EFFECT OF PREOPERATIVE VAGINAL CLEANSING WITH POVIDONE IODINE ON POST-CAESAREAN MATERNAL INFECTIONS AT KENYATTA NATIONAL HOSPITAL; A RANDOMIZED CONTROLLED TRIAL

UNIVERSITY OF NAIROBI

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY

PRINCIPAL INVESTIGATOR:

DR KARANJA DAVID MWANGI

MBCHB

H58/69881/2013

SUPERVISORS:

PROFESSOR JAMES B.O. OYIEKE

MBCHB, MMED

DR JOHN KINUTHIA

MBCHB, MMED, MPH

THIS DISSERTATION IS SUBMITTED IN PARTIAL FULFILMENT FOR THE AWARD OF DEGREE IN MASTERS OF OBSTETRICS AND GYNAECOLOGY

DECLARATION:

I hereby declare that this dissertation is my original work and to the best of my knowledge contains no materials previously published or written by another person, nor material which to a substantial extent has been accepted for the award of any other degree or diploma at the University of Nairobi or any other educational institution.

Name: Dr. Karanja David Mwangi

Registration number: H58/69881/2013

Signature:_____

Date:_____

This dissertation has been submitted for examination with our approval as the university supervisors:

1. Prof. JBO. Oyieke

   Signature:_____

   Date:_____

2. Dr. John Kinuthia

   Signature:_____

   Date:_____

CERTIFICATE OF AUTHENTICITY

This is to certify that this dissertation is the original work of Dr. Karanja David Mwangi, MMed. student registration number H58/69881/2013, Department of Obstetrics and Gynecology, College of Health Sciences, University of Nairobi, supervised by Prof. JBO. Oyieke and Dr John Kinuthia. It has not been presented in any other university for award of a degree.

Signed……

Date…….

Professor Omondi Ogutu,

Associate Professor of Obstetrics and Gynecology,

Consultant Obstetrician and Gynecologist,

Chairman, Department of Obstetrics and Gynecology

University of Nairobi

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DEDICATION

My lovely wife Muthoni thanks for your support, encouragement and understanding.

To my late dad Karanja Senior, a great mentor you were.

My mom, your encouragement and prayers gave me strength to push on.

LIST OF ABBREVIATIONS

ANC- Antenatal care

ASA- American Society of Anaesthologist

CDC- Centre for Disease Control

CI- Confidence interval

CS- Caesarean section

DSMB- Data Safety and Monitoring Board

IQR- Inter-quartile range

KNH- Kenyatta National Hospital

KNH/UoN-ERC- Kenyatta National Hospital/University of Nairobi Ethics & Research Committee

PROM- Premature rupture of membranes

PI- Principal Investigator

SSI- Surgical site infection

USA- United States of America

UTI- Urinary tract infection

WHO- World Health Organization

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ABSTRACT

Introduction

Maternal sepsis accounts for 11% of maternal mortality. Caesarean section is the single most important factor for postpartum maternal infection. Despite different strategies implemented to reduce postcaesarean maternal infection, it is still common, and increases costs of treatment, length of hospital stay and maternal morbidity and mortality. Preoperative vaginal preparation with povidone iodine before caesarean section may reduce postcaesarean maternal infection.

We studied preoperative vaginal cleansing with povidone iodine to reduce post-caesarean maternal infection.

Objectives

In the current study, we aimed to find out if preoperative vaginal cleansing with povidone iodine can reduce postcaesarean maternal infection among women receiving postoperative vaginal toilet with povidone iodine at Kenyatta National Hospital.

The primary outcome was overall maternal infection including endometritis, fever and surgical site infection. We conducted sub-group analysis to evaluate the effect of povidone iodine on endometritis, fever and surgical site infection.

Methods

This was a randomized controlled trial that was carried out at Kenyatta National Hospital Maternity theatre, post-natal wards and postnatal clinic. We enrolled 397 pregnant women scheduled for both elective and emergency caesarean delivery at gestational age of ≥28weeks. Of these, 194 women were randomized in to the intervention group [preoperative vaginal cleansing group], while 191 in to the control group [no preoperative vaginal cleansing group]. All women received postoperative vaginal cleansing/toilet with povidone iodine as standard practice at Kenyatta National Hospital. We followed participants for 2 weeks postpartum for development of endometritis, fever and surgical site infection. Statistical analysis was done as per protocol with intent-to-treat approach. Proportions were compared using Chi2 test, 95% CI, two tailed hypothesis with p value considered significant at <0.05.

Results

The groups were similar in socio-demographic characteristics [age, education level, marital status]. There was no difference between the groups in obstetric and labor characteristics [type of labor, duration of labor, status of membranes and duration of membrane rupture, indication and type of caesarean section done].

There was a significant difference in the incidence of overall maternal infection [the sum of endometritis, fever surgical site infection] among women in the preoperative vaginal cleansing arm, compared to the arm without preoperative vaginal cleansing [7.77% vs. 15.81%, p=0.015]. In the subgroup analysis, there was a non-statistically significant reduction in postcaesarean endometritis [0.97%, 2/201] in the preoperative vaginal cleansing arm, and 3.57% [7/196] in the control arm [p=0.089]. Similarly there was no statistically significant difference in postcaesarean fever [p=0.171] and surgical site infection [p=0.186] between the two arms. There was also no statistically significant reduction in postcaesarean endometritis among women in established labor [1.67% vs. 4.17%; p=0.446], with ruptured membranes [1.14% vs. 5.49%; p=0.108] and emergency caesarean delivery patients [1.18% vs. 4.09%; p=0.093] between the preoperative and no preoperative vaginal cleansing arms respectively.

Conclusion

Preoperative vaginal cleansing with povidone iodine reduces the overall maternal infection but not postcaesarean endometritis, fever or surgical site infection among women who undergo postcaesarean vaginal cleansing/toilet at Kenyatta National Hospital.

Preoperative cleansing with povidone iodine in addition to postoperative cleansing with povidone iodine does not alter postcaesarean endometritis in women with established labor, ruptured membranes and emergency caesarean section.

Preoperative or postoperative povidone iodine did not show any major side effects/local reaction to the vaginal mucosa.

Recommendations

Consistent with the WHO recommendations, preoperative vaginal cleansing with povidone iodine should be considered as an intervention for reducing postcaesarean maternal infection in women even if they undergo postcaesarean vaginal cleansing/toilet with povidone iodine.

Further studies with larger sample sizes are needed to evaluate the benefit of preoperative vaginal cleansing on the incidence of endometritis at 2 weeks and up to 6 weeks postpartum. Since postoperative vaginal cleansing is the standard of care at KNH, it is also important to evaluate its effectiveness compared to preoperative vaginal cleansing.

INTRODUCTION AND LITERATURE REVIEW

INTRODUCTION

Preoperative vaginal cleansing with povidone iodine reduces postoperative maternal infections in mothers with PROM and prolonged labour (1). However it has shown different results in patients without PROM and normal labor: Some studies have shown benefits in reducing postcaesarean maternal endometritis (2) (3), while others have not shown any benefit (4) (5).

Caesarean section [CS] is the leading and the single most important factor for postpartum infections(6) . The incidence of post-caesarean maternal infections in the USA is 7-20% (7), and it is even higher in developing countries. Post-caesarean maternal infections include endometritis, fever, surgical site infection [SSI] and urinary tract infection.

Endometritis, febrile morbidity and surgical site infection are common at Kenyatta National Hospital, with the incidence of endometritis being 20.3% (8), febrile morbidity at 22% (9), and SSI cumulative incidence of 22.3% (10)

Post-caesarean infectious morbidity has led to increased length of hospital stay and high costs of treatment, increased use of antibiotics [and thus resistance], burden to the nursing mother, and ultimately increased mortality (11) (12).

No regional or local studies have been done to ascertain the benefits of preoperative vaginal cleansing, despite the differing socio-demographic characteristics and CS indications among women seen in our setting vis-a-vis those of the developed world.

LITERATURE REVIEW

Caesarean section

Caesarean section is the operative delivery of a fetus through the abdominal incision. The WHO statement on caesarean section rates [2015] noted that at population level, caesarean section rates above 10% does not reduce maternal and neonatal mortality rates (13). Caesarean deliveries account for 15% of all deliveries

in the world, the highest rates being 29.2% in Latin America and the lowest in Africa at 3.5% (14).. The lowest CS rates in Africa are in Chad [0.4%], Niger and Ethiopia at 0.6% while the highest are in South Africa at 15.4 and Egypt at 11.4%. In Kenya, CS rates are at an average of 9% as per the Kenya Demographic and Health Survey data of 2014 (15).

Caesarean section rates have been on the increase over the decade. This is due to increased fetal and maternal monitoring through continuous electronic monitoring and mothers wishes to have caesarean delivery without any obstetric indication (17) (18) (19). A study by Ji et al in Shanghai China showed that up to 17.0% of pregnant women in the third trimester preferred caesarean delivery without any obstetrics indications(20).

Indications for caesarean delivery include maternal and fetal reasons. Maternal indications include antepartum hemorrhage, difficult/prolonged labour, contracted pelvis, cephalopelvic disproportion, previous CS and maternal preference. Fetal indications include Non-reassuring fetal status, vasa previa and breech presentation(21)

Caesarean section complications include intraoperative and postoperative complications. Intraoperative complications include hemorrhage, difficult surgery, organ injury [ureter and gut] and complications due to anaesthesia. Postoperative complications include postpartum hemorrhage, postpartum maternal infections and wound dehiscence(18) (22)

Post-caesarean maternal infections

Post-caesarean maternal infections are infections that occur during the postoperative period as a consequence of caesarean delivery. Maternal infection/sepsis account for 11% of maternal mortality, with Sub-Saharan Africa and Southern Asia accounting for the majority of cases. It's the 3rd commonest cause of maternal mortality after PPH and hypertensive disease (23) (24).

Postpartum infection involves a wide range of morbidities secondary to caesarean or vaginal delivery (25). The route of delivery is the single most important factor in the development of endometritis (26). Caesarean delivery increases the chance of

getting maternal infection 5-20 fold compared to women delivering vaginally(27). Majority of postpartum infections [94%] are diagnosed after discharge from the hospital, and thus some patients may present as late as 42 days postpartum (28).

