevalence of SCD and/or SCT available in English will be included. The primary outcome will be pooled prevalence of sickle cell disease (SCD) and sickle cell trait (SCT) among children and adolescents in Nigeria, while the secondary outcome will be regional and gender variations and associated factors of SCD in Nigeria. All identified articles will be screened, and those that meet the inclusion criteria will be included in the systematic review and meta-analysis. All the studies will be assessed for methodological and statistical heterogeneity. The National Institute of Health (NIH) Quality Assessment Tool for observational studies and the Cochrane tool of risk of bias will be used to assess the quality of selected studies, and publication bias will further be assessed with a funnel plot.

Results: Using random effect models, results will be presented as pooled and regional prevalence along a 95% confidence interval, while odds ratio and 95% will be used to summarise effects size association. A cumulative meta-analysis will assess the time trend, pooled, regional prevalence and variations.

Keywords: Adolescent, Children, Incidence, Sickle cell disease, Sickle cell trait, Prevalence, Nigeria.

This protocol is registered with PROSPERO ID: CRD42024556354.

Introduction

Sickle cell disease (SCD) stands as one of the most pervasive and debilitating genetic disorders in Africa, with significant impacts on the lives of millions of affected individuals and their families.[1,2] The burden of SCD in Africa is not only profound but also multi-faceted, encompassing a complex interplay of medical, social, economic, and cultural factors.[2] It is estimated that around 400,000 babies are born with SCD in Africa each year, with Nigeria having the highest global burden. Though there are studies on the prevalence of SCD among children and adolescents in Nigeria, these studies were carried out across various sub-populations and settings, such as hospitals versus communities, with significant variation.[3–5] Besides, an important driver of the high burden of SCD is the presumed high rate of sickle cell trait (SCT), with the exact burden also unknown in spite of various efforts to reduce both the burden of SCD and SCT in Nigeria. Thus, the national prevalence of SCD and SCT remains unknown, and this hampered adequate planning and resource allocation. This calls for pooled prevalence across the country and establishing the regional burden and associated factors. This study, therefore, aims to document the pooled prevalence, regional and gender variation and related factors (socio-demographics) of SCD and SCT among children and adolescents in Nigeria through a systematic review and meta-analysis.

Objectives

To determine the pooled prevalence, regional variation and associated factors (socio-demographics) of sickle cell disease (SCD) and sickle cell trait (SCT) among children and adolescents in Nigeria.

Review questions

a) What is the pooled prevalence of SCD and SCT among children and adolescents in Nigeria?
b) Is there a regional variation in the prevalence of SCD among children and adolescents across the geopolitical zones in Nigeria?
c) Is there a gender variation in the prevalence of SCD among children and adolescents in Nigeria?
d) What is the relationship between socio-economic status and SCD prevalence in Nigeria?
e) Is there a difference in community and hospital-based prevalence of SCD among children and adolescents in Nigeria?

Methods

Eligibility criteria

Inclusion criteria

a) Children and adolescents in Nigeria from the age of zero days to 18 years.
b) Descriptive studies, cross-sectional studies, longitudinal studies, cohort studies.
c) Articles cited in any form of a review article, including systematic reviews, reporting prevalence or incidence of SCD, study location, settings (hospital/community), and participants' gender with or without socio-demographics.
d) Studies retrievable in the English language.

Exclusion criteria

a) Review articles, including systematic reviews, editorials, commentaries, letters to editors, and case reports.
b) Interventional studies.
c) Studies conducted outside Nigeria**.**

Search period

We will include all published studies up till October 2024.

Search Strategy/Information source.

The search strategy will include MeSH terms, keywords, and entry words from the following databases (AJOL, Google Scholar, Research Gate, PubMed, EMBASE, Cochrane Library, Scopus and Web of Science collections). The search will be conducted using the following words or phrases "sickle cell disease OR sickle cell anaemia OR sickle cell trait" AND "Nigeria" AND "newborns OR infants OR children OR adolescents" AND "associated factors OR sex OR socio-economic status OR sociodemographic" AND "(SCD OR SCA OR SCT)" across the database. The search term will be modified to get more results when a database does not support the Boolean operators and quotations.

