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Factors Associated with Hearing and Visual Impairments in High-Risk Neonates: A Cross-Sectional Study in Cameroon

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Abstract

Background: Early detection of hearing and visual impairments in high-risk neonates is essential to prevent developmental delays, yet data from resource-limited settings like Cameroon are limited. High-risk neonates were defined as those with prematurity (<37 weeks of gestation), low birth weight (<2500 g), or major perinatal complications (e.g., perinatal asphyxia, neonatal infections, or congenital anomalies). This study aimed to determine the prevalence and risk factors for hearing and visual impairments in high-risk neonates at Buea and Limbe Regional Hospitals, Cameroon. **Methods:** A hospital-based cross-sectional study was conducted from January 3 to April 5, 2024, at the neonatology units of Buea and Limbe Regional Hospitals. High-risk neonates were defined as those with prematurity, low birth weight, or perinatal complications, were screened using transient evoked otoacoustic emissions (TEOAE) for hearing and red reflex testing (RRT) for vision. Data on sociodemographic, perinatal, and clinical variables (e.g., APGAR score, duration of oxygen therapy measured in days as a continuous variable from medical records, serving as a proxy for illness severity) were collected via structured interviews and medical records, with validation through cross-checking. Logistic regression identified risk factors for hearing impairment; visual impairment was analysed descriptively due to low event counts. **Results:** Of 260 screened neonates, 22 (8.5%, 95% CI: 5.9% - 12.6%) failed the TEOAE test, indicating possible hearing im-

pairment, and 3 (1.2%, 95% CI: 0.5% - 3.4%) had an absent red reflex, suggesting potential visual impairment. Six (n = 6) of 11 neonates who attended follow-up confirmed positive for hearing impairment via auditory brainstem response (ABR) testing. Duration of oxygen therapy was the only factor associated with hearing impairment (aOR = 1.58, 95% CI: 1.26 - 1.98, $p < 0.001$). **Conclusion:** Possible hearing (8.5%) and visual (1.2%) impairments are notable in high-risk neonates in Cameroon. Prolonged oxygen therapy should prompt targeted screening of hearing impairment in high-risk neonates. Larger studies are needed to assess visual impairment and confirm risk factors like maternal rubella.

Keywords

Hearing Impairment, Visual Impairment, High-Risk Neonates, Screening, Cameroon

1. Introduction

Hearing and visual impairments in neonates represent a significant global health challenge, with profound implications for developmental outcomes [1]-[3]. Globally, approximately 1.4 in 1000 newborns experience hearing impairment, with higher rates (1.2% - 11%) among preterm neonates, and in neonates admitted to the Neonatal Intensive Care Unit (1.6% - 13.7%) [1]. In the same light, an estimated 20,000 to 40,000 children around the world are born with congenital or childhood cataracts annually [4], while retinopathy of prematurity (ROP) affects over 50,000 children globally, with approximately 600 premature infants becoming legally blind each year [5].

With an estimate of 30% - 60% of children with sensorineural hearing loss having coexisting visual impairments [6], early detection of these impairments together is critical, as timely interventions can mitigate developmental delays, improve language acquisition, and enhance cognitive and social outcomes [7]. However, the global burden of these impairments is disproportionately higher in low- and middle-income countries, where limited resources hinder screening programs; correspondingly, age-adjusted rates of severe or extreme visual difficulty are 6% in low-, 5% in middle-, and 2% in high-income countries [8]. In resource-limited settings like Cameroon, challenges in screening for hearing and visual impairments include inadequate infrastructure, limited trained personnel, and low awareness of neonatal sensory impairments [9]. Recent studies in Sub-Saharan Africa highlight similar challenges, with a 2018 Nigerian study reporting a 15.9% prevalence of hearing impairment in high-risk neonates at discharge [10]. Similarly, cataracts are the most treatable cause of childhood vision loss, as community-based surveys in Sub-Saharan Africa indicate that 15% - 35% of childhood blindness results from congenital or developmental cataracts [11], highlighting the regional need for targeted screening programs.

