

Determination of the microbiologic flora on the incision site among obstetric patients who underwent surgical skin preparation with either 10% povidone iodine or 4% chlorhexidine antiseptic solution prior to cesarean section in a tertiary hospital*

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ABSTRACT

Objectives: To determine the microbiologic flora after surgical skin preparation of the incision site using either chlorhexidine or povidone iodine antiseptic solution prior to cesarean section among obstetric patients.

Materials and Methods: This is a cross-sectional study of ninety-two (92) obstetric patients who were admitted for cesarean section. They underwent fishbowl lottery, wherein participants drew from a bag of folded stubs written chlorhexidine or povidone iodine, to determine their distribution to either group. Forty six (46) participants were distributed in each group. Skin cultures were obtained by the researchers from the incision site after surgical skin preparation using chlorhexidine or povidone iodine.

Results: Total of 92 participants enrolled in this study, 46 participants in chlorhexidine group and another 46 participants in povidone iodine group. There was no statistically significant difference between the 2 groups in terms of clinico-demographic characteristics. Out of the 92 participants, only one participant, under the povidone iodine group, showed a growth of 100,000 colony-forming units of *Enterobacter cloacae* and has no statistical significance in the growth of microbiologic flora after effective surgical skin preparation with either chlorhexidine or povidone iodine.

Conclusions: This study showed that chlorhexidine and povidone iodine are both effective in eliminating microbiologic flora after surgical skin preparation prior to cesarean section. Povidone iodine is still a sound choice of antiseptic especially in low resource setting. Due to the descriptive nature of this paper, only assumptions that chlorhexidine and povidone iodine are comparable antiseptic solutions can be deduced from this study.

Keywords: Cesarean Section, Chlorhexidine, Povidone Iodine, Surgical skin preparation

INTRODUCTION

Surgical Site Infections (SSIs) remain a significant cause of disability among surgical patients. Advances have been made in infection control practices but despite these advances, SSIs remain a significant cause of morbidity with associated mortality rate of 3%.¹

SSIs occur in approximately to 20% of patients who undergo intra-abdominal surgery. This leads to prolonged hospital stay and greater hospital costs.² In the Philippines, a number of retrospective and prospective studies have been done since 1982 and demonstrated SSI rate ranging from 0.12 percent to 14.4%.¹

In obstetric cases, SSI happens in about 3-6% of women who had cesarean delivery. According to Habib, surgical site infection rates as high as 15 to 75% were noted in high risk cases and developing countries.³ Hence, it is conceivable that improving skin antisepsis would decrease surgical site infections. The common types of antiseptics used are povidone-iodine, alcohol, and chlorhexidine gluconate.⁴

The composition of skin flora of the body varies from site to site and depends on many factors. It constitutes a major source of organisms responsible for wound infection. *Staphylococcus aureus*, micrococci, saprophytic *Corynebacterium* species, and *Propionibacterium* species are the predominant flora of the skin. *Staphylococcus aureus* regularly inhabits the perineum in about 15% of healthy people.⁵

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Hence suppression of skin flora using antiseptic agents can reduce postoperative wound infection.⁵ Topical antiseptics may be applied to the skin preoperatively to reduce SSI risk.² The Centers for Disease Control and Prevention (CDC) recommend preparing the skin surgical site with antiseptic immediately before incision, but preference as to which antiseptic to use, is still the surgeon's prerogative depending on his training and setting.²

Chlorhexidine and povidone-iodine are commonly used agents for skin disinfection before surgery. Chlorhexidine is a broad-spectrum biocide effective against Gram-positive bacteria, Gram-negative bacteria and fungi. It inactivates microorganisms with a broader spectrum and has a quicker kill rate than other antimicrobials. It kills by disrupting the cell membrane and can kill nearly 100% of bacteria within 30 seconds. Chlorhexidine is safe and effective antiseptic and based on recent studies, it is found to be more effective than povidone-iodine in diminishing microbial skin colonization.⁶ On the other hand, povidone-iodine is a fast-acting, broad-spectrum bactericidal that destroys microbial protein and DNA. It has an excellent in vitro antimicrobial activity and showed optimum bactericidal effect just after 30 seconds of exposure⁽¹⁶⁾. Scherier et al found out that povidone iodine damages bacterial cell function by blocking hydrogen bonding and altering the membrane structure. This ensures rapid death of microbes and helps to prevent the development of bacterial resistance.¹⁵

