THE PREVALENCE AND MORBIDITY ASSOCIATED WITH ECTOPIC PREGNANCIES AT HARARE CENTRAL AND PARIRENYATWA HOSPITALS

A Dissertation Submitted in Partial Fulfillment of
Master of Medicine in Obstetrics and Gynaecology
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BY

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ABSTRACT

Introduction

Ectopic pregnancy is amongst the top causes of maternal morbidity and mortality in the first trimester of pregnancy. It represents one of the commonest gynaecological surgical emergencies in Zimbabwe and other developing countries because most of the women present to health care facilities after rupture has occurred.

Objectives

i. To determine the prevalence of ectopic pregnancy at Harare and Parirenyatwa Hospitals.

ii. To determine the risk factors associated with ectopic pregnancy at Harare and Parirenyatwa Hospitals.

iii. To determine the morbidity and mortality associated with ectopic pregnancy.

Design

Cross-sectional study.

Setting

Harare and Parirenyatwa Central Hospitals in Harare, Zimbabwe.

Subjects

Women attending the two hospitals with suspected ectopic pregnancy from 01 December 2012 to 30 April 2013.
Methods

All women with a suspected ectopic pregnancy who consented to participate in the study were recruited. They were managed by the attending team in the acute phase of the illness. Face to face interviews were conducted to collect information and probe for risk factors of ectopic pregnancy. The management offered to the patient was then analysed using patient’s notes. An HIV test was done on all consenting subjects after pre-counseling. The mortalities were noted and the morbidity was assessed by checking the pre-operative haemodynamic state of the patient, pre-operative haemoglobin count, use of blood or its products, need for intensive care post-operatively and the mean hospital stay.

Results

During the study period there were a total of 11239 deliveries attended at the two hospitals. A total of 138 suspected cases of ectopic pregnancy were recruited into the study. Of these, 126 (91.3%) were surgically confirmed as ectopic pregnancies and the remainder (12) were wrongly diagnosed. The overall incidence of ectopic pregnancy was found to be 1.12%. Most women were in the 21-30 year age group and had 2 children or less. The risk factors identified were a reported history of sub-fertility, previous history of STI, previous abdominal or pelvic surgery and a previous ectopic pregnancy. There was one maternal death due to rupture (case fatality rate of 0.8%). The morbidity was significant with 87.3% presenting after rupture, 38.8% being attended with signs of shock, 11.1% requiring intensive care admission and 77% being transfused with blood. The mean hospital stay was 5 days following salpingectomy via laparotomy. The prevalence of HIV amongst those with ectopic pregnancies who were tested was 13.1%.
Conclusion

The morbidity associated with ectopic pregnancy remains high in young women of low parity as the majority present after rupture. The subsequent impact on future fertility of these women could be improved significantly if health strategists focused on primary prevention and early diagnosis to prevent tubal rupture. This means ensuring universal reproductive health care access thereby working towards achieving Millennium Development Goal 5 (MDG 5) by 2015.
ACKNOWLEDGEMENTS

Glory to God who makes all things possible.

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One wise man said, “Share your knowledge. It is a way of achieving immortality”. I wish to thank my supervisors Dr. T. Magwali and Professor Z.M.Chirenje for their guidance and the priceless knowledge I gained as they mentored me. Indeed they have achieved immortality.

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<tr>
<td>ACOG</td>
<td>American College of Obstetricians and Gynaecologists</td>
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<tr>
<td>b- HCG</td>
<td>beta- Human Chorionic Gonadotrophin</td>
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<tr>
<td>DES</td>
<td>Diethylstilbestrol</td>
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<td>EP</td>
<td>Ectopic Pregnancy</td>
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<td>EPAU</td>
<td>Early Pregnancy Assessment Units</td>
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<td>HDU</td>
<td>High Dependency Unit</td>
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<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>ICU</td>
<td>Intensive Care Unit</td>
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<td>IU</td>
<td>International Units</td>
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<tr>
<td>IUCD</td>
<td>Intra-Uterine Contraceptive Device</td>
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<td>MDG 5</td>
<td>Millennium Development Goal 5</td>
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<tr>
<td>PID</td>
<td>Pelvic Inflammatory Disease</td>
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<tr>
<td>RCOG</td>
<td>Royal College of Obstetricians and Gynaecologists</td>
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<tr>
<td>STI</td>
<td>Sexually Transmitted Infection</td>
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<td>ZDHS</td>
<td>Zimbabwe Demographic and Health Survey</td>
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CHAPTER 1

1.1 BACKGROUND TO THE STUDY

Derived from the Greek word ektos, “aka ekkysis” is defined as the implantation of the blastocyst (fertilized ovum) outside the endometrial lining of the uterine cavity. Ectopic pregnancy (EP) is a tragedy of reproduction, the result of a flaw in human reproductive physiology that ultimately ends in fetal demise or loss. Without timely diagnosis and treatment, it can become a life threatening condition. An EP is 10 times and 50 times as dangerous as a vaginal delivery and induced abortion respectively, thus making it an important cause of maternal mortality in the first trimester.

Epidemiology

The incidence rates vary among different countries depending on the risk factors predominant in the geographical region. It accounts for 0.5 to 2% of all pregnancies. In developing countries, the rates vary from 1 in 44 to 1 in 21 deliveries, while in the developed western countries, the rates are between 1 in 233 and 1 in 280 deliveries. In the US, ectopic pregnancies account for 9% of all pregnancy related deaths. The incidence rose from 4.5 to 16.8 per 1000 reported pregnancies between 1970 and 1987 and it became a major health problem in the USA. The marked increase was attributed to a number of factors including an increase in incidence of pelvic inflammatory disease (PID), smoking in women of reproductive age, use of assisted reproductive techniques and general awareness of the condition facilitated by development of early pregnancy assessment units (EPAUs). The latter tended to include even some EP destined to resorb spontaneously. Other reasons included popularity of contraceptives whose failure predisposed users to getting ectopic pregnancy for example use of tubal sterilization. On the other hand, the mortality and morbidity has drastically declined over the decades due to more accurate diagnostic methods with use of
very sensitive b- HCG assays and trans-vaginal ultrasound scan. The mortality has decreased from 72-90% in 1880 to 0.14% in 1990\textsuperscript{26}. The diagnosis is made early and treatment given before rupture occurs.

However, the situation in the developing countries is quite different with morbidity remaining high due to delay in presentation. Patients present after rupture, require massive blood transfusions, are offered radical surgery and are hospitalized for some days.

**History**

Ectopic pregnancy was first described in the 11\textsuperscript{th} century and until the mid 18\textsuperscript{th} century it was usually fatal. \textsuperscript{ii}John Bard reported the first successful surgery to treat an ectopic in New York (1759). In 1884 Lawson Tait reported success of treatment with salpingectomy. The first conservative technique was salpingotomy by Pronchonwick (1894). In 1953 Stomme described salpingostomy. Early in the 20\textsuperscript{th} century great improvements in anaesthesia, antibiotics and safe blood transfusion contributed to the significant decrease in the maternal mortality rate. The first laparoscopic salpingectomy was by Shapiro and Adler in 1973. The case fatality rate decreased from 35.5 deaths per 10 000 in 1970 to 2.6 per 10 000 in 1992 (CDC).