Patients considered at high risk for these impairments include premature neonates, low birth weight, hypoxic-ischemic encephalopathy (HIE), and maternal infections (e.g., rubella), which are well-documented globally [12]. However, data on factors associated with these impairments in these high-risk neonates in Cameroon are scarce, with most studies focusing on high-income settings, or overall prevalence, leaving a critical knowledge gap in region-specific epidemiology that hinders development of targeted interventions.

Despite sensitive and specific tools like transient evoked otoacoustic emissions (TEOAE) for detecting cochlear function and red reflex testing (RRT) [9], implementation is limited by a lack of localised risk factor profiles to enhance screening efficiency in these high-risk groups. This study investigates the epidemiology of these impairments in high-risk neonates at Buea and Limbe Regional Hospitals in Cameroon to identify specific risk profiles and inform more targeted interventions for resource-limited settings.

2. Methods

2.1. Study Design and Setting

A hospital-based cross-sectional study was conducted from January 3 to April 5, 2024, at the neonatology units of Buea and Limbe Regional Hospitals in Cameroon's Southwest Region. Although these referral centres lack Neonatal Intensive Care Units, they are staffed by paediatricians who manage high-risk neonates (e.g., prematurity, sepsis, HIE), making them ideal for studying hearing and visual impairments. Despite resource constraints (e.g., limited diagnostics), their infrastructure supports TEOAE and RRT screening. Serving diverse urban and rural populations, these hospitals ensure a representative sample, enhancing the study's relevance for resource-limited settings while facilitating reliable data collection and follow-up.

2.2. Participants

High-risk neonates were defined as those admitted to the neonatology unit with conditions such as prematurity (<37 weeks of gestation), low birth weight (<2500 g), perinatal asphyxia, neonatal infections, or congenital anomalies. Inclusion criteria were neonates admitted during the study period whose parents provided informed consent. Exclusion criteria included neonates with incomplete medical records or those whose parents' declined participation. Screening was conducted at discharge or within 7 days of admission to minimize false positives from ear canal debris, with follow-up visits scheduled separately for confirmatory testing.

2.3. Variables

A structured questionnaire, pre-tested for clarity, was used to collect data on sociodemographic characteristics (e.g., maternal age, neonatal sex), perinatal history (e.g., gestational age, birth weight, Apgar score), and clinical risk factors (e.g., ma-

ternal infections, oxygen therapy duration recorded in days as a continuous variable from medical records, used as a proxy for illness severity due to limited NICU monitoring capabilities). Phototherapy was used as a surrogate for severe jaundice, a known risk factor for hearing impairment, due to the lack of routine bilirubin level measurements in the study setting.

2.4. Data Sources and Measurements

Data were sourced from parental interviews and medical records. Parental interviews were necessary due to incomplete or non-standardized medical records for some variables (e.g., maternal infections, perinatal history), which are common in resource-limited settings. Cross-checking with available medical records was performed to minimize recall bias.

Risk factors for hearing impairment were assessed per the Joint Committee on Infant Hearing (JCIH) 2007 guidelines (e.g., maternal TORCH infections, ototoxic medication use) [13], as these were established in local clinical practice and aligned with available diagnostic capabilities. The 2019 JCIH guidelines include additional risk factors (e.g., congenital cytomegalovirus), but these were not feasible to assess due to diagnostic limitations [14]. Risk factors for visual impairment (e.g., hypoxic-ischemic encephalopathy, congenital anomalies) were based on similar risk profiles in literature [15] [16].

