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ORIGINAL ARTICLE

Scoping Review of Predisposing Factors Associated with Sensorineural Hearing Loss in Sickle Cell Disease

Examen de la Portée des Facteurs Prédisposants Associés à la Perte Auditive Neurosensorielle dans la Drépanocytose

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ABSTRACT

PURPOSE: Sickle cell disease (SCD) is a genetically inherited red blood cell disorder that affects people all over the world but is more common among blacks of African ancestry than other races. The condition is linked to sensorineural hearing loss (SNHL). This scoping review aims to evaluate studies that reported SNHL in SCD patients and to identify demographic and contextual risk factors for SNHL in SCD patients.

METHODS: We conducted scoping searches for relevant studies in PubMed, Embase, Web of Science, and Google Scholar. All articles were evaluated independently by two authors. The checklist Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) was used. SNHL was detected at hearing levels above 20 decibels.

RESULTS: In terms of methodology, the studies reviewed were diverse, with 15 being prospective and four being retrospective. Fourteen of the 19 articles chosen from 18,937 search engine results were case-control studies. Sex, age, foetal haemoglobin (HbF), SCD type, painful vaso-occlusive crisis (PVO), blood parameters, flow-mediated vasodilation (FMV), and hydroxyurea use were all extracted. Few studies investigated SNHL risk factors with noticeable knowledge gaps. Age, PVO, and certain blood parameters appear to predispose to SNHL, whereas decreased FMV, the presence of HbF, and the use of hydroxyurea appear to have an inverse relationship with the development of SNHL in SCD.

CONCLUSION: There is a clear gap in the existing literature regarding the knowledge of demographic and contextual risk factors that is required for the prevention and management of SNHL in SCD. **WAJM 2023; 40(2): 209–216.**

Keywords: Sensorineural hearing Loss; Sickle cell disease; Determinants, Risk factors.

RÉSUMÉ

OBJECTIF: La drépanocytose est une maladie héréditaire des globules rouges qui touche des personnes partout dans le monde, mais qui est plus fréquente chez les Noirs d'ascendance africaine que dans les autres races. Cette maladie est liée à la perte auditive neurosensorielle (SNHL). L'objectif de cette revue est d'évaluer les études qui rapportent une perte auditive neurosensorielle chez les patients atteints de DICS et d'identifier les facteurs de risque démographiques et contextuels de cette perte auditive chez les patients atteints de DICS.

MÉTHODES: Nous avons effectué des recherches pour trouver des études pertinentes dans PubMed, Embase, Web of Science, et Google Scholar. Tous les articles ont été évalués indépendamment par deux auteurs. La liste de contrôle Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) a été utilisée. Le SNHL a été détecté à des niveaux d'audition supérieurs à 20 décibels.

RÉSULTATS: En termes de méthodologie, les études examinées étaient diverses, 15 étant prospectives et quatre rétrospectives. Quatorze des 19 articles choisis parmi les 18 937 résultats du moteur de recherche étaient des études cas-témoins. Le sexe, l'âge, l'hémoglobine fœtale (HbF), le type de DICS, la crise vaso-occlusive douloureuse (PVO), les paramètres sanguins, la vasodilatation médiée par le flux (FMV) et l'utilisation de l'hydroxyurée ont tous été extraits. Peu d'études se sont penchées sur les facteurs de risque du SNHL, avec des lacunes notables dans les connaissances. L'âge, la PVO et certains paramètres sanguins semblent prédisposer au SNHL, tandis qu'une diminution de la FMV, la présence d'HbF et l'utilisation d'hydroxyurée semblent avoir une relation inverse avec le développement du SNHL chez les patients atteints de DICS.

CONCLUSION: Il existe une lacune évidente dans la littérature existante en ce qui concerne la connaissance des facteurs de risque démographiques et contextuels qui sont nécessaires pour aider à la prévention et à la gestion du SNHL dans la DICS. **WAJM 2023; 40(2): 209–216**

Mots clés: Perte auditive neurosensorielle; Drépanocytose; Déterminants; Facteurs de risqué.