**Aetiology**

The exact aetiology remains enigmatic but it seems that the common denominator in most theories is a delay in ovum transport. The four main possibilities suggested are anatomic obstruction to the passage of the zygote, an abnormal conceptus, abnormalities in the mechanisms responsible for tubal motility and trans-peritoneal migration of the zygote. The risk factors for ectopic pregnancy include previous tubal pregnancy, previous tubal surgery, pelvic inflammatory disease, medical termination of pregnancy, current intrauterine
contraceptive device users, assisted conception, salpingitis isthmica nodosa, smoking and diethylstilbestrol. The chance of having a subsequent ectopic pregnancy after a previous tubal pregnancy is 10-20%. Following sterilization the absolute risk is reduced though with a higher ratio of ectopic to intra-uterine pregnancy. The relationship between pelvic inflammatory disease (PID), tubal obstruction and ectopic pregnancy is well documented. Infection of the endothelium damages the cilia and intra-luminal adhesions and pockets are formed. The risk increases with successive episodes of PID for example 13% risk after one episode, 35% after two episodes and so on. Chlamydia trachomatis induces tubal damage that is associated with tubal pregnancy. Unfortunately 60-70% of these infections are subclinical and therefore not treated. Although PID is a high risk factor for ectopic pregnancy only 50% of fallopian tubes with ectopics have histology showing salpingitis.

All intra-uterine contraceptive devices (IUCD) prevent both intra-uterine and extra-uterine pregnancies but the risk of tubal pregnancy is 7 times higher when conception occurs with an IUCD in situ as compared to conception without contraception. Induction of ovulation with clomiphene citrate or human menopausal gonadotrophin is a predisposing factor for tubal implantation. Salpingitis isthmica nodosa is a histological diagnosis where diverticula are seen. Smoking increases the risk of ectopic pregnancy and the risk is directly proportional to the number of cigarettes smoked per day. Nicotine inhibits oocyte cumulus complex pick-up by the fimbrial end of the fallopian tube and reduces the ciliary beat frequency.

**Pathology**

Ectopic pregnancies are classified according to the site at which they are found. They can be tubal (more than 95%), cervical, ovarian, abdominal, cornual, intra-ligamentous or over a caesarian scar. In the tube the ectopic gestation can be ampullary (70%), isthmic (12%), fimbrial (11%), interstitial or cornual (2%).
The natural progression of a tubal pregnancy is that it can be unruptured early on, or may rupture as the trophoblast invades the thin antimesenteric border of the tubal wall usually. There can be spontaneous involution with death of the conceptus at an early stage. Complete tubal miscarriage, incomplete tubal miscarriage or a tubal blood mole may be the result of an ectopic pregnancy. The time of rupture varies according to the anatomy of the different parts of the tube affected. The isthmic variant ruptures early at 6-8 weeks gestation as it is the narrowest in diameter. The ampullary one ruptures at 8-12 weeks as it has the widest diameter and the interstitial variant may rupture even later at 12-14 weeks because the surrounding myometrium can hypertrophy to accommodate the enlarging conceptus. Histologically the endometrial glands demonstrate an atypical pattern called the ‘Arias-Stella phenomenon’ characterized by hyperplasia of glandular cells, closely packed glands with evidence of hypersecretion, large irregular hyperchromatic nuclei, cytoplasmic vacuolation and loss of cellular polarity. This is however not specific to ectopic pregnancy as it may be seen in intra-uterine pregnancies.

**Diagnosis**

Despite modern nuances, ectopic pregnancy remains a fascinating, multifaceted relatively common clinical entity whose diagnosis challenges us constantly in our daily practice. There is a high rate of misdiagnosis at the initial visit of up to 40-50%, thus a high index of suspicion by clinicians is very important. It should be considered in any woman of reproductive age who presents with the triad of amenorrhoea, abdominal pain and irregular vaginal bleeding. The presentation may be acute or subacute and depends on whether rupture has occurred or not. Schermers found pain as the most common presenting symptom (96%) and irregular bleeding was second (74%). Other signs and symptoms include shoulder pain, syncope, gastro-intestinal symptoms, adnexal mass or tenderness all usually occurring after 6-10 weeks of amenorrhea. After rupture the patient is often pale, hypotensive, tachycardic
with an acute abdomen. When tubal rupture is gradual the presentation is subacute with mild symptoms, a low grade pyrexia sometimes making the diagnosis more difficult to establish.

**Further investigations**

A single serum b-HCG concentration can be used to detect an ectopic pregnancy but with limited value alone. Serial b-HCG measurements are more informative and an increase of less than 66% over 48 hours is suggestive of an ectopic pregnancy. Another method of diagnosing ectopic pregnancy is when there is a plateau in serum b-HCG levels (defined as a b-HCG doubling time of 7 days or more). Progesterone levels have been used for diagnosis and management of pregnancies of unknown location. A meta-analyses has demonstrated that a single serum progesterone measurement is good at predicting a viable intrauterine or failed pregnancy (less than 16nmol/l), but is not useful for locating the site of the pregnancy. Quantitative assessment of b-HCG levels is essential for accurate interpretation of ultrasound findings where a discriminatory level is used. Failure to visualize an intrauterine gestational sac by transvaginal ultrasound with b-HCG concentrations that are 1000-2000 IU/L or more indicates an abnormal intrauterine pregnancy, a recent miscarriage or an ectopic pregnancy.

Transvaginal scanning has proven to be more accurate than abdominal scanning in detecting ectopics (90% vs 80%) as the proximity of the vaginal probe to the pelvic structures and the use of high-frequency transducers (5-7MHz) significantly improves resolution.

A review of literature by Brown and Doubilet summarized the frequency of various ultrasound features in ectopic pregnancies like empty uterus (28%), empty uterus and adnexal mass (35%), intrauterine or pseudo-gestational sac (25%), empty uterus and ectopic gestation sac (12%), fluid in Pouch of Douglas (25%) Colour and pulsed Doppler increase the sensitivity of transvaginal ultrasound and allow earlier detection.
Diagnostic laparoscopy and culdocentesis are now rarely used for diagnosis with the availability of sensitive b-HCG assays and transvaginal ultrasound.

**Algorithm for management of a woman with suspected ectopic pregnancy (appendix 4)**

**Treatment**

Ectopic pregnancy is one of the few medical conditions that can be managed expectantly, medically or surgically. Over the years the management has evolved from being a surgical emergency to more conservative medical management. The treatment option is influenced by the clinical state of the patient, site of the ectopic gestation, reproductive wish of the patient as well as the availability of facilities and technological expertise. All Rhesus D negative women with an ectopic pregnancy who are not sensitized to D-antigen should be given anti-D immunoglobulin.

