Implementing a Combined Infection Prevention and Control with Antimicrobial Stewardship Joint Programme to Prevent Caesarean Section Surgical Site Infections and Antimicrobial Resistance: a Tanzanian Tertiary Hospital Experience

Elisa Gentilotti (dr.elisagentilotti@gmail.com)
INMI Lazzaro Spallanzani IRCCS https://orcid.org/0000-0001-6018-5295
Pasquale De Nardo
INMI Lazzaro Spallanzani IRCCS
Boniface Nguhuni
Dodoma Regional Referral Hospital
Alessandro Piscini
INMI Lazzaro Spallanzani IRCCS
Caroline Damian
Dodoma Regional Referral Hospital
Francesco Vairo
INMI Lazzaro Spallanzani IRCCS
Zainab Chaula
Dodoma Regional Referral Hospital
Paola Mencarini
INMI Lazzaro Spallanzani IRCCS
Peter Torokaa
Dodoma Regional Referral Hospital
Alimuddin Zumla
University College of London
Emanuele Nicastri
INMI Lazzaro Spallanzani IRCCS
Giuseppe Ippolito
INMI Lazzaro Spallanzani IRCCS

Research

Keywords: Caesarean section, Surgical site infection, Antimicrobial resistance, Antimicrobial stewardship, Resource-limited settings

Posted Date: February 3rd, 2020

DOI: https://doi.org/10.21203/rs.2.22465/v1

Abstract

Background

Surgical site infections after caesarean section are a leading cause of morbidity and mortality, especially in Low and Middle Income Countries. We hypothesized that combining infection prevention and control with an antimicrobial stewardship programme would decrease the rate of post- caesarean section surgical site infections at the Obstetrics & Gynaecology Department of a Tanzanian tertiary hospital.

Methods

A first survey was conducted to assess the burden of post-CS SSI. Thereafter, an intervention was introduced including: 1. formal on-the-job training on infection prevention and control; 2. evidence-based education on antimicrobial resistance and good antimicrobial prescribing practice. A second survey was performed to determine the impact of the intervention. The primary outcome of the study was information on the prevalence of post-caesarean section surgical site infections whereas the secondary outcome was the identification of the determinant factors of surgical site infections before/after the intervention and overall. The microbiological characteristics and patterns of antimicrobial resistance were also established.

Results

A total of 464 and 573 women were surveyed before and after the intervention, respectively. After the intervention, the antibiotic prophylaxis was administered to a significantly higher number of patients (98% vs 2%, p <0.001), caesarean sections were performed by more qualified operators (40% vs 28%, p =0.001), with higher rates of Pfannenstiel skin incisions (29% vs 18%, p <0.001) and of absorbable continuous intradermic sutures (30% vs 19%, p <0.001). The total number of post-caesarean section surgical site infections was 225 (48%) in the pre-intervention group and 95 (17%) in the post intervention group (p <0.001). A low prevalence of gram-positive isolates and of methicillin-resistant Staphylococus aureus was detected in the post-intervention survey.

Conclusions

Further research is needed to better understand the potential of a hospital-based multidisciplinary approach to surgical site infections and antimicrobial resistance prevention in resource-constrained settings.

Background

Health-care associated infections (HAIs) and antimicrobial resistance (AMR) are recognized worldwide as major global health challenges. They are particularly important in Low and Middle Income countries (LMICs) [1, 2] where high level of resistance to commonly prescribed antibiotics together with lack of local AMR surveillance systems need urgent attention [3, 4]. According to the World Health Organization (WHO), HAIs are increasing at alarming high rates in LMICs, being two-to twenty-times higher than in high-income countries [5].

Surgical Site infection (SSI) is the most frequent cause of HAIs in LMICs, affecting up to one third of patients undergoing surgery [6]. In light of this, WHO guidelines for SSI prevention have outlined a roadmap for quality improvement and suggested a multimodal strategy and multidisciplinary approach [7–9]. A cultural and attitudinal change is essential to ensure that protocols for Infection Prevention and Control (IPC) and Antimicrobial Stewardship (AMS) are strictly followed [10]. Although SSIs are largely avoidable, in LMICs they continue to be a leading cause of morbidity and mortality also among women undergoing caesarean section (CS), a life-saving procedure classified as a clean-contaminated operative wound according to the Centre for Diseases Control (CDC) Classification [11].

Dodoma Regional Referral Hospital (DRRH) is one of the few centres of the Dodoma Region, Tanzania, offering CS services. A prospective observational study conducted in 2013 at the Obstetrics & Gynaecology Department (OGD) of DRRH reported an extremely high prevalence of CS-SSIs (48.2%), 40.6% of them caused by Staphilococcus aureus, of which 79% were methicillin-

resistant Staphylococcus aureus (MRSA) [12]. A recent before-after intervention cohort study, conducted in five hospitals of sub-Saharan Africa, found that a multimodal SSI prevention strategy in low-resource settings can reduce the risk of SSIs [13].

Our study aimed to assess the impact of the implementation of a combined IPC with AMS joint programme on the prevalence of CS associated SSIs at DRRH.

Methods

Study design

A before-after intervention cohort study was conducted during two years starting from August 2013 at the OGD of DRRH. The study included a pre-intervention survey (PRE-Int), an intervention and a post-intervention survey (POST-Int). Each of the two surveys lasted three months and were conducted during the dry season. The study was directly supported by the Resource Centre for Infectious Diseases (RCID) of DRRH. The intervention included literature-based education, on-the-job training and the establishment of an AMS multidisciplinary team.

Study sites and study population

DRRH has a bed capacity of 580 and 5 operating theatres, of which one is dedicated to the OGD. Data available from 2013 to 2015 report an average number of 14,800 deliveries per year, with approximately 2,700 (18%) CS.

