

## Surgical Site Infection in Cesarean Section Operation: Risk and Management

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### Abstract

Cesarean sections (CS) are one of the most commonly performed surgical procedures worldwide. There is great variability in the percentage of cesarean sections between countries, varying from 3% to 42.9%<sup>5</sup>. In the US, approximately 32% of deliveries occur through a cesarean section. Overall, a drastic increase in cesarean section rate has been reported reaching its highest level at the present time.

In Brazil, considering the types of births by live births from 2006 to 2016, the national percentage of cesarean section was 52.37%. The variability in this percentage can still be perceived within Brazilian territory. The highest cesarean rate occurred in the Southern region, representing 58.33% of births, while the lowest rate occurred in the Northern region, with 41.79%. It is possible to see the steady increase in the percentage of CS over time, from 45.01% in 2006 to 55.39% in 2016.

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## Introduction

Cesarean sections (CS) are one of the most commonly performed surgical procedures worldwide<sup>1,2,3,4</sup>. There is great variability in the percentage of cesarean sections between countries, varying from 3% to 42.9%<sup>5</sup>. In the US, approximately 32% of deliveries occur through a cesarean section<sup>2,5,6</sup>. Overall, a drastic increase in cesarean section rate has been reported<sup>3,5,7,8</sup>, reaching its highest level at the present time<sup>8</sup>.

In Brazil, considering the types of births by live births from 2006 to 2016, the national percentage of cesarean section was 52.37%. The variability in this percentage can still be perceived within Brazilian territory. The highest cesarean rate occurred in the Southern region, representing 58.33% of births, while the lowest rate occurred in the Northern region, with 41.79%. It is possible to see the steady increase in the percentage of CS over time, from 45.01% in 2006 to 55.39% in 2016<sup>9</sup>.

Surgical site infection (SSI) is reported to be the most common hospital-associated infection in community hospital settings<sup>10</sup>. Moreover, in a recent well-designed multicentre study in England, SSI was estimated to be just under 10% and the readmission rate due to SSI following CS was 0.6%<sup>11</sup>.

Like other surgical procedures, there are risks factors of complications associated with cesarean section<sup>1</sup>. Independent risk factors are not well documented in the literature. In a systematic review of the maternal intrinsic risk factors associated with SSI following CS, obesity and chorioamnionitis were identified as the most significant risk factors for overall SSI (incisional and organ/space)<sup>11</sup>, along with the following factors: lack or improper use of pre-operative prophylaxis antibiotics, duration of rupture of membranes, emergency CS, and CS accompanied by fetal distress<sup>12</sup>.

The present study reviews the current literature related to SSI in CS, risk factors, and potential preventive measure to decrease incidence and severity of that complication.

## Methods

References for this review were identified through searches of PubMed, EMBASE (Ovid), the

Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, and World Health Organization for articles in English published from January 2006 to December 2018 by use of the terms "cesarean infection", "cesarean surgical site infection" and "surgical site infection". We included randomized controlled trials, meta-analysis registries, relevant systematic reviews, cross-sectional, case-control or cohort studies reporting the incidence of SSI following CS, or studies with enough data to allow the estimated information. All studies where the case definition for SSI-incisional and organ/space, met the CDC/National Healthcare Safety Network (NHSN) criteria. Studies which were not published in English, case reports, case-series, editorials, letters and commentaries, were excluded from this review.

## Results

A population-based study between 1988 and 2013 showed 41.375 CS performed during the study period, 1.521 (3.7%) were complicated with SSI<sup>21</sup>. SSI rates significantly decreased over the years, from 7.4% in 1988 to 1.5% in 2012. Using a multivariable regression model, the following independent risk factors for SSI were identified: obesity (OR 2.0; 95% CI, 1.6–2.5); previous cesarean delivery (OR 1.8; 95% CI, 1.6–2.0); hypertensive disorders (OR 1.4; 95% CI, 1.2–1.6); premature rupture of membranes (OR 1.3; 95% CI, 1.1–1.6); gestational diabetes mellitus (GDM, OR 1.2; 95% CI, 1.1–1.4); and recurrent pregnancy losses (OR 1.2; 95% CI, 1.1–1.5)<sup>21</sup>.