**Surgery**

When the EP has ruptured surgery is usually performed. This can be achieved by either laparatomy or laparoscopy the former being the preferred method in haemodynamically unstable patients to achieve immediate hemostasis. These patients should be resuscitated first, intravenous access secured, blood sent for a full blood count and 4 units of blood cross matched in preparation for theatre. Surgery can be radical or conservative. Salpingectomy is the radical form of surgery where the affected tube is resected. It is usually performed particularly if:

- The tube is severely damaged
- There is uncontrolled bleeding
- There is a recurrent ectopic in the same tube already treated conservatively
- There is a large tubal pregnancy of > 5cm
The woman has completed her family

- Previous tubal surgery for infertility
- Previous sterilisation and reversal of sterilisation

Conservative surgery is when a salpingostomy or salpingotomy are done to save the affected tube. Salpingostomy is used to remove a small pregnancy usually <2cm in length and located in the distal third of the fallopian tube. A 10-15mm linear incision is made on the anti-mesenteric border immediately over the ectopic and is left unsutured to heal by secondary intention. This is the gold standard surgical method for unruptured ectopic pregnancy with early diagnosis. Salpingotomy is similar to salpingostomy except the incision is closed with a suture in the former. When evaluated in terms of reproductive outcome, conservative surgery is associated with higher subsequent intra-uterine pregnancy and higher recurrent ectopic rates when compared with radical surgery\textsuperscript{xv}. In the presence of a healthy contralateral tube there is no clear evidence that salpingotomy should be used in preference to salpingectomy\textsuperscript{18}. Laparoscopic salpingotomy should be considered as primary treatment when there is contralateral tubal disease and a desire for future fertility\textsuperscript{18}. Laparoscopic approach in the haemodynamically stable patient is preferable to an open approach because the former is associated with shorter operation times, less intra-operative blood loss, shorter hospital stay and lower analgesic requirements\textsuperscript{18}. It essentially has less morbidity.

**Medical treatment with methotrexate**

This anti-neoplastic drug, a folic acid antagonist, can be used to treat unruptured ectopics in properly selected patients. Success is greatest if gestation is <6 weeks, the fetus is dead, the tubal mass is<3.5cm in diameter and b-HCG is <3000IU/L. Contra-indications include intra-abdominal hemorrhage, breastfeeding, immunodeficiency, alcoholism, liver or renal disease, blood dyscrasias, active pulmonary disease, peptic ulcers and use of concurrent medications
like non steroidal anti-inflammatory drugs. Methotrexate may be given as either a single dose (deep intramuscular injection, 50mg/m²) or a variable dose given on days 1, 3, 5 and 7. Success is monitored by serial b-HCG measurements until undetectable. Prior to administration baseline full blood counts, liver and renal function tests should be carried out. It should be clear to the patient that at any point during treatment, rupture may occur, necessitating surgical intervention. Therefore this mode of treatment is only suitable to those who can quickly access 24 hour emergency surgical services should the need arise. Pregnancy should be delayed for at least three months after treatment because of the teratogenicity of methotrexate.

Mifepristone and methotrexate have been used in combination for medical treatment of ectopic pregnancy\textsuperscript{xvi} but more studies are needed to evaluate the role of mifepristone in this regard.

**Controlled expectant management**

This mode of treatment is offered to a small group of carefully selected cases of unruptured ectopics. In the guidelines for management of tubal pregnancy, the Royal College of Obstetricians and Gynaecologists concluded that success was likely in women clinically stable, with a baseline b-HCG less than 1000IU/L, a hemoperitoneum less than 100ml, a tubal mass less than 2cm and no fetal parts on ultrasound\textsuperscript{xvii}.

Women are followed twice weekly with serial b-HCG measurements and weekly transvaginal ultrasound. Thereafter weekly b-HCG and transvaginal scans are done until b-HCG is less than 20IU/L\textsuperscript{17}.
1.2 STUDY JUSTIFICATION

Ectopic pregnancy is a major problem in gynaecology and accounts for one of the commonest gynaecological surgical emergencies in Zimbabwe as in other developing countries, thus making it a relevant public health indicator. It is an important cause of maternal mortality and morbidity in the first trimester of pregnancy.

In an audit that the author carried out at the two central hospitals in Harare (Parirenyatwa and Harare Central) on ectopic pregnancy, there appeared to be an increase in the incidence of ectopics when the numbers were compared month for month for the years 2011 and 2012 up to June 2012. The total number of ectopics managed at the two hospitals over 18 months was 167. The peak age group was the 25-29 year group with the majority being women of low parity (Para 1 and Para 2). Most striking still was that the bulk of disease (83%) presented after rupture and more than half of the patients required a blood transfusion (51.3%). The other concerning finding was that out of 167 laparatomies done for suspected ectopic pregnancy, 15 of them were not ectopic pregnancies (wrong diagnosis). These women were subjected to the morbidity associated with open surgery.

These figures reflect therefore that the morbidity associated with ectopic pregnancy remains high as most patients present late. It remains questionable why women delay in presenting to health care facilities. As a result of late presentation, most patients are treated with radical surgery (salpingectomy) with the consequence of subsequent reduction in the reproductive capacity in women who are at the peak of their reproductive career.

Ectopic pregnancy rupture leads to massive hemoperitoneum in some cases causing severe anaemia requiring massive blood transfusions. These women are then exposed to the attendant numerous risks of massive or large volume blood transfusions that include acidosis,
hyperkalaemia, citrate toxicity, hypocalcaemia, disseminated intravascular coagulation and hypothermia\textsuperscript{xviii}.

Given the burden of disease posed by ruptured ectopic pregnancy, this study will provide information that will guide local policy in terms of prevention and treatment. Public health strategists will find ways of improving and prioritizing, especially, early pregnancy care in Zimbabwe.

1.3 LITERATURE REVIEW

The incidence of ectopic pregnancy was found to be 0.46\% (2004) in a 5 year Nigerian study
similar to the findings of Majhi et al\textsuperscript{xix} (in India) and Igbarese\textsuperscript{xxi} (Niger Delta). In the Nigerian study, 81.9\% of the ectopic gestations occurred in the 21-30 year age group and single women accounted for 51.4\%. Most of the ectopic pregnancies (51.4\%) occurred in the right fallopian tube. The three most common risk factors in the study were PID (51.4\%), previous abortions (25\%) and infertility (2.8\%). The mortality rate in the study was 1.4\%. Musa et al\textsuperscript{xxii} reported an incidence of 1.74\% in Jos. Anorlu et al\textsuperscript{xxiii} reported 2.31\% in Lagos, whilst Aboyeji et al\textsuperscript{xxiv} reported 1.4\% for Ilorin, Nigeria. In the latter study, a third of the women were between 25 and 29 years of age and 61.4\% were of low parity (0-2). In England and Wales the incidence is said to be 1.2\% and it is 1.9\% in the USA\textsuperscript{xxv, xxvi}.

