



Review article

Prevalence of Use of Herbal Medicines for the Treatment of Sickle Cell Disease in Africa: a Systematic Review and Meta-analysis

S. Awor^{a,*}, F. Bongomin^b, M.M. Kaggwa^c, F.P. Pebalo^a, D. Musoke^d^a Department of Obstetrics and Gynaecology, Faculty of Medicine, Gulu University, Gulu, Uganda^b Department of Microbiology, Faculty of Medicine, Gulu University, Gulu, Uganda^c Department of Psychiatry, McMaster University, Hamilton, Ontario, Canada^d Department of Pharmacology and Therapeutics, Faculty of Medicine, Gulu University, Gulu, Uganda

ARTICLE INFO

Keywords:

Herbal remedies use

Treatment

Sickle cell anaemia

Africa

Systematic review

ABSTRACT

Introduction: Several herbal medicines have been reported to ameliorate sickle cell disease (SCD) complications in many African communities. However, no comprehensive review has evaluated the use of herbal remedies for treating SCD crises. Therefore, this study aimed to determine the prevalence of the use of herbal medicines for the treatment of SCD in Africa.

Methods: Following registration of the review protocol with PROSPERO (CRD42022346755), searched PubMed, Embase, Africa Journal Online, and Web of Science databases using the keywords 'herbal medicine,' 'SCD,' and 'Africa' on 1st August 2022 for peer-reviewed articles without language restriction. We included articles that reported the prevalence of herbal medicine use for SCD treatment in Africa and excluded qualitative studies, letters to editors, case reports, and editorials. All included papers were assessed using the modified Newcastle-Ottawa quality assessment scale for observational studies. We used the random-effect model to calculate the pooled prevalence of herbal medicine use for SCD treatment with STATA 17.0.

Results: Overall, 142 research articles were identified. Of this, three cross-sectional studies involving 702 children with SCD from Uganda (n = 1) and Nigeria (n = 2) met the eligibility criteria and were included. Four hundred thirty-four individuals from the included studies used herbal medicines for the management of SCD. The prevalence of current herbal medicine use in individual studies ranged from 36.4% to 78.0%, with a pooled prevalence of 59% (95% confidence interval: 35.0–82.0, $I^2 = 97.68\%$, $P < 0.001$).

Conclusions: Almost three in five persons with SCD in Africa use herbal remedies as a form of treatment. However, there is limited data detailing the magnitude of the prevalence of use of herbal medicines for the treatment of SCD across different regions. Therefore, further studies are encouraged to explore the prevalence of use of herbal remedies for the management of SCD in Africa.

Background

Five percent of the world's population carried the genes for haemoglobin disorders in 2022 (Wastnedge et al., 2018; World Health Organization, 2022). The prevalence is higher in sub-Saharan Africa, with 20–30% in western and eastern Africa (Wastnedge et al., 2018; World Health Organization, 2022). Sickle cell disease (SCD) is one of the most common inheritable haematological disorders associated with the polymerisation of haemoglobin within the red blood cells, leading to sickling of the red blood cells under low oxygen tension, dehydration, and acidosis (Rees et al., 2010). The cost of screening for SCD ranges from \$3.07 to \$5.09 at point-of-care centres (Mvundura et al.,

2019). Treatment for SCD is not freely accessible in most countries in Africa (Okoh et al., 2019). It costs about \$16,810 annually per patient in the United States of America (Moore et al., 2000) and \$550 in Uganda (Independent Reporter, 2021).

Disease-modifying treatment for SCD, such as hydroxyurea, is limited in Africa (Opoka et al., 2020; Park et al., 2019). For example, hydroxyurea was introduced for treating SCD in Uganda in 2014 through a clinical trial (Anyanwu et al., 2016; Opoka et al., 2020; Park et al., 2019) and later made available for use in most sickle cell clinics in Uganda by 2020 (URN, 2020). As a result, hydroxyurea is the most common medication dispensed in hospitals across Africa to ameliorate the effects of SCD (DeBaun and Galadanci, 2022; Odame, 2022). It

* Corresponding author.