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Abbreviations: FMV, Flow Mediated Vasodilation; **HbF,** Foetal haemoglobin; **HbSS,** Sickle Cell Haemoglobin; **PRISM-ScR,** Systematic Reviews and Meta-Analyses extension for Scoping Reviews; **PVO,** Pain Vaso-Occlusive crisis; **SCD,** Sickle Cell Disease; **SNHL,** Sensorineural Hearing Loss; **WBC,** White Cell Count.

INTRODUCTION

Sickle cell disease (SCD) is a genetically inherited red blood cell disorder that affects people all over the world but is more common in people of African ancestry. In Africa, Europe, and the rest of the world, the estimated prevalence of SCD is 1.12%, 0.04%, and 0.11%, respectively.[1]Nigeria, with a SCD prevalence of 2.28–3%[2-4,] has one of the highest disease burdens. If not treated properly, SCD can lead to chronic haemolytic anaemia, an increased risk of infections, a vaso-occlusive crisis, and end-organ damage. The cochlea is one of the end-organs that can be damaged. A vaso-occlusive event affecting the cochlea's end arterial supply can cause a wide range of hearing impairments, particularly high-frequency sensorineural hearing loss.[5] Individuals who have the sickle cell trait (SCT) are typically clinically stable given their heterozygous genetic formation. However, research on the relationship between SCD and hearing loss is still limited.

The literature supports a link between auditory impairment and SCD.[4,7–13] According to a recent systematic review and meta-analysis,[14] the overall prevalence of SNHL was 26.3% in adults and 19.3% in children with SCD. The coexistence of SCD and auditory impairment is likely to have a negative impact on health-related quality of life. Poor academic achievement, and social and behavioural problems are all consequences of childhood hearing loss.

Knowledge of the associated risk factors for SNHL in SCD patients is essential for effectively developing policies for early screening in children and regular screening in adults to detect and manage sensorineural hearing deficits in all SCD individuals. A scoping rather than a systematic review strategy was used due to a perceived lack of studies on the risk factors of SNHL in SCD patients. As a result, the purpose of this scoping review was to identify individual demographic and contextual risk factors for SNHL in SCD patients.

SUBJECTS, MATERIALS AND METHODS

The scoping review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guideline[15] and the Arksey and O'Malley[16] methodological framework. The steps involved in this review were the following: determination of the purpose of the study, identification of the potential studies to include, screening and selecting studies for inclusion, extracting data, collecting and summarising the results, and synthesising the review's findings.

The scoping review was adopted to provide a view of the available literature on the risk factors of SNHL in SCD and identify knowledge gaps. Therefore, an assessment of the risk of bias in the literature used in this review was not performed.[16]

Eligibility Criteria for Inclusion

1. Studies that included data on the individual demographic and concomitant risk factors that relate to SNHL in SCD patients.
2. The studies that included both children and adults from different regions of the globe.
3. Prevalence studies with focus on predictors or risk factors or determinants of SNHL.
4. Studies that compared SNHL in SCD patients and patients with normal genotype (AA).
5. Studies that detected SNHL at above 20 decibels.

The outcome of interest for inclusion was the presence of SNHL assessed with pure tone audiometry and tympanometry. The 20-decibel loss was used as a cut-off due to the WHO standard and also due to the involvement of both children and adult age groups in this review.

Identifying Relevant Studies

The search for articles was limited to English-language literature. Using PubMed, Embase Ovid, Web of Science, and Google Scholar, searches were conducted for published studies that reported findings on Sickle Cell Disease, Sensorineural Hearing Loss, and Risk Factors. These databases were searched for studies published between January 1969 and September 2022 on predictors or risk factors of SNHL in SCD patients. The text words used in the key term search strategy were "sickle cell disease", "sensorineural hearing loss", "determinants", "risk factors" and "predictors". In addition, we searched some reference lists of relevant articles to find additional relevant literature. The terms used and the search steps are detailed in Supplement Tables S1 and S2. In addition, we removed duplicate publications from the databases.

