

**Determination of C-Reactive Protein Levels in Blood of
Post Caesarean Section Mothers at the University
Teaching Hospital, Lusaka**

By

Emmelia Chileshe

**A Dissertation Submitted to the University of Zambia in Partial Fulfillment of the
Requirement for the Degree of Master of Science in Biochemistry**

**University of Zambia
Lusaka**

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Declaration

I, Emmelia Chileshe, declare that this dissertation is my own work and that all the sources I have cited have indicated and acknowledged using complete references. I further declare that this dissertation has not been previously submitted for any other qualification at this or any other university nor is it being currently submitted for any other degree.

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Certificate of Approval

Dissertation Title: Determination of C - reactive Protein Levels in Blood of Post
Caesarean Section Mothers at the University Teaching Hospital, Lusaka

This dissertation for Emmelia Chileshe has been approved in partial fulfillment of the
Requirements for the award of the Master of Science degree in Biochemistry by the
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Examiner I: Signature.....

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Examiner II: Signature.....

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Abstract

Caesarean section, an obstetric abdominal operation which allows for the delivery of an infant from the uterus poses a risk of infection to women. Most of these cases have been reported in developing countries such as Zambia. Patient records at the University Teaching Hospital in Lusaka show a high number of admissions related to infections associated with Caesarean sections. However, the prevalence of these infections at the hospital is unknown. Most of these infections are usually grouped together with other post-partum infections. Nowadays, most mothers undergoing Caesarean sections are discharged early. An early predictor of septic complications could avoid readmissions, decrease morbidity and allowing safe discharge. Estimation of C-reactive protein levels in blood samples may help in detecting infection in the affected mothers. C-reactive protein is an acute phase protein synthesised by hepatocytes in response to inflammation. The objective of the study was to determine levels of C-reactive protein in blood in post Caesarean section women on the 2nd and 4th day at the University Teaching Hospital.

A cross sectional study was conducted on 240 participants after undergoing Caesarean section. Blood samples from the participants were collected on the 2nd and 4th days post-operatively. The samples were examined on the ABX Pentras 400 Clinical Chemistry Analyser in the Chemistry Laboratory at the University Teaching Hospital. The C-reactive protein levels were dichotomised into below 100mg/l as normal and above 100mg/l as abnormal. The relationship between the means of C-reactive protein values on postoperative day 2 and day 4 were analysed using the Paired t-test. In order to determine the factors that may be associated with C-reactive protein elevation, the Chi squared test and/or Fishers' exact test were used and a p -value of ≤ 0.05 was considered statistically significant.

This study revealed that on both day 2 and 4 the majority of women (155, 64.6% on day 2 and 156, 65% on day 4) had high C-reactive protein levels (>100 mg/L), with the highest recorded abnormal C-reactive protein level being 409mg/l (paired t test; $p=0.000$). In this case, there was no difference in the levels of CRP on both postoperative days; both days had abnormal CRP levels. This may mean that CRP levels are more sensitive to trauma or inflammation thereby rising faster than anticipated, leading to high levels at day 2. The factors (Age, Marital Status, Parity, HIV Status, CD₄ Count, Prenatal HIV Management, Pre-existing medical conditions, Type of C-section, Prophylactic antibiotics, C-section complications) under consideration were not significantly associated with CRP levels on both post operative days ($p>0.05$; Chi-square test). However most of the factors showed high levels of abnormal CRP levels on both postoperative days. Even though, a cut-off value > 100 mg/L may indicate infection, an elevated C-reactive protein on day 2 does not in itself imply infection, but a later rise after day 3 suggests the possibility of infection. Therefore, discharging C-section mothers early on the 4th day postoperatively, requires a check of CRP, which is a good predictor of septic complications allowing a safe discharge, and reduce readmissions. This aspect of the CRP profile can also alert the surgeon of possible septic complications.

Dedication

This work is dedicated to my husband, Bright Kaonga, and my three children – Shupiwe, Towela and Wezi. It is also dedicated to all mothers that delivered by C-section in Zambia during the period of the study.

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List of Abbreviations

ANC	Antenatal Care
APP	Acute Phase Protein
APR	Acute Phase Response
BREC	Biomedical Research Ethics Committee
CD ₄	cluster of differentiation 4
CI	Confidence Interval
CRP	C - reactive protein
C-section	Caesarean Section
DA	Dalton
EDTA	Ethylenediamine Tetraacetic Acid
ESR	Erythrocyte Sedimentation Rate
FC	Fragment Crystallizer
HIV	Human Immunodeficiency Virus
IFCC	International Federation of Clinical Chemistry
MEPI	Medical Education Program Initiative
MSC	Master of Science
NHS	National Health System
PGA	Polyglycolic acid
PGF	Post Graduate Forum
PID	Pelvic Inflammatory Disease
REC	Research Ethics Committee
SACORE	Southern Africa Consortium for Research Excellence
SDF	Staff Development Fellowship
UNZA	University of Zambia
UTH	University Teaching Hospital
WBC	White Blood Cells
WHO	World Health Organization

Chapter 1: Introduction

1.1 Background

Caesarean section (C-section) predisposes women to infections and the majority of cases seem to involve uterine infections arising from vaginal normal flora contamination of the lower uterine segment before or during the operation (Nisula *et al*, 2003). C-section involves making an incision in the abdomen to allow for the delivery of an infant from the uterus (McGee, 2010). Although it is performed under sterile conditions, there is still a risk for infection (Marie, 2012). Infected incisions are the most common cause of sepsis after caesarean section and in some cases, the infection may spread, causing internal tissues becoming infected. If the kidneys or urinary tracts are involved, it may result in urinary tract infection and lead to septicaemia (Cloe, 2011).