E-mail address: s.awor@gu.ac.ug (S. Awor).

reduces the number and severity of painful crises and the risk of blood transfusion and increases the production of foetal haemoglobin (Ofakunrin et al., 2020, 2021). However, it is also associated with neutropenia, bone marrow suppression, hepatic enzyme elevation, anorexia, nausea, vomiting, and reversible dose-dependent leucopenia (Ofakunrin et al., 2020, 2021). That requires close monitoring and dose adjustments (Ofakunrin et al., 2021), thus increasing the cost of care for patients with SCD.

Sickle cell disease is a life-long ailment associated with acute and chronic complications such as painful crises, osteomyelitis, chronic kidney disease, and infectious complications (DeBaun et al., 2022; Rees et al., 2010). For most patients, chemoprophylaxis, vaccination against infectious diseases, folate supplementation, and disease-modifying therapy with hydroxyurea remain the standard of care (Odame, 2022). With recent advances in medicine, gene editing and hematopoietic stem cell transplant are treatment options for a select group of patients (Booth et al., 2022). However, due to sickle cell medical treatment costs (Independent Reporter, 2021; Lubega et al., 2021; Mvundura et al., 2019; Okoh et al., 2019), hope for a cure (Ameh et al., 2012; Misra, 2013), wide availability with a long history of use within the communities (Ameh et al., 2012), and perceived fewer side effects (Lubega et al., 2021), herbal medicine is widely used in many African communities to ameliorate SCD effects.

Before the advent of hydroxyurea in Africa, people with SCD depended on supportive treatments from hospitals and herbal medicines at home (Ogwang et al., 2008; Okagu et al., 2021; Ouédraogo et al., 2019). Several medicinal plants have been identified that reactivate γ -gene transcription through different cellular systems (Pace and Zein, 2006) and increase the production of HbF to relieve the severity of SCD (Bianchi et al., 2009). Herbal medicines are plant parts like leaves, bark, roots, and flowers used to treat different ailments and improve life quality (NHS, 2022). The World Health Organisation (World Health Organization, 2013) has, over the recent past, attempted to make traditional and modern medicines complement each other. However, the only commercially available antisickling agent is *Niprisan* in Nigeria (Obodozie et al., 2010).

In Nigeria, *Niprisan* (made from pepper seeds, clove flower buds, caprium stem, sorghum leaves, and 'trona') (Obodozie et al., 2010; Wambebe et al., 2001) and *Cajanus cajan* (pigeon peas) (Akinsulie et al., 2005; Ekeke and Shode, 1985) are commonly used to treat SCD. These herbs have antisickling properties (Akinsulie et al., 2005; Wambebe et al., 2001). These pigeon peas, pepper, wild fruits, and sorghum are the staple foods of some communities in northern Uganda (Amone, 2014; Onen and Oryem-Origa, 2017). Perhaps that modifies the course of SCD and enables a higher chance of survival beyond 5 years of age. In western Cameroon, Euphorbiaceae plant species are used (Yembeu et al., 2022).

Sub-Saharan Africa has been endemic for using herbal medicines to treat SCD (Ameh et al., 2012; Cordeiro and Oniyangi, 2004). The common herbs used have antisickling properties (Imaga, 2010, 2013; Tchacondo et al., 2012; Towns et al., 2014). In addition, most herbs are used to prevent vaso-occlusive crises (Amoran et al., 2017). The documented prevalence of herbal medicine used to treat SCD ranges from 36.0% to 78.0% in Kampala and Lagos (Busari and Mufutau, 2017; Lubega et al., 2021; Oshikoya et al., 2008). However, this practice in other regions of Africa is unknown. Therefore, this study aimed to determine the prevalence of the use of herbal medicines for the treatment of SCD in Africa. Perhaps this will unlock new research areas into alternative treatments for SCD in Africa.