In 2015, our institution admitted a total of 4,279 obstetric patients wherein 1,899 (44%) delivered via primary or repeat cesarean sections. The antiseptic agent we use for skin preparation depends on the availability, but commonly, povidone iodine is used because of its affordable price. Chlorhexidine was first used in our institution in 2011 but due to its much expensive cost, it is seldom available. Our Infectious Disease section reported a total of 4 Obstetric SSI (2 Superficial SSI and 2 Episiotomy site SSI) last 2015. For the past 5 years, they had a total of 25 Obstetric SSI, mostly Superficial SSI. This resulted in extended hospital stay or readmission and added cost for IV antibiotics. These figures are most probably under reported because it does not include all the cases of SSI that are managed postoperatively. In the out-patient department, patients are also prescribed with antimicrobials causing additional expense for the patients.

This study aimed to determine growth of microbiologic flora along the incision site after surgical skin preparation with either chlorhexidine or povidone iodine antiseptic solution prior to cesarean section among obstetric patients.

OBJECTIVES OF THE STUDY

General Objective: To determine the microbiologic flora of obstetric patients who underwent surgical skin preparation prior to cesarean section.

Specific Objectives:

1. To determine the socio-demographic profile of obstetric participants who underwent surgical skin preparation using either 4% Chlorhexidine or 10% Povidone Iodine antiseptic solution prior to Cesarean Section.
2. To determine the prevalence of the microorganisms that grew from the skin swab cultures of obstetric patients who underwent surgical skin preparation using either 4% Chlorhexidine or 10% Povidone Iodine antiseptic solution prior to Cesarean Section.
3. To determine the sensitivity and resistance pattern of the microorganisms that grew from the skin swab cultures of obstetric patients who underwent surgical skin preparation using either 4% Chlorhexidine or 10% Povidone Iodine antiseptic solution prior to Cesarean Section.

MATERIALS AND METHODS

This study was conducted in the operating room and included pregnant women admitted for cesarean section, either primary or for repeat with the following inclusion criteria: twenty four to forty two (24 to 42) weeks age of gestation, age >18 years old, with intact bag of waters or with ruptured bag of waters less than or equal to 11 hours and patients admitted less than 48 hours. The following are the exclusion criteria: patients with mental disability and incapable of self care, immunocompromised or patients using immunosuppressive agents, patients diagnosed with intra-amnionic Infection and those given antibiotic within the last 2 weeks, other than the prophylactic antibiotic given prior to cesarean section.

This study was a cross sectional design with a ratio of 1:1 for the two antiseptic agents. Based on a prior study by Salama, et al (2016), the post-cesarean section SSI rate from chlorhexidine and povidone-iodine was 3.6% and 12.9% respectively, using an alpha level at 95% and a power of 80% - 82 participants are needed to reject the null hypothesis, that rates of SSI for both agents are equal. An adjustment of 10% was included to account for possibility of withdrawal and attrition due to the nature of the study. Hence, we recruited 92 individuals with 46 pregnant women per treatment group of the study.

After a participant was recruited, an informed consent (Appendix I) was taken and a Patient Case Report Form (Appendix II) was filled up by the investigators. All of them

