**Effect of vaginal antiseptic prior to Caesarean section on the rate of post caesarean complications: A blinded Randomized Controlled Trial**

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**Background**

Caesarean section (CS) is one of the methods of operative delivery in childbirth and its rate has increased internationally over the last 3 decades for various reasons. According to Australian Institute of Health and Welfare ([1](#_ENREF_1)) the CS rate in Australia was 34% in 2016.

Like any other surgical procedure CS has morbidity in the form of infections, which include endometritis in addition to surgical site infection. This is a matter of concern as it has been reported that CS can have ten times higher risk of infections than that of vaginal delivery ([2](#_ENREF_2)). Such infections cause additional burden not only to the mother herself but also to the newborn and her family as a whole. It also increases the risk of hospital readmissions and cost to health care system across the world ([3](#_ENREF_3)). Olsen MA et al., (2010) demonstrated that wound infection and endometritis may incur an additional cost of US$ 4200 and US$4500 to the health systems respectively ([4](#_ENREF_4)). Evidence favours the use of prophylactic antibiotic for CS to reduce post-op infections ([5](#_ENREF_5)), although, there are debates in single vs multiple doses, routes and timing of antibiotic use, types of antibiotics and duration. To reduce the rate of post CS infections further, different antiseptics have been practised inconsistently for skin preparation and vaginal toileting. However, a Cochrane review suggests no clear evidence of favouring the use of chlorhexidine solution before surgery over the other washing products to prevent Surgical Site Infection (SSI) ([6](#_ENREF_6)). While another Cochrane review reported that use of either chlorhexidine or povidone iodine before CS did not make any or might make little difference to the SSI or endometritis ([2](#_ENREF_2)). On the other hand, World Health Organization (WHO) recommends the use of povidone iodine for vaginal cleansing immediately before CS to reduce maternal infection morbidities ([7](#_ENREF_7)). This recommendation is further emphasized in a recent systematic review and network meta-analysis by Roeckner JT, et al. ([8](#_ENREF_8)), and they have reported that the use of 1% povidone iodine for pre-surgical vaginal irrigation among women underwent CS has the most beneficial outcomes in reduction of fever, wound infections and endometritis. Despite the above measures, surgical site infection (SSI) incidence ranges from 3-15% ([9](#_ENREF_9)), perhaps due to variability of practices and individual preferences to one antiseptic agent over the other. Given the current limited data, it is imperative to identify the best evidence based practice for uniform use of antiseptic agents for vaginal toileting to reduce post CS infections or complication and to standardise their practice in a regional Australian hospital for Enhanced Recovery After Caesarean delivery (ERAs).

**Hypothesis**

**H1**: In a blinded randomised controlled clinical trial of using either chlorohexidine or povidone iodine for vaginal irrigation prior to any CS will reduce post-operative infection outcomes by 50% when compared to no vaginal irrigation.

**Methods:**

**General Objective**

To introduce uniform use of vaginal antiseptic wash immediately prior to Caesarean section and to determine the best antiseptic wash material in reducing post-operative infections or complications.

**Specific Aims**

1. To determine the number of post-CS infections among women that will undergo pre-operative vaginal cleansing with either 1% povidone iodine or chlorohexidine or no toileting (control) during elective CS
2. To determine the number of post-CS infections among women that will undergo pre-operative vaginal cleansing with 1% povidone iodine or chlorohexidine or no toileting (control) during emergency CS
3. To compare the rate of infections among the three groups that receiving either 1% povidone iodine or chlorohexidine or no toileting for vaginal irrigation prior to any kind of CS
4. To identify the best antiseptic wash and methods for vaginal irrigation prior to CS for developing a uniform guideline through locally generated evidence
5. To determine the factors that may influence the outcomes such as post-CS infections or related complications

**Outcomes**

*Primary outcome*

Endometritis: defined as core temperature measured >38ºc with uterine tenderness and/or foul smelling vaginal discharge within 28 days of post-CS

*Secondary outcomes*

* Post-operative fever: defined as core temperature >38 ºc at any point until 28 days of post Caesarean section
* Wound infection: defined as itch, redness, pain, swelling and collection of purulent discharge at the surgical incision site within 28 days of CS
* Readmission with infection: defined as representation of post CS patients to the hospital in 28 days of caesarean section with surgical site infection or related infective complications

**Assessment of infection:**

A third person with superior clinical acumen independent to the project will assess the post Caesarean infection to reduce any potential bias. For example, the Obstetrics and Gynaecology (O & G) Consultant on call and O & G Registrar.

**Sample size calculation**

We assume that the interventions will improve the rate of infection including post-operative infective complications (within 28 days of caesarean section from the hospital) by 50% compared to the control. Thus, for sample size estimation in this study we set P1 =8% (as per overall prevalence of post CS infection range 3-15%), P2 = 4%, significance level = 5% and the study power =80%.

Therefore, n ≥ Zα + Zβ 2

 ES

ES= P1-P2

 √P1(1-P1)

n ≥ 361

Here, Zα = 1.96, Zβ = 0.84, P1= 0.08, P2 =0.04, and P1-P2= 0.04.

Considering 5% drop out, the study will require recruiting approximately 375 participants for all the groups and 125 in each group over a period of sixteen (16) months to adequately test the assumption.

