COMPARISON OF SHORT TERM VERSUS LONG TERM ANTIBIOTIC PROPHYLAXIS IN ELECTIVE CAESAREAN SECTION.

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DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE PART II FELLOWSHIP EXAMINATION OF THE NATIONAL POSTGRADUATE MEDICAL COLLEGE IN OBSTETRICS AND GYNAECOLOGY.
DECLARATION

It is hereby declared that this work is original unless otherwise acknowledged. The work has not been presented to any other college for a fellowship nor has it been published or submitted elsewhere for publication.

Dr. A.O. Ijarotimi.
CERTIFICATION

We certify that this work was carried out by Dr. A.O. Ijarotimi of the Department of Obstetrics and Gynaecology under our supervision at Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife. We also supervised the write-up.

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DEDICATION

This work is dedicated to the almighty God; the source of my strength who gave me the wisdom to carry out the study.
ACKNOWLEDGEMENTS

I acknowledge with profound gratitude the dedicated efforts of my supervisors; Prof O.B. Fasubaa, FWACS, the Head, Department of Obstetrics, Gynaecology and Perinatology, Obafemi Awolowo University, Ile-Ife and Dr. E. Orji, FMCOG, Associate Professor, Department of Obstetrics, Gynaecology and Perinatology, Obafemi Awolowo University, Ile-Ife.

I appreciate the useful suggestions of my colleagues: Drs Badejoko, Olaiya and Oyetunji, as well as the contributions of Drs Adeniyi and Adepoju.

I sincerely thank my husband, Segun, my son, Oluwasegun and my entire family for their tremendous love and support. Thanks for being there always.

I thank all the patients involved in this study for their cooperation.

I give God all the praise.

Dr. A.O. Ijarotimi.
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SUMMARY

There is a high level of aversion to Caesarean Section in the developing countries not only because of religious and cultural beliefs but also economic cost. Research into ways of reducing cost, decreasing morbidity and making the experience of caesarean delivery bearable for our women would contribute a great deal to reducing this aversion to Caesarean Section and thereby prevent avoidable maternal morbidities.

The extended use of prophylactic antibiotics for a full 7-day course following an elective caesarean section is still practiced in many centres in Nigeria.

AIM: This study was to determine any significant difference between the incidence of infectious morbidity with the use of a 24 hour antibiotics regimen compared to a 7-day course of antibiotics following elective caesarean section using a cheap and easily available combination of Ampicillin/Cloxacillin and Metronidazole.

METHOD: Two hundred patients planned to have elective caesarean section for various indications and who satisfied the inclusion criteria were enrolled in the study in two groups of 100 patients each. Patients were randomized to receive either Ampiclox as 4 intravenous doses of 1g statim and 500mg each 6 hourly and Metronidazole as 3 intravenous doses of 500mg each 8 hourly both for 24 hours or same combination intravenously for 48 hours and subsequent oral use for 5 days.
**RESULTS:** The mean maternal age, parity, gestational age and indication for caesarean section were similar in the two groups of participants. There was no statistical difference in the incidence of febrile morbidity (17%/18%, \( p=0.852 \)), urinary tract infection (6%/4%, \( p=0.196 \)), wound infection (4%/3%, \( p=0.056 \)) and endometritis (3%/2%, \( p=0.367 \)). The cost of antibiotics per patient (N550) in the short term prophylaxis group was half that of the long term prophylaxis group (N1,410).

**CONCLUSION:** There was no difference in the incidence of infection related morbidity when short term prophylactic antibiotics was used at elective caesarean section compared to long term prophylactic antibiotics.
INTRODUCTION

Infectious complications that occur after Caesarean delivery are an important and substantial cause of maternal morbidity and are associated with a significant increase in hospital stay. There is a high level of aversion to Caesarean Section in the developing countries not only because of religious and cultural beliefs but also economic cost. Research into ways of reducing cost, decreasing morbidity and making the experience of caesarean delivery bearable for our women would contribute a great deal to reducing this aversion to Caesarean Section and thereby prevent avoidable maternal morbidities. The General principles for the prevention of any surgical infection include sound surgical technique, skin antisepsis and antimicrobial prophylaxis. Although antibiotic prophylaxis during caesarean section has been extensively studied and generally found to be effective in preventing infection, surveys suggest inconsistent and variable application of recommendations for its use. The extended use of antibiotics for a full 7-day course following an elective caesarean section is practiced in some centers in the developing countries. The reason for this could be due to the fact that strict asepsis cannot always be guaranteed because of epileptic power supply and inadequate facilities for sterilization.

This study is to determine any significant difference between the incidence of infectious morbidity with the use of a 24 hour antibiotics
regimen compared to a 7-day course of antibiotics following elective caesarean section using a cheap and easily available combination of Ampicillin/Cloxacillin and Metronidazole. The result of this study might facilitate a change or the continuation of the current practice of extended antibiotics use for elective caesarean section in our centre and elsewhere with a similar practice.
LITERATURE REVIEW

HISTORICAL PERSPECTIVE

Caesarean section can be defined as delivery of a fetus through a surgical incision into the uterine wall after 28 weeks of gestation\(^5\). Caesarean section is one of the most commonly performed surgical procedures in obstetrics and it is certainly one of the oldest operations in surgery\(^6\).