Methods

This review was conducted according to the Meta-analysis of Observational Studies in Epidemiology guidelines for systematic reviews and meta-analysis of observational studies (Brooke et al., 2021) and the Preferred Reporting Items for Systematic Reviews and Meta-analyses guideline (Page et al., 2021). It was registered by PROSPERO: CRD42022346755. Based on this, a review question was generated using the Condition, Context, and Population guidelines by the Joanna Briggs Institute (Munn et al., 2015). The condition was 'use of herbal medicine for the treatment of SCD,' the context was 'Africa,' and the population was 'individuals living with SCD.' Therefore, the research question was, 'What is the prevalence of the use of herbal medicines to treat SCD in Africa?' The following keywords were used to identify potential articles on 1 August 2022 from *PubMed*, *Embase*, and *Web of Science*: sickle cell, herbal medicine, and Africa. The search included papers from inception to 1 August 2022. The search strategy is presented in [Supplementary material](#).

All identified articles were entered into Endnote for screening and removal of duplicates. The screen adhered to the following criteria: (1) observational studies reporting the prevalence of herbal medicine use in SCD treatment in Africa, (2) in all languages, and (3) peer-reviewed. Case reports, editorial, and qualitative studies were excluded. Two authors independently screened the title and abstract of each article, and in case of any discrepancies, the third author made the final decision by consensus. The same team followed the same procedure for full-text review, risk of bias, and data entry. The risk of bias was assessed using the Newcastle-Ottawa quality assessment scale for observational studies. The data extracted from each article included: sample size, number of individuals using herbal medications to treat SCD, study design, study setting (country and city), and type of herbal medication used.

Statistical Analysis

Data analysis was performed using STATA version 17.0 (Stata Corp LLC, College Station, Texas, USA). Categorical data from the individual studies were summarised as frequencies and percentages and numerical continuous as mean, standard deviation, median, and interquartile range for parametric or non-parametric conditions. Heterogeneity across individual studies was assessed using Higgins's inconsistency Q statistics and reported as I^2 and P -value. A random-effect model meta-analysis was performed for pooled outcomes with I^2 of $\geq 50\%$, and fixed-effects models for pooled outcomes with I^2 of $< 50\%$. All results will be presented as forest plots. A systematic narrative synthesis was performed to complete the meta-analysis. A $P < 0.05$ was considered statistically significant for all hypotheses testing. Subgroup analysis was not performed, given the limited number of studies included. The regression-based Egger test and visual evaluation of contour-enhanced funnel plots were assessed for small-study effects and publication bias.

Results

We identified 142 research articles, screened them according to the objective, and excluded 132. Ten full-text articles were retrieved and screened, and seven were excluded. Finally, three articles examining the prevalence of herbal medicine used for treating SCD in Africa were included in this review. A summary of the data extraction processes is outlined in [Figure 1](#).