Appendix I

<p>Informed consent form (English version)</p> <p>Part 1: Study Information</p> <p>1. Introduction I am a resident in training, is inviting you to participate in the study entitled "Determination of the Microbiologic Flora on the Incision site Among Obstetric Patients Who Underwent Surgical Skin Preparation with either 10% Povidone Iodine or 4% Chlorhexidine Antiseptic Solution Prior to Cesarean Section in a Tertiary Hospital".</p> <p>My supervising investigator and I, the principal investigator, funds this study. This study has undergone technical and ethical reviews. The technical review was handled by EHRO and gave the necessary approvals.</p> <p>2. Purpose of the study Surgical site infection is a common post-operative morbidity that can take a toll to the physical, mental, social and financial aspects of a patient. Adequate skin preparation is a vital step in the prevention of surgical site infection. To guide the surgeon on what prophylactic antibiotic to use, it is important to know what organism he/she should target. The purpose of this study is to determine the microbiologic flora that persist after surgical skin preparation with Povidone Iodine or Chlorhexidine antiseptic solution among obstetric patients who will undergo cesarean section.</p> <p>3. Type of study Location of study: This study will conducted at the operating room</p> <p>Parts of the study: The first part of the study involves looking for qualified subjects. The principal investigator will take informed consent from the participants. The second part is the skin swab culture sampling after surgical skin preparation with Povidone Iodine or 4% Chlorhexidine antiseptic solution. Lottery system will be done to determine who will be prepped with Povidone Iodine or Chlorhexidine. Specimen will be sent to the Laboratory. A skin culture swab will be taken by either the principal investigator or research assistant and will be sent to the laboratory. The expenses of this study (skin swab culture) will be shouldered by the primary and supervising investigators.</p> <p>Number of subjects: The number of subjects that will be included in the study is 92, 46 for the 10% Povidone Iodine group and 46 for 4% Chlorhexidine group.</p> <p>4. Participation in the study is voluntary. Your participation in the study is voluntary. If you are not able or willing to participate, this will not affect the treatment that you are seeking or undergoing in our institution.</p> <p>5. Possible risks In the course of taking the skin swab cultures, cotton swabs will be used and swiped over the abdomen at the line of incision. This will entail no discomfort, as the abdomen is already anesthetized during this time.</p>	<p>6. Benefits The biggest benefit from the study for the patient is that she will contribute to the knowledge that can be used to determine appropriate prophylactic antibiotics for cesarean section in our local setting.</p> <p>7. Incentives No incentives will be given to the subjects.</p> <p>8. Confidentiality Up to the end of the study, details and other information will be kept confidential.</p> <p>The Ethics Review Panel and regulatory authorities will grant access to participants' records for purposes only of verification of clinical study procedures and data.</p> <p>9. Informing of results Overall results can be disseminated to the participants after the study, if she wishes. Individual results of the skin culture can be accessed by the participants and will be given out by the principal investigator. Results of the culture, if positive, will be revealed to the subject and to the surgeon as soon as available. This information will be helpful in the further care of the subject-patient.</p> <p>10. Right to refuse to join the study If one does not like to become part of the study, she will not be forced to do so.</p> <p>11. Person responsible Should there be questions, please get in touch with the principal investigator of the study.</p> <p>Part II: Signing the informed consent</p> <p>I was invited to participate in the study entitled " The Determination of Microbiologic Flora on the Incision site Among Obstetric Patients Who Underwent Surgical Skin Preparation with either 10% Povidone Iodine or 4% Chlorhexidine Antiseptic Solution Prior to Cesarean Section in a Tertiary Hospital". I am informed of the potential discomfort and benefits of this study. I also know that there is no incentive in this study.</p> <p>I have read the informed consent. I was able to talk to the principal investigator. I agree to participate in the study.</p> <p>NAME OF PARTICIPANT: _____</p> <p>SIGNATURE OF PARTICIPANT: _____</p> <p>DATE: _____</p> <p>NAME OF WITNESS: _____</p> <p>SIGNATURE OF WITNESS: _____</p> <p>DATE: _____</p>
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Appendix II

<p>Patient Case Report Form</p> <p>Title of Study: Determination of the Microbiologic Flora on the Incision site Among Obstetric Patients Who Underwent Surgical Skin Preparation with either 10% Povidone Iodine or 4% Chlorhexidine Antiseptic Solution Prior to Cesarean Section in a Tertiary Hospital</p> <p>CHECKLIST OF FULFILLMENT INCLUSION CRITERIA:</p> <ol style="list-style-type: none"> 1. Pregnant patients twenty four to forty two weeks age of gestation who will undergo cesarean section, either primary or repeat. 2. Ages >18 years old 3. Intact bag of waters or rupture bag of waters for less than or equal to 11 hours 4. Admitted for <48 hours <p>CHECKLIST OF FULFILLMENT EXCLUSION CRITERIA:</p> <ol style="list-style-type: none"> 1. No mental disability and capable of self care (i.e bathing) 2. Not immunocompromised (i.e HIV patient) or using immunosuppressive agents (i.e. steroids, chemotherapy) 3. Reason for cesarean section is not due to Intra-amnionic Infection (IAI). 4. No other antibiotic is given to the patient within the last 2 weeks, other than the prophylactic antibiotic given prior to cesarean section. 	<p>PATIENT INFORMATION:</p> <p>Subject Study Number _____</p> <p>Date of admission: Name: Age/Gravidity/Parity: Civil status: Address: Contact Number: Highest educational attainment: Occupation: Admitting diagnosis: Co-morbid: Medications taken during pregnancy (vitamins, antibiotics etc): When last time patient took a bath? (Date and Time): Reason for Cesarean section: Date of Cesarean section: How many hours bag of water ruptured? (should be less than <11 hours): Skin Swab Culture No. _____ Organism seen: Number of colonies: Sensitivity: Resistant:</p>
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underwent fishbowl lottery, wherein a participant drew from a bag of folded stubs written either Chlorhexidine or Povidone Iodine, to determine their distribution to each group. All patients received preoperative antibiotic, which was Cefazolin (2gm/IV), within 30 minutes from surgical incision, as standard infection prophylaxis. Patients then underwent surgical skin preparation by the 1st assist surgeon of the operation, using either povidone iodine or chlorhexidine antiseptic solution.