The origin of Caesarean Section has always generated debate in most circles. It has been hypothesized that the great Julius Caesar was born in this manner and the mother lived many years after his birth. Critics believed that in 100 B.C. when Julius Caesar was born, this operation would have been fatal resulting in mortality for the mother or the child and do not therefore believe in this hypothesis\(^5\). Probably this term was derived from the decree in Roman law which made it mandatory for the operation to be performed on women dying during childbirth, a term called lex caesarae. Secondly, the latin verb caedere means to cut, an abdominal birth is termed partus caesareus. The first documented operation on a living patient (who died on the 25\(^{th}\) postoperative day) was done in 1610. The first successful caesarean section in the United States was done in a cabin near Staunton, Virginia, in 1794; both mother and baby survived\(^7\).

As the years passed greater care was no doubt given to the technique of the operation, but the maternal death rate showed little if
any improvement\textsuperscript{6}. In 1876, a dramatic modification in technique was introduced by Poro of Italy, this consisted of amputation of the body of the uterus and fixing of the cervical stump to the lower angle of the abdominal wound where bleeding was controlled by pressure. The maternal mortality fell to half its previous figure as a result of this, because the danger of haemorrhage from the unstitched uterus was entirely removed and the other danger of infection greatly lessened. Suturing the uterus was first advocated by Lebas (1769) and later popularized by Kehrer (1881) and Sanger (1882)\textsuperscript{6}. Sanger’s technique which is a median incision of the uterus (the classical incision) and careful stitching of the wound held sway for several decades. However Kehrer again comes into the picture as he was really the father of the ‘Lower Segment Operation’ as employed today\textsuperscript{6}.

The last century opened with much accomplished by improved surgical technique and more rigid aseptic precautions. The results were good for what are termed ‘clean’ or ‘non-infected’ cases but disappointing in ‘suspect’ and ‘infected’ cases. This led to the idea of a technique which would permit access to the uterus without opening the peritoneal cavity. There are two routes by which the uterus can be reached without opening the peritoneal cavity: the lateral and the median approaches. In the lateral approach suggested and employed by Ritgen (1787-1837), a lateral incision parallel to the Poupart’s ligament was made. Then, having cut through the muscles, the peritoneum is lifted up to expose the vagina
at its junction with the cervix. The vagina was incised and the cervix pulled into the abdominal wound. The child was extracted by version. The median approach was suggested by Physick in 1824\textsuperscript{6}. The essential step involves denuding the bladder of a fascial skull cap which remains attached to the peritoneum from bladder fundus to the utero-vesical pouch. The difficulties of both forms of operation include severe bleeding and danger of bladder injury. There may also be difficulty in extracting the child if it is above average size.

**DEFINITION, INCIDENCE AND COMPLICATIONS**

An elective caesarean section is that in which the time of delivery has been determined antenatally before the onset of labour or rupture of membranes. An elective Caesarean section is justified whenever it is deemed that the uterus or fetus could be damaged during labour\textsuperscript{8}. The caesarean section rate is on the increase world wide. The caesarean section rate in OOUTH, Sagamu increased from 10.3\% between 1989-1991 to 23.1\% between 2000-2003\textsuperscript{9}. The caesarean section rate in JUTH is 18\%\textsuperscript{10} while it ranges between 25 to 30\% in OAUTHC and SDA hospital both in Ile-Ife. The incidence is about 15-21\% in most West African countries and would have been higher if there had not been acceptance of vaginal birth after caesarean section and in some types of breech presentations\textsuperscript{5}. Caesarean section rate in the United States in 2002 was 26.1\%, an increase of 7\% over 2001\textsuperscript{11}. This rise has been extraordinary when put in context with the figure of 5.3\% in the early
70’s. The caesarean section rate in Canada has also risen from 13.9% in the late 70’s to 20% in the 90’s\textsuperscript{12}. In Sweden, the incidence of Caesarean section has increased more than ten-fold over the past decades (0.87% in 1946-1950) to 12% in 1995. In England and Wales, the incidence was from 3.1% in 1963 to the current figure of 10-12\%\textsuperscript{13}. The increase in Caesarean Section rates is largely driven by a variety of factors. These include societal demands for improved fetal outcome and protection of the maternal pelvic floor, and the aspirations of obstetricians to meet these demands. Potentially difficult forceps delivery is a thing of the past and similarly, the diagnosis of dystocia is more often managed by caesarean section. The advent of electronic fetal monitoring led to the over diagnosis of fetal distress and delivery of the fetus by caesarean section\textsuperscript{8}. As with other surgical operations, there are risks involved with caesarean section. The risks of Caesarean Section include maternal death, haemorrhage, venous thrombosis, infection and anaesthetic complications.

The maternal mortality rate associated with caesarean section varies in different series from 4 per 10,000 to 8 per 10,000.In one series the risk of death from caesarean section was found to be 26 times greater than with vaginal delivery\textsuperscript{7}. Before the advent of antibiotics, some early workers like Wepley and Chen advocated hysterectomy at the time of caesarean delivery to control bleeding and decrease infection while others
like Latzko (1909) introduced the extra-peritoneal approach to decrease the risk of infection.

Improved anaesthetic techniques, thromboprophylaxis and a wider choice of antibiotics for treatment of infection have made maternal deaths from caesarean section rare. Increasing preference for spinal and epidural anaesthesia over general anaesthesia as well as modifying surgical techniques to shorten the operation time have led to significant reduction in morbidity and increased maternal satisfaction. Infectious complications following Caesarean delivery include fever, wound infection, endometritis, bacteremia, other serious infection (including pelvic abscess, septic shock, necrotizing faciitis and septic pelvic vein thrombophlebitis) as well as urinary tract infection.