Study procedures

A four-step protocol was adopted (Fig. 1). The first step consisted of the PRE-Int, enrolling all consecutive women undergoing a CS during three months from August 19, 2013, with a 30 day-post-CS follow up. During the second step, data from the PRE-Int were shared with the hospital staff. Thereafter, an AMS Multidisciplinary Team was set up, including an Infectious Diseases (ID) Specialist, the head of OGD, a pharmacist, an IPC nurse, a clinical microbiologist and a representative of the hospital management. These professionals identified the prevention measures and the interventions to be prioritized as follows: a) implementing the reporting system; b) strengthening the supply chain for antibiotics, disinfectants and operating room/laboratory disposables; c) proper surgical hand preparation; d) administration of a pre-operative prophylaxis 30–60 minutes before the incision; e) optimizing the appropriateness of antibiotic prescription in the post-operative period; f) improving operating theatre discipline and organization and g) strengthening the capability and capacity of the Microbiology Unit. In particular, the importance of the prophylaxis was underlined. In fact, before the intervention, almost every woman received an antibiotic course lasting 8–10 days post-CS, irrespective of the presence of risk factors or signs/symptoms of infection. The antibiotic course usually included 3 days of intravenous ceftriaxone plus metronidazole, followed by oral penicillin (amoxicillin alone or ampicillin/cloxacillin) plus metronidazole for at least 5 days. The timing was highly variable, ranging from 1 to 24 hours post-CS. A pre-operative prophylaxis with ampicillin 1 g given 30–60 minutes before the incision was suggested, based on drugs availability. The third step consisted of the introduction of the prevention measures into clinical practice and in the organization of seminars focusing on IPC and AMS. Literature-based education was encouraged. On-the-job training was also conducted under the supervision of a pool of ID specialists and clinical microbiologists. Standard Operating Procedures (SOPs), recent publications, guidelines, expert consultation and mentorship on data collection were available at the RCID from Monday to Friday. The last step included the POST-Int, enrolling all consecutive women undergoing a CS during three months starting from April 1, 2015, followed by 30 days post-CS surveillance.

Survey and laboratory procedures

A 30-day follow up was conducted, including a variable number of visits starting from day 7 post-CS. The aim was to have at least one post-operative contact with the patient, either by clinical visit or telephone [14]. Patients were considered lost to follow up after five unsuccessful attempts by telephone. At each visit, an examination of the wound was performed by an ID specialist and the antibiotic treatment history was collected. In case of telephone contact, a structured interview was used to detect SSIs. If SSI was suspected, the patient was referred to the nearest health centre. The classification of SSIs was done according to CDC definitions [11]. In any case, if SSI was suspected, a wound swab was collected. The specimens were processed soon after

collection. Briefly, the specimens were inoculated on blood agar and MacConkey agar and incubated aerobically. Petri dishes were checked after 24 and 48 hours for bacteria detection and identification. Antimicrobial susceptibility of isolates was determined using disc diffusion method. The antibiotics tested included: oxacillin (1 µg), ampicillin (10 µg), amoxicillin (25 µg), amoxicillin/clavulanate (20 µg + 10 µg), clindamycin (2 µg), erythromycin (15 µg), ciprofloxacin (5 µg), trimethoprim-sulfamethoxazole (1.25 µg + 23.75 µg), ceftriaxone (30 µg), chloramphenicol (30 µg), gentamicin (10 µg), tetracycline (30 µg). Vancomycin 5 µg, ceftazidime 10 µg and meropenem 10 µg were also tested in the POST-Int study. Based on Kirby-Bauer susceptibility test, gram-negative bacteria were classified as multidrug resistant organisms (MDROs) if resistances to amoxicillin/clavulanate, ceftriaxone (or ceftazidime), and/or gentamycin, and/or ciprofloxacin were detected. MRSA were identified by using the diffusion method with oxacillin disc [15, 16].

Outcomes

The primary outcome was to report the CS-SSIs rate. The secondary outcome was to assess the determinant factors of SSIs before/after the intervention and overall. The microbiological characteristics and patterns of AMR were determined to provide an overall picture of the SSIs.

Data collection and statistical analysis

All consecutive CS performed during the study period were eligible for inclusion in the analysis. Data were retrieved from different sources, including: hospital medical records, antenatal cards, surgical notes and structured telephone interviews following a standardized questionnaire. Data collection was done by trained staff from the RCID and entered in a dedicated Microsoft Excel dataset. Comparison of mean values was done using the Student's t test. The χ^2 test and Fisher's exact test were used to explore univariate associations between categorical variables. Log binomial regression model was adopted for multivariate analysis to detect the association between predictor variables and SSIs and to assess the impact of the intervention on outcomes. Co-variates with $p < 0.1$ were considered for multivariate analysis. Odd ratios and confident intervals were computed. A $p < 0.05$ was considered significant. The statistical analysis was performed using SPSS (software version 21, NY, U.S.A.).

Results

Comparison of demographic and surgical procedure characteristics

Overall, 1377 women with CS were enrolled, 664 (48.2%) in the PRE-Int study and 713 (51.8%) in the POST-Int study. The follow-up was available for 1040 women, 467 (70%) and 573 (81%) in the two studies, respectively (Fig. 2). A total number of 337 (25%) women (197 and 140 in the two studies, respectively) were lost to follow up. The demographic characteristics were similar in the two populations. In the POST-Int, a higher proportion of women had a college/university education ($p = 0.027$), but SSI prevalence was not affected by the level of education.

Table 1 presents the CS characteristics and the surgical procedures in all enrolled patients with available follow-up and in the two study populations, separately (table 1). The number of elective CS performed was higher in the PRE-Int group ($p = 0.059$). A significantly lower proportion of women with known indication for CS (cephalopelvic disproportion, bad obstetric history, previous CS) was reported in the POST-Int group ($p = 0.043$). In the POST-Int study, a greater CS number was performed by experienced surgeons ($p < 0.001$) and pre-incision antibiotic prophylaxis was administered in more cases ($p < 0.001$). The timing of prophylaxis was reported to be adequate only in 28% of cases in the POST-Int group, but this did not seem to affect SSI prevalence. On the other hand, post-operative antibiotic administration was significantly lower in the POST-Int group ($p < 0.001$). Skin disinfection was performed using povidone/iodine in the majority of POST-Int operations ($p < 0.001$). In the POST-Int group Pfannenstiel incision, absorbable and continuous intradermic/semi-subcutaneous sutures were more often adopted compared to PRE-Int group ($p < 0.001$). The mean number of days of hospitalization was similar in both groups (approximately two days).