Postpartum infections following C-section are a common risk factor for maternal morbidity (Mitt *et al*, 2005; Rauk, 2005). Maternal morbidity related to infections has been shown to be eight-fold higher after C-section than after vaginal delivery (Mitt *et al*, 2005). Maternal morbidity refers to complications that have arisen during the pregnancy, delivery or postpartum period and that every year an estimated 50 million women are affected by maternal morbidity (Vallely *et al*, 2005). Some patients with an internal infection may complicate to septicemia which is as a result of bacterial infection that spreads into the bloodstream and consequently stimulate the release of C-reactive protein (CRP), a systemic marker of infection, in the body (Nisula *et al*, 2003). If infection is a risk factor for maternal complications following C-section, CRP may help detect infection early before manifestation of clinical features (Thompson *et al*, 2010). CRP concentration increases in the blood within a few hours after the onset of infection or other inflammatory injury (Makover, 2011). Infections cause the release of chemical substances such as interleukin-6, an acute-phase inflammatory cytokine, and other cytokines that ultimately

trigger the synthesis of CRP (White *et al*, 1998). These chemical substances rapidly increase the concentration of CRP within 2 to 6 hours of an acute infection or surgery, reaching a peak at 48 hours and decrease by the third day after surgery (White *et al*, 1998). If CRP levels remain elevated 3 days after surgery, this may be indicative of an infection from surgery (Chaudhary *et al*, 2007; Michel *et al*, 2011).

1.1. Statement of the Problem

The single most important risk factor for postpartum infection is delivery by C-section and that maternal morbidity related to infections has been shown to be eight-fold higher after C-section than after vaginal delivery (Mitt *et al*, 2005). Several studies have shown that there is a risk for C-section infection and this can lead to maternal mortality (Emely, 2009). Most of these cases have been reported in developing countries such as Zambia.

The University Teaching Hospital (UTH) records show a high number of post C-section admissions and this is attributed to a number of factors, one of them being post C-section infection (Gynaecology and Obstetrics Register, 2011). However, the prevalence of C-section infection at the UTH is unknown. Cases of C-section infection are usually grouped together with other post-partum infections such as puerperal sepsis and pelvic inflammatory diseases (PID). Among these infections, C-section infections are of great concern and are considered major causes of morbidity among childbearing women.

1.2. Justification of the Study

The standard of care for every C-section (elective or emergency) includes the use of prophylactic antibiotics, skin disinfection, and the use of appropriate surgical techniques, post-operative care and adequate surgical nursing care (UTH C-section protocol, 2012). Despite the above precautions, infections still occur and are diagnosed based on various criteria such as elevated temperature, Erythrocyte Sedimentation Rate (ESR) and White

Blood Cell (WBC) levels. Early detection of infection in post C-section mothers could help in avoiding readmissions and reducing maternal morbidity. As an early predictor of infection, CRP can facilitate safe discharge of the post C-section woman from hospital as it is a sensitive and accurate reflection of the acute phase response (APR) marker to infection (Meyer *et al*, 2007). This study will provide baseline data that will contribute to the effective control methods in the management of post C-section infections and the formulation of the preventive strategies, avoidance of unnecessary exposure to antibiotics, as well as reduced prolonged hospital stay, as the women will be screened for CRP as an indicator for infection before discharge.

1.4 Literature Review

1.4.1. Description of CRP

CRP is an acute phase protein (APP) which reflects a measure of the acute phase response (APR) (Terik *et al*, 2002). It is synthesised by hepatocytes in response to factors released by adipocytes and is classified as an APP on the basis of elevated plasma concentration during infection and inflammation (Ramamoorthy *et al*, 2012). Acute phase is a local and systemic event that accompanies inflammatory local response, which includes vasodilatation, platelet aggregation, neutrophil chemotaxis, and release of lysosomal enzymes (Husain and Kim, 2002). Systemic responses include fever, leukocytosis, and a change in the hepatic synthesis of APP (Terik *et al*, 2002). An APP is one whose plasma concentration increases (positive APP) or decreases (negative APP) by at least 25% during inflammatory disorders (Skovgaard *et al*, 2009).

CRP is a member of the pentraxin family, comprising five identical subunits of non-glycosylated polypeptide of proteins which is a ligand to the leukocyte Fc γ receptors, and its gene is located on the chromosome 1 (1q21-q23). It is a 224-residue protein with a monomer molar mass of 25106 Da (Clyne *et al*, 1999). CRP binds to phospholipids on damaged cells and is easily recognised by phagocytic cells (Husain and Kim, 2002). In this respect, CRP is an important component of the innate immune response.

CRP test is not specific enough to either diagnose a particular disease or show where the inflammation is located (Thompson *et al*, 2010), it is rather a general marker of infection and inflammation that alerts medical professionals that further testing and treatment may be necessary. Moreover, it is a direct and quantitative measure of the acute phase reaction and its serial measurements can be used as a diagnostic tool for infection, monitoring effect of treatment, or early detection of relapse (Husain and Kim, 2002). Plasma levels of CRP in most healthy subjects is usually between 0 -1.0 mg/L, with the normal

concentration being defined as being <10 mg/L and remains elevated during the APR, only returns to normal with the restoration of tissue structure and function (Ramamoorthy *et al*, 2012). It is often the first evidence of inflammation or an infection in the body (Terik *et al*, 2002). An APR concentration increase can vary from approximately 50 to 1000-fold or more for CRP and occur in association with a wide variety of disorders, including infection, trauma, infarction and inflammatory arthritis (Kushner, 2012). An increased concentration of CRP is not only detectable during inflammation and infection, but also during late pregnancy, or in old age, which has a slight increase of 10mg/L (Clyne *et al*, 1999). Mild inflammation and viral infections have been shown to have high levels of CRP (10–40 mg/L), while active inflammation, severe bacterial infection and burns are responsible for higher CRP concentration (>200 mg/L) (Clyne *et al*, 1999). Furthermore, CRP levels in patients with Human Immunodeficiency Virus (HIV) infection have also been demonstrated to be high, although the relationship between CRP concentration and HIV infection is unclear (Triant *et al*, 2009).