**Febrile Morbidity:** Several different definitions of febrile morbidity have been used. The most frequent definition is a temperature of 38°C or greater recorded on two occasions, at least 6 hours apart, more than 24 hours after the surgical procedure. This excludes a fever during the first 24 hours because operative site infections during this time are unusual unless there is preexisting infection at the operative site or gross contamination of the site.

**Endometritis:** Caesarean section and low socioeconomic class are consistently associated with higher rates of endometritis, and caesarean section is easily the most identifiable risk factor for development of puerperal infection. Some series report an infection rate of 40-80%
following caesarean section delivery. Fever and a soft, tender uterus are the most prominent signs of endometritis. The lochia may or may not have a foul odour. In more severe disease, high fever, malaise, abdominal tenderness, ileus, hypotension, and generalized sepsis may be seen\(^7\).

**Urinary tract infections:** About 2-4% of women develop a urinary tract infection postpartum. Following delivery, the bladder and lower urinary tract remain somewhat hypotonic, and residual urine and reflux result. This altered physiologic state, in conjunction with catheterization, birth trauma, conduction anaesthesia, frequent pelvic examinations, and nearly continuous contamination of the perineum, is sufficient to explain the high incidence of lower urinary tract infections postpartum\(^7\).

**Wound infection:** Wound infections may be early or late in onset. Early onset infections are characterized by temperature elevation and cellulitis that develops within the first 48 hours after surgery. Wound breakdown and dehiscence occur if treatment is not initiated rapidly. GP A \(\beta\)-haemolytic streptococci cause most of these unusual infections, but group B \(\beta\)-haemolytic streptococci can also be causative. Parenteral therapy with a penicillin based antibiotic and aggressive wound care are the keys to management. Late-onset infections are characterized by persistent low-grade fever and purulent drainage from the incisions. Occasionally, the patient’s temperature has a single, high spike each day. Causative organisms are S. aureus in 25% of cases and other vaginal contaminants in 75%\(^{17}\).
Infections are commonly polymicrobial. Pathogens isolated from infected wounds and the endometrium include E. coli and other aerobic gram negative rods, group B streptococcus and other streptococcus spp, enterococcus faecalis, S. aureus and coagulase negative staphylococci, anaerobes (including peptostreptococcus spp and bacteroides spp.), Gardnerella vaginalis and genital mycoplasmas. Wound infection caused by S. aureus and coagulase negative staphylococci arise from contamination of the wound with the endogenous flora of the skin at the time of surgery. Adequate skin preparation using antiseptic solution and sterile surgical drapes to isolate the operation field help to decrease contamination.

The infectious morbidity rates quoted vary from 18% to 83%. Extensive study of the epidemiology of wound infections resulted in a classification of operative wounds in relation to contamination and increasing risk of infection. Operative wounds are classified as: Clean, clean-contaminated, contaminated and dirty or infected. Clean procedures include, elective cases, primarily closed, undrained, non-traumatic, uninfected, no break in asepsis and in which the respiratory, gastrointestinal, genitourinary or oropharyngeal tracts are not breached. In clean-contaminated procedures, the alimentary, respiratory, or genitourinary tracts are entered under controlled condition and without unusual contamination. Contaminated procedures are those in which there is gross spillage from the gastrointestinal tract, entrance into
genitourinary or biliary tracts in the presence of infected urine or bile, major break in technique, or incisions in which acute purulent inflammation is present. Dirty procedures include, traumatic wounds with retained devitalized tissues, foreign bodies, faecal contamination, perforated viscus, or acute bacterial inflammation with pus encountered during operation. An elective caesarean section can be classified as a clean contaminated wound.

Culver and colleagues, using the National Nosocomial infections surveillance system, reported the percentage of operations in the United States by wound class and the surgical wound infection rate per 100 operations to be 2.1% for clean, 3.3% for clean –contaminated, 6.4% for contaminated, and 7.1% for dirty or infected case\textsuperscript{17,23}. These rates when compared with infection rates following other surgical procedures that are collected as part of the NNIS system are high. Given the number of operative deliveries performed these rates translate into very large numbers of women with an infectious complication following delivery and significant costs as well as morbidity\textsuperscript{23}. Studies done in various centres in Nigeria revealed wound infection rates of 9.1 to 16.2\%\textsuperscript{24-30}.

It has been said that infection increases the possibility of uterine scar rupture in future pregnancies\textsuperscript{31}, however there is no evidence to support this unless the uterine wound is involved and a history of a wound infection is not an indication for a repeat Caesarean Section\textsuperscript{32}. 
Post operative wound infections have an enormous impact on patients’ life and contribute substantially to the financial cost of patient care. The potential consequences for patients range from increased pain and care of an open wound to sepsis and even death. The seriousness of the above complications and their long term sequelae necessarily support the use of antibiotics. Use of prophylactic antibiotics reduces the incidence of endometritis following elective and emergency caesarean section by two-thirds to three-quarters and the incidence of wound infection by three-quarters\(^23\). Prophylactic antibiotics also lower the incidence of febrile morbidity and urinary tract infection after caesarean section. Also fewer serious complications occur after prophylactic antibiotics\(^33\).