Kasule J and Seeras R\textsuperscript{xxvii} carried out a prospective study from 1981-84 at Harare central Hospital, Zimbabwe. They had a total of 441 ectopic pregnancies out of 162 964 deliveries that were attended in that time period (incidence of 0.27\%), much lower than in other countries. The majority (67\%) of the patients were aged 20-29 years, 88\% being parous. The mean parity was 2.6 and they encountered only one maternal death.

The commonest presenting symptoms in Kasule’s study were lower abdominal pain (96\%), amenorrhoea (78\%) and abnormal uterine bleeding (64\%). At laparatomy 73\% of the women had ruptured and the right tube was involved in 52\% of the cases. A total salpingectomy was carried out in 99\% of patients. Evidence of previous pelvic infection denoted by presence of adhesions and blocked contra-lateral tubes was seen in only 15\% of patients.

A three year Pakistani study\textsuperscript{xxviii} found the gestational age at presentation ranged between 4-11 weeks, the mode being 6 weeks. 33\% of patients had risk factors and amongst them previous abortion was the most frequent factor found. The commonest presenting symptom was abdominal pain in 79\% followed by abnormal vaginal bleeding in 53\% and syncope in 13\%.
On physical examination 84.6% had abdominal tenderness and 64% had cervical excitation tenderness. Serum b-HCG was positive in all cases. Again in Sokoto, Nigeria, Airede LR et al\textsuperscript{xxix} found abdominal pain as the most frequent symptom and the modal duration of amenorrhea was 8 weeks.

In Ilorin, Nigeria, 13.6% of patients were admitted in shock. 75.5% were of low socio-economic status and low education. 57.1% had previous induced abortion and 21% had a previous history of pelvic infection. A previous ectopic was found in 14% of the patients.

A meta-analysis of studies identified 4 factors strongly associated with ectopic pregnancy: previous ectopic, previous tubal surgery, evidence of tubal pathology and in utero exposure to DES\textsuperscript{xxx}. A more recent case-control study in France\textsuperscript{xxxi} identified smoking and a history of sexually transmitted infections as the most important risks. Others were advancing maternal age, history of sub-fertility and tubal surgery.

Previously 85% of ectopics were diagnosed as ruptured and 15% were unruptured. Today, this ratio is reversed in the developed world but remains unchanged in the third world nations\textsuperscript{xxxii}. A Nigerian study had only 1.6% unruptured ectopics and 89.7% of the subjects were offered unilateral salpingectomy as a result of rupture.

In Ghana\textsuperscript{xxxiii}, a study done from 2000-2003 had only 5.4% cases of unruptured ectopics. Lack of awareness of early pregnancy, late reporting by women to health institutions and failure of health care providers to utilize the diagnostic aids for detecting unruptured ectopic pregnancies were cited as the main reasons for low detection rates.

The causes of delay reported in Sudan (2008-2011)\textsuperscript{xxxiv} included being unaware of pregnancy (64%), false reassurance by health provider (28%) whilst 7.5% of patients simply did not take symptoms seriously enough to seek medical attention.
Though surgery is the principal treatment for ectopic pregnancies, early diagnosis allows more conservative forms of treatment to preserve and improve chances of future fertility. A recent meta-analysis showed that laparoscopy is associated with significantly shorter operating time, reduced peri-operative blood loss, shorter duration of hospital stay, shorter convalescence times and is more cosmetic when compared with laparatomy. Laparoscopy thus works out cheaper than laparatomy but the latter may be safer in hemodynamically unstable patients in need of immediate hemostasis.

Randomized control trials have shown no significant difference in future fertility and recurrent ectopic rates between salpingectomy and salpingostomy. Women who underwent surgery with tubal conservation have a tendency towards higher intrauterine pregnancy rates (62-89\%).

The Royal College of Obstetricians and Gynaecologists (RCOG) clinical guideline on management of tubal ectopic pregnancy recommends that laparoscopic surgery be used in preference to laparatomy in clinically stable patients. Salpingostomy should be used in preference to salpingectomy in women with a damaged or absent contra-lateral tube.

The American College of Obstetricians and Gynaecologists (ACOG) guidelines state that comparisons of medical treatment with salpingotomy showed no differences in overall rates of tubal preservation, tubal patency, repeat ectopic pregnancy or future pregnancies.

Guidelines from the Faculty of Sexual and Reproductive Health care of the RCOG on contraceptive use state that the use of hormonal contraception, intrauterine devices and sterilisation should not be restricted in women with a history of ectopic pregnancy.

1.4 OBJECTIVES
Primary objectives

i. To determine the incidence of ectopic pregnancy at Harare and Parirenyatwa Hospitals.

ii. To determine the risk factors associated with ectopic pregnancy at Harare and Parirenyatwa Hospitals.

iii. To determine the morbidity and mortality associated with ectopic pregnancy.

Secondary objectives

i. To determine the HIV sero-status of women presenting with ectopic pregnancy.

ii. To find the proportion of ectopic pregnancies that are ruptured at the time of presentation to the central hospitals.

iii. To determine the treatment options offered for ectopic pregnancy at the two hospitals.

iv. To determine the commonest site of ectopic pregnancy.

v. To determine the proportion of women correctly diagnosed of ectopic pregnancy at the two hospitals in all cases suspected of having an ectopic pregnancy.

1.5 OUTCOME MEASURES

i. The incidence of ectopic pregnancies amongst all the women who delivered at Harare and Parirenyatwa hospitals over the duration of the study.

ii. The demographic characteristics of women suspected of having ectopic pregnancy.

iii. Average gestational age at presentation.

iv. Mean systolic and diastolic blood pressure at presentation.
v. Mean pulse rate at presentation.

vi. Mean haemoglobin count at presentation.

vii. The proportion of patients requiring blood transfusion.

viii. The types of the different surgical modalities used for definitive treatment.

ix. The level of medical practitioner performing the surgery.

x. The proportion of patients requiring post-operative ICU/HDU care.

xi. The mean hospital stay.

xii. The case-fatality rate.

xiii. The proportion of patients who had an HIV test and the proportion with a positive HIV test result.

xiv. The proportion of patients with a false positive diagnosis of ectopic pregnancy.

CHAPTER 2

MATERIALS AND METHODS

2.1 STUDY DESIGN

A cross-sectional study.

2.2 SETTING

Harare central hospital and Parirenyatwa hospital gynaecological units, with a capacity of 36 and 60 beds respectively, making a total of 96 beds. These are the two tertiary hospitals at which all government patients with ectopic pregnancy are referred for management.

2.3 INCLUSION CRITERIA
a) All patients suspected of having an ectopic pregnancy.

b) Patients who agreed to participate in the study.

2.4 EXCLUSION CRITERIA

a) All patients who refused to give informed consent.