A prospective, observational study conducted at the Dijon Hospital in France revealed that CRP at post-operative days 2 and 4 was a good predictor of septic complications. A cut-off of 125 mg/l in the level of CRP at post-operative day 4 yielded a sensitivity of 81.8% and a negative predictive value of 95.8% for the detection of septic complication (Deballon *et al*, 2010). Therefore, CRP ensures safe discharge from hospital after elective surgery and patients with CRP values higher than 125 mg/l on the 4th postoperative day should not be discharged and that patients with lower values than 125 mg/l can safely be discharged from hospital. According to these results, CRP may detect more than 80% of septic complications (Deballon *et al*, 2010)

An Increase in CRP levels constitutes an easy and cheap prognostic alert system and may be used to establish strategies aimed at detecting infection of post-surgical infections (Baez *et al*, 2011). However, a study conducted in England by Cole *et al* (2008), demonstrated that using CRP as a prognostic tool of infection in the first three days of operation may complicate assessment of the presence of infection. This is because trauma of surgery causes CRP level to rise and thus confound results and make interpretation challenging. Therefore, CRP levels should be checked after the 3rd postoperative days if it is to be used for screening for infection. This was confirmed by studies conducted by Coulter (2003) in the United States of America (USA), which also demonstrated that patients undergoing various surgical procedures show increased serum CRP levels within four to six hours after surgery, reaching a peak value between 25 mg/L to 35 mg/L in 48 to 72 hours. However, rising CRP levels from 10 – 40mg/L after the second to third postoperatively day may indicate infection (Coulter, 2003).

The diagnosis of anastomotic leakage was made between the 4th and 11th post-operative day (n=173) in Portugal. The daily average values of serum CRP were significantly higher, starting at the second postoperative day and remained significantly elevated until the diagnosis of leakage (P = 0.003). The cut-off value of 140 mg/L on the third post-operative day maximised the sensitivity (78%) and specificity (86%) of serum CRP in assessing the risk of complication (Almeida, 2012).

With most active infections and inflammatory processes, CRP levels are above 100 mg/L (Weils, 2014) and declining CRP levels are a sign that inflammation is decreasing. A study done by Takahashi *et al*, (2001) in the united Kingdom demonstrated no correlation among CRP and age, gender, body temperature, operating time and blood loss in 52% of the patients who underwent surgery, had elevated CRP 14 days later, although they were not infected. The CRP levels was assessed in 119 HIV positive patients were CRP was

correlated with CD₄ counts; this revealed that CRP was not correlated with CD₄ counts, but levels of CRP was highest in the group with CD4 counts below 200 cells/ μ l (Chaudhary *et al*, (2008).

1.4.2. Post-Caesarian Infection

A prospective multicentre cohort study to assess the frequency and risk factors associated with surgical site infection following C-section in 14 National Health Service hospitals in England in 2009, revealed about 9.6% (394/4107) of women in the study developed a postsurgical infection following C-section, with 5.8% (23/4107) of the women being so severe that they had to be re-admitted for treatment to hospital (Wloch *et al*, 2012). In another pilot study conducted in 11 maternity units in the United Kingdom, revealed that out of 5,563 women, 758 (13.6%) developed surgical site infection, 84% of which developed after discharge (Ward *et al*, 2008). Similarly, in a study to determine post-partum surgical wound infections after C-section in an Italian hospital, results showed that out of 430 mothers studied, a total of 20 (4.7%) had surgical site infection. Through post-discharge surveillance, this study indicated 85% of infections (Charrier *et al*, 2009). Wloch *et al* (2012) also found that C-section results in infections for one in ten women with many readmitted in hospital for treatment. In another study to determine the incidence and risk factors of puerperal morbidity in women who delivered by C-section at Srinagarind Hospital in Thailand, it was shown that the incidence of post-C-section puerperal morbidity in 506 patients was 5.5 per cent and that 6.5% was in patients who did not receive antibiotics (Pothinam, 1992). It was found that the common causes of puerperal morbidity included endomyometritis (35.7%), wound infection (25.0%), urinary tract infection (10.7%) and unknown causes (28.6%).

In a South African study on surgical site infection surveillance following C-section revealed that most wound infections 637/758 (84%) occurred at home after discharge from

hospital (Chunder, 2012), Sixty-four (84%) of the 76 wound infections occurred following discharge from hospital. This was despite the standard practice to prescribe prophylactic antibiotics at the time of C-section was followed and patients given information regarding wound care. Kamau (2005) in Kenya also found that the overall post-C-section wound infection rate (19%) was quite high. This was attributed to prolonged pre-operative duration of labour, prolonged rupture of membranes and long duration of operation are associated with significantly higher incidence of wound infection. Interestingly, in a Nigerian hospital-based survey, it was reported that C-section wound infections were major causes of prolonged hospital stay, high hospital bills, as well as other morbidities and mortality, since recovery from C- section is more difficult for women who develop postoperative wound infection. Rates of postoperative wound infection varied from 0 to 20.5% (Ezechi *et al*, 2009).

A study conducted at the University Teaching Hospital in Lusaka showed that puerperal sepsis and malaria were the leading direct and indirect causes of postpartum morbidity requiring hospital admission. Puerperal sepsis accounted for 34.8% of 365 postpartum admissions in the 6-month period (Valley *et al*, 2005). Malaria and pneumonia, together, accounted for one-fifth of all postpartum admissions (14.5% and 6%, respectively) (Valley *et al*, 2005). According to the Obstetrics and Gynaecology Register at the UTH (records accessed 2011), women are typically discharged from post-natal wards on the 4th day after C-section (Obstetrics register, 2013). Some women usually go back for review with infected wounds and are re-admitted to Gynaecology wards for investigation and treatment. It is assumed that either the woman acquired the infection from the hospital before discharge or after discharge while at home.

Data from most studies seem to suggest that CRP is an acute phase protein (APP) which reflects a measure of the acute phase response. Therefore, if CRP is to be used for

screening for infection, levels should be checked on the 4th and 5th postoperative days because patients undergoing various surgical procedures show increased serum CRP levels within four to six hours after surgery, reaching a peak value between 25 mg/L to 35 mg/L in 48 to 72 hours. However, a rising CRP levels above 100 mg/L after the second to third postoperatively day may indicate infection and declining CRP levels are a sign that inflammation is decreasing (Coulter, 2003). Therefore, using CRP as an indicator of infection before discharge in posts C-section mothers would ensure safe discharge from hospital after surgery. No study has been conducted in Zambia to determine levels of C-reactive protein in post C-section mothers and this study is the first to determine CRP levels in blood of post C-section mothers in the country.

