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Lawal, Okome et al; Preoperative Chlorhexidine-Cetrimide Versus 10% Povidone-Iodine Vaginal Cleansing for Prevention of Post-Caesarean Section Infectious Morbidities: A Randomised Controlled Trial. Arch. Clin. Res. (April); 10(1):pg44-49.

Preoperative Chlorhexidine-Cetrimide Versus 10% Povidone-Iodine Vaginal Cleansing for Prevention of Post-Caesarean Section Infectious Morbidities: A Randomised Controlled Trial

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Abstract

Background: Infectious morbidity is the most common complication of caesarean section. Despite routine antibiotic prophylaxis, post-caesarean infectious morbidity remains a significant source of maternal morbidity, particularly in Nigeria. Preoperative vaginal antisepsis is recommended as an adjunctive preventive measure; however, comparative data on Chlorhexidine-Cetrimide versus the WHO-recommended Povidone-Iodine are scarce. Objective: To compare the efficacy of preoperative vaginal cleansing with 0.3% Chlorhexidine-3% Cetrimide (CC) versus 10% Povidone-Iodine (PI) in the prevention of post-caesarean section composite infectious morbidity. Methods: A prospective, double-blinded, randomised controlled trial was conducted at Irrua Specialist Teaching Hospital, Nigeria. One hundred and seventy-eight women undergoing caesarean section were randomised 1:1 to CC (n=90) or PI (n=88) preoperative vaginal cleansing. Primary outcome was composite infectious morbidity (endometritis, febrile morbidity, and/or wound infection). Follow-up was to six weeks postpartum. Results: Composite infectious morbidity occurred in 4.4% of the CC arm versus 9.9% in the PI arm (RR 0.44; 95% CI 0.20–0.57; p=0.012). CC was associated with significantly lower rates of clinical endometritis (1.1% vs. 3.4%; RR 0.32; p=0.034), febrile morbidity (1.1% vs. 2.3%; RR 0.49; p=0.023), and wound infection (3.3% vs. 4.5%; RR 0.73; p=0.041). Neonatal outcomes and tolerability were comparable in both arms.
Conclusion: Chlorhexidine-Cetrimide demonstrated statistically significant superiority over Povidone-Iodine in preventing post-caesarean infectious morbidity. Both agents were well tolerated. Chlorhexidine-Cetrimide should be considered as an alternative preoperative vaginal antiseptic for caesarean section.

Keywords: *Caesarean section; Chlorhexidine-Cetrimide; Povidone-Iodine; post-caesarean infectious morbidity*

Introduction

Caesarean section is one of the most frequently performed surgical procedures in modern obstetric practice, with rates continuing to rise globally. In Nigeria, caesarean section rates as high as 28.6% have been reported.[1,2] While improvements in surgical technique, anaesthesia, and antibiotic prophylaxis have made the procedure considerably safer, infectious complications remain a major source of postoperative morbidity.[3]

Women undergoing caesarean section face a 5 to 20-fold increased risk of infection compared to those who deliver vaginally.[4] The most frequent post-caesarean infective complications are endometritis (6–27%), febrile morbidity (5–24%), and wound infection (2–9%).[5] These morbidities carry substantial burden, delaying recovery, impairing maternal-infant bonding, and imposing significant economic costs on families and health systems.[3]

Infection commonly originates from ascending microorganisms of the lower genital tract, providing a biological rationale for preoperative vaginal antisepsis.[5] The World Health Organization (WHO) currently recommends Povidone-Iodine (PI) solution for routine preoperative vaginal preparation prior to caesarean section.[6] However, this recommendation was based primarily on randomised controlled trial data not include

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Chlorhexidine-Cetrimide (CC) solution a commonly used surgical antiseptic.[7]

Chlorhexidine-Cetrimide offers some potential advantages. Chlorhexidine maintains antimicrobial activity in the acidic vaginal milieu and in the presence of blood, conditions that inactivate Povidone-Iodine's iodophore component.[8,9] It binds covalently to mucosal proteins, providing prolonged residual bactericidal activity for 24–72 hours, and exerts a bactericidal rather than bacteriostatic mechanism of action.[10] The addition of Cetrimide further reduced the time required for killing organisms.[11] Despite this theoretical basis, comparative evidence between CC and PI remains scarce, particularly in the Nigerian context. This study was conducted to address this evidence gap.