Common maternal infections after caesarean delivery include endometritis, fever, surgical site infection [SSI] and urinary tract infection. Postpartum endometritis is the infection of the decidua [pregnancy endometrium] after delivery. As per Centre for Disease Control and Prevention [CDC], endometritis must meet one of the following criteria(29) :

1. Patient has organism cultured from fluid or tissue from endometrium obtained during surgical operation, by needle aspiration or by brush biopsy'
2. Patient has at least two or more of the following signs and symptoms with no other recognized cause: fever ≥38°C, abdominal pain, uterine tenderness and purulent drainage from the uterus

The United States Joint Commission on Maternal Welfare defines postpartum febrile morbidity as oral temperature of ≥38°C on any 2 of the first 10 days postpartum, excluding the first 24 hours (30)

S.S.I is the infection of the body tissues at the site where the operation was done. CDC classifies SSIs into three; superficial incisional SSI, deep incisional SSI and organ/space SSI (31). SSI is associated with morbidity, and over a third of postoperative deaths are related, at least in part, to SSIs(32).

The incidence of postcaesarean infectious morbidity varies by geographic region, being highest in resource poor settings and lowest in developed countries. A prospective multicenter study in Lagos Nigeria among women scheduled for caesarean section revealed postcaesarean wound infection rate of 9.3% (33). Mpogoro et al found the cumulative incidence of SSI at a hospital in Mwanza, Tanzania to be 10.9%. This was a prospective cohort study of pregnant women who underwent caesarean section and followed for 30 days postpartum (34). Three studies that have been done in KNH have shown almost the same rates of postcaesarean infectious morbidity over time. In 1981, Sinei found the incidence of febrile morbidity to be 22% (9) and in 1987 Plummer et al found the incidence of postpartum endometritis at 20.3% (8). The most recent study in 2015 by Muchiri,

postcaesarean women were followed up for 30 days in the postpartum period. The cumulative incidence of surgical site infection was 22.3% (10).

Common organisms that cause endometritis are commonly found in the lower genital tract, and thus migrate to the upper genital tract to cause infectious morbidity. This include staphylococcus species, streptococcus, anaerobes and gut flora [Escherichia coli] (35) (36) (37). Microbial findings in a case control study in Mozambique found more anaerobes in the vagina, endocervix and uterine cavity among patients that developed postcaesarean endometritis(35). Watts DH et al showed that isolation of Group B streptococcus and Enterococcus faecalis from the upper genital tract at delivery greatly contributed to the development of postpartum endometritis (37).

The most common organisms causing SSI at a referral hospital in Oman was found to be Staphylococcus aureus (66, 31.27%) and the Gram-negative Escherichia coli group (40, 18.95%) (36).

Treatment of postcaesarean endometritis is usually empirical since vaginal swab culture and sensitivity results may delay. In low-resource settings, antimicrobial trials and intrauterine microbiological studies suggest the use of the following antibiotics; oral clindamycin plus intramuscular gentamicin, oral amoxicillin-clavulanate, intramuscular cefotetan, intramuscular meropenem or imipenem-cilastatin, and oral amoxicillin in combination with oral metronidazole (38). A 2015 Cochrane review by Mackeen AD et al found the use of intravenous clindamycin and gentamicin to be superior to penicillin or cephalosporin plus gentamicin (39).

Preoperative vaginal cleansing with povidone iodine

The vaginal flora and the presence of bacteria in the lower uterine segment at the time of caesarean section plays an important role in the development of endometritis (40) (41).

Enzelsberger et al showed that povidone iodine [compared to chlorhexidine, and octenidine] produced the strongest median reduction of the vaginal flora 3minutes after vaginal application, and comparable effects after 30minutes. In addition the residual effect [unwanted local side effects due to the active ingredient or other

ingredients in the antiseptic] after 3-4hours was less pronounced with povidone iodine (42)

Povidone iodine is an iodinated polyvinyl polymer with broad antimicrobial activity, used in surgery as a topical agent, either on skin or mucous membranes. Iodine toxicity towards mammalian cells is minimized by the slow release of iodine from the polyvinyl polymer complex (43)

Preoperative vaginal cleansing with povidone iodine has not been universally adopted due to conflicting results. In 2015, The World Health Organization recommended vaginal cleansing with povidone iodine prior to caesarean section [conditional recommendation based on moderate quality evidence] (44). Some studies have shown benefit in reducing postoperative maternal infection while others have not shown any benefit. Asghania M et al randomized 585 participants scheduled for elective caesarean section into preoperative vaginal cleansing and no preoperative vaginal cleansing groups. The study followed up participants for 6weeks and showed a significant lower incidence of endometritis in women cleansed with povidone iodine preoperative [1.4%] compared to 2.4% in the control group [no preoperative vaginal cleansing] (3). Haas et al in a 2014 Cochrane review showed a significant reduction in the incidence of endometritis in the preoperative vaginal cleansing group [5.4%] compared to the no preoperative vaginal cleansing group [9.2%] (45).

However Virgil C. Reid et al in a 2001 randomized study with 498 participants showed no effect of preoperative vaginal cleansing with povidone iodine [compared to no preoperative vaginal cleansing] on endometritis, fever and surgical site infection [SSI] (5). Similarly, another study by Haas et al in 2010 recruited 155 participants in the vaginal cleansing group and 145 participants in the no vaginal cleansing group. He concluded that preoperative vaginal cleansing may decrease the incidence of postoperative morbidities [6.5% Vs 11.5%] that was not statistically significant [the primary outcome was a composite of fever, endometritis, sepsis and wound infection (46).

Women with PROM and prolonged labor benefit from preoperative vaginal cleansing (1) (3). The incidence of endometritis in PROM was 7.4% in the vaginal cleansing

group versus 21.4% in the no vaginal cleansing group, while in prolonged labor it was 7.8 versus 17.5 respectively (1)

Toxicity after topical application of povidone iodine is very rare, and only case studies have been reported (47). Mild contact dermatitis and allergy have been documented to occur in isolated cases. More severe reactions have been reported when povidone iodine was applied on open wounds or burns wound, including hyperthyroidism and high blood iodine levels (47). A study on 12 non-pregnant women found elevated iodine levels in blood after vaginal application of povidone iodine. However thyroxine levels were not raised during the same period. The risk is higher if povidone iodine is used repeatedly, bur this has been minimized by the slow release of iodine from the polyvinyl polymer complex (43)

Risk factors and outcomes of postcaesarean infectious morbidity

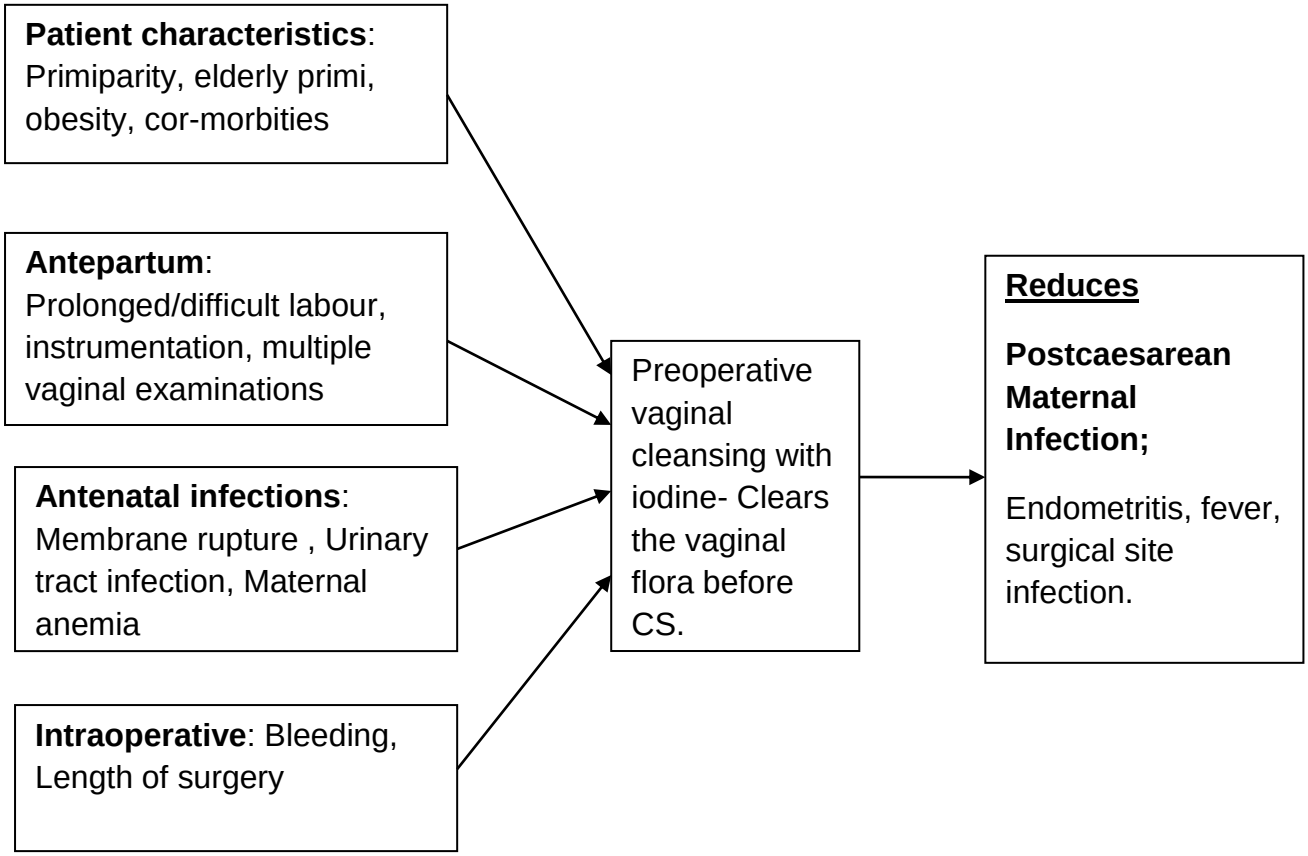
The risk factors for postcaesarean endometritis are young age, pre-existing lower genital tract infection, prolonged labor, multiple vaginal examinations, ruptured membranes, internal fetal monitoring, anemia and low socioeconomic status (48) (26). A study by Koigi Kamau et al in Thika District Hospital, Kenya found that long operation time, labour ≥ 12hours and rupture of membranes ≥12hours were associated with a higher incidence of postcaesarean wound infection (49)

Postcaesarean maternal infections leads to increased length of hospital stay, increased use of antibiotics [and thus resistance], burden to the nursing mother and ultimately increased maternal mortality (50) (51).