An appropriate prophylactic antibiotic should be effective against microorganisms anticipated to cause infection, achieve adequate local tissue levels, cause minimal side effects, be relatively inexpensive and not likely to select virulent organisms\(^34\). The antibiotics chosen for prophylaxis can be those used for active treatment of infection. However the chosen antibiotics must reflect local disease-specific information about the common pathogens and their antimicrobial susceptibility\(^35-41\). A past history of a serious adverse event should preclude administration of a particular antibiotic. A comprehensive risk assessment should be part of the process of choosing the appropriate antibiotic. This should include economic considerations such as the acquisition costs of the
drug and costs of administration and preparation set against consequences of failure of prophylaxis and the possible adverse effects.

Experimental studies published in the early 1960 resulted in a more scientifically accurate approach to antimicrobial prophylaxis. Most important was the report by Burke which demonstrated the crucial relationship between timing of antibiotic administration and its prophylactic efficacy. His experimental studies showed that to greatly reduce skin infection produced by penicillin sensitive staphylococcus aureus, the penicillin had to be in the skin shortly before or at the time of bacterial exposure. This study and others fostered a change in strategy which helped to correct the common error of first administering the antibiotic in the recovery room. In a study of 200 patients in Somalia in which a single dose of ceftriaxone was compared with multiple doses of Ampiclox as prophylaxis against infection at elective caesarean section, there was no statistically significant difference in the incidence of endometritis, wound infection, febrile morbidity or peritonitis. In another study in Saudi Arabia in which cefazolin was compared with placebo, an incidence of 3.3% for febrile morbidity was found.

In spite of clear evidence from Cochrane Database of clinical reviews that the use of penicillin or first generation cephalosporins in single dose therapy is effective, the actual practice is contrary with use of multi agent antibiotics for long periods being very rampant in actual clinical practice. A survey of obstetricians’ practice of using prophylactic
antibiotics in vaginal deliveries and caesarean sections at a centre in India found that a combination of ampicillin/gentamycin/metronidazole for five days was used by 35.5% and 25.5% of obstetricians for elective and emergency caesarean sections respectively.33. Ampiclox is a fixed dose combination of ampicillin and cloxacillin containing 500mg of each per capsule or vial and is vigorously promoted for post operative skin and soft tissue infection.35,44. Metronidazole is an imidazole derivative with broad spectrum activity against anaerobic bacteria such as Bacteroides fragilis, Fusobacterium, Clostridium perfringes, Clostridium difficile, Helicobacter pylori, and anaerobic Streptococci.45.

Very few prospective randomized trials of surgical prophylaxis have included economic evaluation with the study design. There are however some evaluations that combine evidence of effectiveness of prophylaxis with estimates of the additional cost of treating wound infection.41.
OBJECTIVES

GENERAL OBJECTIVE

To determine any significant difference between the incidence of post-operative infectious complications with the use of a 24 hour regimen of combination Ampicillin/Cloxacillin and Metronidazole compared to a 7-day extended course following elective caesarean section.

SPECIFIC OBJECTIVES

1. To compare the incidence of febrile morbidity between the group on short term prophylaxis and those on long term prophylaxis.
2. To compare the incidence of endometritis between the two groups.
3. To compare the incidence of wound infection between the two groups.
4. To compare the incidence of urinary tract infection between the two groups.
5. To compare the cost of treatment using the two regimens.
NULL HYPOTHESIS

There is no difference in the incidence of infection related morbidity when short course prophylactic antibiotics is used at elective caesarean section compared to long course prophylactic antibiotics.
JUSTIFICATION FOR THE STUDY

A systematic review in the Cochrane Library concluded that antibiotic prophylaxis in all cases of caesarean section significantly reduce the incidence of puerperal infections. Although antibiotic prophylaxis during caesarean section has been extensively studied and generally found to be effective in preventing infection, surveys suggest inconsistent and variable application of recommendations for its use. Questions remain about the indications for prophylaxis, the choice of drug (whether a broad spectrum or longer acting agent is better), its route, timing and frequency, the cost-effectiveness of different strategies, adverse effects of antibiotics for the woman and her infant, and the potential for increased use of antimicrobial prophylaxis to be a factor in the development of antimicrobial resistance.

The recommended duration of prescribed antibiotics in many trials has been reduced from greater or equal to five days to three days, then twenty four hours, then to three doses and finally to a single dose. A second review of the Cochrane Library concluded that a single dose of ampicillin or first generation cephalosporins has similar efficacy in reducing puerperal infection. In addition, the benefits are not different from broad spectrum cephalosporins. A study of prophylactic antibiotic prescription for caesarean section in a center in Thailand concluded that the question of why nearly half of the patients who received post-operative prophylactic antibiotics were prescribed subsequent oral
antibiotics regardless of any post-caesarean infections in the study was unanswered and needs further study\textsuperscript{39}. Documented guidelines regarding antibiotic prophylaxis for elective caesarean section have never been established in our center.
METHODOLOGY

Study Location: This comparative study was carried out at the Obstetrics and Gynaecology department of Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State, Nigeria, comprising two obstetric units at Ife Hospital Unit, Ile-Ife and Wesley Guild Hospital (WGH), Ilesha and the Seventh Day Adventist Hospital, Ile-Ife. These hospitals serve as tertiary referral centers for secondary and primary tier hospitals in Ife, Ijesha, Ondo and Ekiti zones of the country. The Three units have an average of 3,240 deliveries per year and caesarean section rates of between 25 to 30%.

Study Design: It is a randomized clinical trial.

Target Population: All booked pregnant women undergoing elective caesarean section during the study period.

Inclusion Criteria: Women in index pregnancy planned for elective caesarean section for various reasons with no added risk factors for infection were recruited to participate in this study.