Rate and determinants of SSIs in the PRE-Int and POST-Int populations

Overall, 320 (30.8%) SSIs were reported in all enrolled women, 225 (48.2%) in the PRE-Int group and 95 (16.6%) in the POST-Int group ($p < 0.001$) (table 1). SSI diagnosis at first visit (approximately 8 days after CS) was higher in the PRE-Int group ($p = 0.037$). The diagnosis of deep/involving organs and/or spaces infections was done in 74 (32.9%) SSIs in the PRE-Int vs 11 (11.6%) SSIs in the POST-Int group ($p < 0.001$). The analysis of CS-SSI determinant factors is shown in table 2 (table 2).

In the overall and per-group analysis the risk of CS SSI was lower in case of Pfannenstiel incision (overall: OR 0.288; 95%CI 0.197–0.420; $p < 0.001$) and of continuous intradermic/semi-subcutaneous sutures (overall: OR 0.322; 95%CI 0.226–0.460; $p < 0.001$). In the PRE-Int group only, a more experienced surgeon was significantly associated with a lower CS-SSI risk (OR 0.644; 95%CI 0.425–0.974; $p = 0.038$). In the POST-Int group, younger age of the patient was significantly associated with higher risk of SSI (OR 2.379; 95%CI 1.384–4.089; $p = 0.001$), whereas the use of absorbable stitches was found to be protective (OR 0.468; 95%CI 0.269–0.814; $p = 0.006$). This finding was confirmed when pooled data from the two studies were combined (OR 0.539; 95%CI 0.387–0.750; $p < 0.001$).

In the PRE-Int and POST-Int studies no significant SSI differences with respect to skin disinfection and body mass index (BMI) were reported. Nevertheless, in all enrolled population, the use of povidone-iodine and a low BMI were significantly associated with a lower SSI risk ($p = 0.031$ and $p < 0.001$, respectively).

At multivariate analysis, no variables associated with SSI were significant in the PRE-Int study. In the POST-Int study, younger age and vertical incision were found to be independent risk factors for SSI (OR 1.893; 95%CI 1.055–3.396; $p = 0.032$ and OR 3.230; 95%CI 1.403–7.435; $p = 0.006$, respectively). Overall multivariate analysis showed an independent association between SSI and lack of pre-incision antibiotic prophylaxis (OR 4.003; 95%CI 2.461–6.513; $p < 0.001$). Conversely, the utilization of absorbable sutures for skin closure was an independent protective factor (OR 0.510; 95%CI 0.276–0.944; $p < 0.032$).

Microbiological characteristics

The rate of microbiologically-confirmed SSIs was considerably higher in the POST-Int study compared with the previous survey (OR 2.534; 95% CI 1.435–4.475; $p = 0.001$). The prevalence of SSIs caused by gram-positive bacteria significantly decreased (OR 0.263; 95% CI 0.126–0.548; $p < 0.001$), and the MRSA prevalence rate dropped from 79–21.4% (OR 0.072; 95% CI 0.016–0.314; $p < 0.001$). All MRSA isolates detected in the second survey had an inducible resistance to clyndamicin (data not available in the first survey). Overall, 16 (43.2%), 5 (13.5%) and 2 (5.4%) MRSA isolates were susceptible to tetracycline, chloramphenicol and cotrimoxazole, respectively. Enterococcus spp was not identified in the PRE-Int study while in the POST-Int, it accounted for 16.1% of the pathogens isolated. Eighty per cent of the Enterococcus spp were resistant to ampicillin. The prevalence of SSIs due to gram-negative (including Klebsiella spp and Pseudomonas spp) significantly increased in the POST-Int study (OR 3.800; 95% CI 1.822–7.926; $p < 0.001$). Overall, more than half gram-negative had a phenotypic profile consistent with MDROs. Finally, no resistances to vancomicin and meropenem were observed.

Discussion

A substantial decrease in SSI rates was observed after the introduction of a combined IPC with AMS joint programme.

Impact of IPC and AMS intervention on CS SSI incidence

This multimodal approach led to a reduction by more than 30% in the CS SSIs rates. Furthermore, less SSIs were detected at first visit (8 days after the CS) in the POST-Int group, possibly suggesting that fewer infections were acquired in the theatre room and during inpatient stay [17]. Strengthening the chain supply for antibiotics and skin disinfectant was a priority. In the POST-Int study almost every CS was preceded by an antibiotic prophylaxis, and the skin disinfection was performed following a standardized procedure in the vast majority of cases. The AMS intervention led to more appropriate antibiotic prescription, as documented also by other studies in LMICs [18]. Post-CS antimicrobial prescription was limited to cases requiring treatment. Administering multiple doses of post-operative antibiotics was not associated with a better outcome compared with pre-operative single dose prophylaxis, as also reported by other authors [19, 20]. Furthermore, by administering a pre-operative prophylaxis instead of a 3 day-intravenous-post-operative course, we estimate that hospital total cost savings can be quantified

at approximately €1500 during the Post-Int study. Moreover, a reduction of post-discharge antibiotics prescription by approximately 70% was achieved. This led to a personal saving of around €3/patient in a country where 28% of the population is estimated to live under the national basic needs poverty line (approximately €14/month per adult) [21]. These findings suggest that AMS programmes are highly recommended in LMICs to improve the prescription attitude and to reduce the burden of health-care associated costs.

The study was not designed to assess the impact of each prevention measure on the occurrence of SSIs. A study with a more robust design, such as an interrupted time series analysis or a controlled randomized clinical trial would be useful to better address this issue [22, 23].

