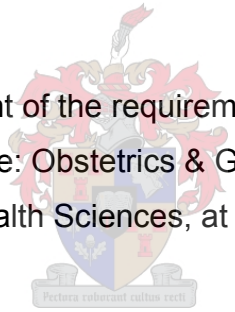
A Retrospective Audit of
Post-Caesarean Sepsis at Tygerberg Hospital

By Dr Marsel Coetzer



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DECLARATION

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ABSTRACT

INTRODUCTION:

Caesarean section (CS) is one of the most common surgical procedures performed worldwide and remains the most important individual risk factor for developing pregnancy related sepsis.

Pregnancy related sepsis leads to an estimated 75 000 maternal deaths worldwide each year, with most of these deaths occurring in low and middle-income countries. According to the 2015 Saving Mothers Annual Report, pregnancy related sepsis remained the 3rd leading cause of direct maternal deaths in South Africa.

In the USA, the attributable costs (per case) of post CS surgical site infection and post CS endometritis were estimated around $3500 and $3900 respectively in 2010.

AIM & METHOD:

To audit post-CS sepsis at Tygerberg Hospital in order to determine the incidence, as well as to describe the risk-factor profile and determine the outcome of women who develop post-CS sepsis. A retrospective audit of patient records of all women who delivered by CS in a three-month period between 1 February 2014 and 30 April 2014 was undertaken. All records were followed up for thirty days after delivery, in order to identify cases with post-CS sepsis. The CDC diagnostic criteria for surgical site infection (both superficial and deep) and endometritis were used.

RESULTS:

During the 3-month study period a total of 1 834 deliveries were managed at Tygerberg Hospital. Eight hundred and forty eight CS were performed, with a hospital-based CS rate of 46.24%. A total of 811 patient records were audited and 38 women with post-CS sepsis were identified. The cumulative incidence for post-CS sepsis was therefore 4.69%.

Patient characteristics illustrated the high-risk nature of the patient population served by Tygerberg Hospital, with a high incidence of known risk factors for post-CS sepsis such as obesity, hypertension and HIV. Risk factors associated with post CS sepsis included: HIV infection without antiretroviral therapy (Risk Ratio 5.83, 95%

Confidence Interval 1.72 – 19.77, p=0.005) and prolonged surgical duration (Risk Ratio 3.01, 95% Confidence Interval 1.10 – 8.19, p=0.03).
Thirty-three women had severe post-CS sepsis and were treated as inpatients. Of these women, 12 required repeat surgery or admission to a high care or intensive care unit.

CONCLUSION:
Despite a post-CS sepsis incidence that compares well with high-income countries (4.69% vs. 3.5 – 8.11%) post-CS sepsis remains a significant contributor to maternal morbidity in the South African setting. Risk factors for post-CS sepsis remain multifactorial and in the setting of a referral hospital, all women should be treated as potentially at risk. Optimization of chronic medical conditions, vigilant intra-partum care, meticulous surgical technique and recognition of early signs of post-CS sepsis are essential in order to prevent maternal morbidity.

OPSOMMING

INLEIDING

Die keisersnit is een van die mees algemene chirurgiese prosedures wêreldwyd en is steeds die belangrikste risiko faktor vir swangerskaps-verwante sepsis. Swangerskapsverwante sepsis is jaarliks verantwoordelik vir ongeveer 75 000 moederlike sterftes wêreldwyd, met die meerderheid van sterftes in lae- en middelinkomste lande. Volgens die 2015 “Saving Mothers Annual Report”, is swangerskapsverwante sepsis steeds die derde belangrikste direkte oorsaak van moederlike sterfte in Suid-Afrika. Die beraamde koste vir die behandeling van wond infeksie of endometritis, na ‘n keisersnit, beloop $3500 en $3900, per geval, in die VSA.

DOEL & METODE:

‘n Retrospektiewe oudit van keisersnitte by Tygerberg Hospitaal vir die tydperk 1 Februarie 2014 tot 30 April 2014 is onderneem. Pasiëntrekords is nagegaan met die doel om die insidensie van sepsis na keisersnit te bepaal, die risikoprofiel van vroue te ondersoek, asook om die uitkoms van vroue met sepsis te evalueer. Pasiëntnotas is opgevolg vir ‘n totaal van dertig dae na keisersnit, met die doel om ook vroue wat na ontslag presenteer, te identifiseer. Die CDC se diagnostiese kriteria vir wond infeksie en endometritis is gebruik.

RESULTATE:

‘n Totaal van 1 834 verlossings is tydens die 3 maande studie periode by Tygerberg Hospitaal hanteer. Agt honderd, agt en veertig vroue (46.24%) is verlos deur middel van keisersnitte. Agt honderd en elf vroue is by die oudit ingesluit en 38 vroue met sepsis na keisersnit is geïdentifiseer. Die kumulatiewe insidensie van sepsis na keisersnit is dus 4.69%. ‘n Hoë insidensie van bekende risiko faktore vir sepsis, onder andere obesiteit, hipertensie en MIV-infeksie is gevind, wat die hoë-risiko profiel van die populasie bevestig. Beide MIV infeksie sonder antiretrovirale behandeling (p=0.005), asook verlengde duur van chirugie (p=0.03) is geidentifiseer as risiko faktore vir sepsis na keisersnitte. Drie en dertig vroue is gediagnoseer met erge sepsis en het binne-pasiënt behandeling ontvang. Van die bogenoemde vroue

het 12 vroue verdere chirurgie, of opname in ‘n hoësorg of intensiewe sorg eenheid benodig.

GEVOLGTREKKING

Selfs al is die insidensie van sepsis vergelykbaar met hoë-inkomste areas (4.69% vs. 3.5 – 8.11%), is sepsis na keisersnitte steeds ‘n noemenswaardige oorsaak van moederlike morbiditeit in Suid-Afrika. Die oorsprong van sepsis na keisersnitte is multifaktorieël en dus moet alle vroue in Tygerberg Hospitaal as hoë-risiko behandel word. Stappe on risiko te verlaag, insluitende optimalisering van mediese siektes, waaksame kraamsorg, noukeurige chirurgiese tegniek en vroeë herkenning van tekens van sepsis, is noodsaaklik om verdere moederlike morbiditeit te vermy. Verdere, prospektiewe studies word benodig.

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LIST OF ABBREVIATIONS

95% CI	95% Confidence Interval
ASA	American Society of Anaesthesiologists
BMI	Body Mass Index (kg/m^2)
CD4	Cluster of Differentiation 4
CDC	Centre of Disease Control
CPD	Cephalopelvic disproportion
CS	Caesarean Section
d	Days
dl	decilitre
ECM	Electronic Content Management
g	grams
HAART	Highly Active Anti-Retroviral Therapy
HELLP	HELLP-syndrome related to pre-eclampsia – Haemolysis, Elevated Liver enzymes, Low Platelets
HIV	Human Immunodeficiency Virus
ICU	Intensive Care Unit
iMMR	Institutional Maternal Mortality Ratio
kg	kilogram
LMIC	Low- and middle-income countries
NICE	National Institute for Health and Care Excellence
NNIS	National Nosocomial Infection Surveillance System (USA)
NS	Not significant
OCCU	Obstetric Critical Care Unit
PE	Pre-eclampsia
RCOG	Royal College of Obstetricians & Gynaecologists
ROM	Rupture of membranes
RR	Risk Ratio
TBH	Tygerberg Hospital
USA	United States of America
UN	United Nations
WHO	World Health Organization

1 INTRODUCTION

Puerperal sepsis leads to an estimated 75 000 maternal deaths worldwide each year and is still the third leading direct cause of maternal mortality in South Africa (1–3). The most important individual risk factor for developing puerperal sepsis is delivery by caesarean section (CS), with some sources quoting up to a 20 fold increased risk compared to vaginal delivery (4). According to the South African Saving Mothers Report for the 2011-2013 triennium, the case fatality rate for pregnancy related sepsis was 1.5 / 10 000 for patients delivered by CS, compared to 0.5 / 10 000 for vaginal delivery (5). Therefore, sepsis is not only more common after CS, but is more likely to be severe and life threatening.

To be able to reach the goal of reducing the global maternal mortality ratio by two thirds, as proposed by the United Nations (UN) Sustainable Development Goal 3.1, post CS sepsis needs to be reduced to a minimum. The UN and World Health Organisation (WHO) have set these goals to build on the initial Millennium Development Goals and the target is set for 2030. The current global maternal mortality ratio is 210 / 100 000 live births and the South African Institutional Maternal Mortality Ratio (iMMR) for the 2011-2013 triennium is 154 / 100 000 (6–8).

Caesarean section is one of the most common surgical procedures performed worldwide, with 1.3 million procedures performed annually in the USA alone (9). The current incidence of post CS sepsis in South Africa, and at Tygerberg Hospital specifically, is unknown and further research is urgently needed. Up to 90% of post CS surgical site infections are diagnosed after hospital discharge and prevalence is often under estimated (9–14). This emphasizes the need for post-discharge surveillance to be able to accurately quantify the incidence of post CS sepsis.

2 LITERATURE REVIEW

Post CS sepsis is a major cause of morbidity in South Africa. By definition it includes both endometritis and surgical site infection (15). Post CS endometritis and surgical site infection are defined as meeting clinical criteria for either endometritis or surgical site infection, occurring within 30 days after CS delivery (15).

According to the Saving Mothers Report, the public sector CS rate in South Africa during the 2011 - 2013 triennium was 23.1%. The CS rate in the Western Cape for 2012 was 29% (5). The global incidence of post CS sepsis range widely from 3.7% to up to 24.2% of caesarean sections (2,10,12,13,16–21), with endometritis and surgical site infection being the first and second most common causes respectively (10,19,21). According to the Royal College of Obstetricians and Gynaecologists (RCOG) and National Institute for Health and Care Excellence (NICE) guidelines, the current average post CS sepsis rate in high income countries is estimated at 8% (22). The occurrence of post CS sepsis significantly contributes to maternal morbidity, influences the quality of life of a large number of women and adds strain to already limited resources. Women undergoing CS are 2.3 times more likely to require readmission to hospital for infectious complications, than after vaginal delivery (23). In the United States of America (USA), the attributable costs (per case) to post CS surgical site infection and post CS endometritis were estimated around $3500 and $3900 respectively in 2010 (24). In an attempt to minimize post CS sepsis, common risk factors have been identified globally. This allows the identification of high-risk women antenatally. Despite risk factors being known however, post CS endometritis and surgical site infections are still common.

2.1 DEFINITION

The detailed definitions of both post CS endometritis and surgical site infection differ widely. Different sources quote different time frames of occurrence, ranging from directly post-operative or 24 hours post-surgery (25) to 14 days

(2,3,14) or up to 30 days post-surgery (11,19,25,15), while others include / exclude organism identification as an essential criteria.

Puerperal sepsis is defined in the International Classification of Disease (ICD) 10 coding system as any temperature > 38°C from more than 24 hours from the day of delivery, up to 10 days thereafter.

The WHO defines puerperal sepsis as an infection of the genital tract, occurring any time between rupture of membranes or labour and forty-two days post-delivery. Clinical criteria that have to be present include: pyrexia and one or more of the following: pelvic pain, abnormal vaginal discharge, offensive discharge and delay in reduction of uterine size (1).

The American Centre for Disease Control (CDC) defines post CS endometritis as:

- Temperature > 38°C

AND

- A tender, sub-involuted uterus, or
- Purulent / offensive lochia, or
- Abdominal pain with no other recognized cause, or
- Diagnosis of endometritis made by attending physician (11,15).