Exclusion Criteria: Women were excluded from the study if they have received antibiotics 2 weeks prior to the operation, if they have any visible infection or elevated temperature at the time of the operation, if they have ruptured membranes prior to the operation or if they are allergic to any of the antimicrobials. Also excluded were those anaemic (PCV < 30%), Human Immunodeficiency Virus positive or if they did not wish to participate in the study.
Sample Size Determination: Accepting a study power of 80%, confidence interval of 95%, study control of 1:1 and an acceptable dropout rate of 10%, the sample size was determined using statistical formula for comparing two proportions as follows:

\[
N = \frac{1}{(1-f)} \times \left( \frac{2x (Z_a + Z_b)^2 x P x (1-P)}{(P_0 - P_1)^2} \right)
\]

N= minimum sample size per group

a= probability of making type 1 error

b= probability of making type II error

\(Z_a=\) level of significance of type 1 error probability; determined from a statistical table based on the value of the level of significance a. For this study, a is set at 0.05. Therefore \(Z_a= 1.96\) for two tailed tests (standard normal variate).

\(Z_b=\) type II error probability determined from a statistical table based on the acceptable power of 80% (0.8). Therefore \(Z_b= 0.84\).

\(P_0=\) The proportion of participants in the control group (long term prophylactic antibiotics) that are expected to exhibit the primary outcome measures of interest (febrile morbidity, endometritis, wound infection and urinary tract infection).

\(P_1=\) The proportion of the participants in the short term prophylactic antibiotics group that are expected to exhibit the primary outcome measures of interest (febrile morbidity, endometritis, wound infection and urinary tract infection).
f= proportion of study participants who are expected to be lost due to exclusion as a result of intrapartum events or withdrawal. For this study f= 10% (0.1).

\[ P = P_0 + \frac{P_1}{2} \]

\[ P = 0.4 + \frac{0.2}{2} \]

\[ P = 0.3 \]

Therefore, the minimum sample size required for each study group for it to be statistically significant is:

\[ N = \frac{1}{1 - 0.1} \times \left( \frac{2 \times (1.96 + 0.84)^2 \times 0.3 \times 0.7}{(0.4 - 0.2)^2} \right) \]

\[ N = 1.11 \times 82.32 \]

\[ N = 91.466 \]

\[ N = 100 \text{ subjects per group} \]

**Methods:** Two hundred patients planned to have elective caesarean section for various reasons were enrolled in the study in two groups of 100 patients each. Patients were randomized to receive either Ampiclox as 4 intravenous doses of 1g statim and 500mg each 6 hourly and Metronidazole as 3 intravenous doses of 500mg each 8 hourly both for 24 hours or same combination intravenously for 48 hours and subsequent oral use for 5 days. All drugs were supplied by the hospitals central pharmacy stores. The CLOXAP brand of ampiclox injection manufactured by Swiss Parenteral Pvt Ltd and the AZCLOX brand of
Ampiclox capsules manufactured by Medreich Sterlab Ltd were used. The Metronidazole injection by Dana/Ashmina Ltd and the tablets, the EMGYL brand by Emzor Pharmaceuticals. The drugs were administered by the anaesthetists and nurses under the supervision of the investigator. All investigations were paid for by the investigator.

After obtaining an informed verbal consent, a complete history of the participants was taken using a standard questionnaire. A physical examination was also performed. All caesarean sections were performed by a standard technique and all post-operative care followed standard clinical practice.

Main outcome measures: The following post-operative complications were recorded:

1) Post-operative febrile morbidity, defined as an axillary temperature of 38.0°C on 2 occasions at least 6 hours apart excluding the first 24 hours.

2) Post-operative infections which include:
   a. Endometritis (fever, uterine tenderness and abnormal lochia).
   b. Wound infection (fever, cellulitis and exudates).
   c. Urinary tract infection.

Once febrile morbidity was identified, patients were examined to localize the potential source of infection (breasts, chest, abdomen and pelvis). Based on the symptoms and examination findings, samples were
collected and sent for investigation. Urine microscopy, culture and sensitivity were done and white blood cell count determined. Blood films (thick and thin) were also taken and stained for malaria parasite. Wound and lochia swabs were sent for microscopy, culture and sensitivity when necessary. All patients who developed post-operative infections were treated based on the antibiotic sensitivity pattern. Patients found to have Malaria fever were treated with a suitable Artemisinin based combination therapy. Wound morbidity was managed by local wound toilet with Normal Saline irrigation and EUSOL. On discharge from the hospital, women were informed to report any fever, wound dehiscence or foul smelling lochia immediately and all women were seen at 6 weeks post-natal visit.

The duration of hospitalization, the need for therapeutic antibiotics and maternal outcome were recorded. Obtained results were statistically processed, using the SPSS 13 and presented in tables. The chi-square test and independent t-tests were used as tests of significance where applicable. A P-value < 0.05 was considered significant.
ETHICAL CONSIDERATIONS

Ethical clearance was obtained for this study from the Research and ethics committee of the Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife. All participants were fully counseled about the study and reserved the right to withdraw for whatever reason without penalty.
RESULTS

During the period of this study, there were 1,453 vaginal deliveries and 505 caesarean sections (25.8%). Two hundred and thirteen (42.2%) of the caesarean sections were elective, while emergency caesarean sections accounted for 292 (57.8%). There were 2 cases of maternal deaths from septicemia following emergency caesarean section. There was no mortality from elective caesarean section according to local hospital statistics from the three centers used in the study.