Hearing screening was performed using a calibrated Interacoustics Titan TEOAE device in a quiet room (<40 dB ambient noise) by trained technicians. Results were recorded as "pass" or "refer", with "refer" indicating potential hearing impairment requiring follow-up. The single-stage TEOAE protocol was chosen due to resource constraints and feasibility in the study setting, though it may overestimate hearing impairment prevalence compared to multi-stage protocols. Visual screening involved red reflex testing using a Welch Allyn ophthalmoscope, conducted by ophthalmology-trained personnel. An absent red reflex indicated potential visual impairment. Screenings were performed at discharge or within 7 days of admission to reduce false positives from ear canal debris. Parents of neonates with "refer" or absent red reflex results were referred for confirmatory testing (e.g., auditory brainstem response [ABR] for hearing, fundoscopy for vision), though follow-up results were not included in this study due to poor compliance, a common challenge in resource-limited settings.

2.5. Bias

Potential biases include selection bias, as only two major referral centres were included, possibly excluding severe cases. Recall bias in parental interviews was minimized by cross-checking with medical records. Detection bias may arise from TEOAE and RRT sensitivity limitations, potentially overestimating impairment prevalence without confirmatory testing (e.g., ABR, fundoscopy). Parental hearing impairment was self-reported and may reflect reporting bias, requiring validation. These biases could affect prevalence estimates and risk factor associations

but were mitigated through standardised protocols and trained personnel.

2.6. Study Size

A minimum sample size of 250 was calculated based on an expected hearing impairment prevalence of 8%, with a 5% margin of error and 95% confidence level [9].

2.7. Quantitative Variables and Statistical Methods

Data were entered daily into a secure database and analysed using SPSS version 26. Due to non-normal distributions, descriptive statistics were presented as medians and interquartile ranges for continuous variables and as frequencies and percentages for categorical variables. Bivariate analyses used chi-square tests for categorical variables and Mann-Whitney U tests for continuous variables (e.g., duration of oxygen therapy, APGAR score, gestational age).

Due to the low prevalence of visual impairment (n = 3), risk factors were reported descriptively without regression analysis. For hearing impairment (22 events), multivariate logistic regression adhered to the 10 events per predictor (EPP) rule, including up to three predictors based on bivariate significance ($p < 0.250$) and clinical relevance [17]. Variables with insufficient events (e.g., Hypoxic Ischemic Encephalopathy with 5 events in the affected group) were excluded from multivariate models to ensure model stability. Model fit was assessed via the Hosmer-Lemeshow test ($p > 0.05$ indicating good fit). Results were reported as adjusted odds ratios (aOR) with 95% confidence intervals (CI).

2.8. Ethical Considerations

Ethical clearance was obtained from the Faculty of Health Sciences Institutional Review Board, University of Buea (Ref: 2023/1234-UB/FHS-IRB). Administrative approvals were secured from the Southwest Regional Delegation of Public Health and hospital directors. Written informed consent was obtained from parents in English or Pidgin English, with verbal explanations provided for low-literacy participants. Data were anonymized and stored securely, accessible only to the research team.

3. Results

3.1. Participant Characteristics

Of 264 eligible neonates, 260 were screened (98.5% participation rate); four were excluded due to parental non-attendance at follow-up. The median gestational age at birth was 38.7 weeks, IQR: 35.1 - 40.2, and median birth weight was 3000 g, IQR: 2103.7 - 3400. Males predominated (57.7%, n = 150; sex ratio 1.4:1). Common admission diagnoses included prematurity (30.4%), neonatal sepsis (72.7%), and hypoxic-ischemic encephalopathy (HIE) (15.8%) (**Table 1**).

Screening was conducted at Buea Regional Hospital (BRH, 73.5%, n = 191) and Limbe Regional Hospital (LRH, 26.5%, n = 69). The median number of antenatal

care (ANC) visits was 5 (IQR: 4 - 6), median patient age at screening was 6 days (IQR: 4 - 12.25), median APGAR score at 5 minutes was 9 (IQR: 7 - 10), median head circumference was 35 cm (IQR: 32.9 - 35.5), median length was 49 cm (IQR: 46 - 50), median duration of hospitalisation was 6 days (IQR: 5 - 8), median duration of aminoglycoside use was 5 days (IQR: 0 - 5), and median duration of oxygen treatment was 3 days (IQR: 3 - 5).