It defines post CS surgical site infection as:

- Temperature >38°C

AND

- Symptoms of redness, pain, tenderness and swelling around surgical site and / or
- Purulent discharge from surgical site and / or
- Spontaneous dehiscence of surgical wound and / or
- Surgical wound deliberately opened by attending physician and / or
- Abscess formation in subcutaneous tissue directly surrounding surgical wound and / or
- Diagnosis of surgical site infection made by attending physician (11,15)

The above-mentioned CDC definitions are most commonly used, as they include all generally accepted symptoms and signs, and also make easy diagnosis possible for attending physicians. More detailed definitions used by the CDC differentiate between superficial and deep surgical site infection.

2.2 CURRENT GLOBAL PREVALENCE

Post CS sepsis occurs in 3.7 to 24.2% of women globally (2,10,12,13,16–20). Unfortunately, very little data on post CS sepsis is available for the South African population. One small study conducted over 6 weeks at Chris Hani Baragwanath Academic Hospital in Soweto, Gauteng, found an incidence of 12.5% when women were followed up for 14 days post CS (2). In this study, all women delivered by CS in a set 6-week period were counselled on the signs and symptoms of surgical site infection and were contacted telephonically on day 14 after surgery. Of the 12.5% of women who reported symptoms of post CS sepsis, only 1.5% had severe enough infection to warrant re-admission. This study was however limited by a short follow-up period, as well as loss of follow-up and was not powered to show the correlation of specific risk factors (2).

According to the Saving Mothers Report of 2011-2013, pregnancy related infection accounted for 9.5% of maternal deaths in South Africa (8). This amounts to a total number of 226 women, including miscarriages and termination of pregnancies. Of those women with pregnancy related infection that reached viability, 100 women delivered by CS and 112 by vaginal delivery. Although these numbers appear fairly equal, when taking into consideration that only 23.1% of women nationally delivered by CS, it becomes clear that pregnancy related infection is more common in the CS group. The Saving Mothers Report expressed these differences by calculating the Case Fatality Rates (CFR) related to the mode of delivery and found that the CFR for vaginal delivery and CS were 0.5 per 10 000 deliveries and 1.5 per 10 000 deliveries respectively. Women delivered by CS therefore have an almost 3 times increased risk of mortality due to pregnancy related sepsis than women delivered by vaginal route (Relative Risk

2.96). Of concern is that 78% of deaths due to pregnancy related sepsis were deemed to be avoidable (8).

Studies done in other LMIC, such as India and Brazil, have reported post CS sepsis incidence rates of 24.2% and 11 - 23.5% respectively (14,19,20). These studies included a follow-up period of 30 days. The post CS infection rate appears to be much lower in high-income countries. The National Nosocomial Infection Surveillance (NNIS) System in the USA classifies the risk of post CS sepsis into 3 risk index categories, ranging from category 1 (no risk factors) to category 3 (multiple risk factors) (17). The NNIS reports an incidence of 3.5% in low risk women after CS delivery and 8.11% in high-risk women (category 2 and 3). It is evident that there is a need for accurate data in the South African population, in order to aid health care workers in identifying high risk women timeously and treating them actively, in order to decrease the number of avoidable maternal deaths.

2.3 ESTABLISHED RISK FACTORS

Known risk factors for post CS sepsis can be categorized into 4 categories:

Demographic / General Risk Factors
Medical Risk Factors
Obstetric Risk Factors and
Surgical Risk Factors.

2.3.1 DEMOGRAPHIC / GENERAL RISK FACTORS

2.3.1.1 BODY MASS INDEX

Women with a raised body mass index (BMI) have been found to be at increased risk of post CS sepsis, especially surgical site infection. A multicentre cohort study by Wloch et al. in England in 2009 reported a BMI > 35 as a significant independent risk factor for post CS surgical site infection (OR 3.7, 95% CI 2.6 – 5.2, when compared with BMI 18.5–25 kg/m^2) (12). Obesity, and especially increased subcutaneous tissue thickness of more than two centimetres, lead to a

larger skin incision and more intra-operative traction, which leads to local tissue damage (9,26). These factors, as well as poor blood supply to adipose tissue, could potentially lead to an increased risk of post CS surgical site infection (19). This risk has been found to be 2 - 3 times higher when compared to women with a normal BMI (21). In a retrospective review study of super obese women (BMI ≥ 50 kg/m^2), done by Alanis et al., the incidence of surgical site complications was 30% (27). This study, done in South Carolina, USA, looked at the incidence of wound complications in super obese women during a 5-year period, from 2005 - 2009. The study also highlighted specific perioperative factors that were associated with surgical site complications in these women. Both smoking and the presence of diabetes increased the risk of surgical site complications with a further 2.7% and 2.1% respectively (27).

Unfortunately, very little data is available on obese women in South Africa, despite obesity being a prevalent risk factor. One study, done at Charlotte Maxeke Hospital in Johannesburg, found that 44% of women who delivered in the 2-month study period were obese (28). A prospective cohort study done at Tygerberg Hospital, Cape Town in 2013 by Nieuwoudt et al. reported an increased risk of pre-eclampsia and gestational diabetes in morbidly obese (BMI 40 - 50 kg/m^2) and super obese women (BMI > 50 kg/m^2). The study also found higher CS rates (41% in morbidly obese women and 54% in super obese women) than in the general population. In women with super obesity, CS procedures had a longer duration (median 50 minutes) and more intra-operative complications when compared to morbidly obese women (29). These factors all potentially contribute to an increased risk of post CS sepsis.

One small study done by Pevzner et al. found reduced tissue concentrations of cefazolin, when given as pre-incisional prophylaxis, in the adipose tissue of obese women (30). Women with a BMI > 40 kg/m^2 had the lowest tissue concentrations when compared with BMI < 30 kg/m^2 and BMI 30 - 40 kg/m^2. These lowered concentrations at the time of incision raises the question of inadequate antimicrobial effect, especially in organisms that are eliminated only by higher concentrations of antibiotics (30). This highlights the possible need for

more rigorous antibiotic cover in obese women, in order to prevent surgical site infection.

On the other end of the spectrum, attention must also be given to underweight and malnourished women. Unfortunately, an electronic search of Google Scholar, PubMed and the Cochrane Database yielded very little data on the outcomes of underweight women, as research worldwide is focussed on obese women. Due to the socio-economic status of many patients in the South African public health care setting, a significant number of women are malnourished and underweight. A study done by Malone et al. in Maryland, USA in 2002, demonstrated malnourishment as a significant risk factor for surgical site infection in the general population (31). Although this study focussed on a large sample group over 5 years, it included 95% males, and no clear evidence that any obstetric or gynaecological procedures were included. Malnourishment was also defined as weight loss in the months before surgery, which is very difficult to define in pregnant women, as the degree of weight gain during pregnancy differs widely.

2.3.1.2 YOUNGER AGE AND NULLIPARITY

Women at a younger age and nulliparity have been found to be at high risk, however the cause remains unclear (20,21). The higher risk in younger women can likely be explained by other factors that relate to younger mothers, such as poorer socio-economic status, limited support after discharge, lower education level, and poor access to antenatal services.

2.3.1.3 SMOKING

Smoking is well known to be associated with poor outcome after surgery, mostly related to surgical site infections and lower respiratory tract infections. In a large, retrospective study published in the Annals of Surgery in 2011, smoking was found to contribute significantly to post-op complications, both in current and past smokers. This study, done by Hawn et al. in Washington, USA included over 390 000 patients and found an increase in risk of surgical site infections in prior

smokers (OR 1.11, 95% CI 1.05 – 1.17) as well as in current smokers (OR 1.18, 95% CI 1.13 – 1.24) (32). The negative effects of smoking can mostly be attributed to nicotine and carbon monoxide. Nicotine stimulates the central nervous system, causes peripheral vasoconstriction and therefore results in relative tissue hypoxia. This tissue hypoxia can lead to delayed wound healing and increased susceptibility to infections. Carbon monoxide causes further tissue hypoxia by competitive binding to haemoglobin. It has a greater haemoglobin binding capacity than oxygen, which leads to a decreased oxygen delivery to tissue (33).

2.3.2 MEDICAL RISK FACTORS

2.3.2.1 ANAEMIA

Anaemia is defined as a blood haemoglobin level of less than 11g/dl. According to the Saving Mothers Report of 2011-2013, 42.7% of maternal deaths were associated with anaemia (8). Anaemia was present in 39.4% of women who succumbed due to pregnancy related sepsis. Especially when severe, anaemia can be associated with a generally diminished resistance to sepsis and slower recovery from infection. Haemoglobin plays a vital role in oxygen delivery to tissue and is therefore essential in the prevention and treatment of sepsis. In a study done by Malone et al., pre- and post-operative anaemia was found to be associated with post-operative sepsis in the general population. It is postulated that a decreased haemoglobin / haematocrit level leads to decreased oxygen tension in tissues that are potentially exposed to pathogens (31). This relative tissue hypoxia can theoretically lead to anaerobic metabolism and therefore increased susceptibility to microbial growth as well as decreased tissue healing (19,25,34).

2.3.2.2 HUMAN IMMUNODEFICIENCY VIRUS

Women with human immunodeficiency virus (HIV) infection are at higher risk of post-operative sepsis, especially women not yet on highly active anti-retroviral treatment (HAART), with low CD4 counts, WHO stage III or IV disease, or with opportunistic infections. With the current burden of HIV in Sub-Saharan Africa and especially the high-risk population of pregnant women, emphasis on prevention of HIV infection, prevention of mother to child transmission and prevention of sepsis is an essential part of obstetric care. Although all HIV-infected women are now initiated on HAART during pregnancy and higher CD4 counts with lower or undetectable viral loads are expected, some women still seroconvert during pregnancy and therefore some women are still diagnosed at the time of delivery. Non-pregnancy related sepsis is the leading cause of maternal mortality in South Africa, with pregnancy related sepsis as the 4th most common cause (35). CS significantly increases the risk of sepsis in HIV-infected women. The current Saving Mothers CS Guideline recommends inpatient

treatment of HIV positive women for 5 to 7 days after CS, as to identify and actively manage any signs of infection (36). Unfortunately, this is often not always feasible in the South African setting, due to limited resources and the high volume of women seen. Therefore HIV-infected mothers who are assessed to be well, are usually discharged after 3 days. Added post-operative antibiotic treatment in the form of ampicillin / gentamycin / metronidazole is recommended (5,36).

2.3.2.3 DIABETES MELLITUS

Diabetes is well known to be associated with a higher risk of developing sepsis after surgical procedures and post CS sepsis is no exception. During pregnancy, diabetes is also often associated with a raised BMI. Several studies have proven a higher risk of post CS surgical site infection, with one study done in Denmark by Leth et al. quoting a 2 fold increased risk (37,38). A particularly large study by Schneid-Kofman et al. including over 19 000 women, reported both gestational and pre-gestational diabetes to be a significant independent risk factor for post CS surgical site infection with an adjusted odds ratio of 1.3 and 1.45 respectively, when compared to non-diabetic women (16). This study was done in Negev, Israel. According to Schneid-Kofman, Negev demographically has a lower socio-economic status and a large proportion of citizens have a lower education level. It therefore compares well to the South African public health care setting. When the increased risk due to diabetes (gestational and pre-gestational) was combined with the added risk of a raised BMI, women were found to have 9.3 fold increased risk of developing surgical site infection after CS (16).

2.3.2.4 HYPERTENSIVE DISORDERS AND PRE-ECLAMPSIA

Evidence of increased risk for post CS sepsis has been reported in women suffering from hypertensive disorders in pregnancy, including chronic hypertension, gestational hypertension and pre-eclampsia (14,16,20,25). Chronic hypertension likely plays a role in increasing risk due to altered peripheral vascular resistance and poor tissue perfusion leading to increased susceptibility of tissue to pathogens and delayed wound healing (14). The

pathophysiology of the relationship between pre-eclampsia and increased risk of infection is less clear, but increased capillary leakage due to endothelial disease and subsequent poor tissue perfusion is postulated as a possible explanation (16).