CONCEPTUAL FRAMEWORK

Risk factors of postcaesarean maternal infection, possible outcomes and the role of preoperative vaginal cleansing

RISK FACTORS



Risk factors for post-caesarean maternal infection can be broadly subdivided in to patients factors, antenatal, intrapartum and postpartum factors. Patient factors include extremes of ages in pregnancy [young primi less than 21years and elderly primi of 35 years and above] and obesity. Other cor-morbid medical conditions also predispose the patient to infection, including poorly controlled diabetes, thyroid disease, chronic renal and liver disease.

In the antenatal period, focused antenatal visits to screen for HIV/AIDs, asymptomatic bacteriuria, haemoglobin level. Untreated and chronic urinary infections, anaemia in pregnancy will increase postpartum infectious morbidity. During labor and immediate postpartum, frequent vaginal examinations, prolonged/obstructed labor, unnecessary instrumentation and operative vaginal delivery are risk factors and must be minimized.

Once infection has set it, several maternal outcomes are expected. Long hospital stay and increased costs of treatment is a burden to the already overstretched health systems. More so, use of antibiotics will be high and thus the risk of developing resistance. Maternal infection like endometritis may lead to chronic pelvic pain and future infertility.

Preoperative vaginal cleansing with povidone iodine clears the vaginal flora that would have otherwise ascended to the upper genital tract to cause postcaesarean infection.

STUDY JUSTIFICATION

Maternal infection/sepsis causes 11% of maternal mortality in Africa. Postcaesarean maternal infection is common and increases costs of treatment, length of hospital stay and is a contributor to maternal mortality. Studies show different results on the benefit of vaginal cleansing preoperatively in women without PROM and normal labor. Despite the differences in the socio-demographic characteristics and risk of maternal infection among our low resource settings as opposed to the developed world, no studies have been done in our setting. This will be the first randomized trial to be undertaken both regionally and locally [in poor resource settings] to ascertain the effect of preoperative vaginal cleansing on postcaesarean maternal infection.

Preoperative vaginal cleansing with povidone iodine if found successful in KNH will be a simple, cost effective and safe mode of preventing postcaesarean maternal infections.

RESEARCH QUESTION

What is the effect of preoperative vaginal cleansing with povidone iodine [compared to no preoperative vaginal cleansing] on post-caesarean maternal infection among women who also receive postcaesarean vaginal cleansing/toilet with povidone iodine at Kenyatta National Hospital?

HYPOTHESIS

Null hypothesis: There is no difference in postcaesarean maternal infection rates between women undergoing preoperative vaginal cleansing with povidone iodine

and those without preoperative vaginal cleansing in addition to postcaesarean vaginal cleansing/toilet wit povidone iodine

Alternative hypothesis: There is a difference in postcaesarean maternal infection rates between women undergoing preoperative vaginal cleansing with povidone iodine and those without preoperative vaginal cleansing in addition to postcaesarean vaginal cleansing/toilet with povidone iodine

BROAD OBJECTIVE

To determine the effect of preoperative vaginal cleansing with povidone iodine on postcaesarean maternal infections among women who also undergo postcaesarean vaginal cleansing/toilet with povidone iodine at Kenyatta National Hospital

SPECIFIC OBJECTIVES

Among women undergoing preoperative vaginal cleansing with povidone iodine versus without preoperative vaginal cleansing in addition to standard of care (postoperative vaginal cleansing with povidone iodine);

1. To compare the incidence of postcaesarean maternal infections overall, and specifically endometritis, fever and surgical site infection.
2. To compare the risk of post-caesarean maternal infection among subgroup of women in labor, ruptured membranes and undergoing emergency caesarean section.
3. To explore the side effects associated with the use of povidone iodine for vaginal cleansing.

METHODOLOGY

Study design

This was a single blind randomized controlled trial that blinded study participants, and research assistants that collected outcome data at follow-up period

Study site and setting

The study was carried out at Kenyatta National Hospital [KNH], a national referral hospital in Nairobi, the capital city of Kenya. KNH serves Nairobi County and its neighboring counties of Kiambu, Kajiado and Machakos. It also receives referrals/ critical cases from peripheral county hospitals for further management. It has a total bed capacity of 1,800. KNH conducts 1000-1300 deliveries per month, with caesarean sections accounting for 40-50%.

The study was conducted in the Maternity Unit [Maternity theatre, postnatal wards and postnatal clinic]

Study population

All mothers admitted and scheduled to undergo caesarean sections at KNH. All pregnant women at ≥ 28weeks gestation scheduled for either emergency or elective caesarean section.

Inclusion criteria

Pregnant mothers undergoing either emergency or elective caesarean sections with a gestational age of more than 28weeks and were willing to participate in the study.

Exclusion criteria

Cord prolapse.

Placenta previa, Antepartum hemorrhage of unknown cause, uterine rupture.

Chorioamnionitis, vulval/ vaginal warts.

Low presenting part making it difficult to perform the intervention- Head descent 1/5

Known hypersensitivity to povidone iodine or related chemicals

SAMPLE SIZE AND SAMPLING PROCEDURE

Sample size

A study by Plummer et al found the incidence of postpartum endometritis in Nairobi to be 20.3% (8). Assuming that preoperative vaginal cleansing using povidone iodine will reduce the rate of endometritis to about 10%, then to have an 80% power and operating at a significance level of 0.05, then the sample size was determined using;

$\mathbf{N= [z_1 + z_2]^2 [p_1(1-p_1)+ p_2(1-p_2)]/ (p_1-p_2)^2}$ Kirkwood and Sterne 2002

- For 0.05 significance level, Z_1=1.96
- For 80% power, Z_2=0.84
- P_1 = proportion of women developing postcaesarean infection in the control arm (assumed 20.3%)
- P_2 = proportion of women developing postcaesarean infection in the intervention arm assumed (10%) in this case

  Therefore n = $(1.96 + 0.84)^2$ *[0.203 (1-0.203) + 0.10(1 – 0.10))/$(0.203-0.10)^2$ = 187 (in each arm)
- A total sample size of 374 participants was required. A 5% adjustment for non-response was included and therefore 397 participants were enrolled into the study.

Sampling procedure

Pregnant mothers were admitted through labor ward or Antenatal clinic. A research assistant screened all mothers who were admitted and review clinical notes to the plan of action of each of the admissions. In addition the research assistant constantly consulted with the nurses on duty to update details on mothers whose mode of delivery may have changed in the course of the admission. The decision for

emergency or elective caesarean delivery was done by consultants and registrars covering the Maternity units. Recruitment into the study was done every day of the week both day and night. After a mother is scheduled for CS, a research assistant screened and consented the mother.

Block randomization was used to determine patient allocation into the study arms (intervention or control) and a ratio of 1:1 was used. This was done by an investigator with no clinical involvement in the trial. Using computer generated random sequences in blocks of 4 and 6 was used to determine the order of intervention allocation and avoid anticipation of the allocation group for the next patient while maintaining a balance in the number of patients recruited in each of the arms at each time point. The randomly generated list of the allocation sequence was printed on small cards each representing the allocation of each patient in the order generated by the software. Each of these cards was sealed in opaque envelopes that was sequentially numbered in the order of the list generated.

After a research assistant (nurse) identified an eligible participant and the consent granted, the next sequentially numbered envelope was opened and determined which arm the patient was allocated to the group listed on the card in the envelope. Each participant was assigned a unique 4-digit number for subject identity and confidentiality.

Study procedures

Intervention arm- Preoperative vaginal cleansing with povidone iodine

Control arm

No preoperative vaginal cleansing with povidone iodine

Primary outcome was postcaesarean endometritis

Secondary outcome- Fever, surgical site infection and side effects of povidone iodine

Description of Intervention

Vaginal cleansing using two 4×4cm gauze in a sponge holding forceps [soaked in povidone iodine] and inserted into the vagina, rotated 360° for 30seconds from the upper to the lower vaginal wall. This was done after spinal/general anaesthesia and during urethral catheterization [if participant did not have a catheter placed previously]. The cleansing was done by research assistants who were nurses working in theatre and routinely do the catheterization and shaving just before a caesarean section is performed.

All participants underwent abdominal scrubbing with povidone iodine, received preoperative antibiotic in theatre [Cefuroxime 1g IV stat], post-operative vulvo-vaginal toilet with normal saline followed by iodine [in a sponge holding forceps], and a 5-day course of post-operative cefuroxime 500mg 12hourly. This is the standard practice at Kenyatta National Hospital.

Determination of outcomes

Participants were assessed daily [excluding the first 24hours] for development of endometritis, fever and surgical site infection for 2weeks postpartum. Patients were discharged on the 3rd post-operative day and clear instructions were given on symptoms of infection and a return postnatal clinic after 2 weeks.

Maternal infection- The occurrence of any of the outcomes described below [endometritis, fever, and surgical site infection]

Endometritis- Temperature of 38°C or higher plus foul smelling vaginal discharge and/or abnormally tender uterus

Fever- Temperature [oral] of 38°C or higher ≥24hours after the operation, not associated with other symptoms/signs of infection

Surgical Site Infection- SSIs were identified using CDC criteria as follows (31)

1. Superficial incisional SSI was defined as infection which occurs within 30 days after the operation [2weeks in our study] and infection involves only skin or subcutaneous tissue of the incision and at least one of the following: purulent drainage, with or without laboratory confirmation, from the superficial incision

or at least one of the following signs or symptoms of infection: pain or tenderness, localized swelling or redness and superficial incision is deliberately opened by surgeon, unless incision is culture-negative, OR diagnosis of superficial incisional surgical site infection (SSI) by surgeon or attending physician.

2. Deep incisional SSI was defined as infection which occurs within 30 days after the operation [in our study 2weeks] and infection involves deep soft tissue (e.g. Fascial and muscle layers) of the incision and at least one of the following: Purulent drainage from the deep incision but not from the organ/space component of the surgical site, OR a deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38C), localized pain, or tenderness, unless site is culture-negative, OR an abscess or other evidence of infection involving the deep incision is found on direct examination, during re-operation.

DATA COLLECTION AND MANAGEMENT

Eligible participants signed an informed consent. An interviewer administered questionnaire (appendix 4) that aimed at collecting socio-demographic and obstetric characteristics was administered after a CS was scheduled. These included age, marital status, level of education, gestation in weeks and parity. Additional information was collected post-caesarean section to document the type of labor, duration of labor, presence of ruptured membranes, duration of ruptured membranes, number of vaginal examinations, type and indication of caesarean section. Upon discharge and at 2 weeks postnatal clinic, the participants medical records to document presence/absence of maternal infection, endometritis as well as data on secondary outcomes [fever and surgical site infection]. Participants were advised to return to hospital in case they developed symptoms of infection [hotness of the body, foul smelling vaginal discharge, persistent/increasing lower abdominal pains, wound discharge, swelling, redness or dehiscence]. Questionnaires were checked for completeness at the end of each day by the PI.