3.2. Prevalence of Impairments

Of 260 neonates, 22 (8.5%, 95% CI: 5.9% - 12.6%) failed the TEOAE test, suggesting potential hearing impairment. Three neonates (1.2%, 95% CI: 0.5% - 3.4%) had an absent red reflex, indicating possible visual impairment; all three also failed TEOAE as shown in Figure 1. Due to the low number of visual impairment cases, no further statistical analysis was conducted for this outcome. Of the 22 infants who failed the TEOAE test, 11 later reported for follow-up control visits as part of the scheduled rendezvous. Of these, 6/11 tested positive for hearing impairment and were referred to ENT specialists for further evaluation and higher imaging testing. Additionally, 2 deaths were recorded among the 22 infants between the initial screening and the time of the scheduled rendezvous.

3.3. Factors Associated with Hearing Impairment

Bivariate analyses identified maternal rubella ($p < 0.001$), HIE ($p < 0.001$), receiving oxygen ($p < 0.001$), duration of oxygen ($p = 0.001$) and APGAR score at 5 minutes ($p = 0.039$) as associated with hearing impairment (Table 2). Other variables, including screening hospital ($p = 0.279$), gestational age ($p = 0.741$), number of ANC visits ($p = 0.578$), age at screening ($p = 0.353$), sex ($p = 0.143$), birth weight ($p = 0.725$), head circumference ($p = 0.319$), length ($p = 0.440$), duration of hospitalisation ($p = 0.943$), neonatal infection ($p = 0.620$), duration of gentamicin ($p = 0.392$), and phototherapy ($p = 0.395$), showed no significant association in bivariate analyses.

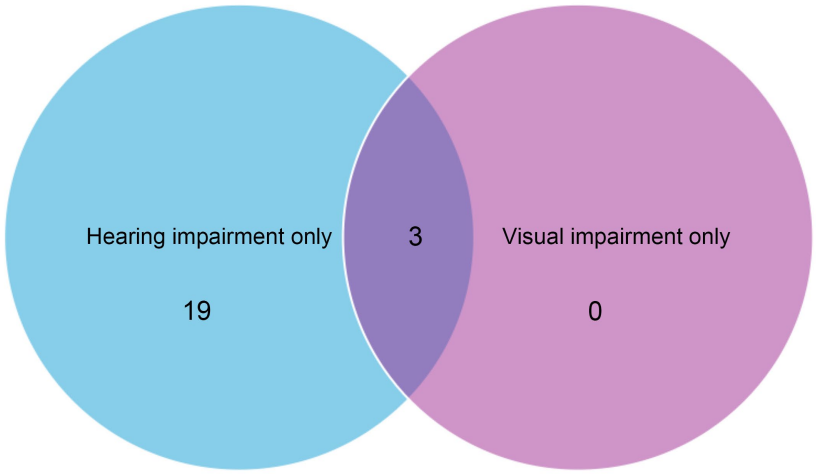

Figure 1. Overlap of hearing and visual impairment outcomes.

Table 1. Baseline characteristics of screened neonates (n = 260).

Variable	Median (IQR) or n (%)
Parental hearing impairment	
One parent	81 (31.2%)
Both parents	4 (1.5%)
Gestational age (weeks)	38.7 (IQR: 35.1 - 40.2)
Male sex	150 (57.7%)
Prematurity	79 (30.4%)
Congenital malformation	3 (1.2%)
Neonatal sepsis	189 (72.7%)
Received phototherapy	67 (25.9%)
HIE (any stage)	41 (15.8%)
Number of ANC visits	5 (IQR: 4 - 6)
Age at screening (days)	6 (IQR: 4 - 12.3)
APGAR score at 5 min	9 (IQR: 7 - 10)
Birth weight (g)	3000 (IQR: 2103.7 - 3400)
Head circumference (cm)	35 (IQR: 32.9 - 35.5)
Length (cm)	49 (IQR: 46 - 50)
Duration of hospitalisation (days)	6 (IQR: 5 - 8)
Duration of aminoglycoside use (days)	5 (IQR: 0 - 5)
Received oxygen	52 (20%)
Duration of oxygen therapy	3 (IQR: 3 - 4.3)

Table 2. Bivariate analysis of risk factors for hearing impairment.