Study Selection

This review included articles that reported potential risk factors for SNHL in SCD patients. Case reports of SNHL in SCD were not considered. Titles and abstracts were extracted and reviewed independently by two authors (TSI and PUI). Full-text articles that met the inclusion criteria were evaluated independently by the two authors (TSI and PUI), and those that were unanimously accepted were included, while those that were rejected were excluded. The ones on which the authors disagreed had to be reanalysed jointly for merits and decisions. It was agreed that if the two authors could not reach an agreement, a third party (EON) would break the tie for the final decision on acceptance or rejection. Eventually, there was no such situation warranting the third author's invitation.

Data Entry

The lead author extracted data on SNHL risk factors in SCD from eligible selected articles and had them reviewed by a second author (PUI). These data were entered and summarised in Microsoft Excel version 2021. This form contained information on authorship, year of publication, study objectives, study type, and relevant patient information. Patients' sex (male/female), age (young and old), foetal haemoglobin (HbF), SCD type, painful vaso-occlusive crisis (PVO), frequency of hospitalisation, blood parameters (haematocrit levels, platelet levels, and white cell counts), flow-mediated vasodilation (FMV), and use of hydroxyurea are all relevant information.

Collating, Summarising and Reporting the Findings

From the included studies, narrative accounts of risk factors for SNHL in SCD were compiled and summarised. Because the majority of the studies did not use the same statistical tool to correlate potential risk factors of SNHL in SCD, the data were thematically synthesised in order to project the research findings, identify research gaps, and make recommendations for future research. To alleviate the narrative account, the authors synthesised the reported risk factors and classified them as protective, non-protective, or equivocal.

RESULTS

The electronic database searches yielded a total of 18,935 hits, with two additional articles discovered from a reference list of relevant articles (Figure 1). After duplicates and title articles lacking information on SNHL in SCD patients were removed, 1895 abstracts were screened for eligibility. Thirty-five full-text articles met the inclusion criteria; however, six case reports and ten articles that did not analyse potential risk factors were excluded.

The final product of a thorough search of the literature in accordance with the inclusion criteria and guidelines as stated in the methodology and study objectives yielded 19 articles.[5, 8–10,12,13–17,28–29] The publication years of the 19 articles ranged from 1973 to 2020. There were fifteen prospective studies[5,8–10,12,18–23,25,26,28,29] and four retrospective studies.[13,17–25,28] There were fifteen case-controlled studies[8–10,12,13,17–25] and four cohort studies.[17,27–29] There was no randomised controlled trial. The details of the relevant information associated with the 19 articles selected for this scoping review are shown in Table 1.

Risk Factors for SNHL in SCD as assessed by the Authors

Sex: Only two studies[8,13] did not analyse the relationship between sex and SNHL in SCD. The rest of the studies did not observe a statistically significant difference between the male and female sexes of SCD with SNHL. Aderibigbe *et al*[5] observed that the female patients' hearing loss was more severe than their male counterparts, but this difference was not statistically significant. Also, Al Okbi[18] observed a preponderance of female over male patients with SNHL, but this difference was not significant. In the Mgbor *et al*[9] study, more male than female children were observed with SNHL, and similarly, this difference was not statistically significant.

Age of Patient: Of the 19 studies, 17 were analysed for the relevance of age as a factor of SNHL in SCD, but only four studies[5,8,18,27] returned significant findings. They discovered that SNHL was more common in older patients recruited for the study and tended to worsen with age. However, Vincent *et al*[27] observed a positive correlation between age and hearing loss in the left ear only. The age groups of patients recruited by all four studies fell between 15 and 56 years of age. They were all case-control studies, with a sample size of 46 for total SCD in the study by Al Okbi *et al*[18] and Aderibigbe *et al,*[5] and 42 and 29, respectively, for controls. Onakoya *et al*[8] had a higher number of cases (167) than controls (100). Onakoya *et al*[8] and Al Okbi *et al*[18] observed more SCD patients with SNHL (68 and 17, respectively) than Aderibigbe *et al.*[5,6] The remaining 14 studies that analysed the effect of age on SNHL in SCD patients did not observe any difference when the ages of those with SNHL were compared with those without. These studies included infants as young as seven months old.