Table 1 shows the maternal age distribution of the participants. Majority of them were in the age range of 26-35 years. There was significant statistical difference in the maternal age distribution between the two groups.

Table 2 shows the distribution of the patients according to their parity. The highest number of cases was recorded among women who were para 1-3 while parity greater or equal to 4 accounted for the least in both groups. The two groups were significantly different statistically in parity distribution.

Table 3 shows that age and parity were however not statistically significant after binary logistic regression. Therefore, they are not independent contributors to the need for therapeutic
antibiotics and there by overall infectious morbidity post-elective caesarean section.

Tables 4 and 5 show that there was no significant statistical difference between the two groups in terms of the gestational age at which the caesarean section was performed and indication for the procedure. Majority of the caesarean sections were performed between 37-40 weeks with few below 37 weeks and above 40 weeks. The commonest indication for an elective caesarean section in this study was one previous caesarean section plus another complication.

Table 6 shows that the two groups were not significantly different statistically in the incidence of febrile and infectious morbidity. Urinary tract infection was the commonest cause of infectious morbidity while endometritis accounted for the least. Eleven percent of the participants had malaria fever.

Table 7 shows the causative organisms of infectious morbidity among the study participants. E-coli was the commonest cause of urinary tract infection while S.aureus was the most frequently isolated organism among the patients that developed wound infection.
Table 8 shows the need for therapeutic antibiotics, mean length of hospital stay and of antibiotics among the study participants. There was significant statistical difference between the two groups in mean length of hospital stay and total cost of antibiotics per patient while the two groups were not significantly different statistically in their need for therapeutic antibiotics.
TABLE 1: AGE DISTRIBUTION OF STUDY PARTICIPANTS

<table>
<thead>
<tr>
<th>Age groups (yrs)</th>
<th>Cases (%) N=100</th>
<th>Control (%) N=100</th>
<th>Total</th>
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<tbody>
<tr>
<td>≤25</td>
<td>6 (6)</td>
<td>10 (10)</td>
<td>16</td>
</tr>
<tr>
<td>26-35</td>
<td>78 (78)</td>
<td>54 (54)</td>
<td>132</td>
</tr>
<tr>
<td>≥36</td>
<td>16 (16)</td>
<td>36 (36)</td>
<td>52</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>Mean</td>
<td>31.56</td>
<td>33.32</td>
<td>_</td>
</tr>
<tr>
<td>SD</td>
<td>4.13</td>
<td>5.09</td>
<td>_</td>
</tr>
<tr>
<td>T-test</td>
<td>0.008</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SD: Standard Deviation, N= Number of participants.
### TABLE 2: PARITY OF STUDY PARTICIPANTS

<table>
<thead>
<tr>
<th>Parity</th>
<th>Cases (%) N=100</th>
<th>Control (%) N=100</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>28 (28)</td>
<td>18 (18)</td>
<td>46</td>
</tr>
<tr>
<td>1-3</td>
<td>72 (72)</td>
<td>72 (72)</td>
<td>144</td>
</tr>
<tr>
<td>≥4</td>
<td>0 (0)</td>
<td>10 (10)</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>200</td>
</tr>
</tbody>
</table>

Mean: 1.00 | 1.50 | 1.50
SD: 0.829 | 1.210 | 1.210
T-test: 0.001

SD: Standard Deviation, N= Number of participants.
TABLE 3: BINARY LOGISTIC REGRESSION ANALYSIS OF THE EFFECT OF DEMOGRAPHIC FACTORS ON THE NEED FOR THERAPEUTIC ANTIBIOTICS

<table>
<thead>
<tr>
<th>Independent Variables</th>
<th>B</th>
<th>OR</th>
<th>P-values</th>
<th>CI Lower</th>
<th>CI Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 1</td>
<td>0.736</td>
<td>2.087</td>
<td>0.523</td>
<td>0.218</td>
<td>19.97</td>
</tr>
<tr>
<td>Age 2</td>
<td>0.398</td>
<td>1.489</td>
<td>0.624</td>
<td>0.303</td>
<td>7.314</td>
</tr>
<tr>
<td>Age 3</td>
<td>_</td>
<td>_</td>
<td>_</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>Parity 1</td>
<td>18.617</td>
<td>0.008</td>
<td>0.999</td>
<td>0.000</td>
<td>_</td>
</tr>
<tr>
<td>Parity 2</td>
<td>18.182</td>
<td>0.007</td>
<td>0.999</td>
<td>0.000</td>
<td>_</td>
</tr>
<tr>
<td>Parity 3</td>
<td>_</td>
<td>_</td>
<td>_</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>Constant</td>
<td>-21.203</td>
<td>0.000</td>
<td>0.999</td>
<td>_</td>
<td>_</td>
</tr>
</tbody>
</table>

Key: Dependent variable:- Need for therapeutic antibiotics, B-coefficient of regression; OR- odds ratio, CI- 95% confidence interval, Age 1: ≤25yrs, Age 2: 26-35yrs, Age 3: ≥36yrs (reference category) Parity 1: 0, Parity 2: 1-3, Parity 3: ≥4 (reference category).