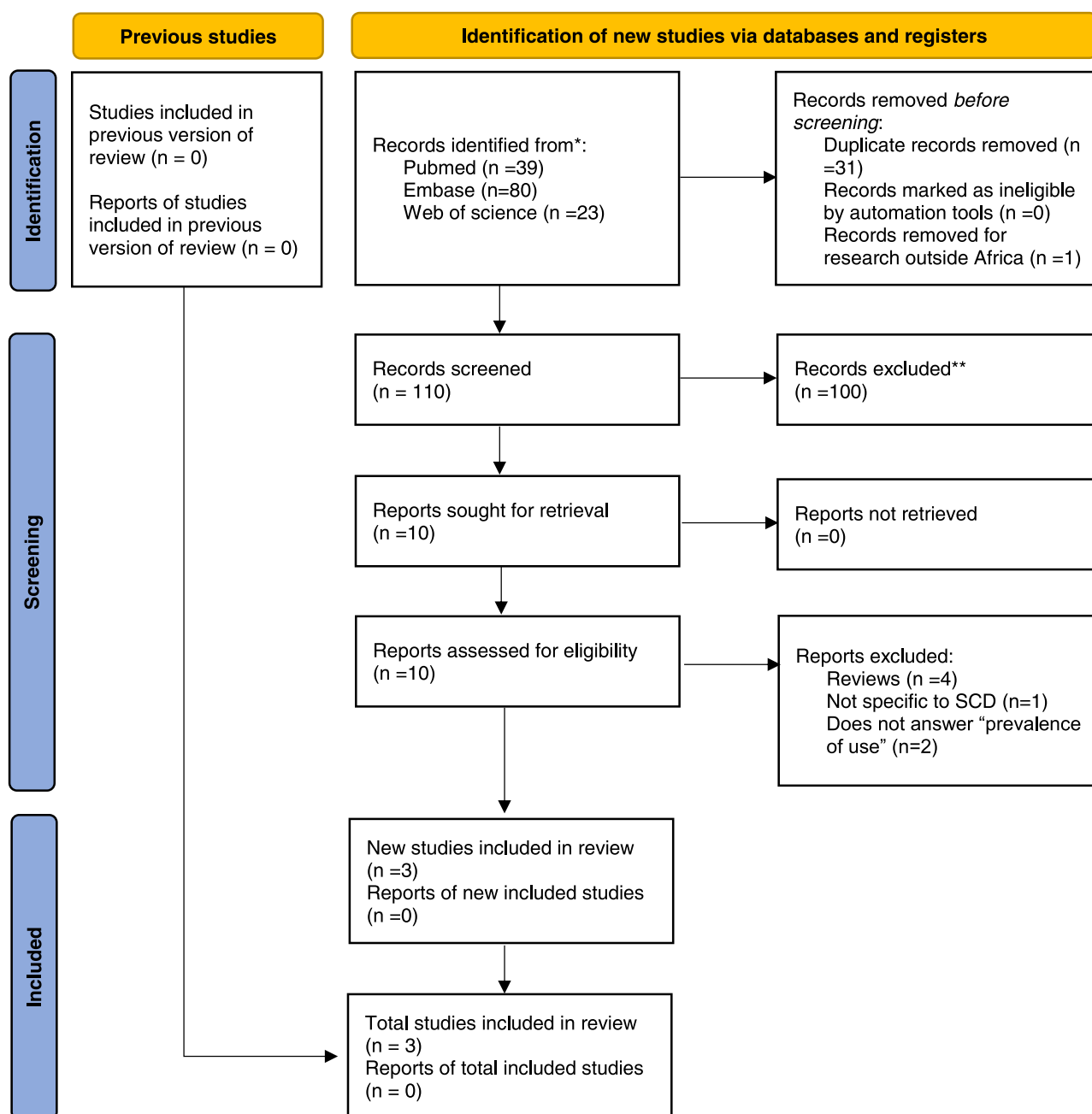


Fig. 1. Flowchart showing the data extraction process [1]. SCD, sickle cell disease.

Types of Herbal Remedies Used for the Treatment of Sickle Cell Disease in Africa

The typical herbal remedies used in different parts of Africa are summarised in Table 1. Different regions of Africa use different extracts. Most of the herbal extracts' effects are dose-dependent. Most exhibit antisickling activities, with a few adding vasorelaxants, anti-fibrinolytic, and neoplastic effects. That may require a deeper look into the safety of the different herbal extracts, especially the zanthoxyloids, which are widely used.

Summary of the Studies Excluded From This Review

Seven studies were excluded (Ameh et al., 2012; Amoran et al., 2017; Cordeiro and Oniyangi, 2004; Imaga, 2010, 2013; Tchacondo et al., 2012; Towns et al., 2014). These were either reviews (Ameh et al., 2012; Cordeiro and Oniyangi, 2004; Imaga, 2010, 2013) or not specific to SCD (Amoran et al., 2017; Towns et al., 2014). One study elaborated more on the different medicinal plants used to treat SCD and not their prevalence of use among people with SCD (Tchacondo et al., 2012).

Table 1

Types of herbal medicines used for the treatment of sickle cell disease in Africa.