2.3.2.5 ANTEPARTUM INFECTION

The presence of active antepartum maternal infection, such as urinary tract infection and chorioamnionitis, can lead to ascending uterine infection and significantly increases the risk of post CS sepsis, especially endometritis (20,25). The risk of surgical site infection is also increased as the endometrium is incised during CS, with possible contamination of the surgical site.

2.3.3 OBSTETRIC RISK FACTORS

2.3.3.1 GESTATION

Idiopathic preterm labour and CS at preterm gestation are often associated with infective pathology, such as urinary tract infection and chorioamnionitis. Other factors such as pre-eclampsia, preterm labour with or without rupture of membranes or severe maternal disease can also lead to preterm CS. These associated factors, rather than the early gestation potentially leads to an increased risk of post CS sepsis.

2.3.3.2 ESTABLISHED LABOUR PRIOR TO CS

The presence of labour prior to CS theoretically increases the risk for ascending infection from the genital tract as it is associated with cervical dilatation, exposure of membranes to vaginal flora, vaginal examinations, as well as rupture of membranes with possible ascending infection. Prolonged labour has been associated with post CS sepsis (21,39). This is thought to be due to increased time for pathogens to ascend into the uterine cavity, as well as due to an increased number of vaginal examinations (21).

2.3.3.3 PRETERM OR PROLONGED RUPTURED MEMBRANES

Preterm or prolonged rupture of membranes (more than 12 hours) is associated with increased risk of ascending infection from the genital tract and therefore increased risk of post CS sepsis, especially endometritis (14,16,19–21,25,40,41). In a study by Devjani et al., 39.2% of women with prolonged rupture were found to develop post CS sepsis (19). This study included 500 consecutive women delivered by CS in an academic maternity hospital in 2013 in New Delhi, India and included a 30 days follow-up after delivery. Pre-labour rupture of membranes for more than 24 hours was reported to more than double the risk of developing post CS sepsis (OR 2.829, *P* value = 0.017) (19). This increase in risk was found despite routine triple therapy antibiotic prophylaxis, given at the time of ruptured membranes in all women. In a different study, Tran et al. in San Francisco in 2008, reported a significant increase in the risk of endometritis after

pre-labour rupture of membranes from as early as 12 hours after rupture, and not 24 hours as previously thought. This retrospective cohort included 3841 women. The adjusted odds ratio at 12 and 16 hours were 2.3 (95% CI 1.2 – 4.4) and 2.5 (95% CI 1.1 – 5.6) respectively (41).

2.3.3.4 MULTIPLE VAGINAL EXAMINATIONS

Contradicting evidence has been found regarding repeated vaginal examinations as a risk factor for post CS sepsis. Devjani et al. found that women with multiple examinations were not at increased risk of surgical site infection (19). However other studies have found different results (21,40). A study done in Athens, Greece by Ziogos et al. found an increased risk of post CS surgical site infection in women who had 6 or more vaginal examinations (OR 6.8, 95% CI 1.4 – 33.4). Vaginal examinations (especially after rupture of membranes) theoretically introduce vaginal organisms to the intrauterine structures, such as the membranes and fetus, even when done under so-called “sterile” conditions. This can lead to ascending infection with chorioamnionitis if delivery is delayed, as well as to post-delivery endometritis. As the uterus is incised during CS, these organisms theoretically spread to the incision site and lead to surgical site infection. A small study done by Imseis et al. in Ohio, USA in 1999, showed a significant increase in the number of different types of bacteria, as well as an increase in the amount of growth of those bacteria, after a single vaginal examination. During this study, vaginal examinations were performed with a sterile glove, after application of a bacteriostatic lubricant (42). A concerning factor is that the increase in organisms did not only include expected vaginal commensals, but also possible pathogenic bacteria such as E.Coli and Group B haemolytic streptococcus species.

2.3.4 SURGICAL RISK FACTORS

2.3.4.1 EMERGENCY CAESAREAN SECTION

The timing of CS also influences the risk of post CS sepsis with emergency CS associated with an increased risk (16,19,21,39). A study done by Schneid-Kofman et al. in Israel reported an increased risk in developing surgical site infection when delivered by emergency vs. elective CS (OR1.3, 95% CI 1.1 – 1.5) while Ghuman et al. in New-Zealand proved an even higher risk (OR 4.22, 95% CI 1.01 – 17.86). This can possibly be attributed to a number of other confounding factors contributing to the total risk. Emergency CS are often performed on women with established labour before CS, rupture of membranes, antepartum haemorrhage with anaemia or women where the maternal or fetal condition is compromised, such as in cases of fetal distress. Theoretically, hastened cleaning and messy surgical techniques could also lead to increased post CS sepsis.

2.3.4.2 GENERAL ANAESTHESIA

Generalised anaesthesia has been associated with increased risk of post CS sepsis, especially surgical site infection, when compared to neuro-axial techniques (spinal or epidural anaesthetic) (10,43). General anaesthesia is most commonly administered only when neuro-axial anaesthesia is contra-indicated. These contra-indications often include women with higher ASA scores (and therefore an increased susceptibility for infection) due to complications such as severe pre-eclampsia and the Haemolysis, Elevated Liver enzymes & Low Platelets (HELLP) syndrome. General anaesthesia is also preferred in women who need emergency caesarean sections, where both maternal and fetal health is compromised and rapid delivery is needed, for example, in the case of abruptio placentae with severe fetal distress. As discussed above, emergency CS has been associated with an increased risk of post CS sepsis when compared to elective CS. Other contra-indications for neuro-axial anaesthesia include women where complicated, prolonged surgery is anticipated. Such cases include, for example, suspected morbidly adherent placenta, where hysterectomy is

anticipated. In these cases, increased blood loss and prolonged surgical time might be the reasons for increased risk of post CS infection and not the general anaesthesia as such. Unfortunately, no large studies have been done focusing on specifically general anaesthesia and post CS infective complications.

2.3.4.3 PROLONGED SURGICAL TIME

Prolonged surgical time is generally regarded as a risk factor for post-operative surgical site infection (9,11,13,20). This is hypothesized to be due to prolonged exposure of tissues to bacterial contact. Antibiotic tissue concentrations also decrease over time, which theoretically puts the surgical field at higher risk. According to the CDC, surgical duration of more than the expected 75th centile is associated with increased risk (15). Unfortunately, no clear cut off time to discern between low and high risk has been established for CS. In 2 studies done in 2006 and 2007 by Johnson et al. and OpØien et al. respectively, two very different approaches were used (10,13).

Johnson et al. classified the duration of the procedure into 3 groups: <30min, 31-60min and >60min. However no significant differences between these groups were found (10). OpØien divided surgical duration into quartiles and calculated the risk for each interquartile group. The fourth interquartile group proved to have a significant higher risk of infection and the cut off between the 3rd and 4th interquartile groups, the 75th centile, was used. This translated to 38 minutes in their setting (13). Caesarean sections with durations exceeding 38 minutes were associated with a 2.4 times increased risk of developing post CS surgical site infection (13). Devjani et al. found a surgical site infection incidence of 53.3% in women with a surgical duration of more than 45 minutes, however no clear explanation for the use of 45 minutes was supplied (19).

2.3.4.4 INEXPERIENCED SURGEON

Surgical experience also plays as a role in post CS sepsis. Inexperienced surgeons or surgeries done as part of training are often associated with prolonged surgical time which can increase the risk for post CS sepsis, as set out above (17,21).

2.3.4.5 SKIN PREPARATION

Prior to all surgical procedures the incision site is prepared in order to obtain a "sterile" surgical field. Various methods of cleaning agents have been used in the past. A randomized controlled trial published in the New England Journal of Medicine in February 2016 included 1147 CS procedures and found pre-operative skin preparation with chlorhexidine in alcohol to be superior to iodine containing agents in preventing surgical site infection (Relative Risk 0.55, 95% CI 0.34 – 0.90, p=0.02) (44).

2.3.4.6 CUTANEOUS STAPLES

The use of cutaneous staples as skin closure method has been found to be associated with an increased risk of surgical site infection when compared to interrupted or subcutaneous sutures (10,17,18,45). A randomised controlled trial done in KwaZulu-Natal, South Africa in 2012, showed a significant increase in post CS surgical site infection associated with the use of skin staples when compared to nylon or polyglycolic acid sutures (45). These results are echoed by the findings of a randomized controlled trial done by Figueroa et al. in the USA (46). Reasons as to why this may be the case is unclear, but postulated to be due to immunological reactions to the metal contained in cutaneous staples. Another possible reason in the South African setting is due to difficulty in placement of staples in the generally obese population. (45)

2.3.4.7 MIDLINE INCISION

Vertical skin incision is thought to be associated with an increased risk of post CS sepsis; however no large study has proven independent significance. Midline incisions are often performed in the emergency setting (which is known to carry an increased risk) or with complicated surgery, and therefore also prolonged operating time is expected (19,21). Midline incisions have also been associated with an increase in surgical site complications in women with a BMI > 50 when compared to transverse incisions.

2.4 CURRENT ANTIBIOTIC PROTOCOLS

Despite numerous clinical trials there is still a considerable difference in recommended antibiotic use as prophylaxis for post CS sepsis.

2.4.1 INDICATION

Firstly, prophylactic antibiotic use has been proven to be effective in preventing post CS endometritis and surgical site infection when compared to placebo. A single dose is as effective as repeated doses and a reduction of between 60-75% in post CS endometritis and up to 75% in post CS surgical site infection has been proven (4,47). Two Cochrane reviews by Smaill et al. found prophylactic antibiotic use to be effective in both high risk procedures (for example emergency CS and women with prolonged rupture of membranes) as well as low risk procedures such as elective CS (4,48,49). The administration of prophylactic antibiotics to all women has also been proven to be cost saving, as the reduction in post CS sepsis with administration of a single dose leads to a significant reduction in costs resulting from post CS sepsis (48).

2.4.2 CLASS

Classes of antibiotics used as prophylaxis differ widely between countries and institutions. This is likely due to different resistance profiles. Multiple organisms can lead to post CS sepsis, which also complicates the choice of antibiotic. Because the uterus is incised during CS there is increased risk of colonization of the surgical site by ascending genital tract organisms. Organisms such as staphylococcus, enterococcus, ureaplasma and anaerobes are some of the more common pathogens isolated from surgical site infections (50). A Cochrane review reported no overall difference in post CS sepsis rates when comparing penicillins and cephalosporins as the prophylactic antibiotic of choice during CS (51). The most commonly used antibiotic, as recommended by the American College of Obstetricians and Gynecologists, is a 1st generation cephalosporin such as cefazolin (9,50). Cefazolin is preferred above penicillins purely due to resistance patterns. The addition of a macrolide (such as azithromycin /

erythromycin) or metronidazole has been proven to be beneficial as the widened antimicrobial cover then also targets organisms such as Ureaplasma urealyticum and anaerobes, which have been shown to cause post CS sepsis (50,52,53). Azithromycin is preferred as it has a long half-life as well as very little fetal transfer; however it is much more costly than metronidazole. Most guidelines however do not include macrolides as routine prophylaxis.