1.5. Research Question

Are CRP levels elevated in post C-section infection at day 4 postoperatively at the UTH?

1.6. General Objective

To determine CRP levels in blood of post C-section women on the 2nd and 4th day at the UTH in Lusaka.

1.6.1. Specific Objectives

1. To determine levels of CRP in blood on the 2nd and 4th days post-operatively
2. To establish the association between CRP levels on day 2 and CRP levels on day4
3. To determine socio-demographic, pre-operative (antenatal), and post-operative factors associated with increased levels of CRP in post caesarean section women.

Chapter 2: Methods and Materials

2.1. Study Design

This was an in-patient cross-sectional study in which CRP levels were assessed on days two and four post operatively.

2.2. Study Setting

The study was conducted at the UTH, Lusaka, in all four postnatal wards. There are only two public facilities in Lusaka that do caesarean deliveries: UTH and Levy Mwanawasa General Hospital. The UTH site was selected purposively because of the large numbers of operative deliveries conducted (approximately 293 per month; UTH C-section register, 2012).

2.3. Target and Study Population

The target population included all women that underwent a caesarean section during the two months of the study (25th December 2013 to 25th February 2014). The study population included those women that met the inclusion and exclusion criteria.

2.3.1. Inclusion Criteria

- Emergency or Elective caesarean section
- All 2nd and 4th day post C-section inpatient participants at UTH who consented to the study during the study period.
- Reproductive age group

2.3.2. Exclusion Criteria

- Participants who did not provide consent to participate in the study.
- Those women that did not have a C-section.
- Those less than reproductive ages.

2.4. Sampling Frame and sampling method

Convenience sampling was used, as all post C-section clients were targeted in the study. According to a preliminary review of C- sections at the UTH, approximately 586 C-sections are conducted per 2 months (UTH Register, 2012). Post C-section women were identified and recruited consecutively for a period of two months from 25th December 2013 to 25th February 2014.

2.4.1. Sample size

The sample size was 240 women who had undergone C- section during the two months of data collection. On average UTH attends to 20 and or more C-section mothers each day. Conveniently, four mothers that met the criteria were selected from postnatal wards for two months of the study period.

2.5. Research Variables

2.5.1. Dependent Variable

C –Reactive Protein level

2.5.2. Independent Variables

Age, Marital status, Parity, HIV Status, CD4 cell count, antenatal HIV management, indication for Caesarean section, C-section type, Existing medical condition, prophylactic medication and post-operative complications

2.6. Determination of CRP levels

Blood samples were collected on the 2nd and 4th day post-operatively for CRP testing. The day 2 CRP was checked to act as a baseline data, as this is an acute phase period where CRP is expected to be elevated soon after C-section. The CRP on day 4 was to check whether it had declined to normal levels or was elevated. The blood was collected by drawing 4mls from a vein using a needle and syringe by the health care practitioner who

was a midwife. Once the blood was collected, it was transferred into an EDTA specimen container, labelled with a study number and immediately sent to the laboratory for analysis. In the laboratory, blood samples were centrifuged for 3 minutes at 3000 rpm in a CLIO IEC centrifuge (Thermo Electron Industries, Chateau-Gontier, France). After centrifugation, plasma was transferred into a sterile plain container and stored at 4°C before being analysed for CRP. CRP was measured by an Immuno-turbidimetric test on the ABX Pentra 400 Automated Clinical Chemistry Analyser (HORIBA ABX SAS, Montpellier, France) following the manufacturer's instructions. Before carrying out the test, controls were used for internal quality control. Each control was assayed daily, and after each calibration according UTH Clinical Chemistry Laboratory protocols.

2.7. Establishment of the Association between CRP levels on Day 2 and Day 4

The SPSS software package data set of CRP levels using the Paired t-test was used to determine the relationship between the means of CRP values on postoperative day 2 and day 4. CRP day 2 was checked to act as a baseline data, as this is an acute phase period where CRP is expected to be elevated as a result of inflammation from surgery and for CRP day 4 was to check if they decline to normal levels or increased.

2.8. Data collection of Socio-demographic, Pre-operative (antenatal), and Post-operative variables

All consenting (240) consecutive post C-section mothers were recruited into the study in December, 2013 and interviewed to obtain socio-demographic data and health information such as HIV status, CD₄ cell count and indication for Caesarean section, existing medical condition, prophylactic medication and post-operative complications. The data was collected on an abstraction form to follow as shown on in Appendix III.

2.9. Data Analysis

Following the data abstraction form, data was double checked for completeness, consistency, legibility and accuracy daily. Numerical codes were used and the flaws were corrected. The data was analyzed by the IBM SPSS Statistical package Version 20.0 for Windows Version (IBM Corp. Armonk, North Castle, Westchester County, NY, USA). The CRP levels were dichotomised into below ($\leq$) and above ($>$) 100mg/l as normal and abnormal respectively. The relationship between the means of CRP values on postoperative day 2 and day 4 were analyzed using the Paired t-test. In order to determine the factors (Age, Marital status, Parity, HIV Status, CD4 cell count, antenatal HIV management, indication for Caesarean section, C-section type, Existing medical condition, prophylactic medication and post-operative complications) that may be predictors to CRP elevation, Chi square test and/or Fishers' exact test (if cell values were less than 5) were used. A p-value of ≤ 0.05 was considered statistically significant.

2.10 Ethical Considerations

The approval to carry out the study was obtained from the University of Zambia Biomedical Research Ethics Committee (UNZABREC) (ref No. 011-03-13). Permission to conduct the study was obtained from the Senior Medical Superintendent of the UTH and the Head of the Department of Obstetrics and Gynaecology. There was very minimal interference to the participants beyond the general standard of clinical care offered by UTH. As such, participants were only followed up at day 2 and 4 postoperatively. Written informed consent was obtained from all participants. In terms of the protection of human subjects, all measures were taken to ensure strict confidentiality. This was possible through training of the research assistants by emphasising on confidentiality. In addition, each participant was assigned a confidential study number, which was used by the staff when collecting and reporting information. There were no names on the data collection instruments.

Chapter 3: Results

This chapter presents results that firstly indicate the levels of CRP in blood on the 2nd and 4th days post-operatively and secondly the results show the association between CRP levels on day 2 and CRP levels on day 4. Lastly, the results showing the Socio-demographic, pre-operative (antenatal), and post-operative factors associated with increased levels of CRP in post caesarean section women.

3.1. Determination of the Levels of CRP on Day 2 and Day 4

3.1.1. Socio-Demographic Characteristics of Participants

Table 3.1: Socio-Demographic Characteristics of Participants (n=240)

Variable	Frequency	Percentage
Age		
< 24	77	32.1
25-35	144	60.0
>35	19	7.9
Total	240	100.0
Marital status		
Unmarried	23	9.6
Married	217	90.4
Total	240	100.0
Parity		
Para 1	78	32.5
Para 2-4	133	55.4
Para 5 and more	29	12.1
Total	240	100.0

These results above below shows that the majority of the participants 144 (60%) were aged between 25 and 35 year s and that most of them were married 217 (90.4%). One hundred and thirty-three (55.4%) had children in the range of 2-4, while 29 (12.1%) had more than 5 children (Table 3.1)

3.1.2: Review Medical Records (HIV Status, CD4 count, pre HIV management) of the participants

In Figure 3.1A below shows that the majority of the participants that had under gone C-section were HIV negative (182, 75.8%), and only 58 (24.2%) were positive (figure 3.1).

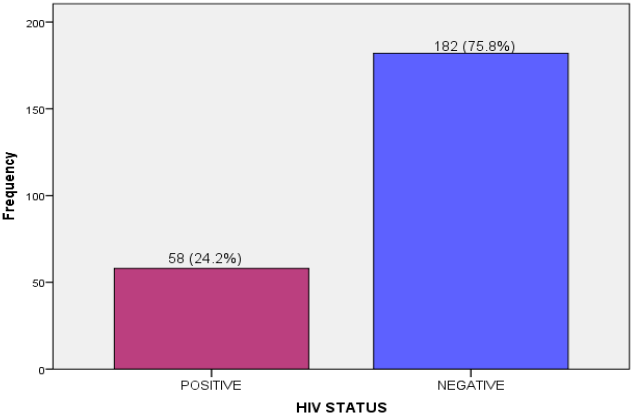


Figure 3.1: A: Frequency of participants HIV Status

3.1.3: participants' CD₄ count

Among the HIV positive participants 53 (22.1%) had their CD₄ > 200cells/μl and 4 (1.7%) had < 200cells/μl (Figure 3.2).

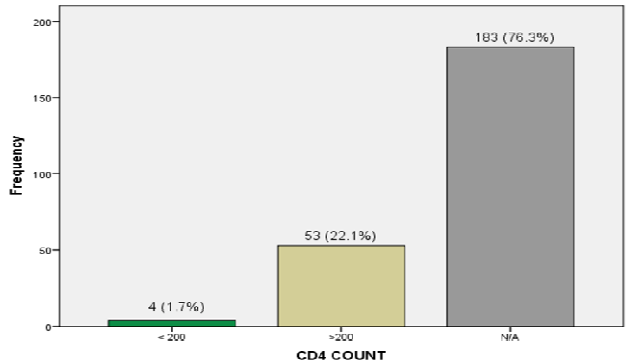


Figure 3.2: Frequency of participants CD₄ count

3.1.4: Participants by Pre HIV Management.

Among the participants that were HIV positive (58, 24.2%) only 14 (5.8%) were on active HAART management and only 10 (4.2%) were on short course ARV therapy Figure 3.3

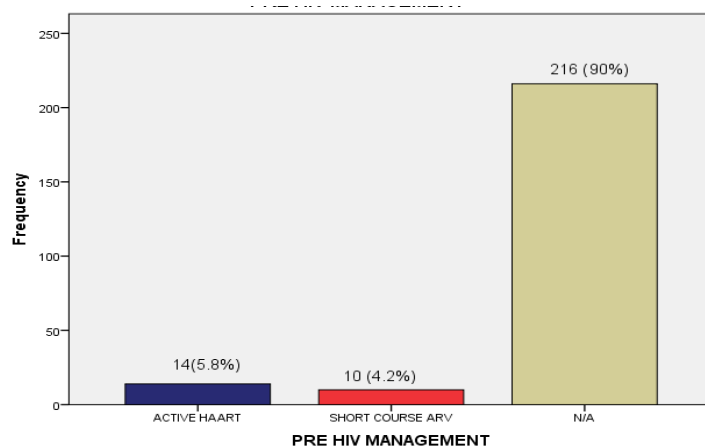


Figure 3.3: Frequency of participants by Pre HIV Management.

3.1.3. Review of antenatal and postnatal factors of participants

Table 3.2: Review of antenatal and postnatal factors of participants (n=240)

Variable	Frequency	Percent
Preexisting medical		
Hypertension	15	6.3
N/A	225	93.8
C-section		
Emergency	203	84.6
Elective	37	15.4
Antibiotics		
Yes	8	3.3
No	232	96.7
C-Section Complications		
Febrile Illness	1	0.4
N/A	239	99.6

Most of the participants (225, 93.8%) were reported not to have any pre-existing medical condition, while only 15 (6.3%) had hypertension and most (203, 84.6%) of the participants had emergency C-Section (Table 3.2). Thirty-seven (15.4%) participants had

elective C-Section. Only 8 (3.3%) had received prophylactic antibiotics, while the rest (232, 96.7%) did not receive any antibiotics. Of all the participants, only 1 (0.4%) was reported to have had a C-section complication (febrile condition) (Table 3.2).

3.1.4: CRP levels of participants on Day 2 and Day 4 post operatively

One hundred and fifty-five (64.6%) participants had day 2 CRP levels above 100mg/l (abnormal), while 85(35.4%) had levels below 100mg/l (Normal) (Figure 3.4).

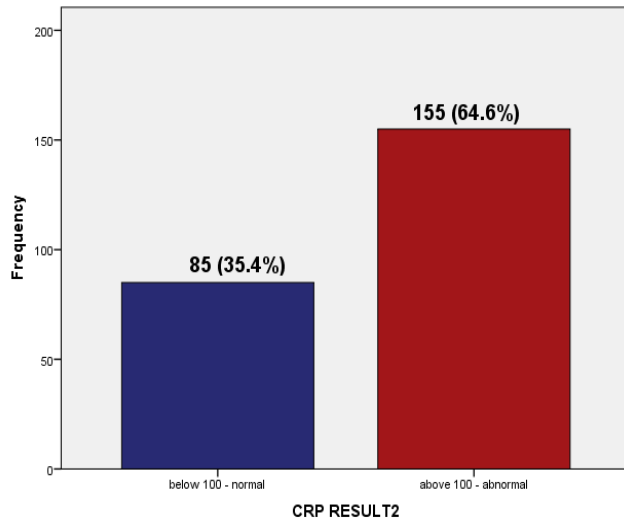


Figure 3.4: CRP levels of participants on Day 2 post operatively

3.1.5: CRP levels of participants on Day 4 post operatively (n=240)

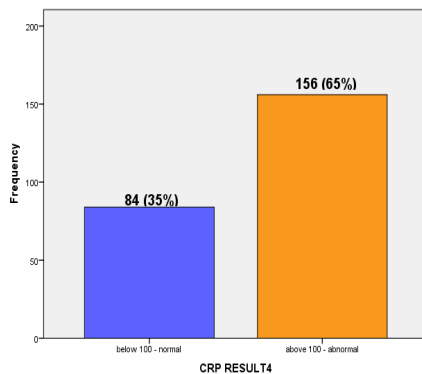


Figure 3.5: CRP levels of participants on Day 4 post operatively (n=240)

3.2. Association between CRP levels on Day 2 and Day 4

The highest CRP value on day 2 was 409 mg/L and 373 mg/l on day 4 postoperatively. The lowest values were, 21mg/l and 10mg/l on days 2 and 4 respectively. Although there was a slight reduction in the means of CRP values on day 2 compared to day 4 (130.0 compared to 127.3), this was highly significant. A day 2 CRP was highly correlated with a day 4 CRP ($r=0.430$, $p<0.001$) (Table 3. 3).

Table 3.3: Determining the association of CRP mean for both postoperative day 2 and 4 (n=240)

Variable	Maximum No (mg/l)	Minimum No (mg/l)	Mean	p-value	Correlation (r)
CRP TEST RESULT 2	409	21	130.0		
CRP TEST RESULT 4	373	10	127.3	0.001	0.430

3.3. Comparison of Socio-demographic, Pre-operative (antenatal), and Post-operative Factors Associated with Levels of CRP

For both day 2 and day 4 the various socio-demographic, medical and operative variables are presented stratified by whether the CRP was $<100\text{mg/L}$ or $>100\text{mg/L}$ (Table 3.4 and Table 3.5 respectively). A comparison was made of categories within each variable (Chi-square or Fisher exact test if cell values were <5) and none of the demographic or clinical factors were associated with a high or low level - all p values were less than 0.05.

A multiple regression model was not created as no factor could be placed in the model as none had a p-value <0.2 which could be considered a cut-off for consideration of a factor as a potential confounder.

Table 3.4: Comparison of Socio-demographic, Pre and post-operative factors with CRP on day 2 (N=240)

Variable	Sub variable	Day 2 CRP levels		*P-Value	Totals (N=240)
		CRP < 100 (%) n=85	CRP > 100 (%) n=155		
^a Age (yrs)	< 24	28 (32.9%)	49 (31.6%)	0.977	77 (32.1%)
	25-35	50 (58.8%)	94 (60.6%)		144 (60.0%)
	> 35	7 (8.2%)	12 (7.7%)		19 (7.9%)
^a Marital Status	Married	76 (89.4%)	141 (91.0%)	0.819	217 (90.4%)
	Not Married	9 (10.6%)	14 (9.0%)		23 (9.6%)
^a Parity	Para1	26 (30.6%)	52 (33.5%)	0.720	78 (32.5%)
	Para 2 – 4	50 (58.8%)	83 (53.5%)		3 (5.4)
	>Para5	9 (10.6%)	20 (23.5%)		29 (12.1%)
^a HIV Status	negative	65 (76.5%)	117 (75.5%)	0.877	182 (75.8%)
	positive	20 (23.5%)	38 (24.5%)		58 (24.2%)
^b CD ₄ Count	< 200	1 (1.2%)	3 (1.9%)	0.856	4 (1.7%)
	> 200	17 (20%)	36 (23.2%)		53 (22.1%)
	N/A	67 (78.8%)	116 (74.8%)		183 (76.2%)
^b Prenatal HIV Mgt	HAART	5 (5.9%)	9 (5.8%)	1.000	14 (5.8%)
	Short ARVs	3 (3.5%)	7 (4.5%)		10 (4.2%)
	N/A	77 (90.6%)	139 (89.7%)		216 (90.0%)
^a Pre-existing conditions	D. M.	0 (0.0%)	0 (0.0%)	0.583	0 (0.0%)
	Hypertension	4 (4.7%)	11 (7.1%)		15 (6.2%)
	N/A	81 (95.3%)	144 (92.9%)		225 (93.8%)
^a Type of C-section	Emergency	71 (83.5%)	132 (85.1%)	0.852	203 (84.6%)
	Elective	14 (16.5%)	23 (14.8%)		37 (15.4%)
^b Prophylaxis	Yes	4 (4.7%)	4 (2.6%)	0.459	8 (3.3%)
	No	81 (95.3%)	151 (97.4%)		232 (96.7%)
^b C-section Complications	Febrile illness	0 (0.0%)	1 (0.6%)	1.000	1 (0.4%)
	Septic wound	0 (0.0%)	0 (0.0%)		0 (0.0%)
	N/A	85 (100%)	154 (99.4%)		239 (99.6%)

^aPearson's Chi-Squared Test (2-sided), ^bFisher's Exact Test (2-sided), *Indicates significant *p*-value at *p* ≤ 0.05.

Table 3.5: Comparison of Socio-demographic, Pre and post-operative factors with CRP on day 4

Variable	Sub variable	Day 4 CRP Levels		*P-value	Totals N=240
		< 100 (%) n=84	> 100 (%) n=156		
^a Age (yrs)	< 24	26 (31%)	51 (32.7%)	0.812	77 (32.1%)
	25-35	50 (59.5%)	94 (60.3%)		144 (60.0%)
	> 35	8 (9.5%)	11 (7.1%)		19 (7.9%)
^a Marital Status	Married	78 (92.9%)	139 (89.1%)	0.372	217 (90.4%)
	Not Married	6 (7.1%)	17 (10.9%)		23 (9.6%)
^a Parity	Para1	23 (27.4%)	55 (35.2%)	0.314	78 (32.5%)
	Para 2 – 4	48 (57.1%)	85 (54.5%)		135 (56.4%)
	>Para5	13 (15.5%)	16 (10.3%)		29 (12.1%)
^a HIV Status	negative	66 (78.6%)	116 (74.4%)	0.529	182 (75.8%)
	positive	18 (21.4%)	40 (25.6%)		58 (24.2%)
^b CD ₄ Count	1. < 200	1 (1.2%)	3 (1.9%)	0.950	4 (1.7%)
	> 200	18 (21.4%)	35 (22.4%)		53 (22.1%)
	N/A	65 (77.4%)	118 (75.6%)		183 (76.2%)
^b Prenatal HIV Mgt	HAART	7 (8.3%)	7 (4.5%)	0.329	14 (5.8%)
	Short ARVs	2 (2.4%)	8 (5.1%)		10 (4.2%)
	N/A	75 (89.3%)	141 (90.4%)		216 (90.0%)
^a Pre-l conditions	D. M.	0 (0.0%)	0 (0.0%)	0.585	0 (0.0%)
	Hypertension	4 (4.8%)	11 (7.1%)		15 (6.2%)
	N/A	80 (95.2%)	145 (92.9%)		225 (93.8%)
^a Type of C-section	Emergency	70 (83.3%)	133 (85.3%)	0.710	203 (84.6%)
	Elective	14 (16.7%)	23 (14.7%)		37 (15.4%)
^b Prophylactic antibiotics	Yes	3 (3.6%)	5 (3.2%)	1.000	8 (3.3%)
	No	81 (96.4%)	151 (96.8%)		232 (96.7%)
^b C-section Complic	Febrile illness	0 (0.0%)	1 (0.6%)	1.000	1 (0.4%)
	Septic wound	0 (0.0%)	0 (0.0%)		0 (0.0%)
	N/A	84 (100%)	155 (99.4%)		239 (99.6%)

^aPearson's Chi-Squared Test (2-sided), ^bFisher's Exact Test (2-sided), *Indicates significant *p*-value at *p* ≤ 0.05.

Chapter 4: Discussion and Conclusion

4.1. Discussion

Of the 240 participants, 155 (64.6%) had their CRP levels above 100mg/l on postoperative day 2, while on day 4, 156 (65%) had their CRP levels above 100mg/l. The mean CRP levels on day 2 were higher than on day 4 ($p < 0.0001$). The highest abnormal value being 409 mg/l on day 2 and 373 mg/l on day 4 postoperatively. The reason for this result may be that CRP is elevated on day 2 as a result of trauma from surgery; unlike on day 4 it may be an indication of infection that need for more attention by the surgeon to investigate the cause. Although an elevated CRP implies infection, CRP on day 2 does not in itself imply infection, but a later rise after day 3 suggests the possibility of infection. These findings are consistent with Coulter (2003), who reported that patients undergoing various surgical procedures show increased serum CRP levels within four to six hours after surgery, reaching a peak value between in 48 to 72 hours. However, rising CRP levels after the second to third postoperatively day may indicate infection. However, this study only recorded one (0.6%) C-section complication (febrile condition) in 156 participants that had abnormal CRP level, although these are so, they are not statistically associated to CRP increase. However, a rising CRP levels above 100 mg/L after the second to third postoperatively day may indicate infection and declining CRP levels are a sign that inflammation is decreasing. This is in support with a prospective, observational study conducted at the Dijon hospital in France that revealed CRP of 125 mg/l at postoperative day 4 as a good predictor for detection of septic complication (Deballon *et al*, 2010).

In correlating the means of CRP on day 2 and day 4, this study, found a that day 2 correlated with day 4; $r^2 = 0.430$, $p = 0.000$ (Paired t test). This suggests that CRP day 2 has an impact on the outcome of CRP day 4. Similarly, Ramanathan *et al*, (2013) in a study to assess the impact of day 2 CRP on the CRP concentrations on days 3 and 4

postoperatively, CRP Correlations between day 2 CRP and Day 3 and day 4 CRP concentrations were examined in 357 participants. He found that Day 2 CRP was directly associated with Day 3 ($r(2) = 0.601$, $p < 0.001$) and day 4 ($r(2) = 0.270$, $p < 0.001$) CRP. These findings could be as a result of the fact that in the acute phase response (first 3 days postoperatively), CRP concentrations are higher and rapidly decrease towards the baseline after the second to third postoperative days. Therefore, it is likely that if day 2 has abnormal CRP levels may predict abnormal CRP levels on day 4 and vice versa.

This study revealed that no factor (Age, Marital Status, Parity, HIV Status, CD₄ Count, Prenatal HIV Management, Pre-existing medical conditions, Type of C-section, Prophylactic antibiotics, C-section complications) under consideration were significantly associated with CRP levels on both post operative days. However, most of the factors showed high levels of abnormal CRP levels on both postoperative days. This result is consistent with data from Ramanathan *et al*, (2013) who demonstrated that Day 2 CRP was not significantly associated with some factors such as age, sex, operation type in 357 participants. Takahashi *et al*, (2001), also found no correlation between CRP and age, gender, body temperature, operating time and blood loss in 52% patients. This could be because CRP elevation is stimulated by inflammation or infection and these factors may be similar in their morphological makeup that will influence CRP levels. In support of these findings, Chaudhary *et al*, (2008) correlated CRP with CD4 counts and found that CRP was not correlated with CD4 counts although levels of CRP being highest in the group with CD4 count below 200cells/ μ l.