2.5 SAMPLE SIZE

All patients presenting with suspected ectopic pregnancy at the two hospitals during the study period were conveniently included in the study after they agreed to participate. The sample size was calculated from a previous study which showed the highest incidence of 2.31% (Lagos, Nigeria) in Africa

The formula used was:-

\[ n = \left( \frac{1.96}{D} \right)^2 \times p(1-p) \]

Where \( p \) = the expected proportion of individuals in the sample with the characteristic of interest

\( D \) = the width of the confidence interval (5% in this study)

1.96 = the Z value at 95 % confidence interval

Therefore \( n = \left( \frac{1.96}{0.05} \right)^2 \times 0.02 \times (1-0.02) \)

\[ = 30 \]

Anticipating a 75% response rate,
\[ N = \frac{30}{0.75} \]
\[ = 40 \]

The researcher increased the sample size to 138 in order to increase the power of the study.

2.6 METHODOLOGY AND DATA MANAGEMENT

The data was collected by the researcher using a standard data collection form (appendix 3) and convenience sampling was used. The researcher went to the gynaecology wards and casualty departments to recruit all patients suspected of having an ectopic pregnancy. Patients who had treatment for ectopic pregnancy were approached after the acute phase was over. The study was explained to each patient and then the researcher asked the patient whether they were willing to give informed consent to participate in the study.

Patients who were willing to participate in the study were asked to sign an informed consent form. The researcher collected part of the data by face to face interviews with the patient and the other part by reviewing the clinical records. The information was entered in a case record file (CRF). The interviews were done in the privacy of the patient’s bed with the curtains drawn. In critically ill patients, the next of kin was asked to sign consent and give a collateral history. Patients were offered HIV rapid tests after pre-test counseling was done. The Determine rapid test kits were used and a positive result was confirmed using the First response rapid test kit.

With the permission of the hospital, sourced documents (post mortem reports and case files) were used to collect information for the deceased participants. The researcher checked all collected data for accuracy before entering it into the excel database. Consistency and data entry errors were checked before analysis.
2.7 STATISTICAL DATA ANALYSIS

The patient’s socio-demographic characteristics and measurement results for the main variables were evaluated using descriptive statistics that is graphs and frequency tables. Descriptive statistics were used to identify the most common factors associated with ectopic pregnancy at the tertiary hospitals. The analysis was performed using Stata version 12.0 (Stata Corporation, College Station, Texas, USA). All statistical evaluations were carried out at 0.05 level of significance. Means, medians (IQR) and standard deviations were used accordingly.

2.8 ETHICAL CLEARANCE

Ethical clearance was granted by the Harare Central Hospital ethics committee and the Joint Parirenyatwa Hospital and College of Health Sciences Research Ethics Committee (JREC) in December 2012. This was followed by approval by the Medical Research Council of Zimbabwe (ref MRCZ/B/442). Only patients who gave informed consent were included in the study. Patient’s names were not used on the data collection forms.

CHAPTER 3

RESULTS

From 01 December 2012 to 30 April 2013, a total of 11 239 deliveries were attended at the two central hospitals (5 114 and 6 125 for Parirenyatwa and Harare Hospital respectively).
There were 138 suspected cases of ectopic pregnancy that were registered and a proportion of 126 (91.3%) of these cases were surgically confirmed as ectopic pregnancy (EP). Of these, 74 cases were managed at Harare Hospital and 52 cases were at Parirenyatwa Hospital. The overall incidence of ectopic pregnancy was 1.12%.

3.1 SOCIO-DEMOGRAPHIC CHARACTERISTICS

The socio-demographic characteristics of the 126 patients with confirmed EP are shown in table 1 below. The age ranged between 18 and 45 years with a median of 30 (IQR: 24–34) years. The majority, 67 (54%) of the patients were in the 21 – 30 year age-group, with 4 (3.3%) aged above 40 years.

Married women accounted for 92% of all the cases with the majority having completed ordinary level education, with median years in school of 11 (IQR: 9–11).

They were mostly unemployed, 179 (62.7%). Patients had a median monthly income of USD 200 (IQR: 150–350) and resided in urban areas with no health insurance cover.

Table 1: Socio-demographic characteristics of the participants, n = 126

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age group (years):</strong></td>
<td></td>
</tr>
<tr>
<td>18 – 20</td>
<td>5 (4.0)</td>
</tr>
<tr>
<td>21 – 30</td>
<td>67 (54.0)</td>
</tr>
<tr>
<td>31 – 40</td>
<td>48 (38.7)</td>
</tr>
<tr>
<td>&gt;41</td>
<td>4 (3.3)</td>
</tr>
<tr>
<td><strong>Marital Status:</strong></td>
<td></td>
</tr>
</tbody>
</table>

xix
<table>
<thead>
<tr>
<th>Status</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td>5 (4.0)</td>
</tr>
<tr>
<td>Married</td>
<td>115 (92.0)</td>
</tr>
<tr>
<td>Widow</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Separated</td>
<td>3 (2.4)</td>
</tr>
</tbody>
</table>

**Occupation:**

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unemployed</td>
<td>79 (62.7)</td>
</tr>
<tr>
<td>Informally Employed</td>
<td>33 (26.2)</td>
</tr>
<tr>
<td>Employed</td>
<td>14 (11.1)</td>
</tr>
</tbody>
</table>

**Monthly income grouping**

<table>
<thead>
<tr>
<th>Income Group</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>27 (21.6)</td>
</tr>
<tr>
<td>100-500</td>
<td>87 (69.6)</td>
</tr>
<tr>
<td>&gt;500</td>
<td>11 (8.8)</td>
</tr>
</tbody>
</table>

**Residence**

<table>
<thead>
<tr>
<th>Residence</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban</td>
<td>83 (65.9)</td>
</tr>
<tr>
<td>Rural</td>
<td>24 (19.1)</td>
</tr>
<tr>
<td>Farming Area</td>
<td>9 (7.1)</td>
</tr>
<tr>
<td>Resettlement/Peri-urban</td>
<td>10 (7.9)</td>
</tr>
</tbody>
</table>

**Health Insurance**
<table>
<thead>
<tr>
<th>None</th>
<th>121 (96.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic Cover</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Comprehensive Cover</td>
<td>3 (2.4)</td>
</tr>
</tbody>
</table>

**Religion**

<table>
<thead>
<tr>
<th>Christian</th>
<th>119 (94.4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (4.0)</td>
</tr>
</tbody>
</table>

Most of the EP occurred in women of low parity (Para 1 & 2). Twenty-three women (18.3%) were nulliparous (see Figure 1) and the mean parity was 2.5. A large proportion of the patients, 73 (58.4%) reported that their sexual debut was after 18 years of age and most reported one lifetime sexual partner, 71 (56.8%).

**Figure 1: Parity of women with ectopic pregnancies**
3.2 RISK FACTORS FOR ECTOPIC PREGNANCY

Table 2 below shows the distribution of patients according to risk factors for EP. The most common risk factors for EP in the study were previous abortion 29 (23.0%), reported sub-fertility 28 (22.2%), reported previous STI, 19 (15.1%) and having had a previous abdominal/pelvic surgery 19 (15.1%). Of those who had abdominal surgery, 9 previously had an ectopic pregnancy. One patient had two previous operations, a previous ectopic pregnancy and appendicectomy. Only one patient indicated being a smoker.