Risk factors for post-CS before and after the intervention

Formal education and on-the-job training of the health-care personnel were essential components of this intervention. In particular, after sharing evidence from literature, including reviews [24–27] and guidelines, we observed improvements in the operating room discipline and a more rigorous compliance to SOPs and reporting tools. The supervision of younger doctors was encouraged according to literature [12, 25, 28]. Therefore, in the POST-Int study, a greater number of CS were performed by more experienced doctors. Overall, an association between younger surgeons and SSIs was detected at univariate analysis. Higher rates of Pfannenstiel incision and of absorbable continuous/semi-subcutaneous sutures for skin closure were also observed in the POST-Int. These variables were associated with an overall lower risk to develop SSIs, and absorbable sutures was associated with lower risk of SSIs even at multivariate analysis. Literature-based evidence suggests that subcutaneous tissue closure is associated with fewer wound complications [29], but the outcome may be different according to the type of CS incision [30]. Further well-designed trials at low risk of bias are needed to provide non-conflicting results on the best type of suturing.

Changes in the characteristics of the isolates after the intervention

A greater proportion of microbiologically-confirmed SSIs in the POST-Int study was reported, possibly related to a better collection and processing of the samples. Also the laboratory diagnostic capability seemed to be improved, as suggested by the detection of Enterococcus spp, which was not identified in the PRE-Int study. In 2016 the DRRH Laboratory has been audited by the WHO AFRO Stepwise Laboratory Quality Improvement Process Towards Accreditation (SLIPTA) Checklist and has met the requirement for “three star” recognition level.

The significant reduction of gram-positive strains isolated and the lower MRSA prevalence in the second survey are noteworthy. This is likely a consequence of the AMS education and on-the-job training which dramatically affected the health care workers’ attitude and behaviour towards antibiotic prescription and IPC [31]. By avoiding unnecessary use of ceftriaxone in the post-operative period, the intervention may have contributed to the reduction in MRSA rates in the second survey. The choice of Ampicillin for prophylaxis depended on the unavailability of cefazolin, which is more widely used for surgical prophylaxis and more effective against Staphilococcus aureus [32]. Probably, this is the reason for which we observed a similar rate in MSSA before and after the intervention. On the other hand, considering the unavailability of second line antibiotics in the majority of health facilities in Tanzania, the high rate of MDROs - including gram-negative bacteria detected in this study is a serious concern. The lack of detailed data on MDROs prevalence throughout the country highlights the need for building an efficient surveillance system in order to guide continuous targeted interventions.

Conclusions

The intervention implemented within this study was a multidisciplinary collaborative strategy involving, among others, hospital management, the pharmacist, the microbiologist and a dedicated nurse. This AMS Multidisciplinary Team worked to improve the SSI prevention, surgical procedures and laboratory capability and cooperated to ensure a better management of wound infections. The participation of different health-care figures could be key to obtain an efficient hospital based surveillance system, able to detect the gap, prioritize interventions and inform national and international institutions on the magnitude of AMR [4].

This multimodal approach demonstrated to be effective in a resource-constrained setting and highlighted the need to improve IPC and AMR education of hospital staff [9]. Improved SSI and AMR surveillance is warranted to better understand the occurrence of SSIs and their microbiological characteristics. Further IPC-AMS joint programmes with robust study designs should be encouraged and scaled up in LMICs.

List Of Abbrevations

AMR - Antimicrobial Resistance

AMS - Antimicrobial Stewardship

BMI - Body Mass Index

CDC - Centre for Diseases Control

CS - Caesarean Section

DRRH - Dodoma Regional Referral Hospital

HAI - Health-care Associated Infection

ID - Infectious Diseases

IPC - Infection Prevention and Control

LMIC - Low and Middle Income Country

MDRO - Multidrug Resistant Organisms

MRSA - Methicillin-Resistant Staphylococcus aureus

OGD - Obstetrics & Gynaecology Department

POST-Int - post-intervention survey

PRE- Int - pre-intervention survey

RCID - Resource Centre for Infectious Diseases

SOP - Standard Operating Procedure

SSIs - Surgical site infections

WHO - World Health Organization

Declarations

Ethics approval and consent to participate

This study was approved by the Hospital Management of DRRH and the Tanzanian National Institute for Medical Research (NIMR/HQ/R.8a/vol. IX/1927). All enrolled patients provided written informed consent. All data were anonymized.

Consent to publication

Not applicable.

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by the Italian Ministry of Health [Ricerca Corrente Linea 1] and the Italian Development Cooperation, Ministry of Foreign Affairs [AID9562].

Authors' contributions

PDN and EG designed the study. Patients were clinically reviewed by PDN, EG, BN, and PM. AP was responsible of the microbiology procedures. EG performed the statistical analysis. EN and FV were involved in drafting the manuscript and reviewing the literature. AZ and GI revised the final paper. All authors read and approved the final manuscript.

Acknowledgements

We thank Prof. Stephan Harbarth, University of Geneva, for his input into scientific advice. We also thank all the staff working at the Obstetrics and Gynaecology Department of the Dodoma Regional Referral Hospital and Post-Natal Care of the Makole Health Centre.

References

1. Laxminarayan R, Heymann DL. Challenges of drug resistance in the developing world. BMJ, **2012**; 344:e1567.
2. Allegranzi B, Bagheri Nejad S, Combescure C, et al. Burden of endemic healthcare-associated infection in developing countries: systematic review and meta-analysis. Lancet, **2011**; 377: 228–41.
3. Tadesse BT, Ashley EA, Ongarello S, Havumaki J, Wijegoonewardena M, González IJ, Dittrich S. Antimicrobial resistance in Africa: a systematic review.BMC Infect Dis, **2017**; 11;17(1):616.
4. Perovic O. Schultsz C. Stepwise approach fr implementation of antimicrobial resistance surveillance in Africa. Afr J Lab Med, **2016**; 31;5(3):482.
5. Bagheri Nejad S, Allegranzi B, Syed SB, Ellis B, Pittet D. Health-care-associated infection in Africa: a systematic review. Bull World Health Organ, **2011**; 89: 757–65.
6. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals. Stockholm: European Centre for Disease Prevention and Control, 2013. Available at: http://ecdc.europa.eu/en/publications/Publications/ healthcare-associated infections-antimicrobial-use-PPS.pdf. Accessed 9 Oct 2018.
7. Allegranzi B, Bischoff P, de Jonge S, et al. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis, **2016**; 16: e276–87.
8. Allegranzi B, Zayed B, Bischoff P, et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis, **2016**; 16: e288–303.
9. WHO surgical safety checklist. Available at: http://www.who.int/patientsafety/safesurgery/checklist/en/. Accessed 18 Jan 2019.
10. Haynes AB, Weiser TG, Berry WR, et al. Changes in safety attitude and relationship to decreased postoperative morbidity and mortality following implementation of a checklist-based surgical safety intervention. BMJ Qual Saf, **2011**; 20: 102–07.
11. Horan TC, Gaynes RP, Martone WJ, Jarvis WR. Grace Emori T. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Am J InfectControl, **1992**; 20:271e274.