2.4.3 TIMING

Some debate still exists regarding the timing of prophylactic antibiotics. For all other surgical procedures, antibiotic administration before skin incision is recommended. However CS may be an exception. Due to concerns that antibiotic administration before skin incision (and therefore well before the time of cord clamping) might lead to difficulty in the culture of organisms causing neonatal sepsis, antibiotic administration after cord clamping has previously been recommended. Newer studies and review articles have shown no adverse neonatal outcome, but significant reduction in risk of post CS infection when administered prior to skin incision (54–59). A prospective, randomized, double blind, placebo-controlled study done by Sullivan et al. proved a significant reduction in especially endometritis, when cefazolin is administered prior to skin incision. No increase in neonatal complications were found (59). The current NICE guideline recommends prophylactic antibiotic administration prior to skin incision as this allows for adequate concentrations in tissue at the time of incision (22,25,50,59).

South African Guidelines contained in the Saving Mothers: Caesarean Section Monograph (3) recommends a single dose of cefazolin 2g intravenously or ampicillin 2g intravenously as prophylaxis at CS. No clear mention is made of timing of administration. A therapeutic course of antibiotics such as ampicillin, gentamycin and metronidazole or cefazolin and metronidazole is recommended in women with:

- Prolonged rupture of membranes (>12 hours)
- Obstructed labour and second stage CS

- Multiple vaginal examinations (>5)
- Immune compromise (HIV positive)
- Intraoperative complications – blood loss > 1000ml / blood transfusion / fetal head disimpacted vaginally (3,5).

2.5 TYGERBERG HOSPITAL

The current incidence of post CS sepsis at Tygerberg Hospital is not known. An average of 280 caesarean sections are done per month, but data is only available on the few women who develop severe sepsis with maternal compromise, or those with resistant strains of bacteria that are identified by Microbiology and the Department for Infection Control. These cases amount to 1 or 2 women per month. When one considers the estimate in the RCOG / NICE guideline on Caesarean Sections of an incidence of 8% in high-income countries (22), one would expect around 20 women with post CS sepsis per month. As these estimates are for developed countries, the possibility of an even higher incidence exists.

The current CS management protocol includes:

- Administration of a single dose of cefazolin 2g intravenously 1-2 hours pre-operatively.
- Ampicillin 2g 6 hourly intravenously and metronidazole 400mg 8 hourly orally for at least 48 hours, then continued orally to complete five days, in women with risk factors as stipulated by the Caesarean Section Monograph and current provincial policy (5,36).

Currently, no post discharge surveillance program exists and therefore the incidence is likely higher than estimated. Due to the large drainage area women with mild / moderate post CS sepsis are treated at less specialised facilities after discharge.

2.6 SUMMARY

Pregnancy related sepsis is still the 3rd most important direct cause of maternal mortality in South Africa (35). Caesarean section is the single most important independent risk factor for pregnancy related sepsis and therefore early detection of high-risk women and adequate management of identified women are essential in order to prevent maternal morbidity and mortality. A comprehensive literature review as set out above found the incidence of post CS sepsis to differ widely, with a significantly higher rate in LMIC. It also emphasizes the diversity of potential risk factors for post CS sepsis. This highlights the importance of the identification of risk factor trends unique to the specified patient population. The calculation of the incidence of post CS sepsis and the identification of risk factors trends among women with post CS sepsis at Tygerberg Hospital were therefore found to be vital. This information will prove beneficial in identifying areas of possible intervention in order to prevent post CS sepsis, as well as guide further research.

3 AIM AND OBJECTIVES

Aim

The aim of this study was to audit post-CS sepsis at TBH.

Objectives

1. To determine the incidence of post CS sepsis at TBH.
2. To identify risk factor trends for post CS sepsis in women who deliver by CS at TBH.
3. To determine the outcomes of women who develop post CS sepsis at TBH.
4. To make recommendations for future research and intervention.

4 METHODOLOGY

4.1 DESCRIPTION OF STUDY DESIGN:

A retrospective audit of patient records of all women delivered by CS at TBH in a three-month period between 1 February 2014 and 30 April 2014 was undertaken. All records were followed up for thirty days after delivery in order to identify post CS sepsis.

4.2 SETTING AND STUDY POPULATION

This research was conducted in the setting of a public sector, academic hospital in Cape Town, South Africa. The obstetric department serves a predominantly low-income community and functions as a specialist and sub-specialist (referral unit for midwife obstetric units as well as district / level 1 hospitals. Women delivering in this unit are therefore at increased risk of obstetric and / or medical complications.

4.3 INCLUSION CRITERIA:

All women that delivered by CS in the above 3-month period were included. Women diagnosed with post CS sepsis within 30 days after surgery were identified and records audited. The CDC criteria for surgical site infection (both

superficial and deep) and endometritis were used for diagnosis, as this is the most commonly used diagnostic criteria globally (15). For the scope of this study, criteria for both superficial and deep infections were included, in order to accurately estimate the entire burden of disease in the study population. The criteria are as follows:

Endometritis

Temperature > 38°C

AND one or more of the following

Tender, sub-involuted uterus

Purulent / offensive lochia

Abdominal pain with no other recognized cause (11,15)

Diagnosis of endometritis made by attending physician.

Surgical Site Infection

Temperature >38°C

AND one or more of the following

Symptoms of redness, pain, tenderness or swelling around surgical site

Purulent discharge from surgical site

Spontaneous dehiscence of surgical wound

Surgical wound deliberately opened by attending physician

Abscess formation in subcutaneous tissue directly surrounding surgical wound.

Diagnosis of surgical site infection made by attending physician (11,15)

4.4 EXCLUSION CRITERIA:

Women transferred to TBH after CS delivery at referral hospitals were excluded in order to accurately calculate the institutional incidence of post CS sepsis at TBH. Women were also excluded if adequate medical records were not available.

4.5 SAMPLE SIZE AND SAMPLING METHOD:

Total population sampling was done. Every woman who delivered during the 3-month study period and met entry criteria was included. The current incidence of post CS sepsis in South Africa is uncertain, but is estimated to be around 12.5% if women are followed up for 14 days after discharge (2). The estimated incidence in high-income countries is 8% according to the most recent National Institute for Health Care and Excellence (NICE) guideline on Caesarean section (22). At Tygerberg Hospital an average number of 280 caesarean sections were done per month in 2013, which leads to a suspected sepsis rate of 20 - 36 cases per month. The sample size of the index study was calculated based on an expected cumulative incidence of 12.5%. The aim was to estimate the incidence of post CS sepsis when assuming a margin of error of 0.02 and a 95% confidence interval. This amounted to a required sample size of at least 802 cases.

Participants were identified by the principal investigator using the CS theatre register as well as cross checking cases in the birth register. Patient records at Tygerberg Hospital are stored electronically on the TBH OpenText Electronic Content Management (ECM) system. All patient files were accessed electronically via the TBH OpenText ECM system in order to obtain clinical records. Women diagnosed with post CS sepsis during inpatient stay or at follow-up at Tygerberg Hospital were identified directly on the ECM system. Records were reviewed and data captured in four (4) main categories:

- General / Demographic (age / smoking / body mass index etc.)
- Medical (Underlying medical conditions, antibiotic use etc.)
- Obstetric (Gravidity / Parity / Time from rupture of membranes / Previous CS etc.)
- Surgical (Surgical time / Surgeon experience / Indication etc.)

According to provincial protocol, women with postpartum endometritis or surgical site infection are managed at district hospitals, or referred for higher-level care if they do not respond within 48 hours of treatment.

The identifiers of all patients included into the study were subsequently reviewed on the Clinicom system, in order to identify women who presented to referral

hospitals in the 30-day follow-up period. Each of these records was manually accessed at the referral hospitals by the principal investigator. Records were assessed in order to identify women diagnosed with post CS endometritis or surgical site infection. Further information on clinical course, outcome, subsequent hospital admission, repeat surgery, severe morbidity and mortality were entered into the database. Referring hospitals participating in the study were:

Khayelitsha Hospital
Helderberg Hospital
Karl Bremer Hospital
Worcester Hospital
Paarl Hospital

5 DATA MANAGEMENT AND STATISTICS

Data were collected and captured electronically by the principal investigator, under supervision of the study supervisor. Data were kept strictly anonymous and confidential at all times by a research code given to each patient case identified for audit. This research code was utilised for data collection, therefore ensuring confidentiality. Research codes and captured data were stored on the study supervisor‘s secure, password protected computer in the Obstetrics and Gynaecology department.

Data were collected in Microsoft Excel® and analysed using Statistica (Statsoft) version 12 of 2014. Data are represented in two ways. Firstly, data are presented descriptively. Continuous data is presented using means and standard deviations with 95% confidence intervals for the population, if data is normally distributed. In the case where the data was non-normally distributed, medians and interquartile ranges were used. Data is presented graphically using pie charts. Nominal data was analysed as frequency distributions, presenting the absolute and relative cell frequencies. For binary proportions such as the primary outcome, the sepsis rate, 95% confidence intervals were presented to estimate the population sepsis rate.

The primary aim of the study was to determine the incidence of post CS sepsis. Thus this objective is descriptive in nature and was analysed using the aforementioned methodology. The other primary objective was determining the factors associated with sepsis in this particular setting. This was done in a univariate sense. If a risk factor is numerical, a T-test was applied if data are normally distributed and a Mann-Witney U test if data is not normally distributed. In the case where a risk factor is nominal then a chi-squared test was used, with exact tests for expected cell frequencies less than five. All significant factors identified from the univariate model were considered for inclusion in the multivariate model. In general, all tests were two-sided with a significance level of 5% used throughout.

6 ETHICAL CONSIDERATIONS

The Health Research Ethics Committee, University of Stellenbosch (S14/08/164), as well as from the Western Cape Department of Health (WC_2014RP43_943), granted ethical approval. Approval was also granted to waiver informed consent for the purpose of this study.

7 RESULTS

7.1 BACKGROUND

A total of eight hundred and forty eight (848) women were identified as having delivered by caesarean section (CS) in the study period (from 1 February 2014 – 30 April 2014). Thirty-seven (37) women were excluded, as minimal or no clinical notes were available. Of the 811 records audited, the number of CS done was equally distributed across the 3-month period, with an average of 271 procedures per month.

Of the 811 included women, 41 presented at referral hospitals within 30 days after CS. Thirty-eight of these patient records were audited. Three women were excluded due to unavailable or incomplete notes. Of the records audited, 5 were diagnosed with post CS sepsis. There were 33 cases of post-partum sepsis diagnosed at TBH. Thus, a total of thirty-eight women with post CS sepsis were identified during the study period (Fig 7.1.1).

During the 3-month study period a total of 1,834 deliveries were managed at TBH. This amounts to a CS rate of 46.24%. Of the 811 CS included, 172 (21.21%) were elective procedures and 639 (78.79%) were emergency procedures. The cumulative incidence of post CS sepsis was therefore 4.69%.