The skin preparation with antiseptic agents has the potential to reduce the SSI risk and is part of a standard operative protocol<sup>2,6,7,13</sup>. Although skin preparation is a well-established recommendation, there is no consensus of the ideal solution<sup>7,14</sup>. Chlorhexidine and povidine-iodine are the antiseptic agents most commonly used in abdominal surgeries<sup>13,14</sup>. Regarding the results of current studies, in order to evaluate the superiority of certain antiseptics to reduce the rate of SSI in CS, they are divergences. The more recently published clinical trials compared the more widely used and effective antiseptics for skin preparation (chlorhexidine in alcoholic solution x iodopovidone, chlorhexidine in alcoholic solution x iodinated alcohol, chlorhexidine in aqueous solution x iodopovidone)<sup>2,6,15,16</sup>. Only one demonstrated the

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reduction of the SSI rate when using alcoholic chlorhexidine compared to iodinated alcohol<sup>2</sup>. Of the three observational studies analyzed, the results also differed, while one showed a superiority of alcoholic chlorhexidine in decreasing the SSI rate, further to reduce the rate of long stay and readmissions to emergency services after cesarean section<sup>17</sup>, the other two showed no difference between the types of antiseptics compared<sup>18,19</sup>. Table 1 summarizes the comparative analysis of these studies.

As main studies carried out on the issue have compared alcoholic chlorhexidine with other products, it is uncertain if the good results are solely due to chlorhexidine, alcohol, or to both. Current guidelines tend to recommend alcohol-soluble antiseptics<sup>2,20</sup>.

As previously reported, in relation to cesarean sections, studies do not show an advantage of alcoholic chlorhexidine in the surgical preparation of the skin, despite several randomized clinical trials in general surgery does. It is believed that this result should not be directly extrapolated to obstetric surgery due to the polymicrobial type of the infection and the physiological immune modulation associated with pregnancy, which may alter the response against infection<sup>2,7</sup>.

In the most recent controlled trial published comparing antiseptic solutions in the preparation of skin on cesarean sections - CAPICA trial, the rate of 7% of SSI was observed when povidine-iodine was used versus 6.3% when using chlorhexidine, showing no statistically significant difference between the infection rate and the level of the infection between the two solutions (RR = 0.90, 95% CI 0.00-1.35, p = 0.38).

## Discussion

SSI is the infection that occurs in the skin and subcutaneous tissue at the incision site and can occur within 30 days after the procedure<sup>13</sup>. The rate of infection varies according to the patient's risk factors, team ability and hospital infrastructure<sup>5</sup>. SSI affects approximately 5-12% of cesareans<sup>2,3,6,7,22</sup>. In limited resource areas, the prevalence of SSI can range from 4-70%<sup>5</sup>. These epidemiological estimates are probably underestimated because infections outside the hospital environment are not considered, even though they are included in the definition<sup>23</sup>. SSI is related to the contamination index of surgeries. (Table 2).

SSI, as well as others operative wound complications, generate problems for the patient, family, and healthcare services<sup>8,22,24</sup>. This condition results in increased physical and emotional burden, as well as maternal postpartum morbidity and mortality<sup>4,7,24</sup>. Due to other factors as physical pain, psychological stress, interference in the mother-baby relationship, impact on the onset and continuation of breastfeeding, delayed return to routine activities, chronic pelvic pain, depression and extra costs, CS represent a concern in public health. For the health system, the financial burden stands out for prolonging maternal hospitalization, care costs and need for readmission<sup>1,4,7,25</sup>. An American study has shown that this financial burden has an average of an additional USD 3,529 per patient with SSI, attributed to readmission and treatment, extra expenses with medical staff, use of pharmaceutical supplies, and an increase in hospitalization time<sup>6,13,22</sup>.