12. De Nardo P, Gentilotti E, Nguhuni B, Vairo F, Chaula Z, Nicastri E, Nassoro MM, Bevilacqua N, Ismail A, Savoldi A, Zumla A, Ippolito G. Post-caesarean section surgical site infections at a Tanzanian tertiary hospital: a prospective observational study. J Hosp Infect., **2016**; 93(4):355-9.
13. Allegranzi B,Aiken AM, Zeynep Kubilay N, Nthumba P, Barasa J, Okumu G, Mugarura R, Elobu A, Jombwe J, Maimbo M, Musowoya J, Gayet-Ageron A, Berenholtz SM. A multimodal infection control and patient safety intervention to reduce surgical site infections in Africa: a multicentre, before-after, cohort study. Lancet Infect Dis, **2018** Mar 5. pii: S1473-3099(18)30107-5. [Epub ahead of print]
14. Nguhuni B, De Nardo P, Gentilotti E, *et al*. Reliability and validity of using telephone calls for post-discharge surveillance of surgical site infection following caesarean section at a tertiary hospital in Tanzania. Antimicrob Resist Infect Control, **2017**; 6: 43.
15. European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 4.0, 2014. Available at: http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/Breakpoint_table_v_4.0.pdf. Accessed 18 Jan 2019.
16. European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 3.1, 2013. Available at: http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/Breakpoint_table_v_3.1.pdf. Accessed 18 Jan 2019.
17. Kawakita T, Landy HL. Surgical site infections after cesarean delivery: epidemiology, prevention and treatment. Matern Health Neonatol Perinatol. 2017; 3: 12.
18. Aiken AM, Wanyoro AK, Mwangi J, Juma F, Mugoya IK, Scott JA. Changing use of surgical antibiotic prophylaxis in Thika Hospital, Kenya: a quality improvement intervention with an interrupted time series design. PLoS One, **2013**; 8(11):e78942.
19. Lyimo, F. M., Massinde, A. N., Kidenya, B. R., Konje, E. T. & Mshana, S. E. Single dose of gentamicin in combination with metronidazole versus multiple doses for prevention of post-caesarean infection at Bugando Medical Centre in Mwanza, Tanzania: a randomized, equivalence, controlled trial. BMC Pregnancy Childbirth, **2013**; 13:123.
20. Abdel Jalil MH, Abu Hammour K, Alsous M, et al. Surgical site infections following caesarean operations at a Jordanian teaching hospital: Frequency and implicated factors. Sci Rep, **2017**; 7(1):12210.
21. The World Bank. Tanzania - Mainland poverty assessment (Vol. 2) : Main report. Available at: http://documents.worldbank.org/curated/en/530601468179976437/Main-report. Accessed 18 Jan 2019.
22. de Kraker MEA, Abbas M, Huttner B, Harbarth S. Good epidemiological practice: a narrative review of appropriate scientific methods to evaluate the impact of antimicrobial stewardship interventions. Clin Microbiol Infect, **2017**; 23(11):819-825.
23. Schweitzer VA, van Heijl I, van Werkhoven CH, Islam J, Hendriks-Spoor KD, Bielicki J, Bonten MJM, Walker AS, Llewelyn MJ; Consensus on Antimicrobial Stewardship Evaluations (CASE) study group. The quality of studies evaluating antimicrobial stewardship interventions: a systematic review. Clin Microbiol Infect, **2018;** S1198-743X(18)30728-6.
24. Nthumba PM1, Stepita-Poenaru E, Poenaru D, Bird P, Allegranzi B, Pittet D, Harbarth S. Cluster-randomized, crossover trial of the efficacy of plain soap and water versus alcohol-based rub for surgical hand preparation in a rural hospital in Kenya. Br J Surg, **2010**; 97(11):1621-8.
25. Mpogoro FJ, Mshana SE, Mirambo MM, et al.Incidence and predictors of surgical site infections following caesarean sections at Bugando Medical Centre, Mwanza, Tanzania. Antimicrob Resist Infect Control, **2014**; 3:25.
26. Dahlke JD, Mendez-Figueroa H, Rouse DJ. Evidence-based surgery for cesarean delivery: an updated systematic review. Am J Obstet Gynecol, **2013**; 209(4):294-306.
27. Mackeen AD, Berghella V, Larsen ML.Techniques and materials for skin closure in caesarean section. Cochrane Database Syst Rev, **2012**; 11:CD003577.
28. Corcoran S, Jackson V, Coulter-Smith S, et al. Surgical site infection after cesarean section: Implementing 3 changes to improve the quality of patient care. Am J Infect Control, **2013**; 41(12):1258-63

29. PergialiotisV, Prodromidou A, Perrea DN, et al. The impact of subcutaneous tissue suturing at caesarean section on wound complications: a meta-analysis. BJOG, **2017**; 124(7):1018-1025.
30. Mackeen AD, Berghella V, Larsen ML. Techniques and materials for skin closure in caesarean section. Cochrane Database Syst Rev, **2012**; (9):CD003577.
31. Bitew Kifilie A, Dagnew M, Tegenie B, Yeshitela B, Howe R, Abate E. Bacterial Profile, Antibacterial Resistance Pattern, and Associated Factors from Women Attending Postnatal Health Service at University of Gondar Teaching Hospital, Northwest Ethiopia. Int J Microbiol, **2018**; 2018:3165391.
32. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, Fish DN, Napolitano LM, Sawyer RG, Slain D, Steinberg JP, Weinstein RA; American Society of Health-System Pharmacists; Infectious Disease Society of America; Surgical Infection Society; Society for Healthcare Epidemiology of America. Clinical practice guidelines for antimicrobial prophylaxis in surgery. M J Health Syst Pharm, **2013**; 70(3):195-283.