Materials and Method

Study Design

This was a prospective, two-arm, parallel-group, single-centre, double-blinded randomised controlled trial.[12] The study was conducted at the Department of Obstetrics and Gynaecology, Irrua Specialist Teaching Hospital (ISTH), Irrua, Edo State, Nigeria, over a six-month period (April-September 2021). The trial was registered on the Nigerian Clinical Trial Registry (NCTR No. 25600625) prior to commencement. Ethical approval was obtained from the ISTH Health Research Ethics Committee (HREC). All participants provided written informed consent.

Study Setting

ISTH is a federal tertiary referral hospital established in 1991, serving Edo State and adjoining states in south-central Nigeria. The department conducts approximately 1,500 deliveries annually with a caesarean section rate of approximately 50%. The study was conducted across the antenatal ward, labour ward, operating theatre, postnatal ward, and postnatal clinic.

Participants

Eligible participants were pregnant women aged ≥18 years undergoing elective or emergency caesarean section at ISTH, irrespective of booking status. Women were excluded if they had: known allergy to either antiseptic agent; active chorioamnionitis; antepartum haemorrhage with a live fetus or cord prolapse; obstructed labour; intrauterine fetal death; face presentation; active genital herpes; pre-operative skin infection; chronic steroid use; diabetes mellitus; HIV infection; or if a hysterectomy was anticipated at decision for caesarean section.

Sample Size

Sample size was calculated using the standard formula for a two-arm randomised controlled trial, with a clinically acceptable margin of 0.1, estimated response rate in the Povidone-Iodine group of 5.5%,[13] α=0.05, and power (1-β) = 0.80. This yielded a minimum of 82 participants per arm. Accounting for 10% attrition, the target sample size was 91 participants per arm (182 total).

Randomisation and Blinding

Participants were randomised 1:1 using a computer-generated random number sequence prepared by an independent statistician. Allocation concealment was achieved using sequentially numbered, opaque, sealed envelopes, stored away from the enrolment area and opened only by the perioperative nurse immediately prior to surgery. Participants, the principal investigator, and research assistants were blinded to allocation. Complete blinding of the executor was not possible due to the differing colours of the two solutions; however, executors were not involved in outcome assessment. To maintain blinding, operation notes recorded only 'preoperative vaginal antisepsis' without specifying the agent used.

Interventions

Participants in the Chlorhexidine-Cetrimide arm (Arm A) received vaginal cleansing with 0.3% Chlorhexidine-3% Cetrimide solution (Purit®, Batch No. P787). Participants in the Povidone-Iodine arm (Arm B) received vaginal cleansing with 10% Povidone-Iodine solution. In both arms, vaginal cleansing was performed using a single piece of 5×5cm sterile gauze saturated with the allocated antiseptic on a sponge-holding forceps, applied for approximately 30 seconds with the patient in the modified lithotomy position under anaesthesia.[14] Caesarean section was performed via transverse lower abdominal incision (pfannenstiel incision) using the department's standard protocol, including routine antibiotic prophylaxis.

Outcome Measures

The primary outcome was composite post-caesarean infectious morbidity, defined as occurrence of one or more of: clinical endometritis, febrile morbidity, or wound infection within six weeks postpartum. Secondary outcomes included individual components of the composite, tolerability (patient-reported vaginal symptoms), and neonatal outcome by 1-minute and 5-minute Apgar scores.