One patient had previous tubal surgery for sub-fertility and one developed an ectopic pregnancy whilst using the IUCD.

Table 2: Distribution of patients according to risk factors for EP

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Para 4+</td>
<td>7.1%</td>
</tr>
<tr>
<td>Para 3</td>
<td>11.1%</td>
</tr>
<tr>
<td>Para 2</td>
<td>28.6%</td>
</tr>
<tr>
<td>Para 1</td>
<td>34.9%</td>
</tr>
<tr>
<td>Para 0</td>
<td>18.2%</td>
</tr>
</tbody>
</table>
Table 3: Reported use of contraception in patients with EP (n=126)

<table>
<thead>
<tr>
<th>CONTRACEPTION</th>
<th>NUMBER</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>59</td>
<td>46.8</td>
</tr>
<tr>
<td>Pills</td>
<td>57</td>
<td>45.2</td>
</tr>
<tr>
<td>Injectables/implants</td>
<td>9</td>
<td>7.1</td>
</tr>
<tr>
<td>IUCD</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Bilateral tubal ligation</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Amongst the women on modern methods of contraception, 85.1% were using oral contraception and 1.5% had an IUCD.

Table 4: Reported treatments for sub-fertility (n=126)

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>NUMBER (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None/not applicable</td>
<td>121(96.0)</td>
</tr>
<tr>
<td>Fertility drugs</td>
<td>0</td>
</tr>
</tbody>
</table>
3.3 CLINICAL PRESENTATION AND INVESTIGATIONS

Clinical presentation of EP occurred within 2 to 12 weeks with a median time after last normal menstrual period (gestation period) of 7.6 weeks. The patients had a median time to admission after onset of symptoms of 0.9 weeks. A slightly greater proportion of patients (52.4%) had symptoms of ill health for more than a week prior to admission. The most common symptoms and signs on admission were as shown in table 5 below.

Table 5: Distribution of patients of clinical symptoms and signs of the patients, n = 126

<table>
<thead>
<tr>
<th>Symptom</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelvic or lower abdominal pain</td>
<td>126 (100)</td>
</tr>
<tr>
<td>Lower Back pain</td>
<td>92 (73.6)</td>
</tr>
<tr>
<td>Vaginal Bleeding</td>
<td>71 (56.4)</td>
</tr>
<tr>
<td>Syncope</td>
<td>49 (39.2)</td>
</tr>
<tr>
<td>Pain radiating to the shoulder</td>
<td>28 (22.4)</td>
</tr>
</tbody>
</table>

Most common clinical symptoms were pelvic or abdominal pain (100%), lower back pain (73.6%) and abnormal vaginal bleeding (56.4%).
Pregnancy tests and ultrasound scans were used in aiding diagnosis for suspected EP cases (Figure 2). In 19.8% of the cases both an ultrasound scan and a urine pregnancy test were not done and in 80.2% of the times an ultrasound scan and pregnancy tests were done.

**Figure 2: Use of urine pregnancy test and ultrasound scan in diagnosing EP**

![Bar chart showing the number of positive, negative, and not done cases for pregnancy test and ultrasound scan.](image)

### 3.4 Morbidity Associated with Ectopic Pregnancy

**Figure 3:** Proportion of confirmed ectopic pregnancies (n=138)
Of the 12 patients that had negative laparotomies (8.7%) for ectopic pregnancy, 3 had ovarian cysts, 1 had perforated bowel and 8 (5.8%) had no identifiable pathology.

There were a total of 110 (87.3%) ectopic pregnancies that were ruptured at the time of laparotomy (Figure 4).

**Figure 4: Proportion of ruptured ectopic pregnancies at laparotomy (n=126)**
Figure 5: Presence of shock on admission

Shock was defined as a systolic blood pressure below 90mmHg and a diastolic blood pressure below 60mmHg with a pulse greater than 100 beats per minute.
The mean pulse rate on admission was 100.4 beats per minute. The average pre-operative haemoglobin was 9.0g/dl (range 2.1-14.3). The average blood that was suctioned as the hemo-peritoneum was 1054 millilitres. It ranged from 100 to 4000 mls.

**Figure 6:** Proportion of patients that required a blood transfusion (n=126)

**Figure 7:** Number of blood units transfused (n=97)
Table 6:  Post-operative care/admission (n=126)

<table>
<thead>
<tr>
<th>WHERE NURSED</th>
<th>NUMBER</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>General gynaecology ward</td>
<td>112</td>
<td>88.8</td>
</tr>
<tr>
<td>Intensive care unit/HDU</td>
<td>14</td>
<td>11.1</td>
</tr>
</tbody>
</table>

The average length of hospital stay by all patients that had an ectopic pregnancy was 5 days. The shortest stay was 3 days and the longest stay was 15 days by one patient that developed wound site sepsis.

Table 7:  Complications (n=126)
The World Health Organisation (WHO) standard definition for anaemia in pregnancy (Hemoglobin less than 11g/dl) was used to define anaemia.

<table>
<thead>
<tr>
<th>COMPLICATION</th>
<th>NUMBER</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia</td>
<td>84</td>
<td>66.7</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>6</td>
<td>4.8</td>
</tr>
<tr>
<td>Wound site sepsis</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Other</td>
<td>1 (bowel perforation)</td>
<td>0.8</td>
</tr>
<tr>
<td>None</td>
<td>32</td>
<td>25.4</td>
</tr>
</tbody>
</table>

3.5 INTERVENTIONS AND OPERATIVE FINDINGS
The main treatment offered was laparotomy (99.2%). One patient initially had a laparoscopy but once diagnosis was made, the operation was converted to a laparotomy. All the patients with an ectopic pregnancy had a salpingectomy done. No conservative surgery was performed. The majority of the operations were carried out by the junior registrars (120 out of 137) and about 12.4% were assisted by a senior registrar or consultant. None of the operations were performed by housemen.

Table 8: Site of ectopic pregnancy (n=126)
Out of the 117 tubal pregnancies, just over half of them were in the right fallopian tube (52.1%) and another 44.4% were found in the left tube. The remainder were not documented.
The proportion of patients with diseased tubes or pelvic adhesions was 17.5%. The women that presented after rupture took a mean of 8.25 hours to get to theatre from the time they were first attended.

3.6 HIV PREVALENCE (n=126)

Most of the participants got tested for HIV, 107 (84.9%). Amongst them, 14 tested HIV positive and 100 were negative. Therefore the prevalence of HIV amongst those tested was 13.1%.

Table 9: Proportion of those with pelvic adhesions/diseased tubes that were HIV positive (n=22)
<table>
<thead>
<tr>
<th>STATUS</th>
<th>NUMBER</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>5</td>
<td>22.7</td>
</tr>
<tr>
<td>Negative</td>
<td>16</td>
<td>72.7</td>
</tr>
<tr>
<td>Not known</td>
<td>1</td>
<td>4.5</td>
</tr>
</tbody>
</table>

3.7 MORTALITY

There was one (0.8% case fatality rate) maternal death due to ruptured ectopic pregnancy. Ectopic pregnancy contributed 1.6% towards the maternal deaths during the study period (63 maternal deaths). Harare Hospital had 33 of the maternal deaths. This was a recently married 22 year old nulliparous woman. She had a ruptured EP and intervention was delayed (one week) because of lack of blood products at the referring provincial hospital. She died 10 hours post-operatively in the intensive care unit of shock and sepsis.