Tables

Table 1. Overall and per-groups analysis of surgical procedure and CS-SSI Characteristics				
	Overall (n=1040) n (col%)	**PRE-Int (n=467) n (col%)**	**POST-Int (n=573) n (col%)**	***p*-value**
CS type				0.059
Elective	76 (7.3)	42 (9.0)	34 (5.9)	
Emergency	964 (92.7)	425 (91.0)	539 (94.1)	
Reason for CS				0.043
CS indication	431 (41.4)	209 (44.8)	222 (38.7)	
No CS indication	606 (58.3)	255 (54.6)	351 (61.3)	
Not known	3 (0.3)	3 (0.6)	0	
Operator grade				0.001
Senior	345 (33.1)	127 (27.2)	218 (38.1)	
Junior	685 (65.9)	337 (72.2)	348 60.7)	
Not known	10 (1.0)	3 (0.6)	7 (1.2)	
Skin disinfection				0.000
Dettol	2 (0.2)	0	2 (0.3)	
Ethanol	94 (9.0)	90 (19.3)	4 (0.7)	
Povidone/Iodine	923 (88.8)	366 (78.4)	557 (97.2)	
Not known	21 (2.0)	11 (2.4)	10 (1.7)	
Tipe of CS incision				0.000
Pfannenstiel	247 (23.8)	82 (17.6)	165 (28.8)	
Midline Vertical	737 (70.9)	341 (73.0)	396 (69.1)	
Not known	56 (5.4)	44 (9.4)	12 (2.1)	
Material used for skin sutures				0.000
Silk (non-absorbable)	693 (66.6)	339 (72.6)	354 (61.8)	
Vicryl (absorbable)	265 (25.5)	91 (19.5)	174 (30.4)	
Not known	82 (7.9)	37 (7.9)	45 (7.9)	
Sutures type				0.000
Type 1[a]	700 (67.3)	327 (70.0)	373 (65.1)	
Type 2[b]	260 (26.0)	96 (20.6)	174 (30.4)	
Not known	70 6.7	44 (9.4)	26 (4.5)	
Abx[c] Prophy[d]				0.000
No	457 (43.9)	451 (96.6)	6 (1.0)	
Yes	572 (55.0)	10 (2.1)	562 (98.1)	

Not Known	11 (1.1)	6 (1.3)	5 (0.9)	
Timing of Abx[c] Prophy[d]				0.017
Appropriate	162 (28.3)	5 (50)	157 (27.9)	
Not appropriate	372 (65)	2 (20)	370 (65.8)	
Not known	38 (6.7)	3 (30)	35 (6.3)	
Abx[c] administration				0.000
No	406 (39.0)	4 (0.9)	402 (70.2)	
Yes	627 (60.3)	459 (98.2)	168 (29.3)	
Not Known	7 (0.7)	4 (0.9)	3 (0.5)	
Day 1° visit, mean, range (±SD)	8.5, 1-38 (3.4)	8.5, 2-37 (2.5)	8.4, 1-38 (4.0)	0.701
Wound infection				0.000
Yes	320 (30.8)	225 (48.2)	95 (16.6)	
No	720 (69.2)	242 (51.8)	478 (83.4)	
Wound infection at 1° visit				0.037
Yes	224 (21.5)	166 (73.8)	58 (61.1)	
No	742 (71.3)	57 (25.3)	37 (38.9)	
Not known	2 (0.2)	2 (0.9)	0	
Type of wound infection				0.000
Type 1[e]	218 (21.0)	138 (61.3)	80 (84.2)	
Type 2[f]	85 (8.2)	74 (32.9)	11 (11.6)	
Not known	17 (1.6)	13 (5.8)	4 (4.2)	

[a]Interrupted; [b]Continuous-intradermic and semisubcutaneous; [c]Antibiotic; [d]Prophylaxis; [e]Superficial; [f]Deep/involving organ and/or space

Table 2. Analysis of risk factors for SSI in patients undergoing CS in the PRE-Int and POST-Int groups and Overall									
	Overall (n=1040)			**PRE-Int (n=467)**			**POST-Int (n=573)**		
	SSI (n=320)	**No SSI (n=720)**	**p-value**	**SSI (n=225)**	**No SSI (n=242)**	**p-value**	**SSI (n=95)**	**No SSI (n=478)**	**p-value**
Age, years			0.403			0.561			0.009
<20	58 (35.2)	107 (64.8)		33 (43.4)	43 (56.6)		25 (28.1)	64(71.9)	
21-34	220 (29.9)	516 (70.1)		164 (48.4)	175 (51.6)		56 (14.1)	341 (85.9)	
>34	39 (29.8)	92 (70.2)		27 (52.9)	24 (47.1)		12 (15.0)	68 (85.0)	
Not known				1 (100)	0		2 (28.6)	5 (71.4)	
BMI, median (range)	27.8 (14-46)	26.9 (16-66)	0.031	27.7 (19-46)	26.7 (18-45)	0.060	27.8 (14-41)	27 (16-66)	0.224
Education			0.327			0.518			0.621
No	46 (35.1)	85 (64.9)		34 (51.5)	32 (48.5)		12 (18.5)	53 (81.5)	
Standard 7[a]	165 (31.2)	364 (68.8)		112 (46.5)	129 (53.5)		53 (18.4)	235 (81.6)	
Form I-VI[b]	88 (30.4)	201 (69.6)		68 (51.5)	64 (48.5)		20 (12.7)	137 (87.3)	
College/University	16 (21.1)	60 (78.9)		7 (33.3)	14 (66.7)		9 (16.4)	46 (83.6)	
Not known	5 (33.3)	10 (66.7)		4 (57.1)	3 (42.9)		1 (12.5)	7 (87.5)	
HIV+			0.097			0.462			0.104
Yes	16 (44.4)	20 (55.6)		10 (58.8)	7 (41.2)		6 (31.6)	13 (68.4)	
No	295 (30.4)	676 (69.6)		211 (48.2)	227 (51.8)		84 (15.8)	449 (84.2)	
Not known	9 (27.3)	24 (72.7)		4 (33.3)	8 (66.7)		5 (23.8)	16 (76.2)	
CS type			0.607			0.469			0.338
Elective	21 (27.6)	55 (72.4)		18 (42.9)	24 (57.1)		3 (8.8)	31 (91.2)	
Emergency	299 (21.0)	665 (69.0)		207 (48.7)	218 (51.3)		92 (17.1)	447 (82.9)	
Indication for CS			0.801			0.558			0.084
Previously known[c]	133 (30.8)	299 (69.2)		104 (49.5)	106 (50.5)		29 (13.1)	193 (86.9)	
Not previously known	187 (30.8)	420 (69.2)		121 (47.3)	135 (52.7)		66 (18.8)	285 (81.2)	
Operator grade			0.006			0.038			1.000