The surgical site is at contamination risk by skin pathogens, which are the main source<sup>2,7,14</sup>. *Staphylococcus aureus* is the most commonly isolated microorganism in SSI, accounting for 15-20% of cases<sup>7</sup>.

Wound infection, which presents with erythema, discharge, and induration of the incision, complicates 2-7% of patients and generally develops 4 to 7 days after CS<sup>26,27,28</sup>. When wound infection develops within 48h of the CS, the offending organisms usually are groups A or B-hemolytic *Streptococcus*. Other common pathogens involved in wound infections are *Ureaplasma urealyticum*, *Staphylococcus epidermidis*, *Enterococcus faecialis*, *Staphylococcus aureus*, *Escherichia coli*, and *Proteus mirabilis*<sup>29,30</sup>.

Some maternal risk factors for SSI were identified in studies such as high BMI, diabetes mellitus, pre-existing infection (eg.: chorioamnionitis), ASA score > 3, nulliparity, high intraoperative blood loss, tobacco use in pregnancy, incision size > 16.6 cm, limited pre-natal care, corticosteroids use, subcutaneous tissue thickness > 3 cm, prolonged second stage of the delivery, hypertensive disease/preeclampsia, premature rupture of membranes and emergency surgery<sup>3,13,31</sup>. A possible explanation for higher SSI rates in the emergency CS is the possible shorter contact duration between the skin and the surgical preparation<sup>3</sup>. Several preventive methods are investigated in an attempt to

Table 1. Comparative analysis of the result of the last studies analyzing skin preparing and surgical site infection in cesarean deliveries

Year	Title	Authors	Type of Study	SSI Rates	
				Control Group	Intervention Group
2012	Chlorhexidine-alcohol compared with povidone-iodine for surgical-site anti-sepsis in cesarean deliveries.	Menderes et al <sup>18</sup>	Retrospective Cohort Review (n=1000)	Povidone-Iodine = 5.8%	Chlorhexidine-Alcohol = 5%
				P = 0.58	
2013	Can we reduce the surgical site infection rate in cesarean sections using a chlorhexidine-based anti-sepsis protocol?	Amer-Alshiek et al <sup>17</sup>	Retrospective Study (n=362)	Povidone-iodine + Povidone-iodine in alcoholic solution = 10.4%	Chlorhexidine + Alcohol = 3.07%
				P = 0.008	
2014	Chlorhexidine gluconate versus povidone iodine at cesarean delivery: a randomized controlled trial	Kunkle et al. <sup>15</sup>	Single-center. Randomized Controlled Trial (n=60)	Povidone-iodine = 4.5%	Chlorhexidine Gluconate = 9.5%
				P = 0.60	
2015	Skin Preparation for Prevention of Surgical Site Infection After Cesarean Delivery: A Randomized Controlled Trial.	Ngai et al <sup>16</sup>	Prospective. Randomized Clinical Trial (N=1404)	Povidone-iodine with alcohol = 4.6%	Povidone-iodine with alcohol + Chlorhexidine with alcohol = 3.9%
				P = 0.85	
2016	A Randomized Trial Comparing Skin Antiseptic Agents at Cesarean Delivery	Tuuli et al <sup>2</sup>	Single-center. Randomized Controlled Trial (n=1147)	Iodine-Alcohol = 7.7%	Chlorhexidine Alcohol = 4.3%
				P = 0.02	
2017	A Randomized Open-Label Controlled Trial of Chlorhexidine-Alcohol versus Povidone-Iodine for Cesarean Antisepsis: The CAPICA Trial.	Springel et al. <sup>6</sup>	Randomized Open-Label Controlled Trial (n=932)	Povidone-iodine = 7%	Chlorhexidine-alcohol = 6.3%
				P = 0.38	
2018	Chlorhexidine-alcohol versus povidone-iodine for skin preparation before elective cesarean section: a prospective observational study	Elshamy et al. <sup>19</sup>	Prospective Observational Study (n=1424)	Povidone-iodine = 4.6%	Chlorhexidine-alcohol = 3.7%
				P = 0.35	