Age and parity were not independent contributors to post-elective caesarean section infections morbidity because they were not statistically significant after binary logistic regression.
<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>Cases (%)</th>
<th>Control (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;37</td>
<td>2 (2)</td>
<td>6 (6)</td>
<td>8</td>
</tr>
<tr>
<td>37-40</td>
<td>94 (94)</td>
<td>90 (90)</td>
<td>184</td>
</tr>
<tr>
<td>&gt;40</td>
<td>4 (4)</td>
<td>4 (4)</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>Mean</td>
<td>37.92</td>
<td>37.91</td>
<td></td>
</tr>
<tr>
<td>Standard deviation</td>
<td>0.97</td>
<td>0.90</td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.352</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TABLE 5: INDICATION FOR PRESENT CAESAREAN SECTION AMONG STUDY PARTICIPANTS

<table>
<thead>
<tr>
<th>Indication for Caesarean Section</th>
<th>Cases (%)</th>
<th>Control (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1c/s + another complication</td>
<td>32 (32)</td>
<td>38 (38)</td>
<td>70</td>
</tr>
<tr>
<td>2 or more previous caesarean sections</td>
<td>12 (12)</td>
<td>18 (18)</td>
<td>30</td>
</tr>
<tr>
<td>Abnormal lie/presentation</td>
<td>14 (14)</td>
<td>12 (12)</td>
<td>26</td>
</tr>
<tr>
<td>Major Placenta praevia</td>
<td>10 (10)</td>
<td>8 (8)</td>
<td>18</td>
</tr>
<tr>
<td>Contracted pelvis</td>
<td>10 (10)</td>
<td>12 (12)</td>
<td>22</td>
</tr>
<tr>
<td>Others</td>
<td>22 (22)</td>
<td>12 (12)</td>
<td>34</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>P.value</td>
<td>0.051</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### TABLE 6: INCIDENCE OF FEBRILE AND INFECTIOUS MORBIDITY AMONG STUDY PARTICIPANTS

<table>
<thead>
<tr>
<th>Morbidity</th>
<th>Cases (%)</th>
<th>Control (%)</th>
<th>% total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary tract infection</td>
<td>6(6)</td>
<td>4(4)</td>
<td>5.0%</td>
<td>0.196</td>
</tr>
<tr>
<td>Wound infection</td>
<td>4(4)</td>
<td>3(3)</td>
<td>3.5%</td>
<td>0.056</td>
</tr>
<tr>
<td>Endometritis</td>
<td>3(3)</td>
<td>2(2)</td>
<td>2.5%</td>
<td>0.367</td>
</tr>
<tr>
<td>Febrile morbidity</td>
<td>17(17)</td>
<td>18(18)</td>
<td>17.5%</td>
<td>0.852</td>
</tr>
<tr>
<td>Malaria fever</td>
<td>10(10)</td>
<td>12(12)</td>
<td>11.0%</td>
<td>0.430</td>
</tr>
</tbody>
</table>
TABLE 7: CAUSATIVE ORGANISMS OF INFECTIOUS MORBIDITY IN STUDY PARTICIPANTS

<table>
<thead>
<tr>
<th>Organisms</th>
<th>Urinary Tract Infection (%)</th>
<th>Wound infection (%)</th>
<th>Endometritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus</td>
<td>2(2)</td>
<td>4(4)</td>
<td>4(4)</td>
</tr>
<tr>
<td>E. coli</td>
<td>6(6)</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>2(2)</td>
<td>2(2)</td>
<td>1(1)</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>_</td>
<td>1(1)</td>
<td>_</td>
</tr>
</tbody>
</table>
TABLE 8: NEED FOR THERAPEUTIC ANTIBIOTICS, MEAN LENGTH OF HOSPITAL STAY AND TOTAL COST OF ANTIBIOTICS PER PATIENT AMONG STUDY PARTICIPANTS

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need for therapeutic antibiotics</td>
<td>8</td>
<td>6</td>
<td>0.096</td>
</tr>
<tr>
<td>Mean length of hospital stay</td>
<td>4.67</td>
<td>5.20</td>
<td>0.000</td>
</tr>
<tr>
<td>Cost of antibiotics (N)</td>
<td>550</td>
<td>1410</td>
<td></td>
</tr>
</tbody>
</table>
DISCUSSION

The caesarean section rate in this study was found to be 25.8%. This is similar to the rate of 23.1% reported by a study in Olabisi Onabanjo University Teaching Hospital, Sagamu for the period between 2000 -2003. This finding is also in keeping with the national and global trend of rising caesarean section rate from 9.4% to 34.6% reported in Abakaliki, Nigeria over a 32 year period and 26.1% in the United States in 2002, an increase of 7% over 2001.

In this study 42.2% of the caesarean sections were elective in contrast to an incidence of 55.8% reported in a study of 200 patients in Somalia. This difference may be explained by the aversion of most of our patients for caesarean section as many of the patients planned for elective caesarean section end up defaulting, only to present as emergencies. This is evidenced by the incidence of almost 60% for emergency caesarean section discovered in the study.

Improved anaesthetic technique and antibiotic prophylaxis have made maternal deaths from caesarean section rare. This is supported by the fact that there was no maternal mortality
recorded following any of the elective caesarean sections in this study.

The extended use of prophylactic antibiotics for a full 7-day course following an elective caesarean section is still practiced in many centres in Nigeria including the Obafemi Awolowo University Teaching Hospitals Complex and the Seventh Day Adventist Hospital both in Ile-Ife.

This study was carried out to test the efficacy of short term against long term prophylactic ampiclox and metronidazole combination in reducing infectious morbidity post-elective caesarean section. The policy of using prophylactic antibiotics in elective caesarean section was justified by the high rate of sepsis in our community with sepsis accounting for about 13% of overall main causes of maternal mortality in Nigeria.