Junior	229 (33.4)	456 (66.6)		172 (51.0)	165 (49.0)		57 (16.4)	291 (83.6)	
Senior	87 (25.2)	258 (74.8)		51 (40.2)	76 (59.8)		36 (16.5)	182 (83.5)	
Skin disinfection			<0.001			0.410			1.000
Dettol/Ethanol	48 (50.0)	48 (50.0)		47 (52.2)	43 (47.8)		1 (16.7)	5 (83.3)	
Povidone-Iodine	265 (28.7)	658 (71.3)		172 (47.0)	194 (53.0)		93 (16.7)	464 (83.3)	
Type of incision			<0.001			<0.001			<0.001
Midline Vertical	280 (38.0)	457 (62.0)		198 (58.1)	143 (41.9)		82 (20.7)	152 (92.1)	
Pfannenstiel	37 (15.0)	210 (85.0)		24 (29.3)	58 (70.7)		13 (7.9)	314 (79.3)	
Skin sutures			<0.001			0.370			0.006
Silk	237 (34.2)	456 (65.8)		167 (49.3)	172 (50.7)		70 (19.8)	284 (80.2)	
Vicryl (absorbable)	58 (21.9)	207 (78.1)		40 (44.0)	51 (56.0)		18 (10.3)	156 (89.7)	
Sutures type			<0.001			<0.001			<0.001
Type 1[d]	268 (38.3)	432 (61.7)		190 (58.1)	137 (41.9)		78 (20.9)	295 (79.1)	
Type 2[e]	45 (16.7)	225 (83.3)		31 (32.3)	65 (67.7)		14 (8.0)	160 (92.0)	
Abx[f] Prophy[g]			<0.001			1.000			1.000
No	216 (47.3)	241 (52.7)		215 (47.7)	236 (52.3)		1 (16.7)	5 (83.3)	
Yes	97 (17.0)	475 (83.0)		5 (50.0)	5 (50.0)		92 (16.4)	470 (83.6)	
Timing of Abx[f] Prophy[g]			0.548			0.428			0.307
Adequate[h]	25 (27.2)	137 (31)		3 (100)	2 (50)		22 (24.7)	135 (30.8)	
Not adequate	67 (72.8)	305 (69)		0	2 (50)		67 (75.3)	303 (69.2)	
Abx[f] administration			<0.001			1.000			0.220
No	64 (15.8)	342 (84.2)		2 (50.0)	2 (50.0)		62 (15.4)	340 (84.6)	
Yes	253 (40.4)	374 (59.6)		220 (47.9)	239 (52.1)		33 (19.6)	135 (80.4)	

[a]Primary education; [b]secondary education; [c] cephalopelvic disproportion, bad obstetric history, previous CS; [d]Interrupted; [e]Continuous-intradermic and semisubcutaneous; [f]Antibiotic; [g]Prophylaxis; [h]30-60 minutes before the surgical procedure.