Authors	Setting	Type of herb used	Effects of the herbs used
Kitadi et al. (2020)	Kikwit, Democratic Republic of the Congo	<i>Justicia secunda</i> , <i>Rungia grandis</i> , <i>Alternanthera bettzickiana</i> , <i>Annona senegalensis</i> , <i>Ceiba pentandra</i> , <i>Carica papaya</i> , <i>Alchornea cordifolia</i> , <i>Bridelia ferruginea</i> , <i>Vigna unguiculata</i> , <i>Milletia laurentii</i> , <i>Hypoxis angustifolia</i> , <i>Leocus africanus</i> , <i>Dissotis brazzae</i> , <i>Albizia ferruginea</i> , <i>Treculia africana</i> , <i>Ficus asperifolia</i> , <i>Ficus tremula</i> , <i>Bougainvillea</i> spp., <i>Hymenocardia acida</i> , <i>Gardenia leopoldiana</i> , <i>Morelia Senegalensis</i> , <i>Stipularia africana</i> , <i>Sterculia bequaertii</i> , <i>Ficus sycomorus</i>	Aqueous extracts of 18 plants (78%) exhibit a change in the shape of a sickled red blood cell into a normal one with a normalised rate of at least 70%.
Ramde-Tiendrebeogo et al. (2014)	Ouagadougou, Burkina Faso	<i>Zanthoxylum heitzii</i>	Moderately inhibits red cells from sickling. Induces vasorelaxation on blood vessels
Nanfack et al. (2013)	Batchingou, Cameroon	<i>C pentandra</i> and <i>Quassia africana</i>	Has antisickling property that is dose-dependent. Inhibits fibrinolytic activities in addition to their antisickling activity.
Nsimba et al. (2013a, 2013b)	Kinshasa, DR Congo		
Adejumo et al. (2012)	Ogun state, Nigeria	<i>Moringa oleifera</i>	Has antisickling activity which is concentration-dependent.
Adejumo et al. (2011)	Ogun state, Nigeria	<i>P alliacaea</i> , <i>C ambrosioides</i> , and <i>E utile</i>	<i>E utile</i> , <i>C ambrosioides</i> , and <i>P alliacaea</i> demonstrated antisickling effects. <i>C ambrosioides</i> leaves had a significantly higher antisickling activity while <i>P alliacaea</i> root had the least.
Adejumo et al. (2010)	Ogun state, Nigeria	<i>P zeylanica</i> and <i>U chamae</i>	Has antisickling activity that is concentration-dependent.
Ouattara et al. (2009)	Ouagadougou, Burkina Faso	<i>Fagara zanthoxyloides</i>	Phenolic compounds isolated, and synergies exist between the different aromatic compounds concerning the antisickling activity
Egunyomi et al. (2009)	Ibadan, Nigeria	Two frequently used recipes consisting of roots, barks, and leaves of recipe 1 (<i>Uvaria chamae</i> , <i>Euphorbia laterifolia</i> , <i>Securidaca longepedunculata</i> , <i>Mangifera indica</i> , <i>Vitellaria paradoxa</i> , <i>Calliandra portoricensis</i> , <i>Zanthophyllum xanthoxyloides</i> , <i>Terminalia superba</i> , <i>Khaya ivorensis</i> , <i>Olex subscorpoidea</i> , <i>Microdesmis keayana</i> , <i>Cassia fistula</i> , <i>Lophira alata</i> Banks, <i>Uvaria afzeliit</i> , <i>Detarium microcarpum</i> , <i>Tetrapleura tetraptera</i> , <i>Alstonia boonei</i> , <i>Plumbago zeylanica</i> , <i>Rauvolfia vomitoria</i> , <i>Gongronema latifolium</i> , <i>Lannea welwitschii</i> , <i>Citrus medica</i> , <i>Anogeissus leiocarpus</i> , <i>Chasmanthera dependens</i> , <i>Xylopia aethiopica</i> , <i>Terminalia</i> spp., <i>Mondia whitei</i>) and recipe 2 (<i>Vernonia amygdalina</i> , <i>Garcinia cola</i> , <i>Mangifera indica</i> , <i>Terminalia catappa</i> , <i>Newbouldia laevis</i> , <i>Z xanthoxyloides</i> , <i>Capsicum frutescens</i>)	Phytochemical screening showed the presence of alkaloids, saponins, cardiac glycosides, and tannins in both recipes. However, the presence of anthraquinones was recorded only in recipe 1 while it was absent in recipe 2
Mpianaa et al., 2008	Lubumbashi city, DR Congo	<i>Bombax pentadrum</i> , <i>Ficus capensis</i> , and <i>Ziziphus mucronata</i>	Flavonoids, anthocyanins, and terpenoids are present in all. Have antisickling activity
Ibrahim et al. (2007)	Zaria, Nigeria	<i>Hymenocardia acida</i>	Has antisickling activity
Moody et al. (2003)	Ibadan, Nigeria	<i>Cissus populnea</i>	Has antisickling activity