PVO-crisis (Painful Vaso-occlusive Crisis): Seven[13,20,22,26,27,29] of the 19 studies examined the effect of PVO-crisis. Five studies[13,20,22,26,29] found a link between PVO-crisis presence and SNHL in SCD. Odetoyinbo *et al*[13] discovered a significant (p 0.05) relationship between the incidence of hearing loss and age at the onset of PVO crisis. Al Jabr *et al*[20] observed that the average number of hospital admissions due to PVO crises per year for the last 10 years in SCD patients with SNHL was significantly higher than controls (p 0.05). Al-Dabbous *et al*[22] observed a significant p value of 0.004 between SNHL patients who had their first PVO crisis at 6 years of age in contrast with SCD patients without SNHL. Lago *et al*[26] observed that all of the SCD patients with SNHL, compared with 62% of SCD patients without SNHL, had PVO crises in the last 12 months of the study. Solomon *et al*[29] (conference proceeding) using bivariate correlation analysis and a multivariate regression model observed a significant correlation (OR, 2.106; 95% CI, 0.019–0.598; p = 0.001) between PVO crisis and SNHL in SCD patients. Conversely, two articles established no relationship between the PVO crisis and the occurrence of SNHL. Onakoya *et al*[8] did not observe a difference in the frequency of PVO crises per year and hearing loss (p = 0.05). The mean number of crises per year from the study was 4.13.4. Similarly, Vincent *et al*[26] used the number of crises per year, and

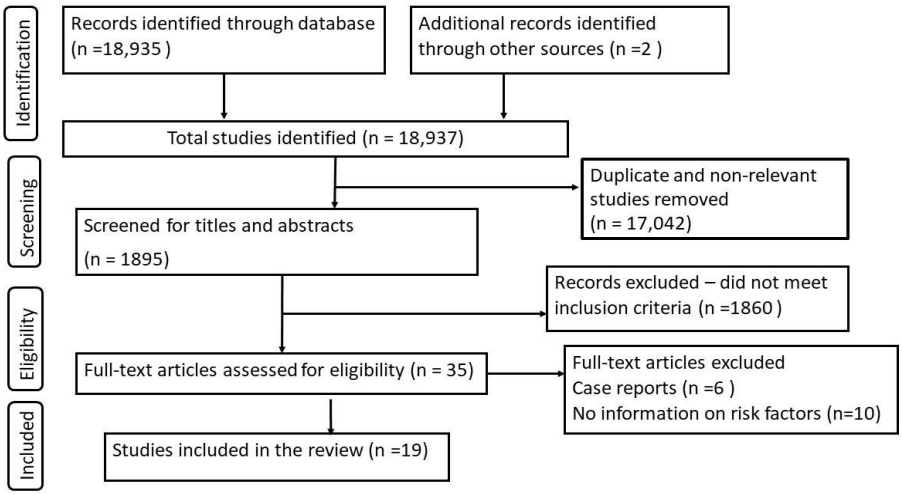

Fig. 1: Flow Chart of the Studies Identified and Selected for the Scoping Review.