Variable	No Hearing Impairment (n = 238)	Hearing Impairment (n = 22)	p-value
Maternal rubella	1 (0.4%)	2 (9.1%)	**<0.001**
HIE	36 (15.3%)	5 (22.7%)	**<0.001**
Received oxygen	40 (16.8%)	12 (54.6%)	**<0.001**
Duration of oxygen therapy	0 (IQR 0 - 0)	3.5 (IQR 0 - 6.0)	**0.001**
APGAR score at 5 min (median)	9 (IQR: 8 - 10)	9 (IQR: 6.3 - 9.0)	**0.039**
Screening hospital (LRH)	61 (25.6%)	8 (36.4%)	0.279
Gestational age (weeks, median)	38.7 (IQR: 35.0 - 40.1)	39.7 (IQR: 36.1 - 41.1)	0.741
Number of ANC visits (median)	5.0 (IQR: 4.0 - 6.0)	5.0 (IQR: 4.0 - 6.0)	0.578
Age at screening (days, median)	6.0 (IQR: 4.0 - 13.0)	6.5 (IQR: 3 - 9.75)	0.353
Sex (female)	104 (43.7%)	6.0 (27.3%)	0.143
Birth weight (g, median)	3000 (IQR: 2150 - 3400)	3000.0 (IQR: 2025 - 3500)	0.725
Head circumference (cm, median)	35.0 (IQR: 33.0 - 35.5)	35.0 (IQR: 32.3 - 35.5)	0.319
Length (cm, median)	49.0 (IQR: 46 - 50)	49.0 (IQR: 46.0 - 50.7)	0.440
Duration of hospitalisation (days, median)	6.0 (IQR: 5 - 8)	8.0 (IQR: 5.3 - 10.0)	0.943
Neonatal infection (yes)	174 (73.1%)	15 (68.2%)	0.620
Duration of aminoglycosides (days, median)	5.0 (IQR: 0 - 5.0)	5.0 (IQR: 0 - 7.0)	0.392
Received phototherapy	63 (26.5%)	4 (18.2%)	0.395

HIE = Hypoxic ischaemic encephalopathy; LRH = Limbe regional hospital; IQR = Interquartile range. Bold values represent p-values at significance threshold.

The multivariable model showed that APGAR score at 5 minutes (aOR = 1.19, 95% CI: 0.86 - 1.65, p = 0.296) was not a significant predictor of hearing impairment. Only duration of oxygen treatment (aOR = 1.58, 95% CI: 1.26 - 1.98, p < 0.001) was significantly associated with hearing impairment (Table 3). The model showed good fit (Hosmer-Lemeshow p = 0.063).

Table 3. Multivariate logistic regression.

Variable	aOR (95% CI)	p-value
Male (Reference = female)	2.14 (0.72 - 6.37)	0.173
APGAR score at 5 min	1.19 (0.86 - 1.65)	0.296
Duration of oxygen treatment in days	1.58 (1.26 - 1.98)	**<0.001**

3.4. Descriptive Findings for Visual Impairment

Only three mothers reported positive rubella serology. Neonates with visual impairment had maternal rubella exposure (n = 2) or HIE stage 3 (n = 1), but the small sample precluded statistical analysis. These cases also had hearing impairment, suggesting possible shared aetiology.