Summary of Studies Included in the Review

Only three studies from two African countries (Nigeria [Busari and Mufutau, 2017; Oshikoya et al., 2008] and Uganda [Lubega et al., 2021]) with 702 participants reported the prevalence of herbal medicine use among people with sickle cell in Africa. In Kampala, 77.6% had ever used herbal medicines while 61.2% were using were current users to treat SCD by 2021. The caregivers and patients of SCD reported faster resolution of symptoms with fewer side effects compared to conventional treatments and other complementary medicines available in Mulago National Referral Hospital (Lubega et al., 2021). In Lagos, Nigeria, 36% of the patients with SCD who presented at Lagos State Teaching Hospital used herbal medicines besides other available treatments by 2007 (Oshikoya et al., 2008) and increased to 78.0% by 2017 (Busari and Mufutau, 2017). They also reported fewer side effects (Busari and Mufutau, 2017; Lubega et al., 2021; Oshikoya et al., 2008) and a lower treatment cost than the conventional therapy for sickle cell provided at the hospital (Busari and Mufutau, 2017), as outlined in Table 2.

Pooled Prevalence of Herbal Medicine Use Among Persons With Sickle Cell Disease

The pooled prevalence of herbal medicine use among people with SCD was 59% (95% CI: 35.0–82.0, $I^2 = 97.68$, $P < 0.001$) (Fig. 2).

Assessment of Publication Bias

The funnel plot is grossly asymmetric, showing a significant publication bias across the three studies, with only 1 study by Lubega et al. (2021) under the funnel (Fig. 3). Therefore, sensitivity analysis was impossible to conduct.

Discussion

In this systematic review and meta-analysis of three studies with 702 persons with SCD across two African countries, about three in five study participants used herbal medicines. This is an underrepresentation of the

Table 2
Prevalence of herbal medicine use among people with sickle cell disease in Africa.

Authors	Setting	Study design	N	Current use n (%)	Type of herbal medicine used
Lubega et al. (2021)	Kampala, Uganda	Cross sectional	384	235 (61.2)	Mixture of different types (not specified); common mixture in Uganda is <i>Zanthoxylum chalybeum</i> (Ogwang et al., 2008)
Busari and Mufutau (2017)	Lagos, Nigeria	Cross sectional	200	156 (78.0)	Mixture of different types (Aloe vera, Forever living, Ginger, Garlic GNLD, Jobelyn, Tianshi, Lemon grass, Ginseng, Ciktavit)
Oshikoya et al. (2008)	Lagos, Nigeria	Cross sectional	118	43 (36.4)	Mixture of different types (Ginger, Herbs, Jobelyn product, Yem-Kem product, Special diet/Nutritional therapy, Lemon grass, Aloe vera, Forever living products)

actual herbal medicine used for the treatment of SCD in Africa, because the use of herbs has been endemic (Ameh et al., 2012; Tchacondo et al., 2012). Hydroxyurea has only been introduced recently in some African countries; therefore, access to it is still limited (Opoka et al., 2017), and Niprisan (herbal treatment for sickle cell) is officially dispensed to sickle cell patients in Nigeria (DailyTrust_reporter, 2022; Wambebe et al., 2001). Some herbal remedies are advertised and sold in marketplaces and communities without regulation (Amaran et al., 2017; Egunyomi et al., 2009; Lubega et al., 2021). These practices mask the true prevalence of the use of herbal remedies for the treatment of SCD in Africa.