Table 1: Summary of Articles Selected

Author/Year	Aim of Study	Sample (n)	Controls (n)	Risk Factors	Outcome
Aderibigbe *et al*[5]/ 2005	Presence and severity of SNHL in SCA patients	46	42	Sex, Age	Females and older age were more predisposed
Onakoya *et al*[8] 2002	Pattern of hearing loss and to identify any correlation with painful vaso-occlusive crisis among adultswith SCD	167	100	Age, PVO crisis	SHNL worsened with increasing age, no difference was observed with PVO
Mgbor *et al*[9]/ 2004	Prevalence and pattern of SNHL in Nigerian children with SCD	52	52	Sex	More male children had SNHL
Kikuhe *et al*[10] /2019	Prevalence, pattern and associated factors of hearing loss among Ugandan children with sickle cell anaemia	132	132	Sex, Age	No association was observed
Taipale *et al*[12]/ 2012	Prevalence of hearing loss and ontological findings among children with SCD in Luanda, Angola	25	28	Sex, Age	No association was observed
Odetoyinbo *et al*[13]/ 1987	Incidence and pattern of hearing loss among homozygous SCD patients	56	30	Age, PVO crisis	No association with age but there was with PVO crisis
Farrell *et al*[17]/ 2018	Audiology results in children with SCD and the prevalence and sequelae of SNHL.	181	Na	Sex, Age	Sex and Age did not influence SNHL in SCD
Al Okbi *et al*[18]/ 2011	Prevalence and pattern of hearing loss in Omani patients with SCD	46	29	Sex, Age, HbF, Blood parameters	More females with SNHL and older age group were more predisposed to SNHL, no association was observed with HbF and Hemo level
Ajulo *et al*[19]/ 1993	Incidence of SNHL in the UK	52	36	Sex, Age	No difference was observed
Al Jabr *et al*[20]/ 2016	Prevalence of SNHL in patients with sickle cell disease with sex and age but with PVO	40	40	Sex, Age, PVO	No difference was observed
Todd *et al*[21]/ 1973	Incidence of SNHL in a group of patients with SCD	83	83	Sex, Age, Blood parameters	No association was observed with sex, age, and Hemo level
Al-Dabbous *et al*[22]/ 1996	Prevalence of SNHL in SCD patients	100	100	Sex, Age, Blood parameters, PVO crisis, HBF	No association was observed with age, sex, and Hemo level but there was with PVO crisis and the presence of HbF
Piltcher *et al*[23]/ 2000	Prevalence of SNHL among HBSS from southern Brazil	28	28	Sex, Age,	No association was observed
Jovanovic-Bateman *et al*[24]/ 2006	Incidence of SNHL in SCD patients	79	40	Sex, Age,	No association observed
Schopper *et al*[25]/ 2019	Prevalence of hearing loss among children with SCD	189	244	Sex	No association was observed
Lago *et al*[26] /2018	Prevalence of SNHL in children and adolescents with SCD and its association with endothelial dysfunction	52	44	Sex, Age, Blood parameters, PVO crisis, HbF, use of hydroxyurea, FMV	No association was observed with sex, age, Hemo level, presence of HbF, and use of hydroxyurea but there was with PVO crisis and FMV

Table 1: Summary of Articles Selected

Author/Year	Aim of Study	Sample (n)	Controls (n)	Risk Factors	Outcome
Vincent *et al*[27]/ 2019	Prevalence of SNHL in adult SCD patients in Lagos	34	na	Sex, Age, PVO crisis	No association was observed for age and PVO crisis but present in age
Towerman *et al*[28]/ 2019	Prevalence and nature of hearing loss in a referred cohort of children with SCD	81	na	Sex, Age	No association was observed
Solomon *et al*[29cp]/ 2020	Identify risk factors of SNHL among children with SCD in Zaria, Nigeria	125	na	Sex, Age, blood parameters, PVO crisis	No association observed with sex and age but was with WBC and platelet level and PVO crisis

na, Not available; FMV, Flow mediated vasodilation; PVO, Painful vaso-occlusive crisis; HbF, Foetal haemoglobin; cp, conference proceeding.

most of the study participants (86.1%) had 3 crises per year.

Blood Parameters: The influence of blood parameters such as haematocrit levels, white blood cell (WBC) levels, and platelet counts was examined in only five studies[18,21,22,26,29] in this review. Al Okbi *et al,*[18] Todd *et al,*[21] Al-Dabbous *et al,*[22] and Lago *et al*[26] found no significant difference in haemoglobin levels and irreversibly sickle cell count between SNHL patients and controls. Solomon *et al*[29] studied WBC and platelet count rather than haematocrit levels and found that high levels of these blood parameters were risk factors for SNHL in SCD (odds ratio [95% confidence interval] = 1.035 [1.020–1.050] and 1.209 [1.070-1.365], respectively; p <0.01).