CHAPTER 4

DISCUSSION

There were 126 cases of surgically confirmed ectopic pregnancies that were registered at the two central hospitals in Harare during the study period and a total of 11 239 deliveries attended over the same time period. The incidence of ectopic pregnancy therefore calculated was 1.12%. This was comparable to Nigerian figures which documented an incidence of 1.4%24. In Nigeria23, Lagos had the highest incidence of 2.31% in 2005 and Musa et al22 reported an incidence of 1.74% in Jos. In 1984, Kasule J et al28 reported a low incidence of 0.27% at Harare Central Hospital, Zimbabwe.
Generally, the incidence of ectopic pregnancy ranges from 1-2 % and varies according to the geographical location and the risk factors prevalent in that region. It appears from the study that the incidence or disease burden associated with EP in Zimbabwe is increasing with time. The prevalence has since almost quadrupled but this might not be the true representation. The incidence is calculated using hospital deliveries, so the more the deliveries attended the lower the incidence. The higher incidence may be partially due to the high prevalence of PID that is partially treated due to the widespread injudicious use of broad spectrum antibiotics for trivial ailments.

During the study one maternal death (case fatality rate of 0.8%) was encountered. Ectopic pregnancy was responsible for 1.6% of all the maternal deaths encountered at the 2 hospitals (63). This death could have been prevented by early diagnosis and availability of blood products at provincial level hospital.

The peak incidence was amongst women in the 21-30 year age group (54%) similar to the findings of Majhi et al20 in Kolkata, India and Igbarese et al21 in the Niger Delta. A significant number of women were between 31-40 years (38.7%) and 3.3% were above 40 years. The majority of women were of low parity (Para 0 -2) and accounted for 81.7% of the subjects. The low mean parity of 2.5 when compared to the national figure could imply underlying sub-fertility in these women though it may still be appropriate because about half of the women were still young (21-30 years).

The nulliparous women affected (18.2%) cannot go without mention as this problem may result in long term repercussions of marriage disruption and emotional stress. This is because of the social and cultural norms in Zimbabwe where a lot of attention is given to child bearing. The mean number of children per woman is 4.11 from the latest ZDHS.
The incidence was highest among married women in contrast to the Nigerian study\textsuperscript{19} in which single women were affected the most. A large proportion (58.4\%) reported that their first sexual encounter was after 18 years of age. This again was in keeping with the results of the Zimbabwe Demographic and Health Survey (ZDHS) 2010-2011 that showed that the median age at first sexual intercourse in women aged 25-49 years was 18.9 years\textsuperscript{40}.

In the study, a greater proportion of the women were on contraception (53.2\%) versus 46.8\% that were not using any method. This result was similar to the country’s contraceptive prevalence rate of 57\%\textsuperscript{40} and so was the distribution and preference for the different methods of contraception used. The pill was the most commonly used (85.1\%), followed by injectables and implants (13.4\% combined). None of the participants had bilateral tubal ligation. Only one woman developed an EP whilst using the IUCD (0.8\%). The IUCD’s role in the aetiology of EP has long been debated but in the study it was difficult to conclude that it is a risk factor for EP because of the small sample size and also the fact that the IUCD is not a popular contraceptive method in Zimbabwe\textsuperscript{40} (less than 1\% use). From the ZDHS, married women use the pill more than condoms whilst the unmarried sexually active women tend to use condoms more than pills. This suggests that married pill users who were populous in the study may have been predisposed to sexually transmitted infections leading to tubal blockage if left untreated or partially treated.

In the aetiology of EP, pelvic infections seem to be an important though not singular factor. The major risk factors identified in the study were reported history of sub-fertility (22.2\%), previous miscarriage (23.0\%), previous history of STI (15.1\%), previous abdominal or pelvic surgery (15.1\%) and a history of previous EP (7.1\%). Aboyeji et al\textsuperscript{24} in Nigeria, similarly reported history of previous induced abortion and a history of STI or PID as risk factors for
EP. In the study it was not ascertained whether the miscarriages noted were induced or spontaneous. The risk is there with induced miscarriages with the risk of sepsis. One woman in the study had a history of tubal surgery for sub-fertility and again this result could not be used to conclude that tubal surgery is a risk for EP because most women from the study that were sub-fertile had not been treated (96%) and tubal surgery is not common practice.

At surgery, 17.5% were noted to have pelvic adhesions which were taken as the gross evidence suggestive of pelvic infection. This was somewhat similar to the findings of Kasule J et al\textsuperscript{27} (15%).

The reported history of STI in the study (15.1%) was slightly higher than the national estimated 10% for women\textsuperscript{40}. Thus, a history of STI may actually be a significant risk factor for EP because the actual proportion may be higher as some infections are asymptomatic and go unnoticed and untreated. No specimens were collected to test for current STI’s in the study.

The prevalence of HIV in the study was 13.1% amongst those tested. Since HIV is a sexually transmitted infection its prevalence was sought to try and estimate the prevalence of the other STI’s. The prevalence estimated was almost the same as that in the general population of Zimbabwe (15%) \textsuperscript{40}. It is therefore likely that other less defined factors like neuro-endocrine, genetic or immunological factors besides pelvic infection may contribute to the aetiology of EP.

The clinical features were similar to those reported in other studies\textsuperscript{27, 28} with the common presenting symptoms being lower abdominal pain (100%), abnormal vaginal bleeding (56.3%) and syncope in 38.9%. The median gestational age at presentation was 7.6 weeks. The primary intervention in all (100%) the cases was laparatomy and the EP was tubal in 92.9%. The operation done was radical to achieve hemostasis by salpingectomy. No
conservative surgical techniques or medical treatment were offered because most (87.3%) presented after rupture had occurred. Most of the operations were done by junior registrars (residents). The right tube was affected in 52.1% of the cases as in the study done by Kasule et al\textsuperscript{27} and the commonest site on the tube was ampullary (59%). In the study quite a significant number of EP were noted to be fimbrial (27.4%) which may have been due to observer differences. Information was retrieved from patients’ notes. Of note was the rate of negative laparotomies (5.8%). These women were subjected to significant post-operative morbidity and higher costs yet they could have benefited from laparoscopy.