Clinical endometritis was defined as postoperative fever (axillary temperature ≥38°C) with uterine tenderness and offensive lochia requiring broad-spectrum antibiotics.[15] Febrile morbidity was defined as axillary temperature ≥38°C more than 24 hours after surgery, excluding identifiable non-infectious causes (mastitis, urinary tract infection, malaria, thrombophlebitis).[15] Wound infection was defined as the presence of erythema or incision disruption with purulent discharge.[15]

Statistical Analysis

Data was coded and analysed using IBM SPSS version 25.[16] Categorical variables were expressed as frequencies and percentages; continuous variables as mean ± standard deviation. Chi-square test was used to assess associations between antiseptic allocation and infectious outcomes; Student's t-test was used for continuous variables. Relative risks (RR) with 95% confidence intervals were calculated for each outcome. Statistical significance was set at $p<0.05$. A stratified analysis was performed across known risk factors for post-caesarean infectious morbidity.

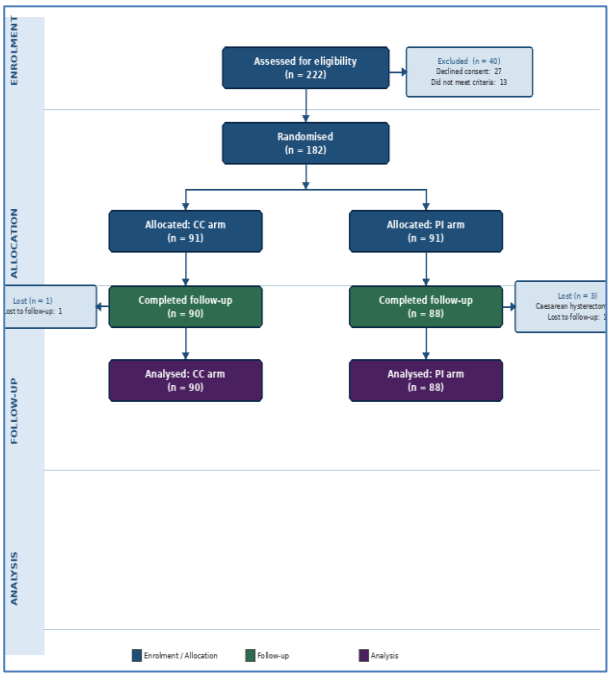

Figure 1. CONSORT flow diagram showing participant enrolment, allocation, follow-up, and analysis.

CC = Chlorhexidine-Cetrimide; PI = Povidone-Iodine.

Results

Participant Flow

During the six-month study period, 222 women were assessed for eligibility. Twenty-seven declined consent and 13 did not meet inclusion criteria, yielding 182 randomised participants (91 per arm). Four participants were subsequently excluded from per-protocol analysis: two who required caesarean hysterectomy and two lost to follow-up. A total of 178 participants (90 Chlorhexidine-Cetrimide; 88 Povidone-Iodine) were included in the final analysis (Figure1).

Baseline Characteristics

Table 1 presents the sociodemographic and obstetric characteristics of participants across both arms. There were no statistically significant differences in any baseline parameter, confirming that the two groups were well matched. The majority were married (97.2%), predominantly Christian (92.7%), and most underwent emergency caesarean section (80.9%). The most common indication was previous caesarean section (23.0%), followed by fetal distress (19.1%).

Table 1. Sociodemographic and Obstetric Characteristics of Participants

Characteristic	CC (n=90)	PI (n=88)	p-value
Age (years), mean ± SD	30.81 ± 4.86	29.82 ± 3.73	0.731
Parity, median (IQR)	3 (2-5)	3 (1-5)	0.912
Gestational age (weeks), mean ± SD	37.80 ± 2.19	37.61 ± 2.05	0.901
BMI (kg/m²), mean ± SD	25.8 ± 4.47	26.34 ± 4.72	0.530
Emergency CS, n (%)	68 (75.6)	76 (86.4)	0.091
In labour at presentation, n (%)	44 (48.9)	42 (47.7)	0.563
Ruptured membranes, n (%)	19 (21.1)	18 (20.5)	0.138
Previous CS history, n (%)	58 (64.4)	49 (55.7)	0.530
Had vaginal examination(s), n(%)	54 (60.0)	59 (67.0)	0.338
No. of vaginal exams, mean ± SD	4(2-5)	4(2-5)	0.973
Duration of surgery (min), mean ± SD	57.61 ± 24.67	58.73 ± 25.09	0.307
Pre-operative haematocrit (%), mean ± SD	32.41 ± 3.92	32.49 ± 3.82	0.491
Estimated blood loss (mL), mean ± SD	550.34 ± 243.41	557.22 ± 247.42	0.902