Foetal Haemoglobin: Three studies,[18,22,26] all in SCD patients, focused on the relationship between HbF and SNHL. Two studies[18,26] included children and adult participants, while one[22] assessed adults only. Al-Dabouss *et al*[22] observed a strong inverse relationship between the presence of HbF and SNHL in SCD patients (p = 0.008). The study inferred that HbF protects against SNHL and other complications of SCD. However, studies by Al Okbi et al.[18] and Lago *et al*[26] found no link between HbF and SNHL in SCD.

Hydroxyurea: The study by Lago *et al*[26] is the only study in this scoping review that considered the effect of hydroxyurea as a possible risk factor for SNHL in SCD. It established no direct relationship ([OR [95% CI] = 0.153 [0.022–1.053]; p = 0.056) in SCD but inferred that it could offer some protection to the integrity of the endothelium of the cochlear vasculature.[26] However, the duration of hydroxyurea therapy was variable and not controlled in this study.

Flow Mediated Vasodilation (FMV): Only one study in this review considered FMV as a possible risk factor for SNHL in SCD. Lago *et al*[26] observed that FMV values were reduced in SCD patients with SNHL when compared with SCD patients without SNHL.
(Odds ratio [95% confidence interval] = 0.614 [0.440–0.858]; p = 0.004).

DISCUSSION

This scoping review has identified and synthesised findings from 19 studies that reported risk factors for SNHL in SCD patients. Due to the low number of papers, we could not categorise the studies geographically, although most of the selected articles were from Africa (six of which were from Nigeria). Below, we discuss the implications of these findings and identify knowledge gaps in order to make recommendations for future research. The authors presented the following risk factors in this review: sex, age, painful vaso-occlusive crises, blood parameters, foetal haemoglobin presence, use of hydroxyurea, and flow-mediated vasodilation, a measure of endothelial dysfunction. Most of the articles excluded had very low numbers of SCD patients with SNHL and so could not be analysed further for risk factors. This is a strong indication that a properly powered study should be designed to investigate SNHL in SCD patients.

Although the number of studies reviewed was quite small, all of them indicated that the sex of the individual did not influence the development of SNHL in SCD. Also, no sex preponderance produced a statistically significant difference in these studies. Thus, we can safely assume that gender is not a risk factor for SNHL in SCD.

Age as a risk factor appears to be significant in adolescent and adult study groups.[5,8,18] The other studies involving children and younger age groups did not observe age as a risk factor for the development of SNHL in SCD; instead, they observed conductive hearing loss and otitis media with effusion.[9,10] The presence of conductive hearing loss and otitis media was not different from the study controls.[12] No specific reason or explanation was given for the significant presence of SNHL in the adult age group; though, we may deduce that the cumulative insults to the cochlear hair cells through their end arterial supplies over time from vaso-occlusive crises can result in hearing loss. However, these three studies did not analyse the effect of vaso-occlusive crises and their possible relationship with age and the development of SNHL. Furthermore, the sample size of most studies was not adequate for this analysis to be performed. To rule out presbycusis, future

studies should use a well-powered sample size of patients under the age of 45.

The frequency of vaso-occlusive crises is considered a risk factor for SNHL in SCD; however, the review found only seven studies that examined this factor. In their studies, these seven studies used different definitions for vaso-occlusive crisis, such as age at first crisis, number of hospital admissions due to crisis in the previous 10 years, number of patients who had first crisis at six years of age, PVO crisis in the last 12 months of the study, and number of crises per year. The studies that looked at the number of crises per year found no statistically significant difference. There is a need for consistency in assessing the relationship between vaso-occlusive crisis frequency and SNHL in SCD. A longitudinal study will best define this relationship.