**Study design, Setting and timeline**

A blinded randomized controlled clinical trial will be carried out in the Obstetrics and Gynaecology Department of GV Health between May 2020 and August 2021. Considering 25% Caesarean Section of a total of approximately 1200 deliveries in GV Health, we may recruit the required number of participants in sixteen months period.

**Eligibility***Inclusion criteria*

Any patients undergoing for either emergency or elective CS that provided voluntary informed consent will be included in the study.

*Exclusion criteria*

* Patients having signs of chorio, intrapartum pyrexia and other signs of infection will be excluded from the study.
* Patients who develop intrapartum pyrexia as a result of syntocinon drip, prolonged labour or obstructed labour and provided voluntary informed consent will be included in the study initially. Their placental swabs will be taken for microscopic examination, culture and sensitivity (m/cs). They will be excluded from the study only if their swab results are positive for m/cs.
* Face presentation

**Follow-up plan**

All the patients included in the study will be followed up for a period of 28 days for the outcome signs and symptoms. We will follow up the patients over the phone fortnightly until 28 days of post caesarean and we will also follow up them during hospital presentations or admissions until 28 days post caesarean section.

**Intervention**

Patients that will be undergoing for elective or emergency CS are randomised either to 1% povidone iodine or chlorohexidine or no vaginal irrigation group.

**Co-intervention**

All the enrolled patients’ skin preparation will follow the same procedure and use of same material of similar quantity (chlorhexidine). Besides all the enrolled patients will receive same health education and wound care advice from the treating team.

**Blinding of intervention and their allocation**

After inclusion in the trial, each prospective CS patient will be assigned either into the intervention (1% povidone iodine or chlorohexidine) or control (no-irrigation) group by using a block randomization technique. A permuted block of six will be used to randomize the patients. A third party not related to the study will generate the permuted blocks and allocate the treatment in sealed opaque envelops.

**Recruitment, consenting and data collection**

Patients undergoing any type of Caesarean Section at GV Health Obstetrics and Gynaecology Department will be approached to participate in the study by the one of the Co-investigators or the Principal Investigator from the treating team. A participant information and consent form (PICF) will be supplied to the patient. After reading the PICF if the patient is agreed to participate, they will have to provide a voluntary signed informed consent to the investigators. Later the patients will pick-up one of the sealed envelopes at random with either an intervention or control. The patient will pass the envelope to the treating team. According to the envelope information the patient will be offered the type of intervention or control.

A predeveloped questionnaire will be completed with patients UR number, socio-demographic characteristics, required clinical and pregnancy related information. All the fever, infection and readmission related information such as duration of Artificial Rupture of Membrane /Spontaneous Rupture of Membrane, duration of labour, BMI, Gestational Diabetes Mellitus (GDM) with current – diet or insulin regime, duration of surgery, Estimated Blood Loss (EBL), Previous Caesarean Section (1/2/3) of elective/emergency nature & Vaginal Examination at Caesarean Section etc. will be completed from either the patient’s or their record or at follow-up visits on the 14th and 28th post-operative days. No identifying information but the aggregated data will be used for analysis and interpretation.

 **(This figure added as an appendix and as a separate document)****Data safety and monitoring**

Collected information will be remained anonymous. Except for the study investigators and the members of the relevant Human Research Ethics Committee (HREC), nobody will have access to the dataset unless there is an institutional or regulatory requirement arises. The principal investigator and the other investigators will maintain a routine and close monitoring of the study activities. Although the proposed interventions are safe, however, during study conduction if any study participant found sick, the investigators will provide adequate suggestions or support on care seeking from appropriate areas of healthcare as per routine standard protocol.

**Data analysis and statistical procedure**

Baseline characteristics of participants including demographic characteristics, morbidity information with severity, current medication/management and satisfaction towards the current management will be compared using the t-test or and χ2 tests for categorical variables to assess the success of the randomization. Summary statistics will be presented for all three groups’ infection information. BMI will be calculated using the weight and height of the participants. If required, analysis will be performed following ‘intention to treat’ analysis method. Primary and secondary outcomes will be compared using ANOVA. Where appropriate, logistic regression analyses will be used to compare the outcomes separately for interventions versus control group. All data will be entered in MS Excel and all statistical analyses will be performed using the STATA 11.0 statistical package.

**Ethical assurance for protection of human rights**

The study will be applied for ethical approval from the Human Research Ethics Committee (HREC), GV Health considering any potential conflict of interests. All participants will be protected after selection. In addition to provide detailed information statement, the research team will clearly explain that participation is totally voluntary. The study will involve vaginal irrigation followed by Caesarean sections using the sealed opaque envelope’s method picked-up by the patient. The surgical procedure will involve all the ethical/legal steps related to any other surgery in the hospital. There will be additional risks as in other surgeries. Also the research team will explain clearly that the study will collect some basic information, measure height and weight, follow up telephone calls/visits and collection of information during any sudden health facility visits for infection or post-operative complications. Additionally, the trial will be registered with the Australia New Zealand Clinical Trial Registry (ANZCTR).

**Dissemination**

Study findings will be presented internally in the Goulburn Valley Health hospital for service improvement, externally in national or international conferences. A full scientific article will be developed and published in peer reviewed journal/s.

**References:**

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