4. Discussion

This hospital-based cross-sectional study of 260 high-risk neonates in Cameroon identified a suspected hearing impairment prevalence of 8.5% (95% CI: 5.9% - 12.6%) and visual impairment prevalence of 1.2% (95% CI: 0.5% - 3.4%) using TEOAE and RRT. Duration of oxygen therapy (aOR = 1.58, 95% CI: 1.26 - 1.98, p < 0.001) was the only significant predictor of hearing impairment. Maternal rubella (n = 2) and HIE stage 3 (n = 1) were prominent in patients with visual impairment cases (n = 3).

The 8.5% hearing impairment prevalence aligns with regional estimates, as in Cameroon, where 8% of both high and non-high-risk neonates have hearing impairment [9]. Because the study population includes only high-risk groups, prevalence was anticipated to be higher. However, the early screening (median = 6 days) in our cohort (versus 13 days [9]) could justify this finding, as later age at screening has been associated with a higher chance of a false-positive result (1.5% false positive when screened within 5 days, and 4% between 26 - 31 days) [18]. Prevalences as high as 15% have been reported in 100 Indian high-risk neonates [19], a finding that probably relates to historical trends, as several public health strategies have now been implemented to mitigate this burden [20].

The 1.2% prevalence of visual impairment aligns with reported ranges of 0.01% to 30.9% [21]. In contrast to high-income studies focusing on prematurity, perinatal asphyxia, and oxygen therapy [15] [16], our results emphasize maternal rubella as a key factor in resource-limited settings, consistent with findings in India, where 1.92% of congenital rubella syndrome cases develop cataracts [22]. However, larger, statistically robust studies are required to confirm these associations.

Lower 5-minute APGAR scores were associated with hearing impairment in

univariate analysis, potentially indicating perinatal asphyxia that leads to cochlear damage [23]. In Sub-Saharan African contexts like Cameroon, diagnostic limitations (e.g., lack of blood gas analysis) imply that APGAR scores may reflect a broader range of stressors, including hypoglycaemia or infection, beyond just hypoxic ischemic encephalopathy (HIE) [24] [25]. However, the APGAR score was not significant in multivariable analysis, possibly due to these unmeasured factors. This lack of significance could be attributed not only to APGAR reflecting various other conditions that contribute to reduced scores, but also to the inherent bias in the Apgar score that is associated with systematically lower score reporting in people of colour [26] [27].

Prolonged oxygen therapy, usually more associated with visual impairment [28], was the sole factor associated with hearing impairment in this sample, which probably reflects increased risk via middle ear effusion from unregulated oxygen delivery, common in settings with limited monitoring [29] [30]. However, this finding may more likely relate to oxygen therapy being the closest proxy indicator of disease severity in the sample, as NICU services are limited in Cameroon [31] [32]. The overlap of visual and hearing impairment cases points to shared aetiologies, such as congenital infections or syndromes like Usher syndrome [33] [34]. The impact of these aetiologies on combined hearing and visual needs to be further explored in resource-limited settings.

This study has several limitations that warrant consideration. First, the focus on two referral centers in Cameroon's Southwest Region may introduce selection bias, potentially excluding severe cases from other facilities and limiting generalizability to the broader neonatal population. However, the high-risk cohort (e.g., 30.4% prematurity, 72.7% neonatal sepsis, 15.8% HIE) aligns with established risk profiles, supporting the study's relevance for targeted screening in similar settings. Second, the lack of confirmatory testing (e.g., ABR for hearing, fundoscopy for vision) may overestimate prevalence, particularly for hearing impairment (8.5%), as TEOAE screening can yield false positives, especially in preterm infants (30.4% of the sample) with immature auditory systems [15]. Ciorba *et al.* (2019) note that many preterm infants who fail initial TEOAE pass follow-up testing by 7 months, highlighting the need for confirmatory diagnostics [35]. In our study, poor follow-up compliance, a common challenge in resource-limited settings, precluded comprehensive confirmatory testing, though partial follow-up data suggested some true positives. Third, the low number of visual impairment events (n = 3) prevented statistical analysis of risk factors, limiting conclusions about visual outcomes. Fourth, reliance on parental interviews for some variables (e.g., maternal infections) due to incomplete medical records may introduce recall bias, despite cross-checking with available records. Fifth, the use of continuous variables (e.g., APGAR score, duration of oxygen therapy) without defined cutoffs may reduce clinical interpretability, but it was chosen to identify associations for future research in settings where standardized thresholds are not well-established. Similarly, phototherapy was used as a proxy for severe jaundice due to the lack of rou-