Data was then be entered onto a REDCap electronic database with inbuilt consistency and range checks. No patient-identifiable information was collected on

the questionnaires nor entered on to the REDCap database. The database was password protected and only authorised personnel had access to the data. The questionnaires were stored in lockable cabinet and only the PI or the persons granted permission by the PI had access.

DATA ANALYSIS

Intention to treat analysis was the data analysis plan. The study population was described by summarizing categorical data as frequency (n) and percentage (%) while continuous data were summarized and presented as mean and standard deviation. Inferential statistics to establish associations for post-caesarean maternal infection and the various risk factors was done using Pearson chi-square and Fisher's exact tests. The findings of this study was also presented using frequency tables and bar graphs. A p-value of <0.05 was considered significant.

Data was analysed using SPSS version 21. The main/primary outcome for this study was the proportion of women who developed post-caesarean endometritis. The secondary outcome was the proportion of women who developed fever and surgical site infection. Local reaction [vaginal itchiness or burning sensation] and anaphylaxis to povidone iodine was also assessed. Proportions in each study arm were compared for the primary and the secondary outcome. Subgroup analysis was also done among women at risk of developing endometritis [women in established labor, ruptured membranes and emergency caesarean section].

ETHICAL CONSIDERATIONS

Ethical Review

The study protocol and the template informed consent form found in appendix 2, were reviewed and approved by the Kenyatta National Hospital/University of Nairobi Ethics Research Committee prior to initiation of the study, with respect to scientific content and compliance with applicable research and human subjects regulations.

The study protocol, the informed consent form, and any other requested documents, as well as any subsequent modifications, were reviewed and approved by the Ethical Review Committee.

Safety and progress reports were to be submitted to the KNH/UoN ERC. No reports were submitted since there was no severe adverse event reported nor was the study terminated.

Informed consent

We obtained a written informed consent from participants. Adequate explanation and counseling was done before consenting. The informed consent form described the purpose of the study, the procedures to be carried out, the risks and benefits in accordance with applicable regulations. The consent form was verbally translated into Swahili for ease of understanding.

Literate participants appended their signatures at the provided space in the consent form. Non-literate participants were to document their approval by marking the form using their thumbprint, in the presence of a literate third party witness [we did not have such a case].

Risks

Risks were anticipated and addressed accordingly. Side effects of povidone iodine are rare and minor. Contact dermatitis could easily be picked by the participant once itching or a burning sensation occurs after anesthesia wears off. None of our participants had such a complaint. Any side effects that was to be reported would have been managed by standard practice [usually managed conservatively and resolves within 72hours]. Rare adverse events have been reported in case studies, including anaphylactic reactions and allergy to povidone iodine. This is common in exposed wounds/ burns as opposed to intact mucosal membranes. The registrar and consultant on duty were to be immediately informed and the Hospital protocol for managing acute anaphylactic reactions would have been followed. All these events/occurrences were to be documented and presented to the DSMB. However, no severe adverse event or local reaction to povidone iodine[addition] was reported in our study.

We ensured the participants privacy and confidentiality was maintained at all times.

Benefits

There was no direct benefit to the participants irrespective of the study outcome. We planned to share the study findings with staff in the reproductive department and this may change/advise on practise. This will help institute measures targeted towards reducing postcaesarean maternal infection.

Confidentiality

Each participant was allocated a 4-digit code number for confidentiality. All the information on the participants and the study as a whole were stored and secured at the study site and stored in locked file cabinets only accessible by study staff. All databases were secured with password-protected access systems.

Study discontinuation

The study's goal was to achieve ≥ 95% participant retention. We made every reasonable effort to retain any enrolled study participant to completion of the study. Participants were at will to withdraw from the study if they were unwilling or unable to comply with the required study procedures.

Finally the study would have been discontinued at any time by the KNH/UoN-ERC if they deemed necessary.

Data Safety and Monitoring Board

This study was monitored by the Data Safety and Monitoring Board, with one online meeting to monitor the safety of patients and signals of efficacy, futility or harm. The members of the board included the Chair Dr.Nelly Mugo, senior researcher RH KEMRI/Prof James Kiarie, WHO. Other member included Dr.Franklin Onchiri,PhD Biostatician CDC and Dr. Andrew Mujugira, senior Researcher University of Washington.

Interim analysis for efficacy and effectiveness was not conducted.

Study registration and permission

Once the study was approved, it was registered with the Kenyatta National Hospital Research and Programs Office (registration number- R. Health/113/2016) and a study registration certificate was issued.

Permission to carry out the study at the RH department was sort and granted by the Assistant Director, department of Reproductive Health.

Study Funding

The study was fully funded by Kenyatta National Hospital. The hospital also provided the povidone iodine that was used during the study. However the hospital was not involved in the study design, enrolment, randomization or analysis

RESULTS

We screened 432 participants during the study period. Of these, 21 participants declined to participate in the study, and 14 participants were excluded due to various reasons as summarized in Figure1. A total of 397 patients were assigned in to either vaginal cleansing arm [201] or no vaginal cleansing arm [196]. In the vaginal cleansing group, 3 participants were lost to follow-up, 2 participants delivered in theatre vaginally after recruitment, 1 participant was cleansed with chlorhexidine instead of iodine and one data extraction form was missing. In the control group, 1 participant was lost to follow up, 1 participant delivered vaginally in theatre after recruitment, 2 data extraction forms were missing and 1 participant withdrew from the study.

Age, marital status, level of education, gestational age and parity did not differ between women in the vaginal cleansing arm and those in the no vaginal cleansing arm [Table1].

Type of labor, duration of labor, whether membranes were intact or ruptured and number of vaginal examinations were similar between the two groups (Table2).

Similarly, type of caesarean section and indication of caesarean section did not differ between the vaginal cleansing and no vaginal cleansing arm.

Figure 1: Flow diagram of study participants from enrolment, allocation, follow-up and analysis

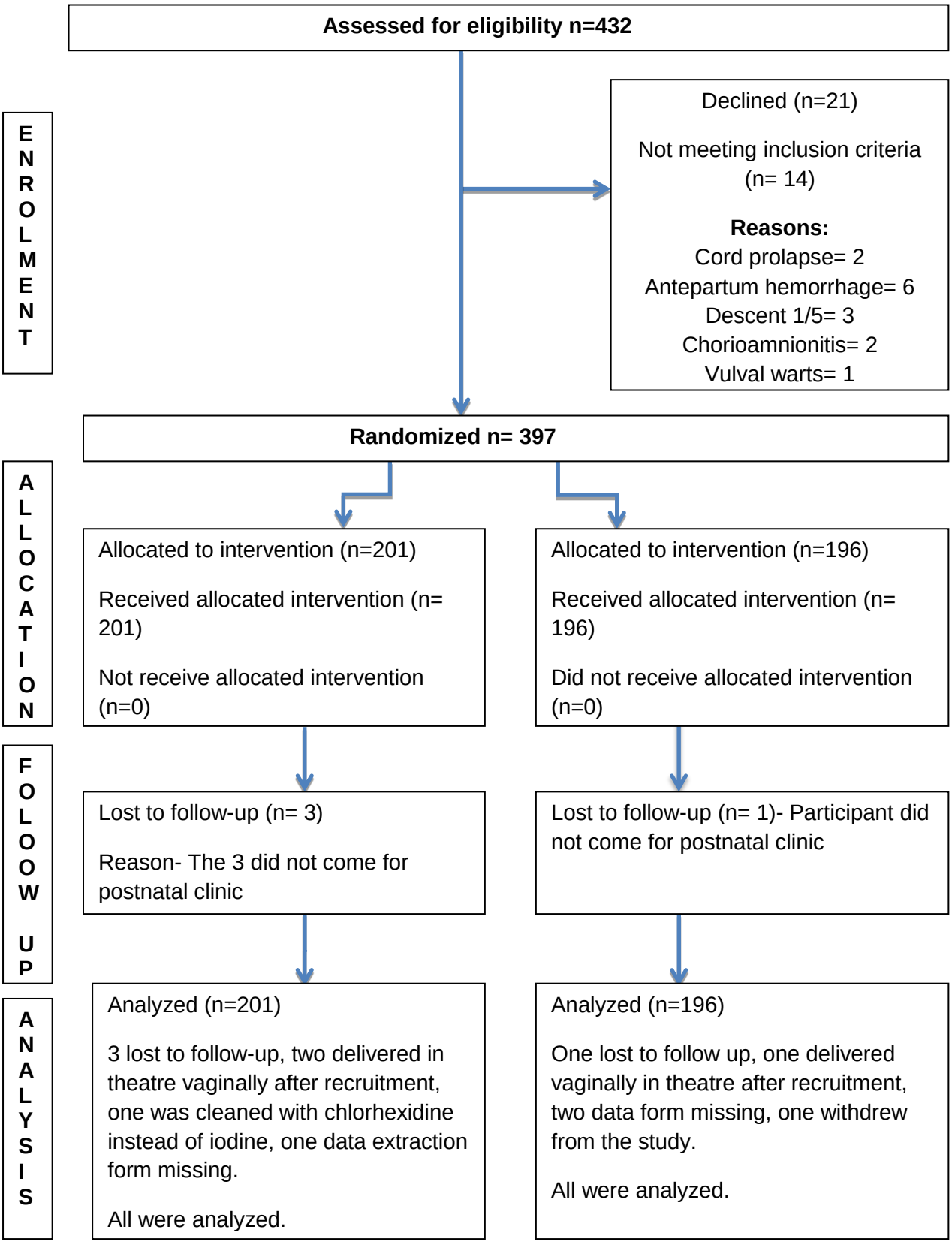


Table 1; Comparison of demographic and obstetric characteristics of participants between the vaginal cleansing and no vaginal cleansing arm

	Vaginal cleansing arm [n=201]	No vaginal cleansing arm [n=196]	p-value
Age [mean]	28.41 ± 5.63	28.70 ± 5.72	0.066
<24	52	56	
25-29	69	49	
30-34	49	56	
35-39	20	31	
>40	11	4	
Marital status			
Single	24	21	
Married	177	176	0.784
Level of education			
None	0	1	
Primary	50	36	0.235
Secondary	75	87	
Post-secondary	76	73	
Gestation [mean]	38.71 ± 2.15	38.46 ± 2.16	0.655
<37	22	28	
37-38	56	56	
39-40	92	86	
41-42	31	26	
Parity			
Primiparous	64	63	
Multiparous	136	131	0.830
Grandmultiparous	1	2	

Table 2; Comparison of labor, status of membranes, number of vaginal examinations and indications for caesarean section between the vaginal cleansing and no vaginal cleansing arm.