This study demonstrated an incidence of post-operative febrile morbidity of 17% for the short term prophylaxis group and 18% for the long term prophylaxis group. There was no significant statistical difference between the two groups. Results of a similar study in which single dose ceftriaxone was compared with multiple doses of Cefoxitin also failed to show a significant statistical difference in the incidence of febrile morbidity\(^{52}\).
The incidence of 17-18% of febrile morbidity found in this study is higher than 8.1% reported by a study in the United States which compared a 24 hour course of Ampicillin against a 3-day course of same drug\textsuperscript{53}. The high incidence recorded in this study may be due to the high incidence of malaria (11%) which is endemic in this region.

The incidence of urinary tract infection from this study ranged between 4%-6% and there was no significant statistical difference between the two groups. This compared favourably with an incidence of 7.3% for urinary tract infection reported by Rehu et al in a prospective study of 774 patients\textsuperscript{54}. This study demonstrated that the incidence of endometritis was similar in both groups. The figure of 2-3% reported for endometritis in this study is in keeping with an incidence of 1.5% recorded when single dose ceftriaxone was compared with Ampiclox in multiple doses in a study of 200 patients carried out in Somalia\textsuperscript{35}.

The incidence of wound infection from this study of 3-4% was comparable in the two groups and similar to the incidence of 2.2% reported by Elliot et al in a similar study when short course Ampicillin prophylaxis was compared to extended course prophylaxis\textsuperscript{53}. It is also in keeping with the finding of 3.8% of
wound infection post-elective caesarean section obtained in a multicenter study of 1,032 patients in Copenhagen\textsuperscript{55}.

In this study, the commonest causative organism isolated for urinary tract infection was E. coli while S. aureus was more common in wound infection. This is similar to findings from a study done in South Africa, comparing cefoxitin prophylaxis with placebo in elective caesarean section\textsuperscript{56}. There was no significant statistical difference in the need for therapeutic antibiotics between the two groups. The 7\% average incidence of the need for therapeutic antibiotics represents the true incidence of overall febrile morbidity after correcting for malaria and overlapping of the three main causes of infections morbidity considered in the study. The 7\% incidence of need for therapeutic antibiotics obtained from this study is similar to the incidence of 5.1\%-6.3\% reported by the South African study\textsuperscript{56}.

This study demonstrated a significant statistical difference in the mean length of hospital stay between the two groups with a mean of 4.67 for the cases and 5.20 for the controls. This difference may be attributed to the fact that a patient on extended antibiotics is less likely to be discharged early compared to a patient that has
completed a 24 hour course of antibiotics. A short hospital stay will reduce the incidence of nosocomial or hospital acquired infections.

In this study, the cost of antibiotics per patient in the long term prophylaxis group is more than double that of the short term prophylaxis group which is not unexpected. The short term use of antibiotics, apart from reducing costs will also reduce the risk of emergence of antibiotic resistant strain of organisms. This is of benefit not only to the patients, but to the hospital and the community at large.

It is not surprising that both regimens of antibiotics failed to completely eliminate infectious morbidity post-caesarean section. These findings are comparable to other investigations which demonstrated that prophylactic antibiotics were effective in reducing (not eliminating) by approximately two thirds, infectious morbidity post-caesarean section⁵⁰.
CONCLUSIONS

Short term (24 hours) course of Ampiclox and Metronidazole was as effective as a long term (7-day) course of same combination in preventing post–elective Caesarean section infection related morbidity. It is cheaper, easier to administer and may also save nursing time.
RECOMMENDATIONS

1. A 24-hour course of Ampiclox and Metronidazole can be used for prophylaxis against infection at elective Caesarean section in patients with no added risk factors for infection.

2. A follow-up study to determine the effectiveness of short term antibiotic prophylaxis in emergency Caesarean section will be useful as the risk of infection is much higher.
SCOPE AND LIMITATION

1. The incidence of infection at elective Caesarean section is generally low.

2. The use of microbiological criteria and the translation into clinical settings may be conflicting as some patients with clinical symptoms of urinary tract infection may have no microbiological evidence of infection.
REFERENCES


<table>
<thead>
<tr>
<th>No.</th>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Hospital Number:</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Parity</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>No of previous abdominal surgery:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a. caesarean sections:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. others(specify):</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Indication for index caesarean section:</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Duration of surgery:</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Febrile morbidity(Temp &gt;/= 38°C on 2 occasions after 24 hrs of surgery):</td>
<td>Yes:                      No:</td>
</tr>
<tr>
<td>8.</td>
<td>Malaria parasite staining result:</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>Symptoms of endometritis:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a. Yes(specify):</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. No:</td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>If Yes, endocervical swab mcs result:</td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td>Symptoms of wound infection:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a. Yes(specify):</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. No:</td>
<td></td>
</tr>
<tr>
<td>12.</td>
<td>If Yes, wound swab mcs result:</td>
<td></td>
</tr>
<tr>
<td>13.</td>
<td>Symptoms of urinary tract infection:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a. Yes(specify):</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. No:</td>
<td></td>
</tr>
<tr>
<td>14.</td>
<td>If Yes, urine mcs result:</td>
<td></td>
</tr>
</tbody>
</table>
15. Duration of prophylactic antibiotics:

16. Therapeutic antibiotic required:

17. If Yes, duration of therapeutic antibiotics:

18. Length of hospital stay:

19. Total cost of antibiotics/ Total cost of admission:
