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Surgical site infection and antimicrobial use following caesarean section at QECH in Blantyre, Malawi: a prospective cohort study

Amos Tumizani Kachipedzu^{1,3*}, David King Kulapani¹, Samuel James Meja² and Janelisa Musaya¹

Abstract

Background Surgical site infections (SSIs) are one of the most common healthcare-associated infections and preventable complication of surgical procedure; continue to threaten public health with significant effects on the patients and health care human and financial resources. Therefore, this study aimed to determine the incidence of SSIs, risk factors and common microorganisms associated with SSI and assess the practice of antimicrobial use in women following Caesarean Section (CS) at Queen Elizabeth Central Hospital (QECH).

Methods This was a hospital-based quantitative prospective study design involving pregnant women who underwent a CS between February, 2023 and July, 2023 at QECH with 30 day-follow-ups. Wound specimens (wound swabs) were collected from all infected CS wounds and processed at QECH main laboratory, and susceptibility testing was conducted using the Kirby-Bauer disk diffusion method with results reported only as susceptible, intermediate, or resistant and the collected data was analyzed using Stata.

Results The overall cumulative incidence of SSI recorded at QECH during the study period was 9.61% (20 cases out of 208). Of these, 19 (95%) of them reported superficial SSI following CS. The mean age was 26.1 years with a standard deviation of 6.2. All pregnant women who underwent for CS received antibiotic prophylaxis. This study revealed that 138 (66.35%) patients received both preoperative antibiotics (ceftriaxone) and post-CS antibiotics without knowing the specific bacterial organism isolated. This study revealed that ruptured membrane had twice the incidence of SSIs compared to intact membrane ($\chi^2 = 2.0922$), though not statistically significant. The majority of patients with SSIs (n = 12, 60%) were readmitted and 5 (25%) out of 20 with SSIs had antimicrobial resistance following susceptibility testing. *Staphylococcus aureus* was the most common organism (3, 60%) and other bacterial isolates included were *Enterobacteriaceae* and *Acinetobacter baumanni*.

Conclusion The incidence of SSIs and inappropriate antimicrobial use following CS remains a challenge at QECH. Therefore, due to increased number of SSIs following CS with relative emergence of AMR ensure intensive infection prevention and control practices, establishing AMS program and routine surveillance of SSIs at QECH.

Keywords Surgical site infections, Healthcare-associated infections, Antimicrobial resistance, Incidence, Risk factors

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Background

Caesarean section (CS) is a lifesaving operative technique in which a foetus, placenta, and membranes are delivered through an abdominal and uterine incision. Surgical site infection (SSI) is defined as an infection that occurs at or near the surgical incision within 30 days of the operation or after 1 year if an implant is placed [1-3]. Globally, SSI is the second most reported health-care associated infection (HAI), accounting for 19.6% of HAIs [4]. Numerous studies have reported incidence rates of post-CS SSIs, for example, 2.85% in India [5], 21% in Ethiopia [6] and 7-9.6% in Nigeria [5, 7]. HAIs and antimicrobial resistance (AMR) are major global health challenges recognized worldwide. However, the spread of HAIs and AMR is particularly alarming in low- and middle-income countries [8]. SSI accounts for 20% of all HAIs and is associated with a 2-11 fold increase in the risk of mortality, with 75% of SSI-associated deaths directly attributable to SSI [9, 10].

There are limited data on surgical site infections (SSIs) in African countries such as Malawi [11]. A prospective survey conducted by Borgstein at QECH in Blantyre showed an overall infection rate of 25.8% and that for clean wounds of 14.8% [12]. In many SSIs, the responsible pathogens originate from the patient's endogenous flora [13]. The causative pathogens depend on the type of surgery; the most commonly isolated organisms are *Staphylococcus aureus*, coagulase-negative *staphylococci*, *Enterococcus spp.* and *Escherichia coli*. Other studies have shown that *Staphylococcus aureus* is a commonly isolated organism in SSIs, accounting for 20–30% of SSIs occurring in hospitals [5, 13, 14]. A survey revealed that caesarean section procedures carry a risk of infection 5–20 times that of normal delivery [6].

Different studies have shown that the rational use of antimicrobials in women of childbearing age is important because it affects this population as well as their offspring. The indiscriminate use of antibiotics may result in the appearance of drug-resistant organisms [15]. The use of antimicrobial prophylaxis for caesarean section has been shown to be effective in reducing postoperative morbidity, cost and duration of hospitalization. Another study reported the incidence of infection even after antimicrobial prophylaxis due to pre-existing infection, debilitating disease or prolonged rupture of membranes [15].

In addition, another study reported that once antibiotics are intensively misused, they are undoubtedly the main factor associated with the high numbers of antibiotic-resistant pathogenic and commensal bacteria worldwide [16, 17]. Similarly, a study by Classen et al. revealed that a delay in surgery reduces patient protection and can lead to the occurrence of postoperative infections [18]. Consequently, with the increasing number of surgical cases in LMICs, surgical site infections (SSIs) are becoming more prevalent due to anecdotal evidence of AMR, despite limited data on resistance patterns. The criteria for defining surgical site infection (SSI) were established according to the US Centres for Disease Control (CDC) and Prevention [19]. Therefore, this study aimed to determine the incidence of SSIs, risk factors and common microorganisms associated with SSI and assess the practice of antimicrobial use in women following CS at QECH in Blantyre, Malawi.

Methods and materials

Study setting, design, period and population

This was a hospital-based quantitative prospective cohort study among all women who underwent a caesarean section procedure at QECH from 1st February 2023 to 31st July 2023, and they were followed up for a 30-day period to assess wound outcome (SSI). QECH has an average of 300 CS procedures performed per month and is found in Blantyre in the southern region of Malawi. QECH provides secondary and tertiary levels of care and serves as the referral hospital for the health centres in Blantyre and district hospitals in the region (primary and secondary health care). Surgical wound sites on discharge from hospital were inspected and classified according to the CDC [19]. The study excluded all women who underwent CS in other health facilities.

Sample size and sampling technique

The study enrolled 208 pregnant women who delivered through CS at QECH. This sample size was calculated in OpenEpi version 3, assuming that 15% of the subjects in the study population developed surgical site infections and that they received antimicrobial agents. To determine significant differences in the proportions of surgical site infections between the two groups, a power of 80%, two-sided significance of 95% confidence and a design effect of 2 were used [20]. These two groups considered those that developed SSI and those that did not develop SSI following CS procedure and antimicrobial use.

The assumption on the percentage was based on the results from a prospective survey conducted by Borgstein at QECH in Blantyre, which showed an overall infection rate of 25.8% and that for clean wounds of 14.8% [12]. Furthermore, the assumed percentage was also based on the point prevalence survey by Bunduki, which revealed HAI of 11.4%, including surgical site infections [11].

Data collection and procedure

The data were collected electronically using Open Data Kit (ODK) software. The information included sociodemographic characteristics, obstetrics-related factors, and

operation- and anaesthesia-related factors. The dependent variable of this study was the incidence of SSIs following CS. The suggested independent variables included were sociodemographic variables such as maternal age, maternal educational status, occupational status, religion, and antenatal care visits. Relevant maternal medical history, such as HIV status, BMI, previous history of CS, and/or hypertensive disorder, was collected. Surgical intervention-related variables included type of CS (elective or emergency), type of incision (vertical, horizontal), type of skin closure (Interrupted or continuous), premature rupture of membranes, number of vaginal examinations, duration of the procedure, anaesthetic technique (general, spinal), indication for CS, gestational age, CS performed by a doctor (e.g., international clinical officer, clinical officer, medical officer, student or consultant) and/or antibiotic use. Wound swab samples were collected from the infected surgical wounds and processed using the Kirby-Bauer (KB) test via the disc diffusion method [21].

As part of routine clinical care, the samples collected from the patients were quickly tracked; wound swabs or pus aspirates were sent to the QECH main laboratory for microbiology culture and sensitivity. Furthermore, the data were collected by the principal investigator and research assistants, who were qualified nurse midwives and microbiologists. The data for cases post CS were identified through the phone interviews by the principal investigator at least three contacts (day 3 / or on discharge, day 7 and day 30 post discharge). Those that reported signs and symptoms for SSIs as defined by CDC were asked to visit the hospital and have wound swab sample collected for further microbiology analysis. Some patients were not admitted as per doctor's recommendation after proper assessments and they were followed up through the phone interviews. For consistency in the data collection process, the research assistants were oriented to the data collection instrument by the principal investigator prior to the actual data collection process.

Data management and statistical analysis

After data collection to ensure completeness, consistency and correct methods of data entry, quality control was performed on a daily basis. The data were subsequently transferred to a password-protected computer and downloaded to an electronic server for storage. The server was secure, with access only granted to study data managers.

The statistical analyses were performed by means of Stata version 14, and statistical significance was defined by a p value ≤ 0.05 (95% confidence level). Descriptive analysis was also conducted. For the continuous variables, means (standard deviations) and interquartile

ranges (IQRs) were calculated, and the summarized results are presented in a table.

Descriptive data analysis was also used for frequencies and percentages. These studies were mainly focused on sociodemographic characteristics, medical-related and obstetric-related factors, and operation and anaesthesia factors. Chi-square (χ^2) and Fisher's exact tests were performed for observations less than or equal to 4 to determine the potential risk factors associated with the SSI at the 95% confidence level. The analyses were performed to determine the potential risk factors or crude odds ratios. Risk factors with a p value < 0.05 in the univariate analysis were selected for inclusion in the multivariable logistic regression model. However, multivariable analysis was not performed to assess whether the relationship between C-sections and SSIs was confounded by other risk factors because χ^2 showed no direct association between the variable and the outcome of interest (SSI).

Results

Socio-demographic and clinical characteristics

A total of 208 pregnant women who underwent CS were enrolled, and 30 days of follow-up were used to assess SSI outcomes (Fig. 1). The minimum age of the study participants was 15 years, while the maximum age limit for the study participants was 42 years.

The mean age was 26.1 years, with a standard deviation of 6.2 years. Approximately 111 (53.37%) of the women responded with no previous history of CS, and 20 (9.6%) of the women were HIV positive in this study (Table 1). Among the enrolled women, 20 patients developed SSI following CS either clinically or through microbiological culture diagnosis.

Caesarean section indications

Among mothers who underwent caesarean section, previous scarring was the most common indication (63 (30.29%)), followed by cephalopelvic disproportion (61 (29.33%)) (Table 2).

Medical-related and obstetric related characteristics

Among the 208 women, 115 (55.5%) had a BMI greater than 25, and 22 (10.58%) had an ASA score equal to or greater than two. Furthermore, 93 (44.71%) of the patients experienced membrane rupture before CS was performed. In addition, approximately 169 (81.25%) of the participants' gestational age was not less than 37 weeks (Online supplementary Table 3).

Anaesthesia and operation-related characteristics

The average duration after the first dose of antibiotic prophylaxis to the start of the CS procedure was 12.85 min, with a standard deviation of 8.44 (IQR=8,



Fig. 1 Flow chart of patient recruitment and case identification process

25th percentile=7, 75th percentile=15). Furthermore, 134 (64.4%) CS procedures were performed by intern medical officers (IMOs), and 206 (99.04%) of the procedures involved spinal anaesthesia. Approximately 113 (54.3%) of the operation procedures were completed in more than 60 min, and 120 (57.7%) and 63 (30.3%) of the 208 patients underwent emergency and urgent CS, respectively. (Online supplementary Table 4).

Incidence of surgical site infection

The overall incidence of SSIs recorded at QECH during the study period was 9.61%. Of these, 19 (95%) reported superficial SSI, and 1 (5%) reported deep SSI following CS (Table 3). The majority of patients with SSIs (n=12; 60%) were readmitted, and 5 (25%) out of 20 patients with SSIs had antimicrobial resistance following susceptibility testing.

This study revealed that ruptured membrane had twice the incidence of SSIs compared to intact membrane, though not statistically significant. This might be due to the small sample size included in this study. The tested factors that other studies reported include skin closure technique, BMI, education level, age range in years, HIV status, parity, membrane status pre-CS, ANC visits, gestational age (weeks), duration of CS and SSI [22]. Hence, we did not perform any logistic regression model analysis because no P value < 0.05% indicated statistical significance (Table 3).

Antimicrobial use

This study also revealed that all the women who underwent the CS procedure received preoperative antibiotic prophylaxis. However, 138 (66.35%) patients received both preop antibiotics (ceftriaxone) and post-CS antibiotics (Online supplementary Table 6). The most common post-CS-prescribed antibiotics were metronidazole and ceftriaxone combined therapy, even for patients with noncomplicated CS. No patient had a known infection or specific bacterial organism isolated in the current study at the time these antibiotics were prescribed and administered which may increase the risk for antimicrobial resistance spread. The average duration from the first dose of antibiotic prophylaxis to the start of the CS

Chi-square P value

Variable Frequency **Proportion (%)** Mean (SD)Age 26.05 (±6.18) Age in years 156 75 ≤30 30 52 25 Marital Status Married 171 82.21 Others* 37 17.79 Previous history of CS Yes 97 46.63 No 53.37 111 Education Level Primary 84 40.38 59.62 Secondary or More 124 Occupation Employed 7.21 15 Business 37.50 78 Housewife 92 44.23 Other* 23 11.06 **HIV Status** Positive 20 9.62 90.38 Negative 188

Table 1 Socio-demographic and clinical characteristics of the study participants

Married _Others * (Single, Divorced, Widowed),

Occupation_ Other * (dwellers, none)

Table 2 Indications for caesarean section

| Indication | Frequency | % |
|------------------------|-----------|-------|
| CPD*1 | 61 | 29.33 |
| Previous scar | 63 | 30.29 |
| Cord prolapse | 4 | 1.92 |
| Eclampsia | 14 | 6.73 |
| Antepartum haemorrhage | 7 | 3.37 |
| Breech presentation | 12 | 5.77 |
| Fetal Distress | 12 | 5.77 |
| Prolonged labour | 17 | 8.17 |
| Other*2 | 18 | 8.65 |

CPD*1 Cephalopelvic disproportion

Other*2 (placenta previa, twin gestation, IUGR, PROM, polyphromnious and postdates)

procedure was 12.85 min, with a standard deviation of 8.44 (IQR = 8).

Bacterial isolates and susceptibility pattern

Wound swabs from infected CS wounds for culture and sensitivity were collected for 11 (55%) of the clinically suspected postoperative CS infections. Among the

| | $\overline{\text{Yes (n = 20)}}$ No (n = 188) | | | | |
|-----------------------------|---|-------------|--------|-------|--|
| Skin closure tech- nique | | | 0.3675 | 0.544 | |
| Interrupted | 7 (35.00) | 13 (65.00) | | | |
| Continuous | 79 (42.02) | 109 (57.98) | | | |
| BMI | | | | | |
| ≤25 | 11 (55.00) | 9 (45.00) | 0.9475 | 0.330 | |
| >25 | 82 (43.62) | 106 (56.38) | | | |
| HIV status* | | | | | |
| Positive | 4 (20.00) | 16 (80.00) | | 0.109 | |
| Negative | 16 (8.51) | 168 (89.36) | | | |
| Age range* | | | | | |
| ≤30 | 16 (80.00) | 4 (20.00) | | 0.787 | |
| > 30 | 140 (74.47) | 48 (25.53) | | | |
| Education level | | | | | |
| Primary | 8 (40.00) | 12 (60.00) | 0.0014 | 0.971 | |
| Secondary or More | 76 (40.43) | 112 (59.57) | | | |
| Duration of CS (min) | | | | | |
| ≤60 | 11 (55.00) | 9 (45.00) | 0.0916 | 0.762 | |
| >60 | 110 (58.51) | 78 (41.49) | | | |
| Membrane status pre-CS | | | | | |
| Ruptured | 12 (60.00) | 8 (40.00) | 2.0922 | 0.148 | |
| Intact | 81 (43.09) | 107 (56.91) | | | |
| Parity | | | | | |
| ≤2 | 10 (50.00) | 10 (50.00) | 1.1379 | 0.286 | |
| >2 | 71 (37.77) | 117 (62.23) | | | |
| ANC visits | | | | | |
| ≤4 | 11 (55.00) | 9 (45.00) | 0.1218 | 0.727 | |
| >4 | 111 (59.04) | 77 (40.96) | | | |
| Gestation age (weeks)* | | | | | |
| < 37 | 3 (15.00) | 17 (85.00) | | 1.000 | |
| ≥37 | 36 (19.15) | 152 (80.85) | | | |

 Table 3
 Univariate analysis of possible risk factors for SSIs in women who underwent CS

SSI

Variable/factor

* *p* value according to Fisher's exact test, ANC Antenatal care

20 cases recorded, 10 (50.0%) had microbiology culture results, and 1 sample was reportedly missing from the laboratory. Five of the 10 cultures exhibited positive/bacterial growth (Fig. 1). Among the few etiological agents isolated, 3 (60%) were gram-positive cocci (clusters). *Staphylococcus aureus* was the most common organism (3, 15%). Other isolates included *Enterobacteriaceae* (1, 5%) and *Acinetobacter baumanni* (1, 5%) (Table 3).

The *Staphylococcus aureus* bacteria isolated were resistant to most antibiotics, including clindamycin, erythromycin, gentamicin, and cefoxitin. However, *Enterobacteriaceae* were sensitive to ciprofloxacin, meropenem, amikacin and tigecycline and resistant to chloramphenicol and Trimethoprim / sulfamethoxazole. Only *Acinetobacter baumannii* Baumanni was sensitive to gentamicin and resistant to ceftriaxone, ciprofloxacin, cefotaxime and tigecycline (Table 4).

Discussions

This is the first study in Malawi to determine the extent of surgical site infections (SSIs) and antimicrobial use following cesarean section at QECH in Blantyre. The overall incidence of SSI during the study period was 9.61% (20 of 208 patients). Most patients were given antibiotics either prophylactically or post-CS without performing culture to ascertain AMR. Similarly, this finding is consistent with findings in Vietnam (10.9%) [23]. Of course, Borgstein's prospective survey findings at QECH in Blantyre revealed a 25.8% overall infection rate in general surgeries [12]. Similarly, other studies reported incidences of 21% in Ethiopia [6] and 7–9.6% in Nigeria [5, 7]. The incidence of SSIs in this study was greater than that in developed nations [24, 25].

In the present study, among the extremely few isolated etiological agents, 3 (60%) were gram-positive cocci (clusters). However, *Staphylococcus aureus* was the most common organism. This finding is in line with previous findings that *Staphylococcus aureus* is the most common cause of SSIs following post-CS [26, 27]. Similarly, other studies have shown that *Staphylococcus aureus* is a commonly isolated cause of SSI, accounting for 20–30% of SSIs occurring in hospitals [6, 14, 28]. Furthermore, other isolates identified in our study included *Enterobacteriaceae* and *Acinetobacter baumannii*. In the present study, the *Staphylococcus aureus* isolates were resistant to most antibiotics, such as clindamycin, erythromycin, gentamicin and cefoxitin, similar to the findings of Fantahamu et al. [29]. Furthermore, *Enterobacteriaceae* were sensitive to ciprofloxacin, meropenem, amikacin and tigecycline, and the same bacteria were resistant to chloramphenicol and trimethoprim-sulfamethoxazole. However, *Acinebacter Baumanni* was sensitive to gentamicin and resistant to ceftriaxone, ciprofloxacin, cefotaxime and Tigecycline, as also reported in other studies [29, 30].

This study also revealed that 138 (66.35%) patients received both preop antibiotics (ceftriaxone) and post-CS antibiotics. The most common post-CS-prescribed antibiotics were metronidazole and ceftriaxone combined therapy, even for patients with noncomplicated CS. However, the WHO panel recommends against the prolongation of surgical antibiotic prophylaxis (SAP) administration after completion of the operation for the purpose of preventing SSIs [31]. A study by Lamont et al. indicated that a single dose of antibiotics could be as effective as multiple doses given preoperatively [32]. No patient had a known infection or specific bacterial organism isolated in the current study at the time these antibiotics were prescribed and administered; hence, this may also promote antimicrobial resistance spread due to unnecessary use of antibiotics in our hospitals.

| Antibiotic given after | Type of organism identified | Medications | Interpretation | | |
|----------------------------|-----------------------------|--|----------------|----------------|-------------|
| surgery | | | R-Resistant | I-Intermediate | S-Sensitive |
| Yes Acinetobacter baumanni | Acinetobacter baumanni | Ceftriaxone | R | _ | - |
| | | Ciprofloxacin | R | - | - |
| | | Gentamicin | - | - | S |
| | | Cefotaxim | R | - | _ |
| | | Tigecycline | R | - | _ |
| Yes Enterobacteriaceae | Enterobacteriaceae | Chloramphenicol | R | - | - |
| | | Ciprofloxacin | - | - | S |
| | | Trimethoprim /Sulfamethoxazole | R | - | - |
| | | Gentamicin | - | I | - |
| | | Meropenem, Amikacin and Tigecycline | - | - | S |
| Yes | Staphylococcus aureus* | Clindamycin, | R | - | - |
| | | Erythromycin, | R | - | - |
| | | Gentamicin | R | - | _ |
| | | Cefoxitin | R | - | - |