Many different herbal extracts are used in different parts of Africa. For example, frequently advertised herbal treatments for SCD in Uganda and Nigeria contain *Zanthoxylum* species (Ogwang et al., 2008; Okagu et al., 2021). Nigeria also uses root extracts of the *Cissus populnea* plant in the south (Ameh et al., 2012; Moody et al., 2003), and leaves, stems, roots, and fruits of *Plumbago zeylanica* and *Uvaria chamae* in other parts of the country (Adejumo et al., 2010; Ameh et al., 2012). *Alchornea cordifolia*, *Alternanthera bettzickiana*, *Annona senegalensis*, *Dissotis brazzae*, *Hypoxis angustifolia*, and *Justicia secunda* are used in Congo and Togo (Kitadi et al., 2020; Tchacondo et al., 2012). *Euphorbiaceae* is the dominant family plant used in western Cameroon (Yembeau et al., 2022).

Almost all the articles reviewed reported faster resolution of symptoms with herbal remedies compared to conventional treatment for sickle cell (Busari and Mufutau, 2017; Lubega et al., 2021; Oshikoya et al., 2008). That could be because the plants contain phytochemical compounds (especially polyphenols and alkaloids), which may exert their pharmacological effects through antioxidant and antisickling activities (Egunyomi et al., 2009; Imaga, 2010; Kitadi et al., 2020; Yembeau et al., 2022). They also stabilise red blood cell membranes and reduce the haemolysis rate (Imaga, 2010). Some plant extracts have been associated with reduced thrombin activity and prolonged plasma clotting time (Nsimba et al., 2013b). In addition, the extracts may decrease the activity of both tissue-type plasminogen activator (t-PA), urokinase-type plasminogen activator (u-PA), and plasminogen activator inhibitor type-1 (PAI-1) (Nsimba et al., 2013b). Only one study in Lagos, Nigeria (Oshikoya et al., 2008) reported some clients discontinuing herbal medicine to treat sickle cell due to severe unwanted side effects.

While in many African countries patients with SCD look for herbal medicine in their communities, in Nigeria and Asia, these medicines are prescribed and dispensed to them in health care centres by trained professionals (Chen et al., 2018; DailyTrust_reporter, 2022; Gour et al., 2022); hence, their access and use are widespread.

Limitations and Strengths of the Study

Although herbal medicines are widely used in Africa, they are rarely documented. Therefore, we could not perform a sensitivity analysis because of the few studies identified in this review with few participants in only two cities in Africa. These are people living in cities with better access to health care. There were no studies done in rural or peri-urban areas.

Researchers’ Impression About the Quality of Evidence Presented

There were only three articles included in this review with only 702 participants from two African countries. This is not representative of the whole African continent. Besides, before the advent of Western medicine, Africans depended on herbal remedies. I expected a lot more than three articles with millions of participants. Perhaps the studies documenting the prevalence of the use of herbal medicines in Africa never get to be published due to publication bias.

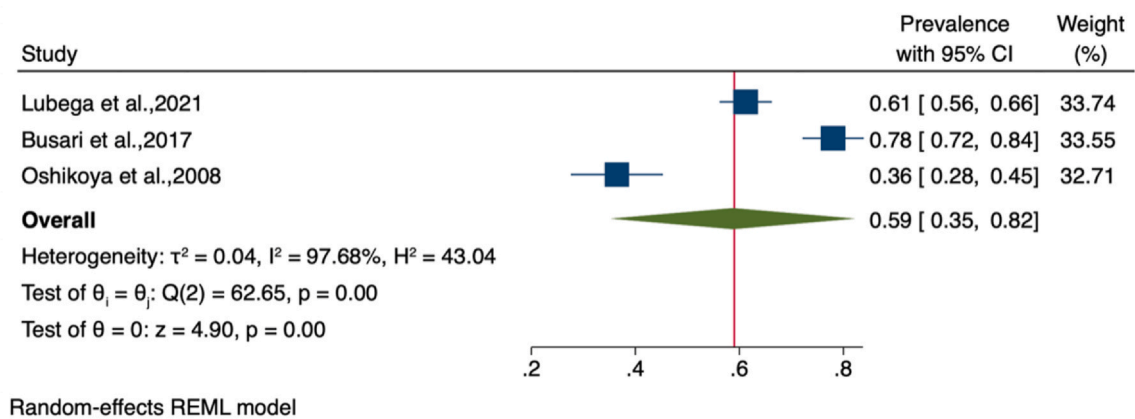


Fig. 2. Forest plot for herbal medicine used to treat sickle cell disease in Africa. REML, Restricted Maximum Likelihood.