The surgical skin preparation was done, first with a surgical scrub, wherein the surgical site was thoroughly scrubbed with the antiseptic solution then rinsed with sterile water. The first swipe was done at the line of incision (violet dotted line, Figure 1), then the succeeding swipes were done in circular clockwise or counterclockwise manner going outwards the incision the site (blue arrow lines). The same manner was done with a Pfannensteil incision (Figure 1). The procedure was done thrice before wiping it dry with a sterile cloth or towel. The next part was applying again the surgical site with the antiseptic solution in the same manner, but this time without rinsing with sterile water. This is for a more concentrated coat of the antiseptic solution at the surgical site. The whole surgical skin preparation lasted less than 5 minutes. Aslan et. al concluded that 5-minute scrub were statistically more effective at reducing bacterial counts than the scrub for 1 minute.⁸ The antiseptic solution was allowed to dry for 30 seconds after which samples of skin swab cultures were taken. After donning sterile gloves, sterile cotton swabs were used and sample was collected at the line of incision. The cotton swabs were placed in a sterile container. The samples were sent for culture studies in the laboratory, within 12 hours at the time of collection and kept in room temperature (18-25°C). Specimens of skin culture swabs are said to be stable for at least 24 hours.¹⁴ The samples were plated using Blood, MacConkey and Chocolate agar and incubated for 2 days before reading the microbiologic growth, if present.

Descriptive statistics such as the mean and standard deviation for continuous variables; and frequency and percentage were used for the categorical data variables, to provide an overview of the study population. These clinico-demographic variables were compared between the two study groups (Chlorhexidine and Povidone-iodine) using the independent t-test, chi-square test of association and Fisher's exact test.

The level of significance for all sets of analysis was set at $p < 0.05$ using two-tailed comparisons.

RESULTS

A total of 92 patients were included in the study. Forty-six (46) were in the chlorhexidine surgical skin preparation group and another 46 for the povidone iodine group.

Table 1 shows the socio-demographic characteristics of the study participants. There was no statistically significant difference between the 2 groups in terms of clinico-demographic characteristics, except for gravidity, which was significantly higher among women assigned to the povidone-iodine group. This suggests that there was effective randomization performed during the conduct of the study.

Trends would show that there is a higher percentage of participants with co-morbid conditions, more hours from last bath prior to the cesarean section, and emergency indication for abdominal delivery assigned in the povidone iodine group (Table 1). These factors could be seen as having a negative impact to patient's well-being and are postulated factors that may contribute to wound dehiscence. Indirectly, one would suspect that patients in the subset of povidone iodine would have growth of microorganisms, however, it showed no significance. On the other hand, the Chlorhexidine group was noted to have a higher percentage of participants with intact bag of water and previous abdominal delivery (Table 1). Despite the disparity in the percentages, all of these variables showed no significant difference between the two groups. Since both groups are almost the same, in terms of baseline demographic characteristics and other factors like co-morbidities, time last bath was taken before the procedure and number of hours the bag of waters had ruptured, all of these factors have shown no significance in the microbiologic growth after surgical skin preparation with either Chlorhexidine or Povidone Iodine.