Table 2. Infection according to wound classification

Clean	Non-traumatic, elective surgery, GI, respiratory and GU tract not entered	Mastectomy, vascular, hernias	2%
Clean-contaminated	Respiratory, GI, GU tract entered with minimal contamination	Gastrectomy, hysterectomy	< 10%
Contaminated	Open, fresh, traumatic wounds, uncontrolled spillage, minor break in sterile Technique	Rupture app, emergent bowel resect	20%
Dirty	Open, traumatic, dirty wounds; traumatic perforation of hollow viscus, frank pus in the field	Intestinal fistula resection	28-70%

reduce the infection rate of surgical site, with the proper preparation of the skin playing an important role <sup>1,3,13</sup>.

SSI rates are high not only in CS, but also in surgical procedures in general. Currently, researches focus on use of different resources and at various operative moments, to supplement already established and scientifically proven measures for the prevention of infection. One conception that has been explored in recent years is the irrigation of the operative site with numerous solutions to prevent contamination and SSI.

Prophylactic intra-operative wound irrigation (PIOWI) is defined as promoting the flow of a solution across the wound surface to achieve tissue hydration, removing and diluting body fluids, metabolic wastes, bacteria, blood clots, and necrotic cell debris from the surgical field prior to closure <sup>1,32,33</sup>. This would be a good measure to reduce local bacterial contamination <sup>34</sup>, concomitant with the facilitation of the healing process, as well as to promote a better visualization and evaluation by the surgeon of the affected area, immediately before the end of the surgery<sup>35</sup>.

The healing stages of the wound include hemostasis, inflammation, epithelization, fibroplasia and maturation. Failure or modification of some point in this sequential process can lead to noninfectious complications such as hematoma, bruise and dehiscence, in addition to SSI <sup>1</sup>. Whether bacteria and residual debris remain in the surgical site, healing will be affected with prolonged and excessive inflammatory phase, with late or inappropriate angiogenesis and

excess granulation of the tissue, which increases SSI risk and possible complications such as sepsis <sup>35</sup>.

Contamination can also alter collagen synthesis, cause tissue anoxia, and decrease phagocytic cell function<sup>35</sup>. PIOWI would be a method easily performed by professionals, as well as being an economically accessible option to reduce the risks of SSI <sup>1,33,34</sup>. This approach have already being used in clinical practice by some surgeons according to individual preference or hospital protocols <sup>34</sup>, although, there is no standardization regarding patient population, application surface, technique and solutions applied <sup>32,35</sup>. Studies with PIOWI show mixed, and often, divergent results due to different methodologies applied, so no convincing evidence of irrigation effectiveness exist, becoming, therefore, a practice not widely accepted<sup>35</sup>.

International guidelines such as the NICE (National Institute for Health and Care Excellence - UK) do not recommend irrigation of operative wound (OW) with saline solutions containing antibiotics or antiseptics due to potential adverse effects such as tissue toxicity and systemic side effects, without proven efficacy with any irrigated solution<sup>36</sup>. The WHO <sup>37</sup> and CDC <sup>20</sup> guidelines concluded that PIOWI with saline solution isolated is not efficient and that solutions containing antiseptics such as povidone-iodine may have potential benefit in preventing SSI.

About the solution used to perform PIOWI in cesarean sections, saline solution (sodium chloride 0.9%) is the most commonly used because of its safety, but there are limited data on its effect<sup>1</sup>. Three clinical

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trials have been conducted in recent years to evaluate OW irrigation in cesarean sections. Güngördük et al. compared the incidence of wound infection between irrigation with saline versus non-irrigation and did not obtain a significant difference<sup>38</sup>. Aslan et al. recently also made the same comparison between saline irrigation vs. no irrigation and reached the same result<sup>1</sup>.

Corroborating with the previous results, Al-Ramahi et al. conducted a study evaluating the efficacy of saline irrigation in the incidence of OW infection after gynecological surgeries, showing no difference in infection rate, stating that saline solution lavage did not reduce OW contamination<sup>39</sup>.