CC = Chlorhexidine-Cetrimide; PI = Povidone-Iodine; BMI = Body Mass Index; CS = Caesarean Section; SD = Standard Deviation; IQR= Interquartile Range. Continuous variables expressed as mean ± except parity and number of vaginal examination which are expressed as median (IQR

Primary Outcome

Composite infectious morbidity occurred in 4 of 90 participants (4.4%) in the Chlorhexidine-Cetrimide arm compared to 8 of 88 (9.9%) in the Povidone-Iodine arm (RR 0.44; 95% CI 0.20–0.57; p=0.012), representing a 56% reduction in relative risk with Chlorhexidine-Cetrimide.

Secondary Outcomes

Table 2 presents the individual infectious morbidity outcomes by allocation. Clinical endometritis was significantly less frequent in the Chlorhexidine-Cetrimide arm (1.1% vs. 3.4%; RR 0.32; 95% CI 0.28–0.59; p=0.034), representing a 68% reduction in risk. Post-caesarean febrile morbidity was lower in the Chlorhexidine-Cetrimide arm (1.1% vs. 2.3%; RR 0.49; 95% CI 0.475–0.578; p=0.023). Abdominal wound infection was also significantly less frequent with Chlorhexidine-Cetrimide (3.3% vs. 4.5%; RR 0.73; 95% CI 0.56–0.83; p=0.041).

Table 2. Post-Caesarean Section Infectious Morbidities by Allocation Group

Outcome	CC n=90 (%)	PI n=88 (%)	RR (95% CI)	p-value
Composite infectious morbidity	4 (4.4)	8 (9.9)	0.44 (0.20–0.57)	0.012*
Clinical endometritis	1 (1.1)	3 (3.4)	0.32 (0.28–0.59)	0.034*
Post-operative febrile morbidity	1 (1.1)	2 (2.3)	0.49 (0.475–0.578)	0.023*
Abdominal wound infection	3 (3.3)	4 (4.5)	0.73 (0.56–0.83)	0.041*

** p<0.05 (statistically significant). CC = Chlorhexidine-Cetrimide; PI = Povidone-Iodine; RR = Relative Risk; CI = Confidence Interval*

Neonatal Outcomes

Neonatal outcomes were comparable across both arms (Table 3). Birth asphyxia (5-minute Apgar <7) occurred in 2.2% in the Chlorhexidine-Cetrimide arm versus 2.3% in the Povidone-Iodine arm (RR 0.96; 95% CI 0.75–1.04). SCBU admission rates were similarly comparable (5.6% vs. 4.5%). Cases of birth asphyxia were attributable to the underlying indication for caesarean section rather than the antiseptic intervention.

Table 3. Neonatal Outcomes Across Study Arms

Outcome	CC n=90 (%)	PI n=88 (%)	RR (95% CI)
1-minute Apgar <7, n (%)	8 (8.9)	7 (8.0)	1.10 (0.67–1.23)
5-minute Apgar <7, n (%)	2 (2.2)	2 (2.3)	0.96 (0.75–1.04)
SCBU admission, n (%)	5 (5.6)	4 (4.5)	1.20 (0.82–1.25)

CC = Chlorhexidine-Cetrimide; PI = Povidone-Iodine; SCBU = Special Care Baby Unit; RR = Relative Risk; CI = Confidence Interval

Tolerability

No significant adverse effects or patient-reported vaginal symptoms (dryness, burning, itchiness, unusual discharge, or pain with urination) were recorded in either arm during the study period. Application of antiseptics under anaesthesia likely minimised the perception of any mild irritative symptoms.

Stratified Analysis

Stratified analysis across key infectious risk factors, number of vaginal examinations (<4 vs. ≥4), body mass index (<30 vs. ≥30 kg/m²), and membrane status, showed no statistically significant differences in antiseptic performance across subgroups. However, subgroup sample sizes were small and results should be interpreted with caution given limited statistical power.