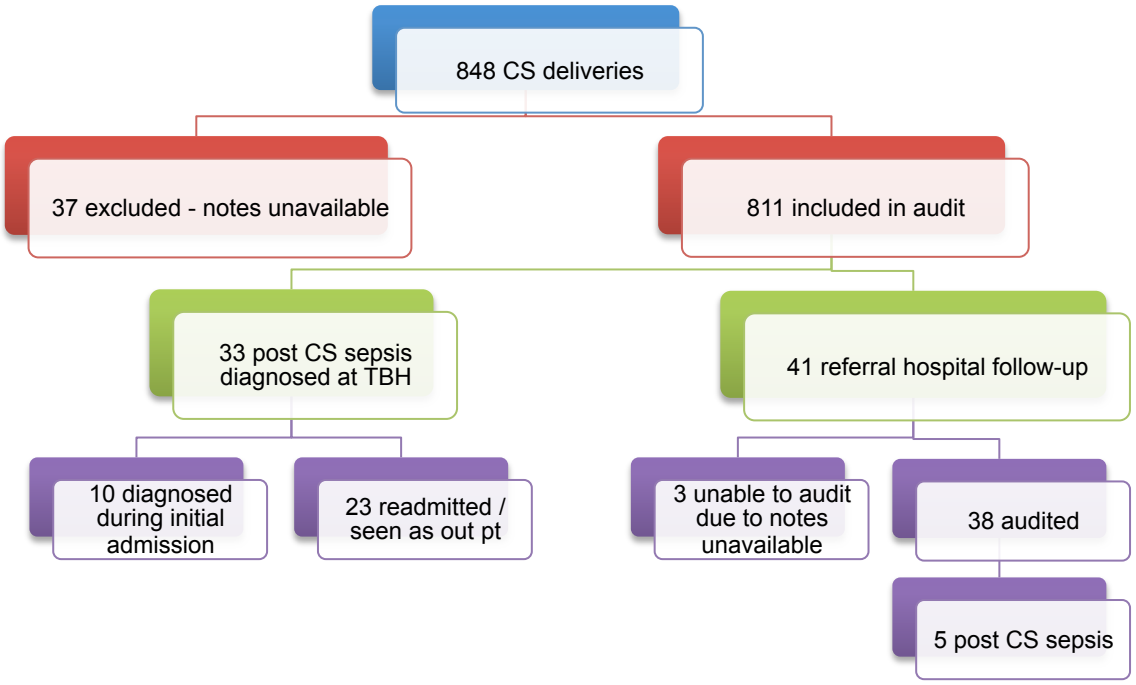

Figure 7.1.1 – Audit profile

7.2 PATIENT AND CAESAREAN SECTION CHARACTERISTICS

The median age of the patient population was 29 years with a range of 15 – 49 years. Teenagers (women younger than 20 years of age) comprised 7.40% of the patient population and 11.22% of women were older than 37 years.

Most women were multiparous (72.13%) and 226 women (27.87%) were in their first pregnancy.

Almost two thirds (61.16%) of CS included were performed on women without a prior CS. When isolating emergency CS only, 70.89% of CS performed where first time procedures.

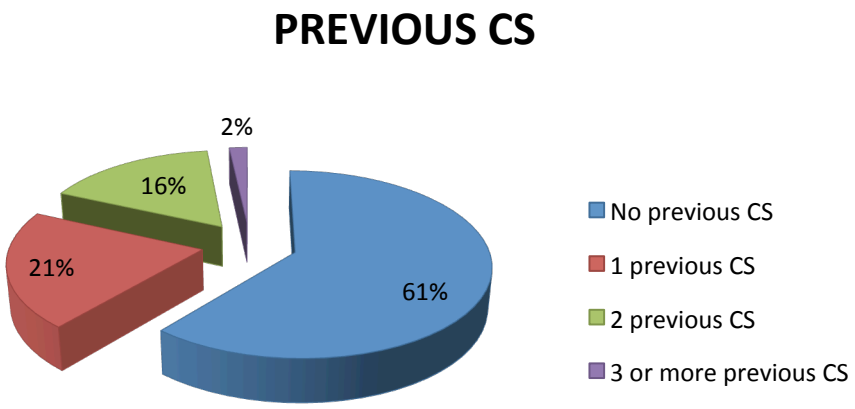

Figure 7.2.1 - Number of previous CS

The median BMI of the study population was 31kg/m^2 with a range of 14 – 74kg/m^2. Importantly, only eighteen percent of women had a normal BMI. A total of 17.20% of women could be classified as morbidly obese (BMI 40 – 49.9) and 4.67% as super obese (BMI > 50).

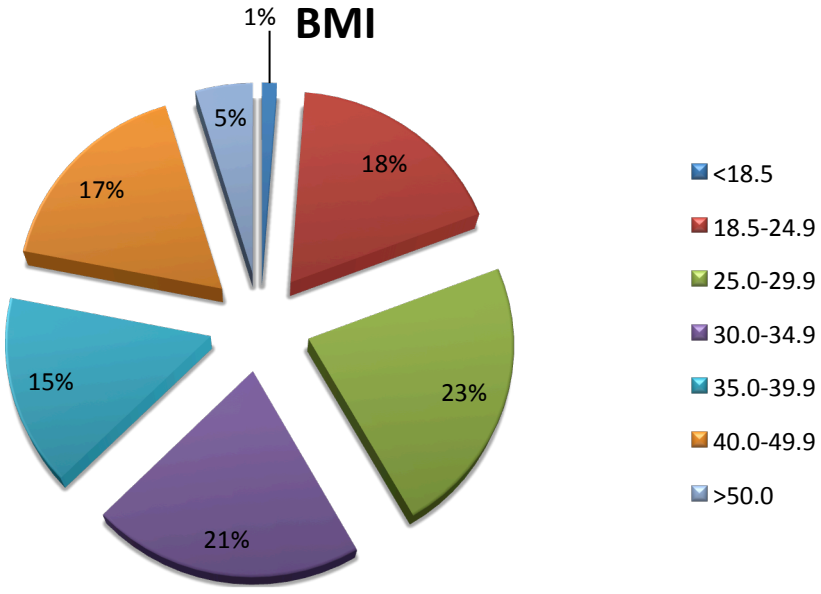

Figure 7.2.2 – Distribution of BMI subgroups

The median haemoglobin (Hb) was 11.7g/dl, ranging from 5.6g/dl to 17.0g/dl. Approximately one fifth of women (21.70%) were known, or newly diagnosed to be HIV positive. Of these women, 169 (94.94%) were known, or newly initiated on HAART during the pregnancy. The median CD4 count was 411 with a range of 41 - 1320.

Diabetes Mellitus was diagnosed or known in 8.14% of women. This includes both pre-gestational and gestational diabetes.

Hypertensive disorders were present in 47.60% of women included, with pre-eclampsia diagnosed in 29.60%.

The median gestational age (in completed weeks) at delivery was 38 weeks, with a range of 26 to 42 weeks. However, when dividing data between emergency and elective CS, the median gestational age for elective CS was 39 weeks (range 38 to 42 weeks) and emergency CS 37 weeks (range 26 to 40 weeks).

Of the 639 women who delivered by emergency CS, 209 (32.79%) had spontaneous onset of labour and 197 (30.82%) had induced labour. Of all the women in labour, one hundred and twenty five women progressed to the active phase of the first stage of labour (defined as regular, strong uterine contractions with cervical dilatation >4cm). This amounts to 30.78% of the total number of women in labour and 19.56% of all women delivered by emergency CS.

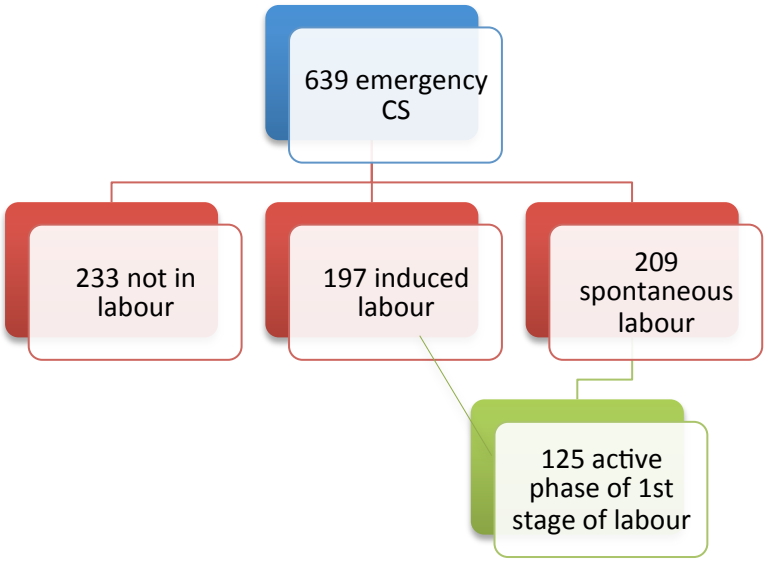

Figure 7.2.3 – Distribution of patients in labour

Upon investigation of the 125 women in active labour, approximately one third (32.80%) were in active labour for more than 6 hours before CS.
Rupture of membranes (ROM) during labour was present in 185 women (28.95%) that delivered by emergency CS. The median duration of ROM was 11 hours (range 1- 45 hours).
Vaginal examinations were performed in 635 of 639 women who delivered by emergency CS. Of these women, 37 (5.82%) received more than 6 documented examinations before CS.

Around one fifth of women included (21.21%) had planned, elective procedures, while 78.79% had emergency CS, with both groups having similar sepsis rates (4.65% vs. 4.69%). When comparing elective procedures to emergency procedures, a clear difference in indication was found, as tabulated below.

Indication	Emergency		Elective	
	number	%	number	%
Fetal distress / compromise	349	54.62	0	0.00
Cephalopelvic disproportion / Poor Progress	75	11.73	0	0.00
Failed induction of labour	51	7.99	0	0.00
Previous CS x1 – declined VBAC	31	4.85	37	21.51
Previous CS x2/more (emergency CS – in labour)	45	7.04	82	47.67
Malpresentation	32	5.01	6	3.49
Multiple gestation	29	4.54	18	10.46
Maternal Condition	10	1.56	3	1.74
Placenta Praevia	10	1.56	9	5.24
Macrosomia	0	0.00	11	6.40
Other	7	1.10	6	3.49

Table 7.2.1 – Indication for caesarean section

The level of surgical experience was categorized as the surgery being performed by an intern (and therefore a training procedure), medical officer, registrar and consultant obstetrician. Medical officers and registrars performed the bulk of CS, 61.31% and 28.92% respectively. Interns performed 6.55% and consultants were responsible for 3.21% of CS.

The majority of CS were performed via a transverse skin incision (93.10%) with uterine entry through a lower segment transverse incision in 96.11% of cases. Surgical duration was classified according to quartiles.

	Duration (minutes)
< 1st quartile	Less than 28 minutes
1st to 2nd quartile	29 - 37
2nd to 3rd quartile	38 - 50
> 3rd quartile	51 minutes and longer

Table 7.2.2 - Duration of procedure

Intra-operative complications occurred in 20.86% of procedures. The 3 most common complications were:

- Difficult adhesiolysis (35.97%),
- Difficult haemostasis (24.39%) and
- Uterine tears (13.41%).

One woman required a hysterectomy at the time of CS due to major post-partum haemorrhage. A general anaesthetic was indicated in 88 (10.94%) of cases. The mean postoperative inpatient days were 3.25 (Standard Deviation ± 1.90).

Nine women out of the total sample group had a pre-operative diagnosis of chorioamnionitis. However, none of these women developed post CS sepsis. Six women out of the total sample group were diagnosed with non-obstetric causes of sepsis (urinary tract infection / respiratory tract infection). Eleven women were found to be pyrexial during labour and were started on antibiotics before delivery.

A single dose of prophylactic, pre-operative antibiotics was administered in 96.05% of women. Thirty-two women (3.95%) had no documentation that a prophylactic dose was administered.

A therapeutic course of antibiotics was administered in more than one third (37.37%) of women during the post-partum period.

7.3 RATE OF POST CS SEPSIS

This audit identified 38 women diagnosed with post CS sepsis, which translates to a cumulative incidence of 4.69%.