In this review, the haematocrits level as a risk factor for SNHL in SCD patients showed no statistically significant difference from non-SNHL participants.[18,21,22,26] This does not support the long-held hypothesis that chronic anaemia is the cause of SNHL in SCD patients.[21] Other blood parameters have not been thoroughly studied. Solomon *et al,*[29] for example, discovered that high WBC and platelet count correlated positively with SNHL in SCD patients. Thus, in SCD, the higher the WBC and platelet count, the greater the likelihood of developing SNHL. This is, however, the only study in the literature. Similarly, Al-Dabbous *et al* [22] discovered that SCD patients with SNHL had significantly lower mean corpuscular volume than those without hearing loss. This was explained by the presence of the alpha-thalassemia trait in the study population. More global studies on the effect of the aforementioned parameters in these patients are encouraged.

Only one study in this review reported foetal haemoglobin to be a protective factor against SNHL in SCD patients, while the other two found no link. This demonstrates that this factor is understudied, despite the widespread belief that it protects against the occurrence of vaso-occlusive crises and the negative effects of SCD. Similarly, studies on the use of hydroxyurea and SNHL are scarce. In SCD patients, hydroxyurea is used to raise HbF levels.[30,31] Flow-mediated vasodilation is thought to be an early indicator of vascular changes in SCD.[26] These vascular changes cause a decrease in blood flow and supply to the cochlea, resulting in the death of the outer hair cells. Although lower FMV correlated with SNHL in SCD in a study under this review, more studies are required to confirm this correlation.

CONCLUSION

While only a few studies met the inclusion criteria and were chosen for this scoping review, we found the following as potential risk factors for SNHL in SCD patients: older age, increased vaso-occlusive crisis, blood parameters including HbF, use of hydroxyurea, and decreased flow-mediated dilatation. More research is needed to confirm the role of haematocrit levels, other blood parameters, HbF, hydroxyurea, and FMV as risk factors. In this review, only a few studies (with insufficient power) assessed risk factors for SNHL in SCD. There is a significant knowledge gap regarding the risk factors for SNHL in SCD patients. Studies are required because knowledge application will aid in the prevention and management of SNHL in SCD.

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Duality of Interest

None.

Statements and Declarations

Ethics approval and consent to participate-Not applicable.

Competing Interests

None.

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SUPPLEMENTARY TABLES AND MATERIALS

Supplementary Table S1: Search Strategy for PubMed/Medline

Search	Terms	Translations	Number of Articles
#1	Sickle cell disease	"sickle cell disease"[All Fields] OR "sickle cell anaemia"[All Fields] OR "HbSS"[All Fields] OR "HbSc"[MeSH Terms]	17,179
#2	Sensorineural hearing Loss	(((("sensorineural hearing loss"[All Fields] OR ((((("Sensory hearing loss"[MeSH Terms] OR ("sensorineural deafness"[All Fields] AND "sensorineural hearing disorders"[All Fields]))	22,387
#3	Determinants	"determinants"[MeSH Terms] OR "Predictors" OR "Risk factors" [All Fields]	4,313,116
#4	–	#1 AND #2 AND #3	15,921
#5		Filters: English	114

Word search on EMBASE and Web of Science: ((((("sickle cell disease"[All Fields] OR "sickle cell anaemia"[All Fields] OR "HbSS"[All Fields] OR "HbSc"[MeSH Terms] All Fields])) AND ((((("sensorineural hearing loss"[All Fields] OR ((((("Sensory hearing loss"[MeSH Terms] OR ("sensorineural deafness" OR "sensorineural hearing disorders"[All Fields] AND "determinants"[MeSH Terms] OR "Predictors" OR "Risk factors" [All Fields]

Supplementary Table S2: Search Strategy for Google Scholar

Find articles with all the words:	"sickle cell disease" "sickle cell anaemia" "HbSS" "HbSc"
with the exact phrase:	Sickle cell disease Sensorineural hearing Loss Determinants
with at least one of the words:	
without the words:	
where my words occur:	Anywhere in the article
Year	2022
Stage 1:	

Stages	Details
1	identifying the research question
2	identifying relevant studies
3	study selection Stage
4	charting the data Stage
5	collating, summarising and reporting the results