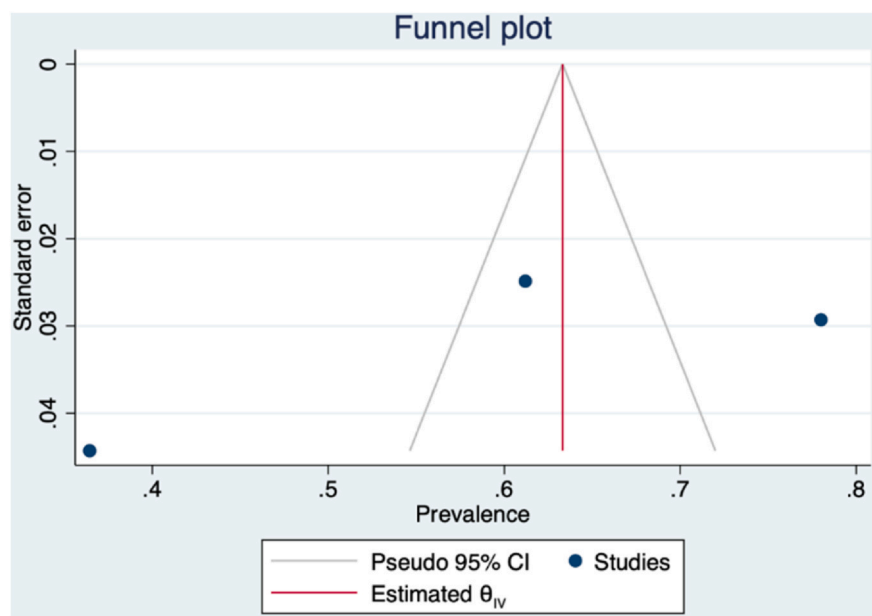


Fig. 3. Funnel plot for publication bias of herbal medicine used to treat sickle cell disease in Africa.

Conclusion

Several medicinal plants in Africa have antisickling properties. However, limited data are available on the prevalence of the use of these herbs for the treatment of SCD. The pooled prevalence of the use of herbal medicines for the treatment of SCD from three studies in Africa consisting of over 700 individuals with SCD was 59%. This study confirms the high prevalence of herbal medicine use among persons with SCD in Africa. We recommend further prospective and interventional studies to investigate the safety and efficacy of these herbal medicines in controlled clinical studies.

Implication of Findings

This is a wake-up call to African researchers to document the prevalence of the use of herbal medicines for the treatment of SCD in their communities. Future studies should be encouraged to document the types and prevalence of the use of the different herbal remedies for treating sickle cell in the different regions of Africa. That will enable people with SCD to be aware of alternative treatments within their environment or communities, and the researchers will be able to identify the best available treatment for SCD in Africa.

Ethical approval

Not applicable. Registered in Prospero CRD42022346755.

Standards of reporting

Followed the Preferred Reporting Items for Systematic Review and Meta-Analysis strategy.

Author contributions

Silvia Awor drafted the research protocol, registered it in Prospero, did data screening processes, and drafted the manuscript. Felix Bongomin provided expert advice on the subject, did data screening and analysis, and reviewed the manuscript. Mark Mohan Kaggwa did data extraction and reviewed the manuscript. Francis Pebolo Pebalo proofread and reviewed the manuscript. David Musoke guided in the protocol writing and reviewed the manuscript.

Acknowledgements

Declared none.

Financial support statement

There was no funding for this project.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.hermed.2023.100735.

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