Discussion

This randomised controlled trial demonstrates that preoperative vaginal cleansing with Chlorhexidine-Cetrimide is superior to 10% Povidone-Iodine in the prevention of composite post-caesarean section infectious morbidity, as well as all individual infectious morbidity outcomes, in a Nigerian tertiary care setting. Both solutions were equally well tolerated.

The overall composite infectious morbidity rate of 6.7% is lower than rates reported in comparable Nigerian studies — 10.2% in Gwagalada[17] and 23% in Abeokuta.[18] This difference may be attributable to the use of an active comparator in both arms and the application of stringent operational definitions for outcome measures. The exclusion of identifiable non-infectious causes of postoperative fever likely explains the lower febrile morbidity rate of 1.7% in the present study compared to

8.8% reported in the Abeokuta study, which did not apply equivalent exclusion criteria.

The 56% reduction in composite infectious morbidity with Chlorhexidine-Cetrimide (RR 0.44; p=0.012) is consistent with the pharmacological properties of the combination agent. Chlorhexidine maintains antimicrobial activity in the presence of blood and in the acidic vaginal environment — conditions known to substantially inactivate Povidone-Iodine's iodophore component.[11] Furthermore, Chlorhexidine's covalent binding to mucosal proteins provides prolonged residual bactericidal activity for 24–72 hours after a single application, a property not shared by Povidone-Iodine.[11] The bactericidal action of Chlorhexidine, compared to the bacteriostatic activity of Povidone-Iodine, may also contribute to the superior reduction in infectious outcomes observed.

The 68% reduction in clinical endometritis differs from findings of the GUCCI trial,[19] which used 4% Chlorhexidine gluconate and did not demonstrate a significant reduction compared to Povidone-Iodine. The superior performance in the present study may be attributable to the combined Chlorhexidine-Cetrimide formulation, which has broader antimicrobial activity than individual components.[11] This finding is, however, consistent with placebo-controlled studies from Abakaliki and Egypt that demonstrated significant endometritis risk reduction with Chlorhexidine-based agents.[20,21]

The statistically significant reduction in wound infection with Chlorhexidine-Cetrimide is consistent with findings from a United States randomised trial that reported significantly lower wound infection rates in the Chlorhexidine arm compared to Povidone-Iodine (0.6% vs. 2.0%; p=.039).[22] The higher absolute rates in the present study likely reflect differences in baseline infectious risk between high-income and resource-limited settings.

Neonatal outcomes were comparable in both arms and no adverse effects attributable to either antiseptic solution were observed. This is consistent with established safety data for both agents.[11,23]

Limitations

This was a single-centre study; generalisation of findings to other settings should be done with caution. Clinical rather than microbiological definitions of outcomes were used, which while reflective of real-world practice, may affect diagnostic specificity. Complete blinding of the executor was not achievable due to visible colour differences between the solutions, though executors were not involved in outcome assessment. Subgroup sample sizes in the stratified analysis were small, limiting statistical power to detect subgroup-level differences.

Conclusions

Preoperative vaginal cleansing with Chlorhexidine-Cetrimide demonstrated statistically significant superiority over 10% Povidone-Iodine in the prevention of composite post-caesarean section infectious morbidity and all individual morbidity outcomes. Both solutions were well tolerated. Chlorhexidine-Cetrimide should be considered as an evidence-based alternative to Povidone-Iodine for preoperative vaginal antisepsis prior to caesarean section, particularly where Povidone-Iodine is contraindicated or unavailable. A multicentre trial is recommended to further validate these findings.

Acknowledgement

The authors acknowledge the support of consultants of the department of Irrua specialist teaching hospital. The authors also acknowledge the research assistants, perioperative nursing staff, and statistical support from the independent statisticians who contributed to the successful conduct of this trial. This study was self-funded by the principal investigator. No external grant funding was received.

Conflict of Interest

The authors declare that we have no known competing financial interests that could have influenced the findings reported in this paper.

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