Selection process

The search data obtained will be uploaded into the Rayyan software manager for data management. Duplicates will be removed after exporting all the search literature into the Rayyan software. Two independent and blinded reviewers will screen eligible studies' titles, abstracts, and full texts, forming the basis for selecting studies for inclusion in systematic review and meta-analysis. Where there is a disagreement in decision between the two reviewers, the third reviewer will be a tiebreaker. Authors of eligible studies with any missing data will be contacted with queries via email and telephone and given adequate time to respond.

Data collection process

Three main tools will be used for data extraction and management:

i) Rayyan Systematic Review Screening Tool.

ii) Microsoft Excel®

iii) MedCalc statistical software package for biomedical research (version 23).

The following levels of data screening will be used for searched studies:

Level 1: Only observational studies, retrievable in the English language, will be selected from the entire database.

Level 2: This will involve screening of selected studies in the titles and abstracts using entry terms, keywords, and MeSH terms.

Level 3: Selected articles that scaled through the abstract and title screened will have their full text retrieved. Further screening will be carried out by reading the full articles.

Level 4: Additional extracts of grey literature, including those obtained from a manual search of literature that meets the inclusion criteria, will be added.

Studies that include the primary outcome with or without a secondary outcome will be included.

For the studies whose titles and abstracts are screened and meet the inclusion criteria but whose full texts are unavailable, the corresponding authors will be written to request the full texts and data. A reasonable length of time (four weeks) will be allowed for the authors to respond, and those who respond and meet the inclusion criteria will be added to the study.

Data extraction/items

The data extracted from the included articles will be entered into a standardized Microsoft® Excel spreadsheet. Extractable data will consist of the first author's name, year of publication, location of study, study design, study population (age range), hospital, or community-based study, sample size, gender, diagnostic method, prevalence, incidence, and sociodemographic.

Review Outcomes

Primary

The pooled prevalence of SCD and SCT among children in Nigeria.

Secondary

Regional variation in the prevalence of SCD and SCT in Nigeria.

Gender variation in the prevalence of SCD among children in Nigeria.

Associated factors (socio-economic status) with the prevalence of SCD in Nigeria.

Effect sizes

The random effect model will be used to report the measure of the effect size of pooled prevalence along with a 95% confidence interval (CI) of SCD and SCT, while the odds ratio along with 95% CI will be used to report the effect size for the association.

Synthetic methods

a) The NIH quality evaluation tool will be used to extract studies with acceptable methodological quality. The results will be displayed in a tabular manner, along with quotes/comments from the study.
b) The meta-analysis will incorporate the following:

i. The percentage of children and adolescents with SCD and SCT.
ii. Categorical variables used in subgroup analysis.

Risk of bias

Two independent co-authors will use the NIH Quality Assessment Tool for observational cohort and cross-sectional studies to assess the studies.[6] Where there is a disagreement, the senior co-author will re-assess the study, and his assessment will be used. The assessment tool has 14 criteria that range from whether the research question or objectives are clearly stated and, where applicable, if potential confounders are accounted for in the analysis. Each study will be assigned an overall good, fair, or poor rating. Also, we will add direct quotes from the study report to support the assessment. This will be cross-checked against the Cochrane tool of risk of bias assessment. Sensitivity testing using the include/exclude function will be applied to studies with extreme bias risk. Also, a funnel plot of all included studies will be used to assess publication bias.

Results

The study selection process will be depicted in a flow diagram following the PRISMA 2020 Statement guidelines and the PRISMA-P Checklist. A table detailing the search strategy employed across various databases, including text words, MeSH terms, and entry terms, will also be provided. The included studies will be summarized in another table. Quantitative data, such as pooled prevalence and regional prevalence, will be reported with their measure of uncertainty, such as 95% confidence intervals, p-values, relative weights assigned to studies and heterogeneity tests. The results will be presented in forest plots. Furthermore, a table showcasing the quality scores and risk of bias for each eligible study will be included. Sub-group analyses will be illustrated through forest plots, and sensitivity analyses conducted will be depicted in both figures and tables.

Study selection

The search results and numbers will be reported in a flow diagram.

Study characteristics.

A table will be used to summarize studies along with their characteristics.

Discussion

The results of the review will be interpreted and discussed under the following subheadings:

General interpretation, level of evidence including limitation of the review process and implication of the results for policy review, redistribution of resources and future research.

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