The bacterial isolates were supposed to be tabulated and presented using frequency and percentage, across antiseptic agents. Chi-square test of association was supposed to be done to ascertain association between the two antiseptic agents and the presence of bacterial isolates in the swab. The same procedure was supposed to be conducted to compare the two antiseptic agents

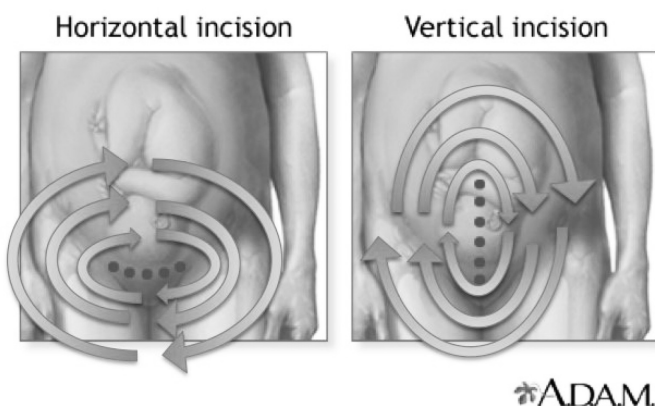


Figure 1. Manner of Surgical Skin Preparation

Table 1. Baseline Characteristics of the Study Participants

Characteristics	Povidone-iodine (n=46)	Chlorhexidine (n=46)	p-value
Age in years	30 ± 1.00	29 ± 0.89	0.45
Age of gestation	38 ± 0.36	38 ± 0.35	0.76
Highest educational attainment			
Elementary	2 (4.35%)	1 (2.17%)	
High school	26 (56.52%)	24 (52.17%)	0.46
Vocational	1 (2.17%)	5 (10.87%)	
College level	17 (36.96%)	16 (34.78%)	
Married	18 (39.13%)	18 (39.13%)	0.58
Unemployed	35 (76.09%)	39 (84.78%)	0.29
Gravidity	3 ± 0.26	2 ± 0.17	0.03*
Parity	2 ± 0.25	1 ± 0.15	0.18
Presence of Co-morbidities	7 (15.22%)	6 (13.04%)	0.50
Intact bag of water	37 (80.43%)	40 (86.96%)	0.40
12 hours or more from last bath	18 (39.13%)	14 (30.43%)	0.38
Emergency Indication for CS	18 (39.13%)	11 (23.91%)	0.12
Repeat CS	21 (45.65%)	27 (58.69%)	0.32

and presence of antimicrobial sensitivity and resistance pattern among cultures. However, these steps were not performed since only one participant had a positive microbiologic growth during the course of the study.

Out of the 92 participants, only one participant, under the povidone iodine group, showed a growth of 100,000 colony-forming units of *Enterobacter cloacae*, which was sensitive to amikacin, ampicillin and sulbactam, cefixime, ciprofloxacin, cotrimoxazole, levofloxacin, meropenem, tetracycline and resistant to ampicillin, aztreonam, cefepime, vancomycin. The indication for the cesarean section for this patient was fetopelvic disproportion. Her bag of waters had ruptured for 6 hours and she was admitted for 4 hours in our labor room before cesarean section was called. Since only one out of all the participants had shown a positive culture growth after surgical skin preparation, this suggests that using either chlorhexidine or povidone iodine in surgical skin preparation showed no significant difference in the growth of microbiologic flora after effective surgical preparation.

DISCUSSION

The skin flora's composition varies from site to site and depends on many factors, including the amount of

sebum, location of sweat glands, and moisture content. The skin constitutes a major source of organisms responsible for wound infection and for this reason, prolonged suppression of skin flora might be associated with reduction in postoperative wound infection.⁵

Preparing the skin at the surgical site with antiseptic solution immediately before incision has already been the standard of care. Skin disinfection before surgery is universally accepted as an essential component of surgical practice. CDC strongly recommends this practice but the preferred antiseptic solution was not indicated. Many products are available to reduce resident and transient skin flora but the common agents used among institutions are chlorhexidine and povidone iodine, both of which are bactericidal.

Povidone-iodine has been used for preoperative skin preparation since 1955 and is preferred universally. It exerts its antiseptic properties in two ways, first it substitutes the covalently bound hydrogen groups and second, it is an iodophor and reacts with the oxygen containing functional groups. Iodine solutions have rapid, broad-spectrum antimicrobial activity against gram-positive and gram-negative organisms, viruses, and fungi.