Table 4 Antibiotic susceptibility tests against the identified organisms

* Three patients with staphylococcus aureus and no antibiotic was indicated as to be sensitive

This study revealed that ruptured membrane had twice the incidence of SSIs compared to intact membrane (χ^2 =2.0922), though not statistically significant. Further, other potential factors like skin closure, BMI, HIV status, education level, age, duration of CS, parity, ANC visits and gestational age were not significant risk factors in our study sample in contrast to the previous studies [25, 29, 33, 34]. Additionally, Kaye et al. reported that age was a powerful predictor of SSI [35]. However, other studies have also reported contamination or dirt operation as a risk factor [25] and wound classification as clean contamination for the CS procedure [19].

The present study revealed that all the women who underwent CS were given antibiotic prophylaxis with ceftriaxone. The average duration from the first dose of antibiotic prophylaxis to the start of the CS procedure was 12.85 min, with a standard deviation of 8.44 (IQR=8). The prevalence of SSI and the timing of antibiotic prophylaxis in clinical practice have not been thoroughly investigated, but some clinical trials have indicated a relationship [18]. In the same study by Classen et al. [18], few patients developed SSI among those who received antibiotic prophylaxis early before the start of surgery compared to those who received antibiotics later after surgery. Furthermore, in the present study, three patients who received post-CS antibiotic prophylaxis and two patients who did not receive antibiotics after surgery had antimicrobial resistance. Of course, these patients without any confirmed infection diagnosis received antimicrobial treatment after caesarean section; hence, this therapy cannot be applied as an indicator of SSI. The inappropriate use of antimicrobial agents needlessly exposes patients to potential toxicity and risks that promote the development and spread of antimicrobial resistance, leading to increased medical care costs in healthcare facilities [25]. However, the rational use of antimicrobials in women of child-bearing age is important because it affects this population as well as their offspring. [15].

The strengths and limitations of the study

The strengths of the study include that the study revealed the emergence of AMR in the Malawian setting and that the study used primary data for SSIs following CS. However, the study was limited to SSIs following CS, and the number of HAIs occurring in other settings, such as surgical departments or wards for various hospitals for general surgery, cannot be estimated. Some patients who developed SSIs did not return to the hospital again for review, which could lead to a lack of microbiological data related to SSIs. Last, the small sample size or small number of isolates could have affected the outcomes of interest.

Conclusion

This study concludes that the incidence of 9.61% SSI following the CS procedure was relatively greater than that in other developing countries. Most patients were continued on antibiotics post CS procedure without performing culture to ascertain AMR. The inappropriate use of antibiotics may result in antimicrobial resistance. Therefore, due to the increased number of SSIs following CS and the relative emergence of antimicrobial resistance to some microorganisms, including Acinetobacter baumanni and Staphylococcus aureus, intensive infection control practices are needed and establish AMS programs and routine surveillance of SSIs at QECH. In addition, there is a need to conduct further studies on bacterial isolates and antimicrobial resistance patterns and how to best address AMR through one health approach.

Abbreviations

| AMR | Antimicrobial resistance |
|--------|---|
| AMS | Antimicrobial stewardship |
| ASA | American Society Anaesthesiologists |
| Abx | Antibiotics |
| CDC | Centres for Diseases Control and Prevention |
| COMREC | College of Medicine Research Ethics Committee |
| CS | Caesarean section |
| ESBLs | Extended-spectrum β-lactamases |
| HAIs | Healthcare-associated infections |
| IQR | Interquartile range |
| IPC | Infection prevention and control |
| KUHeS | Kamuzu University of Health Sciences |
| LMIC | Low- and middle-income countries |
| QECH | Queen Elizabeth Central Hospital |
| SSIs | Surgical site infections |
| US CDC | United States Centre for Diseases Control |
| WHO | World Health Organization |

Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s13756-024-01483-5.

Additional file 1.

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Author contributions

ATK originated the research idea and analyzed the data. DKK, SJM and JM contributed to supervision, data analysis and writing the manuscript. All authors reviewed the manuscript.

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Availability of data and materials

Data is provided within the manuscript and the datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Competing Interests

The authors declare no competing interests.

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