tine bilirubin measurements, which may have masked associations with hearing impairment. Finally, the use of JCIH 2007 guidelines instead of the 2019 version reflects local practice and resource constraints, potentially missing newer risk factors like congenital cytomegalovirus. Despite these limitations, the study's strengths include a relatively large sample size (n = 260), high participation rate (98.5%), and use of validated TEOAE and RRT methods, enhancing applicability in resource-limited settings. Future multi-center studies with confirmatory diagnostics and larger samples are needed to validate findings and refine screening strategies.

Multi-center, national studies with confirmatory diagnostics and larger samples are needed to validate findings and explore visual impairment risks. Integrating TEOAE and RRT into routine neonatal care, targeting neonates with low APGAR scores or prolonged oxygen therapy, is feasible. Policy should prioritise standardized oxygen delivery, asphyxia prevention, and training programs for neonatology staff. Community education to improve follow-up compliance could enhance screening effectiveness, supporting pilot universal newborn screening programs in Cameroon.

5. Conclusion

This study confirms a significant burden of possible hearing impairment (8.5%) and a lower prevalence of possible visual impairment (1.2%) in high-risk neonates in Cameroon. Prolonged oxygen therapy is a key factor associated with hearing impairment. Maternal rubella and HIE require further investigation due to low event counts. Pilot programs for universal newborn hearing screening, integrated with improved perinatal care (e.g., standardised oxygen delivery and asphyxia prevention), are feasible next steps for Cameroon. Larger, multi-center studies with confirmatory testing are essential to validate these findings and refine screening strategies for both hearing and visual impairments.

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Authors' Contributions

Study concept and design: YDP, LF and EMML. Data collection: LF. Analysis and interpretation of data: EMML. Manuscript writing: YDP, FL, EMML, GV, BV, YW, CEE, BDM, DA, WA, SFK, and SN. SN supervised the study. YDP, LF and EMML had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. All authors agreed to submit the manuscript in its current form.

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Data Availability

The data supporting this study's findings are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

Ethical clearance was obtained from the Faculty of Health Sciences Institutional Review Board, University of Buea (Ref: 2023/1234-UB/FHS-IRB). Written informed consent was obtained from parents in English or Pidgin English, with verbal explanations provided for low-literacy participants.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Supplementary Materials

Table S1. STROBE checklist for cross-sectional studies.

Item	No	Recommendation	Page
Title and abstract	1	a) Indicate the study's design with a commonly used term in the title or the abstract	1
		b) Provide in the abstract with an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	2 - 3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	Give the eligibility criteria, and the sources and methods of selection of participants	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3 - 4
Bias	9	Describe any efforts to address potential sources of bias	4
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4 - 5
Statistical methods	12	a) Describe all statistical methods, including those used to control for confounding	4 - 5
		b) Describe any methods used to examine subgroups and interactions	5
		c) Explain how missing data were addressed	5
		d) If applicable, describe analytical methods taking account of sampling strategy	5
		e) Describe any sensitivity analyses	N/A
Results			
Participants	13*	a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		b) Give reasons for non-participation at each stage	5
		c) Consider use of a flow diagram	N/A
Descriptive data	14*	a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders	6
		b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers of outcome events or summary measures	6
Main results	16	a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6 - 9

Continued

		b) Report category boundaries when continuous variables were categorized	6 - 9
		c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarize key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9 - 10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for exposed and unexposed groups. Note: An explanation and elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLOS Medicine at https://journals.plos.org/plosmedicine/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at https://www.strobe-statement.org/.