It quickly penetrates microorganisms and attacks nucleotides and it inhibits protein synthesis by oxidizing thiol groups.¹⁸ Povidone iodine is effective in reducing the bacterial counts up to one hour of surgical procedure without any local postoperative complications.²¹ Systemic toxicities, like metabolic acidosis and acute renal failure, were seen in a group of burn patients with more than 25% of the total body surface area burned.²⁰

Chlorhexidine is a cationic biguanide that binds to the negatively charged surface of bacterial cell wall leading to alteration in permeability, leading to leakage of cytoplasmic contents and cell death.¹⁸ It has been shown to be effective against all microorganisms. However, it does not have a wide spectrum of antiviral activity as povidone-iodine. Chlorhexidine creates a protective bacteriostatic film on the skin that maintains a high level of activity against organisms. In contrast with povidone iodine, its antimicrobial activity is not affected by presence of body fluids such as blood.²¹ Due to its significantly shorter contact time, Chlorhexidine may be of value in emergency situations. The prolonged residual effect and adherence of chlorhexidine to the stratum corneum, extends its duration of action for several hours (at least 6 hours), makes it a preferable agent for cutaneous antiseptics.¹⁸ This ability of antiseptic solutions to bind to and penetrate the stratum corneum is important for effective clearance of the microorganisms. Up to 20% microorganisms live deep within the dermis and these may be an important source of contamination

and subsequent colonization.¹⁸ There have been a few reported cases of irreversible corneal eye damage caused by eye contact during facial skin preparation before surgery.²⁰ The use of flammable alcohol-based products in the operating room poses a small risk of fire or chemical skin burn.¹⁹

Numerous studies have stated that an Alcohol based chlorhexidine 0.5 to 2% is superior than Povidone iodine 10% for cutaneous antisepsis. In a study conducted by Mimoz et al, they assigned patients to either skin preparation with 0.5% chlorhexidine or povidone-iodine. The contamination rates were much lower in the chlorhexidine group ([1.4% vs. 3.3%]; odds ratio, 0.40 [95% CI, 0.21-0.75]; P=0.004).¹⁸ Other studies have contradicting results. Girard et al. evaluated the effect of povidone-iodine and chlorhexidine over the next year for catheter-related infections. They found a significant reduction in colonization with chlorhexidine (1.12 vs. 1.55 P=0.041), however, the reduction in infections and bacteremia were not significant. Langgartner et al showed no difference between the two and concluded that chlorhexidine 0.5% was 'as effective as' povidone-iodine 10%.¹⁸ Although studies may suggest that Chlorhexidine can have greater reduction in microbiologic growth, the clinical significance in terms of infection rate may not differ that much compared with Povidone iodine.²⁰ In a prospective randomized open-label controlled trial done by Springel et al,¹⁸ they found that preoperative preparation with chlorhexidine-alcohol was not superior to povidone-iodine in the reduction of cesarean-related surgical site infection. As such, they believe that povidone-iodine remains an acceptable method of preoperative surgical site antisepsis prior to cesarean delivery.

In this study, no demonstrable significant difference in the microbiologic growth after surgical skin preparation of either antiseptic was noted. Despite the widespread acceptance of chlorhexidine as a superior antiseptic than povidone iodine, it can be inferred from this study that povidone iodine is still a sound choice of antiseptic especially if there is scarcity of funds and supply of Chlorhexidine. Based on the DOH 2014 Drug Price Reference Index (Second Edition), 1 gallon of chlorhexidine costs approximately Php 1,500 while a gallon of povidone iodine costs only Php 400. This price discrepancy is quite steep in developing countries. There was one sample under the povidone iodine group, which grew Enterococcus on skin culture but the result was insignificant. However, due to the descriptive nature of this study, it will be difficult to draw a strong conclusion and comparison between the 2 commonly used antiseptic agents. It is helpful though that since we were able to complete our sample size, it somehow strengthens the idea that chlorhexidine and povidone iodine are both effective for surgical antisepsis.

CONCLUSION

This study showed that chlorhexidine and povidone iodine are both effective in eliminating microbiologic flora after surgical skin preparation prior to cesarean section. Out of the 92 samples, only one sample exhibited microbiologic growth, which showed no significant difference in the microbiologic growth in the culture samples of the 2 antiseptics after skin preparation. Despite numerous studies that show superiority of chlorhexidine than povidone iodine, povidone iodine can still be a sound choice of antiseptic especially in low resource setting.

LIMITATIONS

The limitation of study is lack of blinding of the participants and the investigators. And due its descriptive nature, only assumptions that chlorhexidine and povidone iodine are comparable antiseptic solutions can be deduced from this study.

RECOMMENDATIONS

Skin cultures taken before and after the surgical skin preparation or before and after surgical operation are may be better ways to determine the microbiologic flora that may persist or grow after surgical skin preparation or operation using Chlorhexidine or Povidone Iodine. Blinding of participants and investigators, if possible, can be done to eliminate any biases.

FUNDING

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