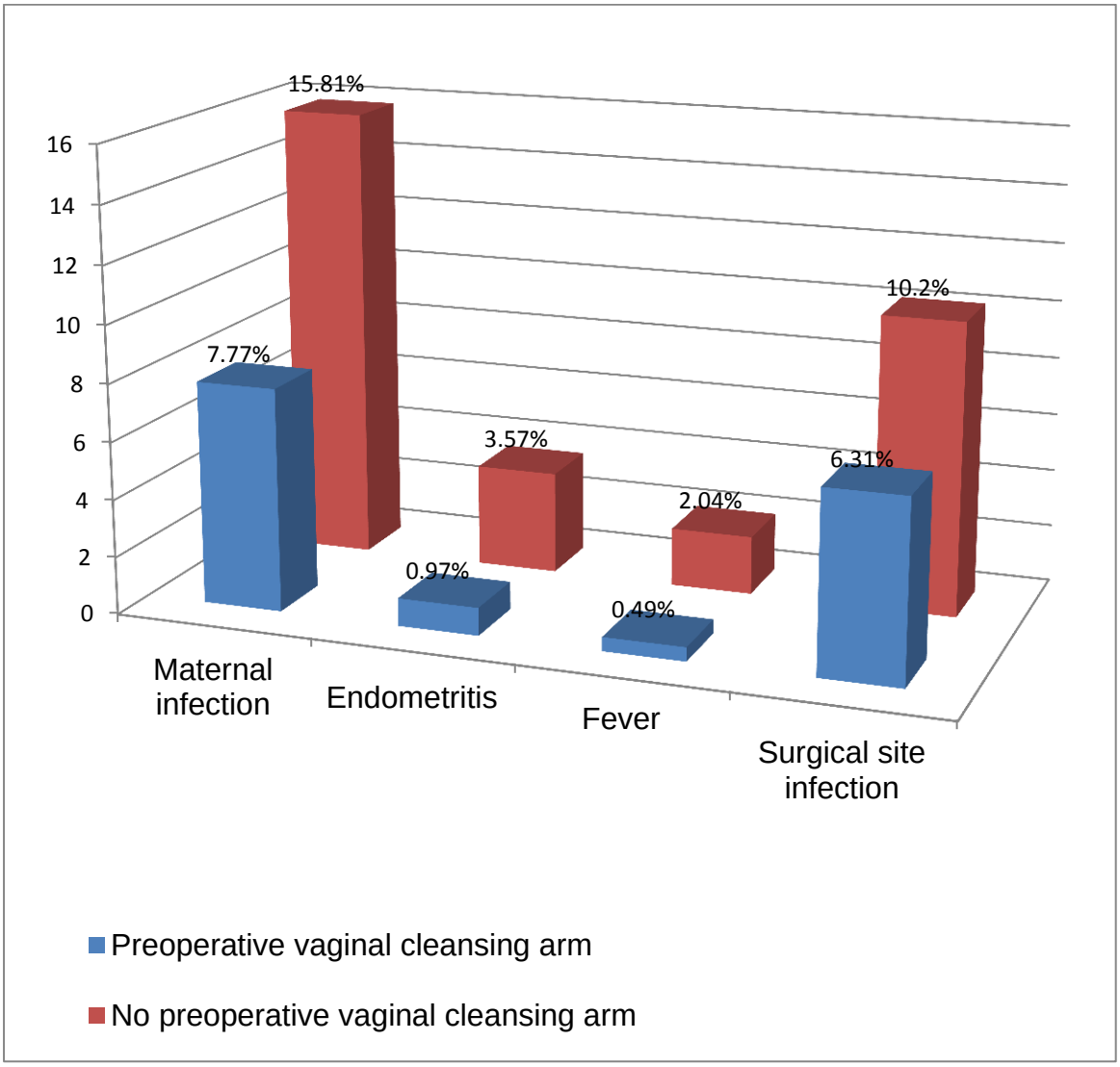
	Vaginal cleansing arm [n=201]	No vaginal cleansing arm [n=196]	p-value
Type of labor;			
None	78	74	
Spontaneous	86	91	0.878
Induced	12	9	
Augmented	18	17	
Duration of active labor in hours [mean]	11.932 ± 6.46	11.168 ± 5.53	0.557
1-7.9	36	32	
8- 12	34	42	
>12	48	45	
Presence of ruptured membranes;			
Yes	85	89	0.583
No	109	102	
Membrane rupture in hours [mean]	8.39 ± 5.11	7.42 ± 4.19	0.301
1-8	53	64	
9-18	31	24	
>18hours	5	3	
Number of vaginal examinations [mean]	2.87 ± 2.63	2.61 ± 2.19	0.452
0	38	39	
1-4	113	121	
5-8	35	27	
>8	8	4	
Indication for CS;			
Non-reassuring fetal status	25	22	
Meconium stained liqor	22	39	
Prolonged labor/poor progress	21	20	
One previous CS	53	37	
Two previous CS	23	33	0.079
Breech presentation	14	13	
Failed induction	6	2	
Others	23	23	
Type of caesarean			
Elective CS	21	18	0.637
Emergency CS	168	169	

Postcaesarean maternal infection [the sum total of endometritis, fever and surgical site infection] occurred in 31 [15.81%] of women in the no vaginal cleansing arm compared to 16 [7.77% of women in the vaginal cleansing arm [p=0.015]. Endometritis occurred in 7 [3.57%] of women in the no preoperative vaginal cleansing arm, and in 2 [0.97%] of vaginal cleansing arm [p-value 0.087]. Four [2.04%] of women in the preoperative vaginal cleansing arm compared to 1 [0.49%] in the vaginal cleansing arm developed post-operative fever [p-value 0.171]. Postoperative surgical site infection developed in 20 of 196 [10.20%] in the no vaginal cleansing arm, compared to 13 [6.31%] in the vaginal cleansing arm [p-value 0.186] [Table3].

Table 3; Comparison of incidence of post-caesarean maternal infection between women in the vaginal cleansing and no vaginal cleansing arm.

	Vaginal cleansing group [n=206]	No vaginal cleansing group [n=196]	p-value	RR (95% CI)
Maternal infection	16 [7.77]	31 [15.81]	0.015	0.50 (0.29 – 0.89)
Endometritis (n, %)	2 (0.97)	7 (3.57)	0.087	0.28 (0.06 – 1.34)
Fever (n, %)	1 (0.49)	4 (2.04)	0.171	0.25 (0.03 – 2.18)
Surgical site infection (n,%)	13 (6.31)	20 (10.20)	0.186	0.64 (0.33 – 1.25)

Figure 2; Comparison of the incidence of postcaesarean maternal infection between women in the vaginal cleansing and no vaginal cleansing arm.



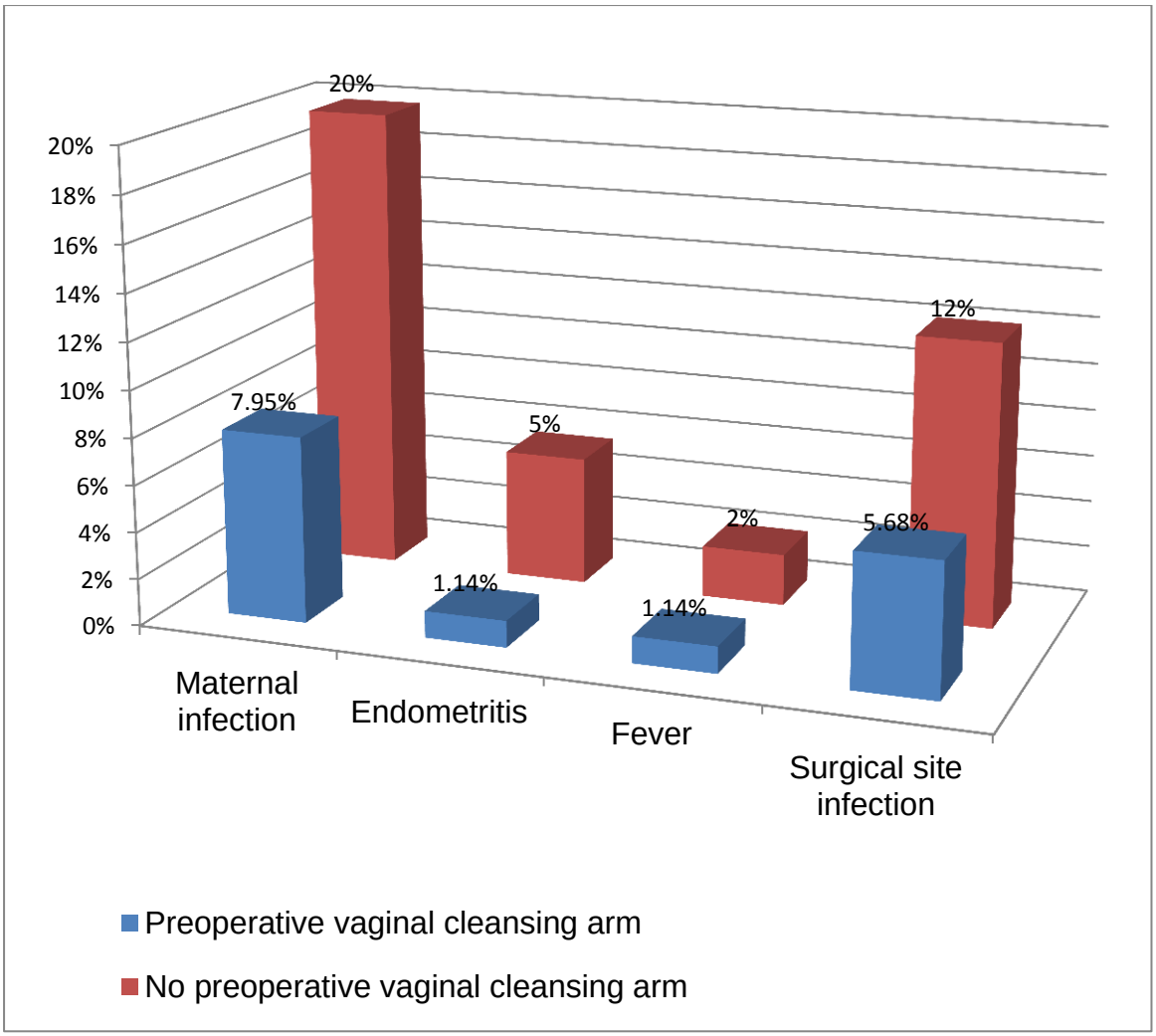
The incidence of developing post-caesarean maternal infection, endometritis, fever and surgical site infection in women with ruptured membranes is summarized in (Table4 and Figure 3). Eighteen [19.78%] of women in the no vaginal cleansing arm developed maternal infection and 7 [7.95%] of women in the vaginal cleansing arm. There was no statistically significant difference noted in the incidence endometritis between women in the vaginal cleansing arm as compared to no vaginal cleansing arm[1.14% vs. 5.49%, p= 0.108]. Similarly there was no significant difference noted in the incidence of fever [1.14% vs. 2.20%: p= 0.588] and surgical site infection [5.68% vs.12.09%: p= 0.139].