Using a distinct solution, Mahomed, Ibiebele and Buchanan (2016) compared a group irrigated with aqueous solution of povidine-iodine (PI) versus a group receiving no irrigation prior to wound closure, desiring to assess the incidence of SSI in both groups. The result was similarity between the incidence, making it clear that PI did not prevent or decrease SSI<sup>40</sup>.

Since cesareans are considered clean-contaminated surgeries, OW irrigation can hydrate the bed, allow better visualization, remove clots, tissue remains, and organic fluids, but it does not affect the bacteria, thus not influencing the rate of infections<sup>38</sup>. To further support this hypothesis, a systematic review and meta-analysis by Mueller et al. with the objective of determining the current knowledge regarding PIOWI, showed that non-colorectal surgeries, ie clean or contaminated clean, did not have a beneficial effect on SSI with any solution used in irrigation, regardless whether it was performed with saline, antiseptics or antibiotics<sup>34</sup>.

Another resource that has been explored as a measure to prevent SSI is the intra-abdominal irrigation. Two studies have not demonstrated a reduction of SSIs with intra-abdominal irrigation of normal saline<sup>41,42</sup>. In a randomized controlled trial of 236 women undergoing CS, intra-abdominal irrigation did not demonstrate decreased OW infection risks and endometritis, but was associated with intra-operative nausea (RR 1.62; 95% CI 1.15, 2.28)<sup>41</sup>. Similarly in a randomized controlled trial of 196 women undergoing CS, intra-abdominal irrigation by normal saline did not reduce intrapartum or postpartum maternal morbidity<sup>42</sup>. Evidence does not support use of routine intra-abdominal irrigation.

One study compared irrigation of the abdominal cavity prior to closure with saline solution versus low molecular weight povidone-iodine solution diluted with normal saline ("Betadine group"). Postoperative infections were statistically significantly lower in "Betadine group" - endometritis were 3.7% in "Betadine group" versus 5.9% in "No Betadine group" and wound infections 2.3% in "Betadine group" versus 6.3% in "No Betadine group", both with p value <0.05. As the only study comparing these groups, the authors concluded that the results are promising, but they should be considered preliminary<sup>43</sup>.

As mentioned above, cesareans present an SSI rate of approximately 5-12%, and extensive efforts have been made to reduce these rates, including the following methods: use of preoperative prophylactic drugs such as intravenous antibiotics, use of antiseptic solutions in preparation of the skin, pre and postoperative vaginal cleaning with antiseptics, skin incision techniques, different forms of placental removal, closure with layer sutures, subcutaneous drainage and use of pressure dressings<sup>1,38,40</sup>.

Hauk et al.<sup>44</sup> conducted a prospective randomized study on 1,504 patients, and their demographic information, risk factors and surgical indications were recorded. Postoperatively, patients were monitored for signs of SSI. Out of 1,504 patients, 13% developed SSI, - prolonged hospital stay, wound class, ASA class, antibiotic prophylaxis and type of caesarean showed significant association with SSI. They concluded that the reasons for SSI were higher than developed countries were tertiary care hospital dealing with high risk pregnancies, late referrals from peripheries, prolonged hospital stay, heavy rush of attendants, faulty supervision where dose of antibiotics is actually missed, and no proper segregation of cases.

## Conclusions

SSI following CS represent complex clinical situations and are caused by many factors such as patient characteristics and peri-operative management. In addition, SSI represents significant financial burden to health care systems. Creating bundles of evidence-based elements may decrease the rates of post-CS SSI, as has been demonstrated in non-obstetric patients.

Literature strongly recommend each hospital to consider the evidence-based information presented in

creating its own surgical bundle to decrease the rates of SSI after CS. Independent risk factors for post-cesarean SSI include obesity, gestational diabetes mellitus, hypertensive disorders of pregnancy, premature rupture of membranes, and recurrent pregnancy losses. Information regarding higher rates of SSI and preventative measures should be provided to these high-risk women prior to surgery.

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