4.1. Conclusion.

This study revealed that on both days 2 and 4, the majority of women had a high CRP with the highest recorded abnormal CRP on day 2. Although all the factors under consideration had showed abnormal CRP levels on both days, statistically were not significantly associated with CRP, $p > 0.05$. Even though, a cut-off value $> 100 \text{ mg/L}$ may indicate infection, an elevated CRP on day 2 does not in itself imply infection, but a later rise after day 3 suggests the possibility of infection. Even if it is so, this study only showed one participant with a febrile condition observed as a post C-section complication and the rest had no complication recorded. However, statistically, this was not significantly associated with CRP, $p = 0.999$. Most patients who undergo C-section at UTH are discharged early on the 4th day postoperatively. An early predictor of septic complications could avoid readmissions and decrease morbidity. CRP could be a good predictor allowing a safe discharge and this aspect of the CRP profile can alert the surgeon of possible septic complications.

4.2. Study Limitations

Some participants refused to be recruited as they did not want to have their blood withdrawn for any purpose and others withdraw before collection of the second sample, on day 4 postoperatively. The other challenge was that some participants were discharged on the 3rd day, which meant that 4th day blood collection was not done.

4.3. Recommendations

All post C-section mother should have their CRP levels measured on the 4th day before they are discharged from hospital and 6th day as follow up when they come for review. This would allow safe discharge of C-section mothers from the hospital and detection of both overt and covert infection (post C-section complications).

Future research should focus on the following:

There is a need to explore CRP levels on the review date as a follow up, as this would help in the identification of both overt and covert infections that could occur after the patient is discharged.

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6.0 APPENDICES

Appendix I

PARTICIPANT INFORMATION SHEET

Title: “C-reactive protein levels in plasma as a marker for detecting infection in post

Caesarean Section Mothers at the University Teaching Hospital, Lusaka”.

Principal Investigator: Ms Emmelia Chileshe

Sponsor: UNZA- Staff Development Fellowship

Dear Participant,

I invite you to participate in this study being conducted by Ms Emmelia Chileshe as part of the requirement for the award of a Master of Science in Biochemistry. We are doing a study to find out the presence of infection using protein called CRP, that rises in infection and this study will be done among the women that has undergone C- section at UTH. CRP will be checked on days 2 and 4 following operation. We are doing this research because it will help us to detect and manage infection in our women following C-section early before complications occur.

Anyone who has undergone a C-section can be part of this important study. You have been chosen because you have undergone C-section operation. If you agree to take part in this study, you will be asked some questions to help us know you better, while some other information will be extracted from your medical records, concerning your pregnancy and your social status information. For us to do this study, we will require to withdraw about 2mls of blood from your vein using a needle and a syringe. The site to puncture will be cleaned with antiseptic and an elastic band will be wrapped around the upper arm to apply

pressure to the area and make the vein swell with blood. Once the blood has been collected, the needle is removed, and the punctured site is covered to stop any bleeding and a bandage may be placed over the area if there is any bleeding. When the needle is inserted to draw blood, you may feel moderate pain, or feel only a prick or stinging sensation.

Your participation in this study is completely voluntary and you may withdraw at any time without penalty. We will not interfere in the way the doctors have planned to take care of you in this pregnancy. The study will not in any way influence the plan of care your doctors have for you.

The information we will have about you will not be shared with anyone. The study will ensure strict confidentiality and will not reveal any information related to any individual participant to anyone. The research assistants will see you on day 2, and day 4 while you will be in hospital before you are discharged. If you agree to take part, please sign this consent form, which will allow us to enrol you in the study.

Appendix II

PARTICIPANT CONSENT FORM

“Determining C-reactive protein levels in blood as a marker for detecting infection in post Caesarean Section Mothers at the University Teaching Hospital - Lusaka”.

I understand all that has been explained to me as above and it is clear to me what this study is all about and so I voluntarily consent to take part in the study. I agree to participate in the study on my own without coercion.

Name -----

Signature -----Date -----

Thumb stamp (Those that can't write)

Witness 1 Name_____ Sign_____ Date_____

NB. Consent form to be kept separate from the data collecting tools.

Appendix III

Data Abstraction Form

Date of Interview.....

Place of Interview.....

Name of Interviewer.....

Phone No of the Client

Residential address

.....

Serial Number

Instructions to Interviewer

1. Introduce yourself to the respondent
2. Explain the purpose of the interview
3. Get verbal and written consent from the respondent
4. Reassure the respondent that all responses will be held in strict confidence
5. Thank the respondent at the end of each interview.

Abstraction Form

Part I - Demographic Data			
		Option Answers	Indicate Answer Here
1.	Age (years)	a. < 24 b. 25-35 c. > 35	(Write exact age)
2.	Marital Status	a. Married b. Not Married	
3.	Parity	a. Primigravida (Para1) b. Para 2 -4 c. Para5 and more	(Write exact parity)
Part II – Medical Records			
4.	HIV Status (from antenatal record)	a. Positive b. negative	
5.	CD4 Count (Option) if available	a. < 200 b. > 200	(Write exact CD4 count)
6.	Prenatal HIV Management	a. Active HAART b. Short course ARVs c. N/A	
7.	Pre-existing medical conditions	a. Diabetes Mellitus b. Hypertension c. N/A	

8.	Type of C-section	a. Emergency b. Elective	
9.	Prophylactic antibiotics	a. Yes b. No	
10.	C-section complications (Indicate day of complication)	a. Febrile illness b. Septic wound c. N/A)	
Part III (Laboratory Test Results)			
15	CRP levels Test results (Indicate figure)	2 nd day of C-section	
		4 th day of C-section	