In sub-analysis among women with intact membranes (Table 4), there was no significant difference found in the incidence of maternal infection [7.96% vs. 12.38, p=0.279], endometritis [0.92% vs. 1.96%: p= 0.522], fever [0% vs. 1.96%] and surgical site infection [7.34% vs. 8.82%; p= 0.692] between the vaginal cleansing arm and no vaginal cleansing arm respectively.

Table4; Comparison of the incidence of post-caesarean maternal infection between women who had vaginal cleansing or not stratified by whether they had intact or ruptured membranes

	Vaginal cleansing arm	No vaginal cleansing arm	p-value	RR (95% CI)
Intact Membranes	[n=113]	[n=105]		
Maternal infection	9 [7.96]	13 [12.38]	0.279	0.64 (0.29 – 1.44)
Endometritis	1 (0.88)	2 (1.90)	0.522	0.46 (0.04 – 5.08)
Fever	0 (0.00)	2 (1.90)		
Surgical Site Infection	8 (7.08)	9 (8.57)	0.692	0.83 (0.33 – 2.07)
Presence of ruptured membranes	[n=88]	[n=91]		
Maternal infection	7 [7.95]	18 [19.78]	0.022	0.40 (0.18 – 0.92)
Endometritis	1 (1.14)	5 (5.49)	0.108	0.21 (0.03 – 1.76)
Fever	1 (1.14)	2 (2.20)	0.588	0.52 (0.05 – 5.67)
Surgical Site Infection	5 (5.68)	11 (12.09)	0.139	0.48 (0.17 – 1.31)

Figure3; Comparison of the incidence of post-caesarean maternal infection among women with ruptured membranes in the vaginal cleansing and no vaginal cleansing arm



Among women in established labor [Table 5], there was a significant difference in the incidence of maternal infection between the vaginal cleansing arm as compared to the no vaginal cleansing arm [7.50% vs. 15.83%, p=0.044]. The incidence of endometritis among women in established labor was 1.72% in the vaginal cleansing arm compared to 4.27% in the no vaginal cleansing arm [p= 0.446]. The incidence of fever [0.0% vs. 1.71%] and surgical site infection [6.03% vs. 10.26, p= 0.239] was not different between women in the vaginal cleansing and no vaginal cleansing arm [Table 5 and Figure4]

The incidence of maternal infection, endometritis, fever and surgical site infection was not statistically different between women in the vaginal cleansing arm and those in the no vaginal cleansing arm; [8.64% vs. 15.79%, p=0.170], [0% vs. 2.63%], [1.23% vs. 2.63%, p= 0.529], [7.41% vs. 10.53%, p= 0.506] respectively.

Table5; Comparison of the incidence of post-caesarean maternal infection between women who had vaginal cleansing or not stratified by whether they were in established labor or not.

	Vaginal cleansing arm	No vaginal cleansing arm	p-value	RR (95% CI)
No labor	[n=81]	[n=76]		
Maternal infection [n,%]	7 [8.64]	12 [15.79]	0.170	0.55 (0.23 – 1.32)
Endometritis (n, %)	0 [0.00]	2 (2.63)		
Fever (n, %)	1 [1.23)	2 (2.63)	0.529	0.47 (0.04 – 5.12)
Surgical site infection	6 (7.41)	8 (10.53)	0.506	0.71 (0.26 – 1.95)
Labor present	[n=120]	[n=120]		
Maternal infection [n,%]	9 [7.50]	19 [15.83]	0.044	0.47 (0.22 – 1.00)
Endometritis (n, %)	2 (1.67)	5 (4.17)	0.446	0.40 (0.08 – 2.04)
Fever (n, %)	0 (0.00)	2 (1.67)		
Surgical site infection	7 (5.83)	12 (10.00)	0.239	0.59 (0.24 – 1.44)

Figure 4; Comparison of the incidence of post-caesarean maternal infection among women in established labor between the vaginal cleansing and no vaginal cleansing arm.

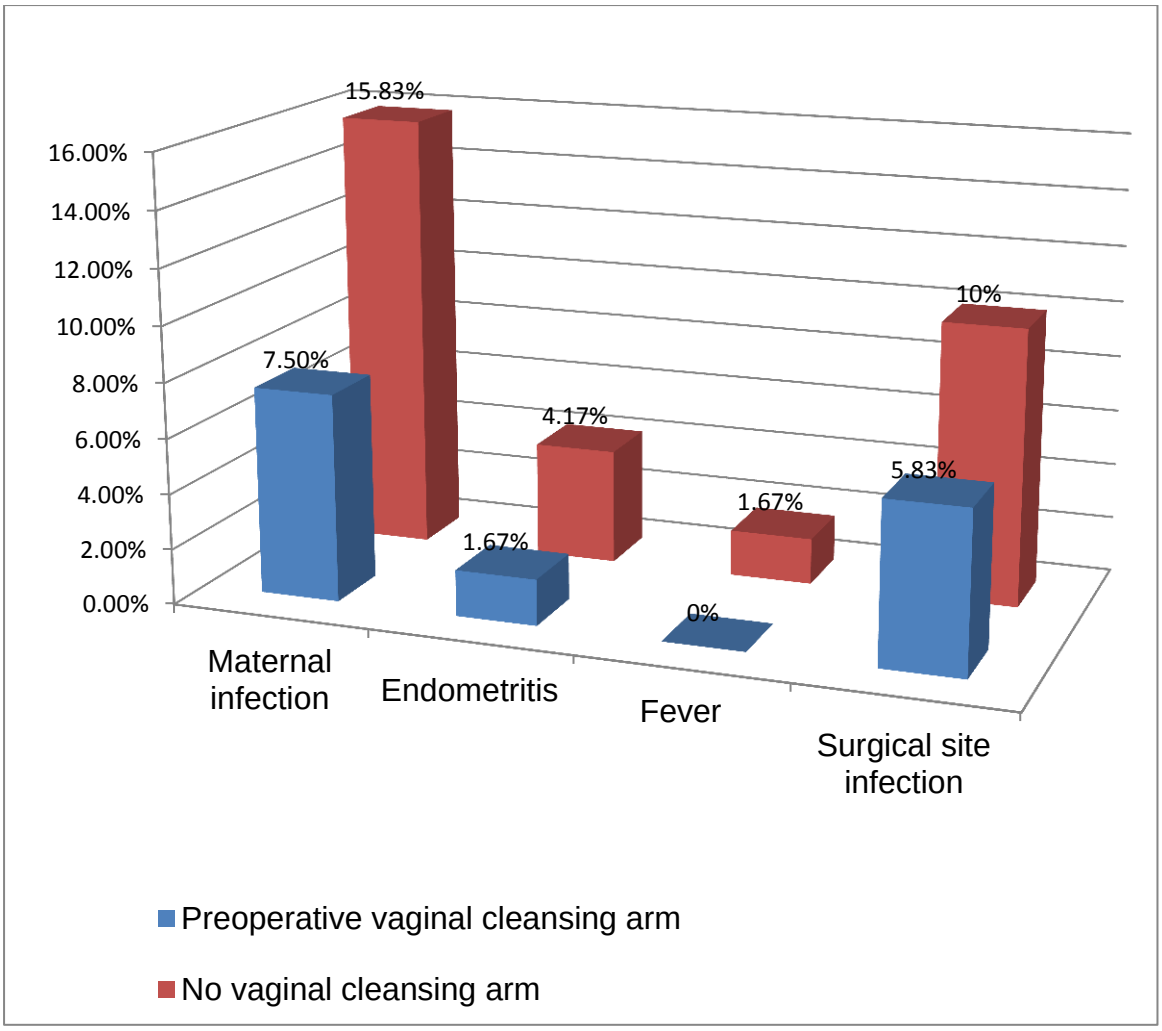


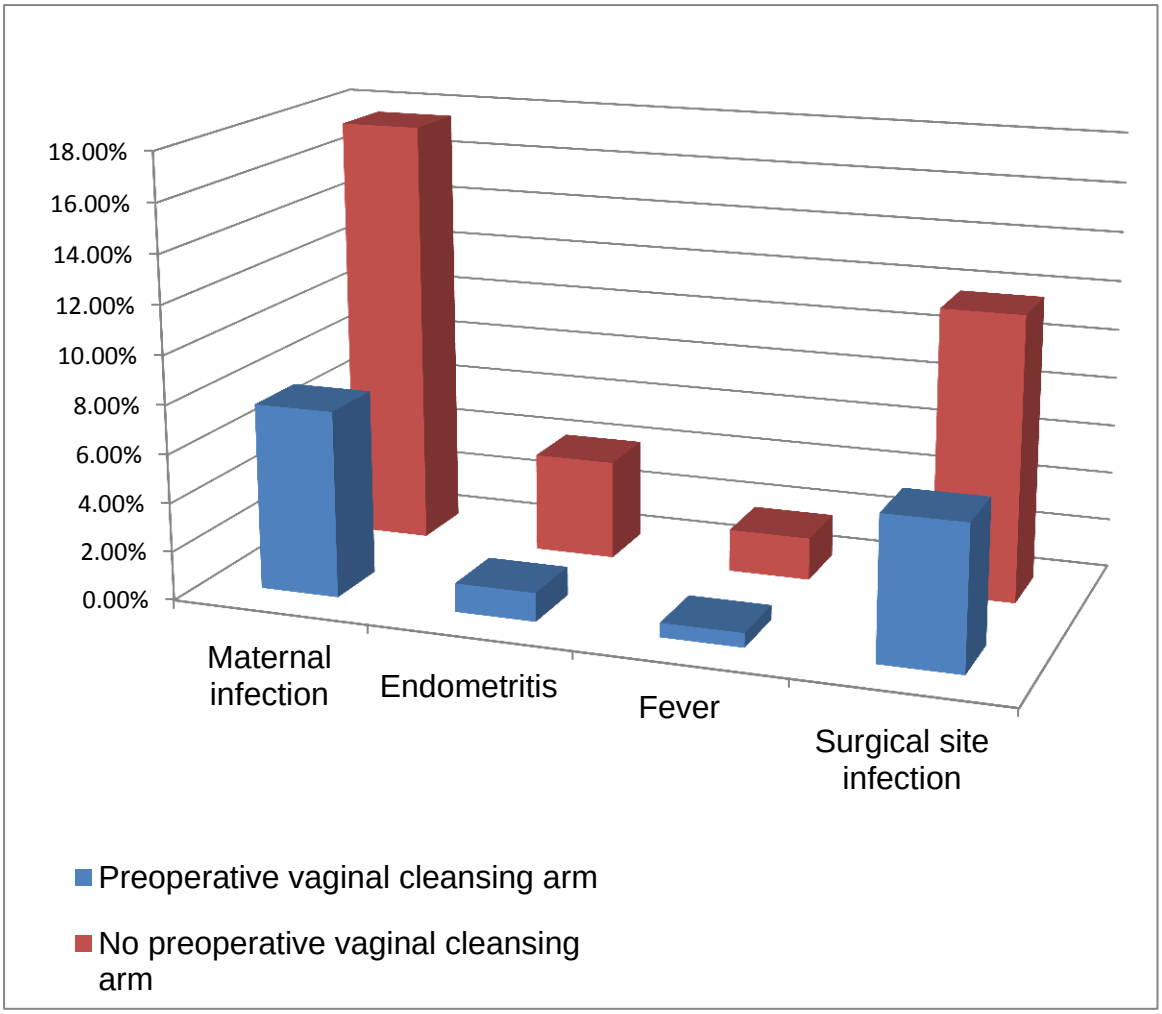
Table 6 summarizes subgroup analysis of outcomes stratified by whether they underwent elective or emergency caesarean section. Among patients undergoing emergency caesarean section, there was a significant difference in the incidence of maternal infection between the vaginal cleansing arm compared to the no vaginal cleansing arm [7.65% vs. 17.54%, p=0.006]. The incidence of developing endometritis, fever and surgical site infection did not differ between the vaginal cleansing and no vaginal cleansing arm; [1.18% vs. 4.09%, p= 0.093], [0.59% vs. 1.75%, p= 0.317], [5.88% vs. 11.70%, p= 0.058].

In patients who underwent elective caesarean section, no participant developed endometritis in either group. Only one patient in the control group developed fever, while surgical site infection developed in 3 participants in the intervention group as opposed to none in the control group.

Table6;Comparison of the incidence of post-caesarean maternal infection between women who had vaginal cleansing or not stratified by whether they underwent elective or emergency caesarean section.

	Vaginal cleansing arm	No vaginal cleansing arm	p-value	RR (95%CI)
Elective caesarean section	[n=23]	[n=20]		
Maternal infection	3 [13.04]	1 [5.00]	0.390	2.42 (0.27- 21.63)
Endometritis	0 [0.00]	0 [0.00]		
Fever	0 [0.00]	1 [5.60]		
Surgical site infection	3 [14.3]	0 [0.00]		
Emergency caesarean section	[n=170]	[n=171]		
Maternal infection	13 [7.65]	30 [17.54]	0.006	0.43 (0.23 – 0.80)
Endometritis	2 [1.18]	7 [4.09]	0.093	0.29 (0.006-1.36)
Fever	1 [0.59]	3 [1.75]	0.317	0.34 (0.04 –3.19)
Surgical site infection	10 [5.88]	20 [11.70]	0.058	0.50 (0.24 –1.04)

Figure 5; Comparison of the incidence of post-caesarean maternal infection among women who underwent emergency caesarean section between the vaginal cleansing and no vaginal cleansing arm



There were no severe adverse events reported among participants. Neither did any participant report local reaction to povidone iodine.

DISCUSSION

We found a significant difference in the incidence of maternal infection among women who underwent preoperative vaginal cleansing compared to no preoperative vaginal cleansing. The benefit of preoperative vaginal cleansing was also found among participants who had ruptured membranes, were in established labor and those who underwent emergency caesarean section. However, in the subgroup analysis, there was a non-statistically significant reduction in postcaesarean endometritis in the preoperative vaginal cleansing arm compared to the arm that did not receive preoperative vaginal cleansing. Similarly there was no statistically significant difference in postcaesarean fever and surgical site infection between the two arms. There was also no statistically significant reduction in postcaesarean endometritis among women in established labor, with ruptured membranes and those who underwent emergency caesarean section between the preoperative and no preoperative vaginal cleansing arms.

Our study had a small sample size [397 participants], and the incidence of endometritis was low, thus the possibility of an underpowered study. We needed a larger sample size to show any significant difference. The subtle differences in preoperative vaginal cleansing technique, the amount of povidone iodine used, its distribution and contact time with the vaginal mucosa/flora may explain the difference in our findings compared to studies that found vaginal cleansing to be beneficial in reducing postcaesarean endometritis. As highlighted earlier, all women in our study underwent post-operative vulvo-vaginal toilet, a 5-day course of antibiotics and were followed up for 2weeks only post-operative. This too might explain why we found no difference in the incidence of endometritis between the two study arms.

Previous studies did not look at the overall maternal infection rates, but instead looked at endometritis, fever and surgical site infection. We looked at the overall maternal infection since the specific infectious morbidities are not mutually exclusive.

Our findings are in keeping with study findings by Reid et al, Haas et al and Shahnaz barat et al, that preoperative vaginal cleansing with povidone iodine [compared with no vaginal cleansing] does not reduce post-caesarean endometritis, fever and surgical site infection (5) (46) (53). Shahnaz barat et al recruited women at low risk of developing post-caesarean infection, since the participants included

women scheduled for elective caesarean delivery only. The study did not show a significant difference in the post-caesarean infection rates in both arms (53). Our study recruited women scheduled for elective and emergency caesarean delivery, and thus captured women at high and low risk of postcaesarean infectious morbidity. Reid et al randomized 247 women in to the vaginal cleansing arm and 251 women in the no vaginal cleansing arm. There was no difference in the incidence of fever, endometritis or wound infection between the two arms. The limitation of this study was the post-randomization exclusion of 68 women with chorioamnionitis, which theoretically may predispose to a selective reporting bias.

Several studies have shown the benefit of vaginal cleansing before a caesarean section on reducing the risk of developing endometritis, although the practice has not been universally adopted. Asghania M et al showed a significant lower incidence of endometritis in women cleansed with povidone iodine [0.4%] compared to women in the no vaginal cleansing arm at 2.4% (3). This study did not follow block randomization rules since women were recruited alternately [non-random], and as such the risk of selection bias. A Cochrane review by Haas et al in 2014 showed a significant reduction in the incidence of endometritis between the vaginal cleansing arm [4.3%] as compared to the no vaginal cleansing arm [8.3%] (45). This review included seven randomized trials, of which three trials [Haas et al, Starr et al and Guzman et al] showed a benefit of vaginal cleansing with iodine, one trial by Yildrim et al showed significant difference only in women who were in established labor and ruptured membranes,, while one study [Reid et al] showed no benefit. The Cochrane review and the study by Asghania et al found that the effect of povidone iodine cleansing on reducing endometritis was strong among women with ruptured membranes and those in established labor. Our study did not show a difference on the risk of developing endometritis even in women with ruptured membranes and those in established labor. This is despite studies showing the risk of post-partum endometritis is increased with prolonged rupture of membrane and in prolonged labor. Starr and colleagues concluded that vaginal cleansing with povidone iodine reduces endometritis, although there was a risk of reporting bias. The study excluded a large number of participants in the analysis since they excluded reporting outcomes in participants whose data were not complete. More so, the study excluded 92 of 400 [23%] participants after randomization, thus selective reporting

bias. An observational case control study by Shahneela Memon et al concluded that preoperative vaginal cleansing reduced post-operative endometritis (54). Participants were not randomized [this was a case control study] and thus selection bias was a limitation. More so the sample size was small with a total of 200participants [100 cases vs. 100 controls].

Some studies have shown benefit of vaginal cleansing in only selected cases that are at increased risk of endometritis,that is women with established labor and ruptured membranes. A randomized trial by Yildrim et al also showed a lower incidence of endometritis in women cleansed with povidone iodine compared to those who had no vaginal cleansing that was statistically significant [6.9% vs. 11.6%; RR = 1.69; 95% CI = 1.03-2.76] (1). The reduction in the incidence of endometritis was only found to be significant in women with ruptured membranes and prolonged labor. This study had a larger sample size of 334 in the vaginal cleansing arm and 336 in the no vaginal cleansing arm.

We found a low incidence of endometritis in both the vaginal cleansing arm and the no vaginal cleansing arm. This is a good finding since post-caesarean infection is associated with increased length of hospital stay and high costs of treatment, increased use of antibiotics [and thus resistance], burden to the nursing mother, and ultimately increased maternal mortality (11) (12). The low incidence may be explained by the fact that all participants received pre-operative prophylactic antibiotic as well as post-operative 5-day course of antibiotics. In addition, all participants underwent post-operative vulvo-vaginal toilet with normal saline and povidone iodine [standard practice in Kenyatta National Hospital], and this may have cleared the vaginal flora of infectious bacteria in both arms. Participants were followed up for 2-weeks post-operative, compared to 6weeks in other studies (3) (45) (52). This might have affected our incidence since infections that occurred after 2 weeks postpartum might have been missed.

Studies that showed comparable incidence of endometritis include Asghania M et al study, which found the incidence of endometritis in women cleansed with povidone iodine to be 1.4%, compared to 2.4% in the no vaginal cleansing arm (3). However this study excluded women who underwent emergency CS due to fetal distress and antepartum hemorrhage, and this might explain the low incidence of endometritis.