Figures

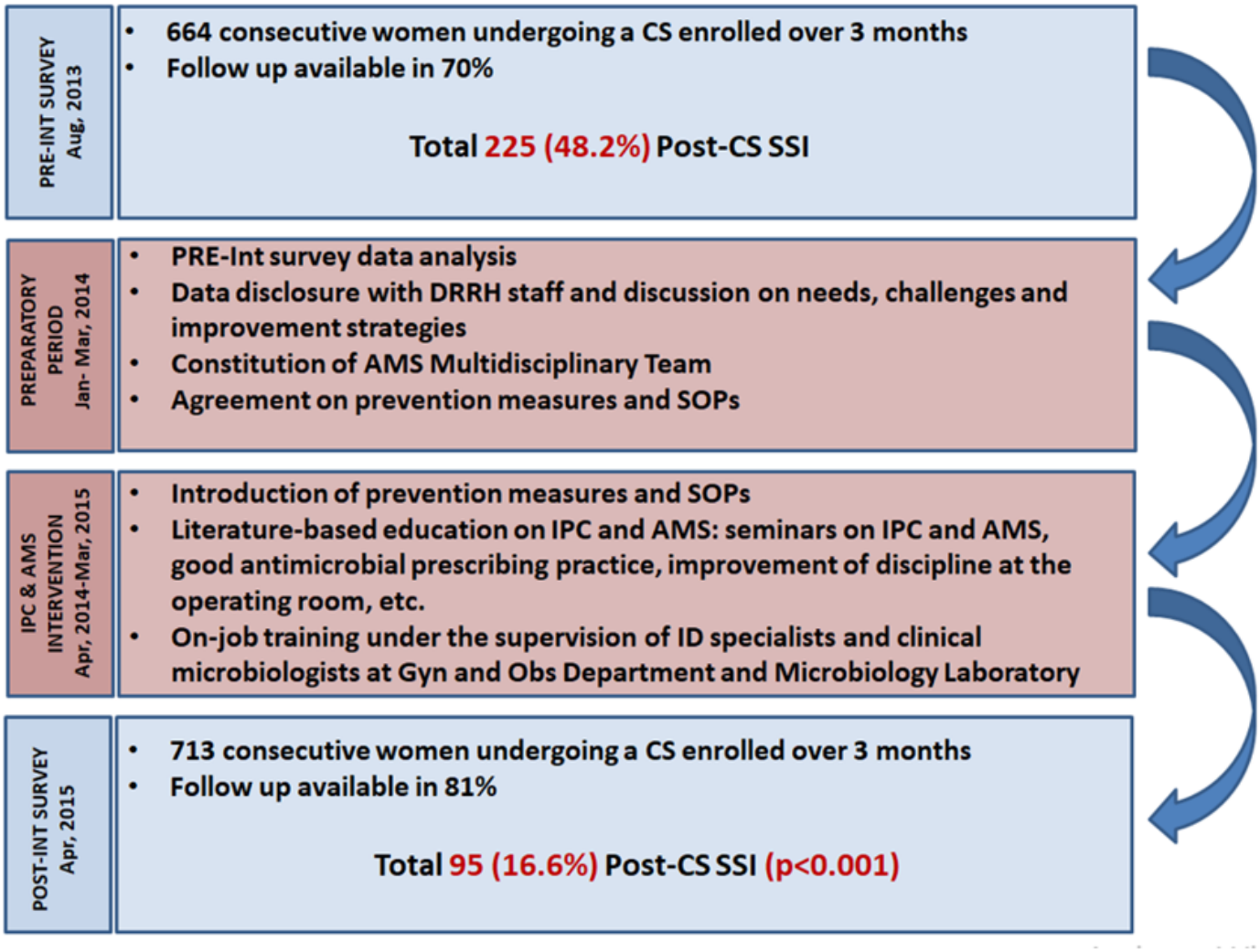

Figure 1

Four-steps protocol of the study. PRE-Int=pre-intervention; CS=caesarean section; SSI=Surgical Site Infections; DRRH=Dodoma Regional Referral Hospital; AMS=Antimicrobial stewardship; SOPs=Standard Operating Procedures; IPC=Infection Prevention and Control; ID=Infectious Diseases; OGD= Obstetrics & Gynaecology Department; POST-Int=post-intervention.

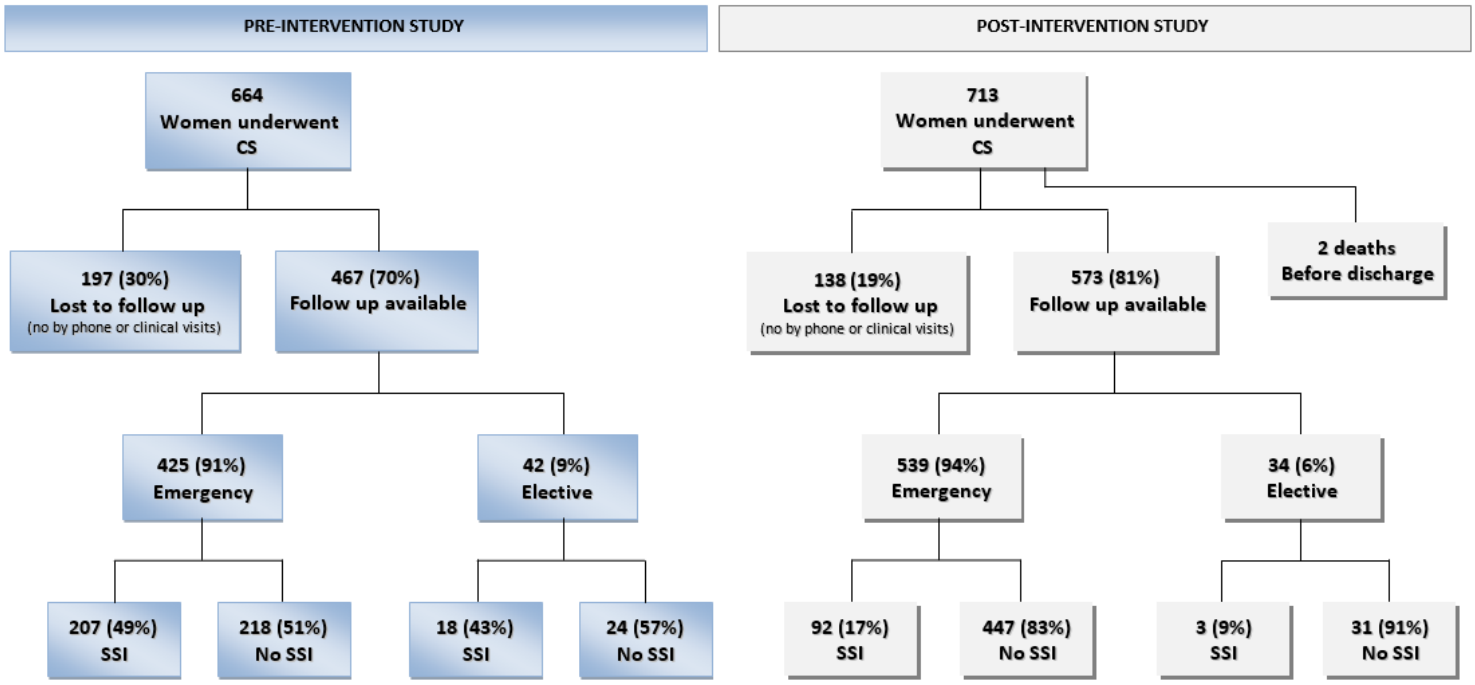

Figure 2

Number of patients surveyed for post-CS SSI in the Pre-Intervention and Post-Intervention groups. CS=caesarean section; SSI=Surgical Site Infections.