Twenty-seven women (71.05%) had surgical site infection, while 7 (18.42%) had endometritis and 4 women (10.53%) met criteria for both. Therefore, the incidence for post CS surgical site infection was 3.82% and for post CS endometritis, 1.35%. The median time from CS to diagnosis of sepsis was 7 days (range 2 – 30 days). Twenty-four women (63.15%) needed re-admission to hospital, with a median hospital stay of 5 days (range 2 – 32 days). In the 10 women (26.31%) diagnosed before initial discharge, the median post-operative hospital stay was 6.5 days (range 3 – 38 days). Therefore only 4 women (10.52%) that presented with post CS sepsis were deemed to be well enough for outpatient management. Ten women (26.31%) required repeat surgical intervention of which five (13.15%) required hysterectomy. Five women (13.15%) required multiple surgeries of which 3 had an explorative laparotomy and a total abdominal hysterectomy and 2 women had an explorative laparotomy and subsequent wound debridement. Nine women (23.68%) required admission to the Obstetric Critical Care Unit (OCCU) / Surgical ICU. These cases are discussed in more detail in section 8.3 below.

7.4 RISK FACTOR ANALYSIS

When identifying risk factors for post CS sepsis, all patient- and caesarean section factors mentioned above were analysed as possible risk factors. The majority of factors were found to not reach statistical significance.

Risk Factor	With Post CS sepsis n=38 (%)	Without Post CS sepsis n=773 (%)	Risk Ratio (RR)	Confidence Interval (CI)	p-value
Age					
Median	29	29			
< 20 years	4 (10.53)	56 (7.24)	1.47	0.53 - 4.02	NS
≥ 37 years	4 (10.53)	112 (14.49)	0.97	0.35 - 2.68	NS
Parity					
Nulliparous	13 (34.21)	213 (27.59)			
Parous	25 (65.79)	559 (72.41)	0.74	0.39 - 1.43	NS
Smoking	7 (18.42)	139 (18.68)	0.96	0.40 - 2.29	NS
Alcohol use	6 (15.79)	127 (17.09)	1.04	0.44 - 2.46	NS

Table 7.4.1 - Demographic Risk Factors

The first group of risk factors identified focused on patient demographics. No statistically significant differences were found for maternal age or parity. Approximately one fifth of women were found to be regular tobacco users and around 16% used alcohol in pregnancy.

Risk Factor	With Post CS sepsis n=38 (%)	Without Post CS sepsis n=773 (%)	RR	CI	p-value
BMI (kg/m2)					
< 18.5	1 (2.63)	8 (1.12)	3.86	0.92 - 16.19	NS
18.5 – 24.9	8 (21.05)	128 (17.90)			
25.0 – 29.9	6 (15.79)	163 (22.80)	0.68	0.24 - 1.99	NS
30.0 – 34.9	8 (21.05)	148 (20.70)	0.99	0.37 - 2.66	NS
35.0 – 39.9	5 (13.16)	111 (15.52)	0.83	0.27 - 2.55	NS
40.0 – 49.9	5 (13.16)	124 (17.34)	0.75	0.24 - 2.30	NS
>50	2 (5.26)	33 (4.20)	1.10	0.24 - 5.07	NS
Haemoglobin (g/dl)					
➢ **>11**	27 (71.05)	500 (65.27)			
➢ **< 11**	11 (28.95)	263 (34.33)	0.78	0.39 - 1.56	NS
➢ **< 7**	0 (0.00)	3 (0.39)			

Table 7.4.2 - Medical Risk Factors

No significant differences were found in maternal BMI at booking in women with or without Post CS sepsis despite the high percentage of obese patients. Anaemia as risk factor did not reach statistical significance and only 3 women presented with severe anaemia.

Risk Factor	With Post CS sepsis n=38 (%)	Without Post CS sepsis n=773 (%)	RR	CI	p-value
Human Immunodeficiency Virus	8 (21.05)	169 (21.92)			
With antiretroviral therapy	5 (13.16)	165 (21.40)	0.60	0.24 - 1.53	NS
Without antiretroviral therapy	3 (7.89)	4 (0.52)	5.83	1.72 - 19.77	0.005
CD4 count					
≤ 200	1 (2.63)	21 (2.72)	0.95	0.10 - 8.71	NS
200 – 500	1 (2.63)	77 (9.96)	0.27	0.03 - 2.53	NS
≥ 500	3 (7.89)	60 (7.76)			

Table 7.4.3 - HIV as Risk Factor

Upon investigating HIV infection as a risk factor, women with HIV who were not on HAART were found to be at 5.83 times greater risk to develop sepsis than women without HIV. However, this should be interpreted with caution due to the low number of women in this group.

Risk Factor	With Post CS sepsis n=38 (%)	Without Post CS sepsis n=773 (%)	RR	CI	p-value
Hypertension	20 (52.63)	365 (45.18)			
Chronic Hypertension	5 (13.16)	68 (8.82)	2.02	0.82 - 4.96	NS
Gestational Hypertension	1 (2.63)	25 (3.24)	0.96	0.13 - 6.93	NS
Pre-eclampsia	13 (34.21)	227 (29.44)	1.26	0.60 - 2.65	NS
Diabetes Mellitus	3 (7.89)	63 (8.15)	0.97	0.31 - 3.06	NS

Table 7.4.4 - Medical Risk Factors Continued

Despite hypertension being prevalent in a large number of women included in this audit, no statistically significant differences were found between groups when compared to non-hypertensive women. Diabetes in pregnancy (both gestational and pre-gestational) was also found to be non-significant.

Risk Factor	With Post CS sepsis n=38 (%)	Without Post CS sepsis n=773 (%)	RR	CI	p-value
Prophylactic pre-op antibiotics					
None administered	1 (2.63)	22 (2.86)	1.00	0.14 - 7.02	NS
In theatre	34 (89.47)	746 (97.14)			
Pre-CS therapeutic antibiotics					
None	34 (89.47)	739 (95.97)			
Administered	1 (2.63)	31 (4.03)	0.71	0.10 - 5.03	NS
Therapeutic post partum Antibiotics					
None	20 (52.63)	479 (62.61)			
Administered	17 (44.74)	286 (37.39)	1.11	0.54 - 2.28	NS

Table 7.4.5 - Antibiotic usage

Antibiotic administration pre-delivery, prophylactic antibiotic administration in theatre and post-operative antibiotic administration were similar in both groups.

Risk Factor	With Post CS sepsis n-38 (%)	Without Post CS sepsis n=773 (%)	RR	CI	p-value
Previous CS					
No previous CS	27 (71.05)	469 (60.67)			
Prev C/S x1	8 (21.05)	159 (20.60)	0.88	0.41 - 1.90	NS
Prev C/S x2 or more	3 (7.89)	145 (18.81)	0.37	0.11 - 1.21	NS
Emergency / Elective					
Emergency	30 (78.95)	608 (78.76)	1.01	0.47 - 2.16	NS
Elective	8 (21.05)	164 (21.24)			

Table 7.4.6 - Surgical risk Factors

Upon investigation of the surgical risk factors previous CS and emergency vs. elective CS, no statistical significance was found.

Risk Factor	With Post CS sepsis n-38 (%)	Without Post CS sepsis n=773 (%)	RR	CI	p-value
Anaesthetic					
General	6 (15.79)	82 (10.68)	1.58	0.68 - 3.67	NS
Regional (spinal and epidural)	30 (78.95)	686 (89.32)			
Skin suture type					
Non-absorbable interrupted	35 (94.59)	672 (87.27)			
Absorbable continuous	2 (5.41)	65 (8.44)	0.60	0.15 - 2.45	NS
Skin Clips	0 (0.00)	33 (4.29)			
Skin Incision					
Midline	2 (5.26)	54 (7.08)	0.73	0.18 - 2.99	NS
Lower transverse	36 (94.74)	709 (92.92)			

Table 7.4.7 - Surgical Risk Factors continued

Anaesthetic choice and choice of skin closure technique and skin incision yielded no significant differences between groups.

Risk Factor	With Post CS sepsis n-38 (%)	Without Post CS sepsis n=773 (%)	RR	CI	p-value
Level of experience surgeon					
Intern	3 (7.89)	50 (6.49)	1.08	0.34 - 3.45	NS
Medical Officer	26 (68.42)	470 (60.96)			
Registrar	7 (18.42)	227 (29.44)	0.57	0.25 - 1.30	NS
Consultant	2 (7.89)	24 (3.11)	1.47	0.37 - 5.85	NS
Duration					
< 1st Quartile	5 (13.16)	197 (25.79)			
Between 1st & 2nd Quartile	11 (28.95)	196 (25.65)	2.15	0.76 - 6.07	NS
Between 2nd and 3rd Quartile	6 (15.79)	197 (25.79)	1.19	0.37 - 3.85	NS
> 3rd quartile	14 (36.84)	174 (22.77)	3.01	1.10 - 8.19	0.03
Vaginal disimpaction of fetal head	1 (2.63)	21 (2.73)	1.02	0.15 - 7.09	NS

Table 7.4.8 - Surgical Risk Factors Continued

Medical officers and registrars performed the majority of CS. Procedures with a duration of 51 minutes or longer (above the 3rd quartile) were found to have a 3 times higher risk of developing post CS sepsis, when compared to procedures with a duration less than 28 minutes (below the first quartile).

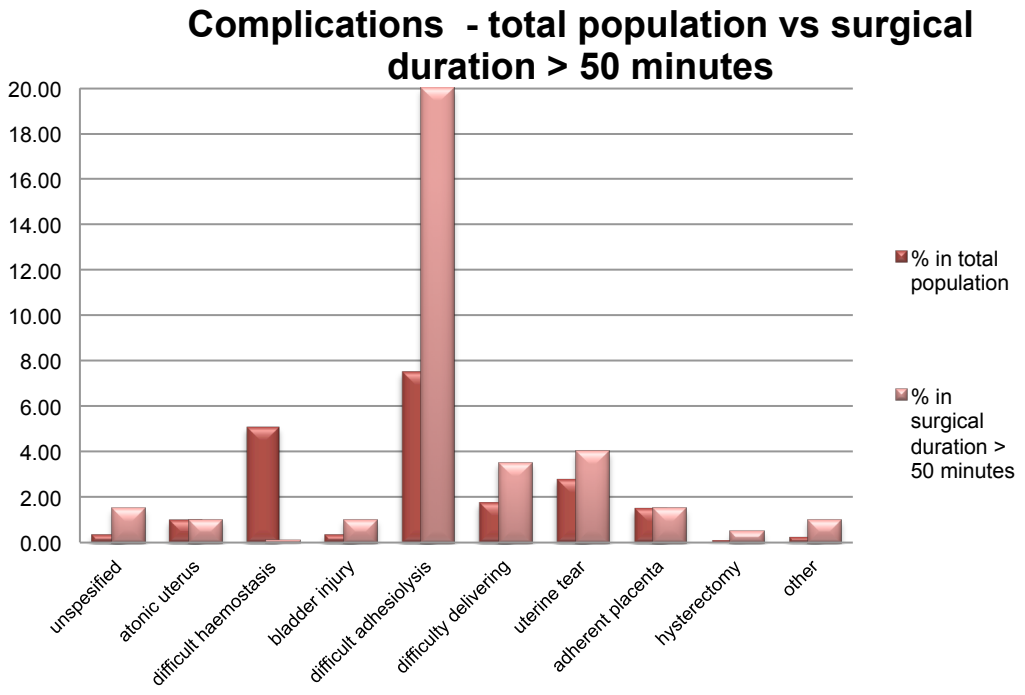

Figure 7.4.1 - Complications - total population vs. surgical duration > 50 minutes

As set out above, a higher incidence of intra-operative complications were found in these prolonged procedures, when compared to the total study population.

Risk Factor	With Post CS sepsis n=38 (%)	Without Post CS sepsis n=773 (%)	RR	CI	p-value
Gestation					
<27 weeks	0 (0.00)	9 (1.16)			
27 – 33 weeks	11 (28.95)	173 (22.38)	2.05	0.84 - 4.99	NS
34 – 36 weeks	7 (18.42)	128 (16.56)	1.77	0.66 - 4.79	NS
37 – 38 weeks	12 (31.58)	198 (25.61)	1.96	0.81 - 4.70	NS
≥ 39 weeks	8 (21.05)	265 (34.28)			
Labour					
Not in labour	18 (47.37)	384 (49.68)			
Spontaneous	10 (26.32)	202 (26.13)	1.06	0.50 -2.25	NS
Induced	10 (26.32)	187 (24.19)	1.13	0.53 - 2.41	NS

Table 7.4.9 - Obstetric Risk Factors

Obstetric risk factors were investigated to assess for an association with post CS sepsis. Gestation at delivery and the presence of labour was found to be statistically non-significant.

Risk Factor	With Post CS sepsis n=38 (%)	Without Post CS sepsis n=773 (%)	RR	CI	p-value
Method of induction					
Medical induction	4 (10.53)	90 (48.13)			
Amniotomy	2 (5.26)	43 (22.99)	1.19	0.21 - 6.77	NS
Balloon catheter & amniotomy	3 (7.89)	31 (16.58)	1.86	0.33 - 10.40	NS
Duration of ROM					
none	26 (68.42)	561 (73.05)			
≤ 12 hours	5 (13.16)	113 (14.71)	0.98	0.37 - 2.59	NS
12 – 24 hours	4 (10.53)	63 (8.20)	1.40	0.49 - 4.02	NS
≥ 24 hours	2 (5.26)	31 (4.04)	1.40	0.34 - 5.79	NS
Duration of active labour					
none	28 (73.68)	654 (84.82)			
< 6 hours	5 (13.16)	80 (10.38)	1.52	0.59 - 3.94	NS
> 6 hours	4 (10.53)	37 (4.80)	2.49	0.90 - 6.95	0.08
Number vaginal examinations					
< 6 examinations	34 (89.47)	736 (95.58)			
≥ 6 examinations	3 (7.89)	34 (4.42)	1.86	0.59 - 5.88	NS

Table 7.4.10 - Labour-related Risk Factors

Upon further exploration of obstetric risk factors no statistically significant differences were found for induction method or duration of active labour. A trend was recognized in women in active labour for more that 6 hours, however numbers were small.

7.5 OUTCOMES OF WOMEN WITH SEPSIS

Of the 811 women included in the index study, 38 (4.69%) presented with post CS sepsis. Twenty-seven women (71.05%) had surgical site infection, while 7 (18.42%) had endometritis and 4 women (10.53%) met criteria for both.

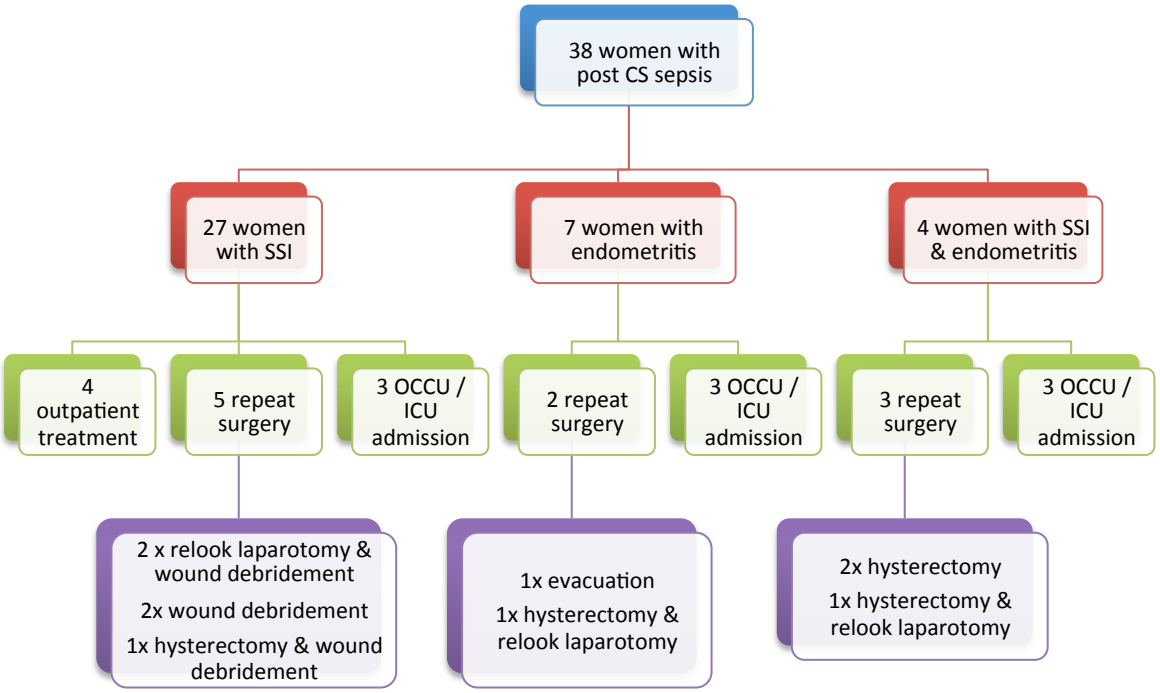

Figure 7.5.1 – Outcomes of women with post CS sepsis

Twenty-eight (73.68%) women were discharged and presented to a health care facility with a diagnosis of post CS sepsis within 30 days, while 10 women were diagnosed prior to initial discharge. Twenty-four (82.14%) of the 28 women that presented after discharge from hospital, required re-admission. Ten women (26.31%) required a repeat surgical intervention, five of which needed hysterectomy. Five of the women with repeat surgical interventions required multiple surgical procedures including explorative laparotomy, wound debridement and negative pressure dressing changes in theatre. Only 3 of the women requiring surgery were managed in a general ward, with 7 requiring a higher level of care.

8 DISCUSSION

This research was conducted in the setting of a public, academic hospital in Cape Town, South Africa. The obstetric department serves a predominantly low-income community and functions as a level 2 and 3 referral unit for both midwife obstetric units and district / level 1 hospitals. Women delivering in this unit are therefore at increased risk of obstetric, medical and / or surgical complications.

8.1 Rate of post CS sepsis

According to this index study, the post CS sepsis cumulative incidence for the 3-month study period was 4.69%. The rate for post CS surgical site infection specifically, was 3.82%. The study group included both superficial and deep surgical site infection in this study in order to identify all patients with sepsis related morbidity. The reported incidence compares well to current data on incidence rates from high-income countries. According to the RCOG and current NICE guideline, the current mean post CS surgical site infection rate in high income countries is 6.4% and 8% respectively (22). The National Nosocomial Infection Surveillance System in the United States of America reports an incidence of 3.5% in low risk patients and 8.11% in high risk patients undergoing CS (17). Data from LMIC have shown a much higher post CS sepsis incidence. A prospective study, by Devjani et al., done in India in 2013, reported a post CS surgical site infection rate of 20.4% (19).

Unfortunately data on post CS sepsis in South Africa is less readily available. Johnson et al., in research conducted at Chris Hani Baragwanath Hospital in Johannesburg, found a post CS surgical site infection rate of 12.5%, with 1.5% of women requiring re-admission.

We postulate that the significant difference in incidence between the index study and data from international and local sources is two-part. Firstly, as this study had a retrospective design and identified women who presented with sepsis prior to initial discharge, or who presented to a health care provider at a level 1 hospital or higher, the possibility exists that the index study was biased towards identifying women with more severe post CS sepsis. This could explain our lower incidence compared to other low-income countries, as well as the significantly higher re-admission rate than

found by Johnson et al. We do, however, feel that symptoms mild enough to not prompt women to seek medical advice, or require referral from primary health care facilities, would likely not significantly contribute to maternal morbidity or mortality. Secondly, Johnson et al. identified women by telephonic follow-up, which relies on patient opinion and interpretation, without verification of the diagnosis by a health care provider. This potentially allows for over-estimation of the incidence of post CS sepsis.

8.2 Specific risk factors for post CS sepsis

Despite including a large number of women in this study (811 in total), the number of women diagnosed with post CS sepsis was small – only 38 women. Due to this small number, identifying specific risk factors proved difficult, with most factors not reaching statistical significance. However, interesting trends towards significance were identified.

8.2.1 Body Mass Index

Although a raised BMI was not found to be a significant risk factor for post CS sepsis in the index study, it was clear that the prevalence of obesity in the study population was exceptionally high, with only 18% of the study population presenting with a normal BMI at booking for antenatal care. This high prevalence of obesity could explain the lack of statistical significance found in the index study, when compared to studies that include the general population.

8.2.2 Anaemia

Anaemia has commonly been described as an associated factor for the development of post-operative sepsis. However, in the index study anaemia as risk factor did not reach statistical significance. This is likely due to a very low incidence of severe anaemia, with only 3 patients presenting with a Hb below 7g/dL. A study by Malone et al. found pre- and post-operative anaemia to be associated with post-operative sepsis in the general population, however in this study a haematocrit cut-off of <36 was used to define anaemia (31). As

haematocrit is not routinely used to quantify anaemia in our study population, it is difficult to directly compare our findings. It is generally accepted that a Hb of 11g/dL translates to a haematocrit of 33%, however there are exceptions. The study by Malone et al. also did not specify the severity of anaemia in the patients included, which makes comparison difficult.

8.2.3 HIV on HAART

As the national guideline states that all women known with (or newly diagnosed with) HIV in pregnancy should be initiated on HAART at first contact with antenatal care, most of the women in our study received anti-retroviral therapy (96.05%). The remainder of women were diagnosed intra-partum or shortly prior to CS and received PMTCT. As expected, women not initiated on HAART were more susceptible to developing post CS sepsis and were found to be at 5.8 times the risk than women without HIV.

Our results in women living with HIV, but not treated with HAART, echo the findings by Rodriguez et al., in a study done in Atlanta, USA (60). This study found that women with HIV were 2.7 times more likely to present with minor postoperative complications. Complications regarded as minor were fever, surgical site infection, post-partum endometritis and urinary tract infections. A systematic review and meta-analysis by Calvert and Ronsmans also found a close to 6 times increase in risk of puerperal sepsis in HIV infected women who underwent CS, when compared to women without HIV (pooled OR 5.81, 95% CI 2.42–13.97) (61). A large number of studies included in this meta-analysis were from low and middle-income countries and should therefore compare well with our patient population. However, the risk of post CS sepsis in women living with HIV and treated with HAART where found to be similar than those without HIV. When compared to those women not receiving HAART, this clearly demonstrates the benefit of anti-retroviral treatment in preventing infective complications in women with HIV.

We also speculate that other factors might contribute to the relatively low incidence of post CS sepsis in women with HIV on HAART. Firstly, we postulate that health care providers in our setting tend to identify these women as at

increased risk antenatally. This increased vigilance potentially leads to subtle adjustments in patient care, such as earlier initiation of preventative measures, routine post-operative antibiotic treatment and meticulous wound care, which in turn might lead to less sepsis. Secondly, as per departmental protocol, women with HIV do not undergo amniotomy during labour. This eliminates the added risk of a prolonged duration of rupture of membranes. Although not found to be statistically significant in our study, prolonged rupture of membranes has be proven to be an individual risk factors for post CS sepsis, especially endometritis (16,19,20).

8.2.4 Diabetes

In the index study diabetes was not found to be a statistically significant risk factor for post CS sepsis. This is likely due to only 67 women (8.27%) with diabetes included in the study. Schneid-Kofman et al. found that the highest risk of sepsis exists in women with pre-gestational diabetes, but that women with gestational diabetes are also at increased risk (16). The study group acknowledges this proven increased risk, but postulates that diabetes in pregnancy, in our study population, is not one of the major contributors to the burden of post CS sepsis. Great care is taken in the TBH setting to achieve optimal glycaemic control, in order to decrease other risks related to diabetes in pregnancy. The great majority of women have well-controlled diabetes with little, or no target-organ involvement by the time of delivery. This, together with the relatively low numbers included, might explain the lack of statistical significance in this study.

8.2.5 Pre-eclampsia

The risk of post CS sepsis was found to be somewhat higher in women with chronic hypertension and pre-eclampsia, but in comparison with the normotensive women, did not reach statistical significance. This might be attributed to a very high incidence of hypertensive disorders in the study population (47.48% of women). Analysis of the general population will likely yield different results.

8.2.6 Antepartum Infection

Antepartum infection, such as chorioamnionitis has been well established as a significant independent risk factor for post CS sepsis, especially endometritis (20,25). However, the index study did not yield a statistically significant result as only 32 women presented with antepartum infection and of these, only 1 woman also had evidence of sepsis after CS. This could indicate that antenatal infection is not the most significant contributor to sepsis in the TBH setting and that women in this study population rather develop sepsis due to multiple other risk factors, however numbers are too small to draw accurate conclusions.

8.2.7 Preterm Gestation

In the index study, preterm delivery was not found to be associated with post CS sepsis. We postulate that this is due to the high-risk nature of the study population. In the general population, spontaneous preterm delivery is often initiated by an underlying infective process and associated inflammatory response and could therefore be associated with an increased risk of especially endometritis. However, in this study, the indication for pre-term CS delivery was predominantly due to severe maternal illness or fetal compromise, rather than established preterm labour or antepartum infection.

8.2.8 Active labour

A trend towards developing post CS sepsis was identified in women with longer durations of active labour. For the purpose of this study, active labour was defined as the presence of regular uterine contractions and a cervical dilatation of ≥ 4cm with or without rupture of fetal membranes. This definition was chosen as the current National Maternity Care guideline and referral criteria utilize the above definition. An arbitrary duration of 6 hours was chosen to investigate whether longer durations of labour were associated with post CS sepsis. Ghuman et al. found the presence of active labour prior to CS to be an independent risk factor for post CS sepsis (39). The study group acknowledges the previously proven association between active labour and post CS sepsis and postulates that this

was not replicated in the index study for two reasons. Firstly, due to very few women with both active labour and sepsis included (only 9 out of 811 women), it is very difficult to draw accurate statistical conclusions. Secondly, due to the high-risk nature of the study population, a woman without active labour might have numerous other risk factors and therefore develops sepsis due to these other factors.

8.2.9 Surgical duration > 3rd quartile

In the index study, a procedure of longer than 50 minutes represented a surgical duration above the 3rd quartile. For the purpose of this study therefore, all surgical durations of 51 minutes and longer were classified as prolonged. Prolonged procedures resulted in a 3 times increased risk of developing post CS sepsis when compared to procedures less than 28 minutes, or below the 1st quartile. This is in keeping with that quoted by OpØien et al., who found these women at a 2.4 times greater risk (13). In that study however, the 3rd quartile represented a surgical duration of 38 minutes. The study group postulates that the surgical times in the index study were generally longer due to the more complicated nature of the patient profile (raised BMI, multiple previous surgeries etc.). Upon exploration of characteristics of women who had prolonged surgery, we noted a higher incidence of intra-operative complications in these women, as set out in Figure 7.4.1. The most common complications were difficult adhesiolysis, uterine tears and difficult delivery of the baby.

Thirty-nine procedures with a prolonged duration (18.06%) where performed by medical interns, under supervision and were therefore training procedures. OpØien also found that women with both a prolonged procedure and a raised BMI (BMI >30) were at an even increased risk of post CS sepsis. This was not reproduced in the index study.

The acknowledgement that women with prolonged surgical duration are at increased risk raises the question as to possible interventions aimed at reducing sepsis in these women. Some studies have suggested a repeat dose of prophylactic antibiotics in such cases. During the study period no formal

guideline regarding repeat antibiotic doses were in practice. Antibiotic guidelines have since been updated and a repeat dose of cefazolin is now given when surgical duration exceeds 1 hour. This ensures adequate tissue concentrations for the duration of the procedure and therefore potentially reduces the sepsis risk. Therapeutic post-operative antibiotics could also be considered in these patients, especially in women with additional risk factors. Women with anticipated complicated surgery should have a senior surgeon involved from the start of the procedure. Early recognition of intra-operative complications and rapid escalation to care by a senior surgeon is paramount, in order to avoid unnecessarily prolonged surgical durations. Continuous surgical skills training are essential to ensure competent surgical staff.

8.3 Outcomes of women with post CS sepsis

Of the 811 women included in the index study, 38 (4.69%) presented with post CS sepsis. Twenty-eight (73.68%) of these women were discharged and presented to a health care facility with a diagnosis of post CS sepsis within 30 days, while 10 women were diagnosed prior to initial discharge. Interestingly, 24 (82.14%) of the 28 women that presented after discharge from hospital, required re-admission. This is markedly higher than the 1.5% reported by Johnson et al. in the study done at Chris Hani Baragwanath hospital (2). Again, the study group postulates that this is due to the index study's design favouring women with more severe sepsis, who seek medical attention.

Little data is available on the incidence of repeat surgery for sepsis after CS in the South African setting. An audit by Janse van Vuuren published in 2016 investigated the indications for peri-partum hysterectomy at Tygerberg Hospital over a 5-year period. Of the 151 women included in this audit, 123 delivered by CS. Pregnancy related sepsis was identified as the most common indication for peri-partum hysterectomy, resulting in 60 hysterectomies (62). Of these 60 women, 52 (86.7%) delivered by CS and 5 women demised. Direct comparison with the index study is difficult as the audit by Janse van Vuuren also included women delivered at other facilities and later transferred to Tygerberg Hospital. However, this does highlight

the impact of specifically post CS sepsis on the peri-partum hysterectomy rate in the Tygerberg Hospital setting.

In the index study the significant burden of post CS sepsis on maternal morbidity is evident. Of the 38 women identified with post CS sepsis, nine women (23.68%) required admission to the Obstetric Critical Care Unit (Level 2 critical care) or Intensive Care Unit (Level 3 critical care). Supportive interventions included a wide spectrum of care, ranging from detailed observation and invasive monitoring to inotropic support, non-invasive continuous positive airway pressure (CPAP) ventilation as well as airway intubation and ventilation, as set out in Figure 7.5.1 and Appendix A.

Maternal morbidity and related prolonged hospital stay have a significant socioeconomic impact. In the LMIC setting, this places an added burden on the available health resources. The estimated attributable costs (per case) to post CS surgical site infection and post CS endometritis were estimated around $3500 and $3900 respectively in 2010 in the USA (24). When considering the number of deliveries managed and the severity of post CS sepsis in the index setting, the burden is significant.

Maternal morbidity also has a negative impact on the initiation and continuation of breastfeeding, bonding of the mother and baby, maternal psychological wellbeing and adds significant psychosocial stressors to the family and caregivers.

9 STRENGTHS AND LIMITATIONS

This study was the first audit of such scale done on post CS sepsis in the TBH setting. It included a relatively large number of women and was well powered to accurately estimate the post CS sepsis rate. It provided valuable insight to the demographics and known risk factors in this study population.

Firstly, we have to acknowledge that post CS sepsis is multifactorial and that no woman has only one risk factor. The multitude of demographic, medical, surgical and obstetric risk factors at play makes risk stratification complex. The study population is also at higher risk than women in less specialised centres of care (for example Level 1 hospitals) and therefore have very different patient profiles and outcomes.

The study group initially expected to find clear associations between known risk factors (emergency procedures, raised BMI etc.) and post CS sepsis; however this was not the case. This raises awareness that due to the patient profile and multi-factorial aetiology, even women that are usually regarded as “lower risk” (for example non-HIV infected women, women with a normal BMI or elective procedures) are at significant risk of post CS sepsis and that a general increased vigilance in prevention and early detection is essential in all women who are delivered by way of CS.

Secondly, this study highlighted the burden of disease caused by post CS sepsis. Although the cumulative incidence is relatively low, the numbers in this study still suggests that more than 12 women per month (average of 3 women per week) presents to this department with post CS sepsis, two thirds of which require admission to hospital. This adds substantially to the patient burden of the already overwhelmed health care system, as well as significantly influencing the affected women’s quality of life.

This study also found that women from this population often only seek medical care once symptoms become severe. Improved patient education could possibly lead to earlier detection and intervention and therefore a decrease in morbidity due to

sepsis. Areas of intervention that could be considered includes detailed education pre-operatively, highlighting danger signs pre-discharge as well as providing women with a detailed discharge letter explaining the signs of post CS sepsis and advising on routes of access if any symptoms are observed.

Some limitations have to be acknowledged. Due to the retrospective nature of the study design, it relies heavily on accurate note keeping and a number of patients had to be excluded due to inadequate or unavailable notes. Despite the relatively large number of women included, the results yielded a lower than expected post CS sepsis rate. Although this can be interpreted as a reassuring finding, it did lead to a very small number of women with post CS sepsis included. Due to this low number it was difficult to identify individual, statistically significant risk factors specific to this population accurately. The study design also likely favoured women with more severe disease, as indicated by the high hospital admission rate.

10 AREAS FOR FUTURE RESEARCH

A prospective, matched case-control study is advised in order to assess whether trends in this study do reach statistical significance when adequately powered. Qualitative research into patient perception of post CS sepsis, the impact on quality of life as well as barriers to seeking early medical intervention should be undertaken.

11 CONCLUSION

Despite a post-CS sepsis incidence that compares well with high-income countries (4.69% vs. 3.5 – 8.11%), post-CS sepsis remains a significant contributor to maternal morbidity in the South African setting. Risk factors for post-CS sepsis remain multifactorial and in the setting of a referral hospital, all women should be treated as potentially at risk. Optimization of chronic medical conditions, vigilant intra-partum care, meticulous surgical technique and recognition of early signs of post-CS sepsis are essential in order to prevent maternal morbidity. Further prospective research is needed in order to identify specific, individual, modifiable risk factors.

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13 APPENDICES

Appendix A: Description of women requiring OCCU / ICU

Nr	Age	Parity	Indication for CS	Risk Factors	Description
1	24	0	Cephalopelvic disproportion	Pre-eclampsia, BMI 51, active labour	4d OCCU, TAH, 18d inpatient care. Wound care follow-up until 45d post CS
2	22	0	Fetal distress	Pre-eclampsia, ROM	6d OCCU, TAH, Relook laparotomy, 12d inpatient care.
3	39	2	Placenta praevia with APH	BMI 47, smoker	4d OCCU, wound debridement, developed pulmonary embolism, 13d inpatient care
4	35	2	Breech presentation, twins	HIV, active labour	4d OCCU, TAH, wound exploration, massive blood transfusion, 17d inpatient care.
5	22	0	Cephalopelvic disproportion	BMI 35, Pre-eclampsia, active labour	4d ICU, TAH, Relook laparotomy, inotropic support. 38d inpatient care
6	21	0	Failed assisted delivery	Prolonged ROM	3d OCCU, 6d inpatient care
7	40	4	Fetal distress due to abruptio placenta	Smoker, CHT,	7d ICU, inotropic support, TAH, acute kidney injury, 4x wound debridement and finally skin graft. 28d inpatient care.
8	20	0	Fetal Distress	Pre-eclampsia with HELLP syndrome	4d OCCU, re-look laparotomy, wound debridement, acute kidney injury, 15d inpatient care
9	22	0	Cephalopelvic disproportion	Pre-eclampsia, Active labour	3d OCCU, 7d inpatient care