Other studies had a slightly higher incidence of postcaesarean endometritis. Haas et al showed the incidence of endometritis after caesarean section to be 4.3% in the vaginal cleansing arm and 8.3% in the no vaginal cleansing arm (45). This was close to Yildrim et al study, incidence of endometritis was 6.9% and 11.6% in the vaginal cleansing and no vaginal cleansing arm respectively (1).

No severe adverse events or local reaction to povidone iodine was reported in this study. The Cochrane review did not report any severe adverse events from the seven studies that were reviewed (45).

The strengths of our study included adhering to strict block randomization rules. Participants demographic characteristics were comparable between the vaginal cleansing arm and the no vaginal cleansing arm [age, marital status and education level]. Gestation in weeks, parity, type of labor, duration of labor, duration of membrane rupture, type and indication of caesarean section were also similar between the two arms. More so we had a high retention rate in our study since only 4 participants were lost to follow-up. Both participants and research assistants who collected data were blinded in the study.

There were several limitations in our study. Our study followed up women for 2weeks postpartum, yet other studies followed up patients for 6weeks postpartum, thus we might have picked less postoperative infections and thus the low incidence of endometritis. More so, all patients received a course of antibiotic for 5 days as is the standard practise in KNH, meaning that infections occurring within the first 48hours were cleared by the antibiotics. During the study, research assistants [nurses] who were doing the vaginal cleansing had to be reminded of the technique in terms of timing and duration of vaginal cleansing. This was necessary since it was noted some research assistants were in a hurry in cases of emergency caesarean section. This might have affected the contact time and distribution of the povidone iodine with the vaginal flora.

From this study therefore, preoperative vaginal cleansing with povidone iodine showed a difference in the overall postcaesarean maternal infection compared to no preoperative vaginal cleansing. However no benefit was shown in reducing the incidence of endometritis, fever and surgical site infection.

Conclusion

Preoperative vaginal cleansing with povidone iodine reduces the overall maternal infection but not postcaesarean endometritis, fever or surgical site infection among women who undergo postcaesarean vaginal cleansing/toilet at Kenyatta National Hospital.

Preoperative cleansing with povidone iodine in addition to postoperative cleansing with povidone iodine does not alter postcaesarean endometritis in women with established labor, ruptured membranes and emergency caesarean section.

Preoperative or postoperative povidone iodine did not show any major side effects/local reaction to the vaginal mucosa.

Recommendations

Consistent with the WHO recommendations, preoperative vaginal cleansing with povidone iodine should be considered as an intervention for reducing postcaesarean maternal infection in women even if they undergo postcaesarean vaginal cleansing/toilet with povidone iodine.

Further studies with larger sample sizes are needed to evaluate the benefit of preoperative vaginal cleansing on the incidence of endometritis at 2 weeks and up to 6 weeks postpartum. Antibiotics postoperatively without evidence of infection should also be omitted. Since postoperative vaginal cleansing is the standard of care, it is also important to evaluate its effectiveness compared to preoperative vaginal cleansing.

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APPENDICES

APPENDIX 1: STUDY BUDGET

Components	Unit of Measure	Duration/ Number	Cost (Kshs)	Total (Kshs)
Personnel				
Research Assistants	5			274,500.00
Statistician	1			30,000.00
Printing				
Consent Form	1 copy	3 pages	10.00	30.00
Questionnaires	1 copy	2 pages	10.00	20.00
Final Report	1 copy	70 pages	10.00	700.00
Photocopying				
Consent Form	410 copies	3 pages	3.00	3,690.00
Assent Form				
Questionnaires	410 copies	2 pages	3.00	2,460.00
Final Report	5 copies	70 pages	3.00	1,050.00
Final Report Binding	6 copies		500.00	3,000.00
Other costs				
ERC Fees				**2,000.00**
Total				317,450.00

APPENDIX 2: STUDY TIMELINES

September 2015	Proposal presentation
January- May 2016	KNH/UoN-ERC review and approval
June-July 2016	Training of Research assistants
July- October 2016	Enrolment and data collection
October 2016	Data analysis
November 2016	Results presentation and dissemination
November 2016	Submission of final Thesis book

APPENDIX 3: CONSENT FORM

STUDY TITLE: EFFECT OF PREOPERATIVE VAGINAL CLEANSING WITH POVIDONE IODINE ON POST-CAESAREAN MATERNAL INFECTIONS AT KENYATTA NATIONAL HOSPITAL

Principal Investigator

I am Dr Karanja Mwangi, a postgraduate student in the Department of Obstetrics and Gynaecology in the University of Nairobi. I am carrying out a study as part of the requirement for Master of Medicine in Obstetrics and Gynaecology. My contact is 0725780067

Supervisors:

1. Prof. J.B.O. Oyieke, Professor of Obstetrics and Gynaecology, Department of Obstetrics and Gynaecology, University of Nairobi

2. Dr John Kinuthia, Consultant Obstetrician and Gynaecologist, Department of Obstetrics and Gynaecology, University of Nairobi

Study introduction

Maternal infection/sepsis accounts for a high number [11%] of maternal death/mortality. Caesarean section [delivery by operation] is the single most important factor for post-delivery maternal infection. Postcaesarean maternal infection is common, and increases costs of treatment, length of hospital stay and maternal death/mortality. Vaginal cleansing/preparation with povidone iodine [antiseptic solution] before caesarean section may reduce postcaesarean maternal infection.

Purpose Of Study

To find out the effect of preoperative vaginal cleansing with povidone iodine on post-caesarean maternal infections at Kenyatta National Hospital

Study Procedure

If you agree to participate there will be 2 arms, one arm involve vaginal preparation with povidone iodine before caesarean section, while the other arm will not be done

vaginal preparation [they will be given the standard of care as practiced in Kenyatta National Hospital]. We will then find out the rate of maternal infection after 3days and at 2weeks and compare the 2 arms. The ward nurse and/or the doctor covering the ward will be monitoring and recording your progress while in the ward, and you will be informed of the progress accordingly. In case of any complications/undesired events/infection sets in, you will be informed about it and the treatment/intervention to be undertaken.

Benefits

The study will confer no direct benefits to the participant but the information obtained will help us improve on the management of other women in future who will be undergoing caesarean section and may develop maternal infection after the operation.

Risks

Though rare, you may react to the iodine solution that will be used during the study. This is a local reaction that is self limiting within a few days. In case you develop an infection due to the operation, we will offer you the standard of care as per the hospitals protocol.

Compensation

There will be no form of compensation for participating in this study.

Participation

Participation in the study will be purely voluntary, you may choose not to participate or withdraw at any point of the study. You will not be penalized or intimidated in any way if you wish to withdraw your participation from the study.

Confidentiality

All information provided by the participant will be completely anonymous. The information collected will be treated and kept confidential and in the custody of principal investigator and used only for the purpose of the study.

Study approval has been given by the Kenyatta National Hospital Administration and Kenyatta National Hospital/University of Nairobi Ethics and Research Committee {KNH/UON-ERC}.

I am requesting your participation in this study.

Your agreement to participate in the study will be taken as a voluntary consent to participate in this study.

For Further Information Please Contact:

Dr. Karanja Mwangi

Tel: 0725780067

E-mail: mwangikaranja001@gmail.com

OR

Kenyatta National Hospital / University of Nairobi Ethics and Research Committee

P.O. Box 20,723-00,202

Tel: (254) 020 7263 00 EXT 44102, 44,355

E-mail: uonknh_erc@uonbi.ac.ke

CONSENT FORM

I have fully understood the information provided in the consent form above and have been given opportunity to ask questions. I give my voluntary consent to participate.

Participant's signature…….. Date……

Investigator's signature…… Date……

APPENDIX 4:

DATA EXTRACTION FORM

PATIENT NUMBER ☐☐☐☐☐☐☐☐☐☐
PATIENT CODE ☐☐☐☐

DATE OF ADMISSION (DD MM YYYY) ☐☐ ☐☐ ☐☐☐☐
DATE OF OUTCOME (DD MM YYYY) ☐☐ ☐☐ ☐☐☐☐
LENGTH OF HOSPITAL STAY (DAYS) ☐☐☐

INFORMED CONSENT: 1. YES ☐
2. NO ☐

SOCIODEMOGRAPHIC

AGE (YEARS) ☐☐

MARITAL STATUS: SINGLE ☐ MARRIED ☐ OTHER ☐

YEARS OF EDUCATION: NONE ☐ PRIMARY ☐ SECONDARY ☐
POST-SECONDARY ☐

OBSTETRIC

GESTATIONAL AGE (WEEKS) ☐☐
PARITY: .....

GROUPS:
VAGINAL CLEANSING GROUP ☐
NO VAGINAL CLEANSING GROUP ☐

PRESENTATION
TYPE OF LABOR: NONE☐ SPONTANEOUS ☐ INDUCED ☐ AUGMENTED ☐

DURATION OF LABOR IN HOURS:

PRESENCE OF RUPTURED MEMBRANES: YES ☐ NO ☐

DURATION OF MEMBRANE RUPTURE IN HOURS:

NUMBER OF VAGINAL EXAMINATIONS:

TYPE OF CAESAREAN SECTION; ELECTIVE ☐ EMERGENCY☐

INDICATION FOR CAESAREAN SECTION:

TIMING OF ANTIBIOTIC USE:

PREOPERATIVE ☐
INTRAOPERATIVE☐
POSTOPERATIVE ☐

POSTOPERATIVE VULVOVAGINAL TOILET: DONE☐ NOT DONE☐

POSOPEARTIVE VVT SOLUTION USED: IODINE ☐ CHLORHEXIDINE ☐ NORMAL SALINE☐

MATERNAL POSTCAESAREAN INFECTION YES ☐ NONE☐
IF YES, STATE;
Temperature of ≥38°C ≥24hours after the operation and/or foul smelling vaginal discharge and/or abnormally tender uterus [any two]: ☐

Temperature of ≥38°C or higher ≥24hours after the operation, not associated with other symptoms/signs of infection: ☐

Purulent discharge from the skin incision: ☐

Redness, localized tenderness or swelling: ☐

Incision spontaneously dehisces: ☐

Abscess [purulent discharge in the presence of induration at the incision site]: ☐

MATERNAL POVIDONE IODINE SIDE EFFECT/ADVERSE EFFECTS:

ANAPHYLACTIC REACTION: ☐

LOCAL VAGINAL REACTION: ☐