The morbidity associated with EP has drastically dropped in the developed world in recent years with improved early diagnostic tools and service provision (early pregnancy assessment units). In the early 20\textsuperscript{th} century the commonest presentation was after rupture (85%) but this ratio has reversed with rupture occurring in 15% or less. However in the study, morbidity remained very high with most women being admitted after rupture (87.3%). This proportion was even greater than the 73% documented in the study done at Harare central Hospital more than 30 years ago\textsuperscript{27}. Slightly more than a third were admitted in shock and 77% received a blood transfusion. Three women required massive transfusion of 5 and 6 units of blood. The clinical diagnosis of a ruptured EP is fairly straight forward and usually does not require an ultrasound scan for confirmation but an unruptured EP may cause a diagnostic challenge. In 19.8% of the cases, no pregnancy tests or ultrasound scans were done to facilitate diagnosis.

In a study population of mostly low income individuals (median monthly income of USD$200), it remained questionable whether this could have contributed to delay in making an early diagnosis before rupture. Most patients had symptoms of ill-health for more than a week prior to admission implying poor health seeking behaviours or late referrals.
Intensive care was required to nurse 11.1% of the women and the most common morbidity was anaemia (66.7%) as defined by WHO (haemoglobin<11g/dl). This was similar to Aboyeji’s findings. Two women developed wound site sepsis and one had bowel perforated at laparatomy as it was adherent to pelvic structures. Undoubtedly, the morbidity has remained high and the effect of HIV infection on the morbidity could not be assessed or ascertained because the study did not determine the CD4+ counts, viral loads and whether the subjects were on anti-retroviral therapy or not. The average hospital stay was 5 days.

As with all descriptive studies, they give a broad overview of the features of a disease and its burden but because there is no comparison group, conclusions about causes of disease are not allowed. The actual incidence of EP could be better assessed by doing a population based cohort study and over a longer period of time to remove the bias of possible seasonal variations. The study duration was short (5 months) and at least 1 year would have been better to measure the incidence of EP. All the data was collected over a short period of time in the immediate post-operative period. This eliminated the problem associated with following up participants but on the other hand, limited information concerning long term morbidity. Patient’s clinical records were used to gather information on intra-operative findings and these were observer dependant hence introducing bias because different team members (not researcher) performed the operations and recorded their findings.

CONCLUSION

Ectopic pregnancy is a life threatening gynaecological emergency whose incidence was found to be 1.12% of all deliveries. There was significant morbidity in the first trimester of
pregnancy because the commonest presentation was after rupture had occurred (87.3%) in young women of low parity who probably desired future fertility. The majority of women required a blood transfusion (77%), some required intensive care and the mean hospital stay was 5 days. Signs of shock were present in 38.8% of the cases. Early diagnosis of EP with use of sensitive b-HCG assays and ultrasound scan to prevent rupture was uncommon in the study. The risk factors for EP identified in the study included a history of sub-fertility, previous history of STI, previous abdominal or pelvic surgery and a previous ectopic pregnancy. The HIV prevalence in the study was similar to that for the general population of Zimbabwe\textsuperscript{40}.

**RECOMMENDATIONS**

i. Emphasis should be placed on primary prevention and early detection of EP. Clinicians must have a high index of suspicion in any woman of reproductive age group with symptoms and risk factors for EP and have ready access (24 hours) to sensitive b-HCG assays and ultrasonography at the hospitals. This will contribute towards achieving MDG 5 by 2015.

ii. Women should be empowered by providing them with knowledge on risk factors and symptoms of EP.

iii. Treatment of STI’s and PID should be comprehensive with emphasis on contact tracing and completion of antibiotic courses.

iv. Treatment of both spontaneous and induced miscarriages should be prompt and effective to prevent post- abortal sepsis.

v. Establishment and promotion of subsidized early pregnancy assessment units (EPAUs) will certainly increase the proportion of unruptured EP. This will make
conservative therapy more appropriate and will reduce the overall maternal morbidity associated with ruptured EP.

vi. Gynaecological surgeons ought to have on-going training in operative laparoscopic surgery.

vii. A population-based study (cohort study) may be done to evaluate the actual incidence of EP in the population and give trends.

viii. A further study is required to find out why most women still present after rupture of EP have occurred.

APPENDIX 1

SUBJECT INFORMED CONSENT
PROTOCOL TITLE: THE INCIDENCE AND MORBIDITY ASSOCIATED WITH ECTOPIC PREGNANCY AT HARARE CENTRAL AND PARIRENYATWA HOSPITALS

NAME OF RESEARCHER: DR. TARISAI ELLEN CHINOKWETU-MARERE

PHONE: +263 773 361 701

PROJECT DESCRIPTION: A CROSS-SECTIONAL STUDY

YOUR RIGHTS

Before you decide whether or not to volunteer for this study, you must understand its purpose, how it may help you, the risks to you, and what is expected of you. This process is called informed consent.

PURPOSE OF RESEARCH STUDY

i. To determine the incidence of ectopic pregnancy at Harare and Parirenyatwa Hospitals.

ii. To determine the risk factors associated with ectopic pregnancy at Harare and Parirenyatwa Hospitals.

iii. To determine the morbidity and mortality associated with ectopic pregnancy.

PROCEDURES INVOLVED IN THE STUDY

Information is going to be gathered from the patient with the aid of a questionnaire about the current pregnancy or problem as well as other issues about your reproductive health. This will be done in hospital in private after you have received treatment.

DISCOMFORTS AND RISKS

The study is not going to add any discomfort to you as no other additional tests or treatments are going to be carried out on you.

POTENTIAL BENEFITS

The benefits might not be directed to the patient as such. Other women of reproductive age group from the society will benefit from the results of the study. They will learn the magnitude of the disease and risk factors associated with it.

It will also encourage women with symptoms to seek medical attention early to prevent serious complications and morbidity.

STUDY WITHDRAWAL
You may choose not to enter the study or withdraw from the study at any time without loss of benefits entitled to you.

CONFIDENTIALITY OF RECORDS

The patient’s names will not be used on the data collection forms or in any publications emanating from the study. After the data has been collected it will be kept in a lockable cabinet stored in a lockable room. Only the researcher and the supervisor will have access to the data. When entered into the computer, the information will be password protected and only the researcher will have access to it.

PROBLEMS/QUESTIONS

Please ask questions about this research or consent now. If you have any questions in the future please ask. You may contact the Medical Research Council for more information on 791792/791193 or telefax (263)-4-790715.

AUTHORIZATION

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I know being in this study is voluntary. I choose to be in this study. I know I can stop being in the study and I will not lose any benefits entitled to me. I will get a copy of this consent form. (Initial all the previous pages of the consent form)

__________________________________
Client Signature

__________________________________
Client Name (Printed)

__________________________________
Researcher Signature

__________________________________
Witness Signature

APPENDIX 2
SUBJECT INFORMED CONSENT (SHONA)

PROTOCOL TITLE:  THE INCIDENCE AND MORBIDITY ASSOCIATED WITH ECTOPIC PREGNANCY AT HARARE CENTRAL AND PARIRENYATWA HOSPITALS

NAME OF RESEARCHER:  DR. TARISAI ELLEN CHINOKWETU-MARERE

PHONE:  +263 773 361 701

PROJECT DESCRIPTION:  A CROSS-SECTIONAL STUDY

KODZERO DZENYU
Musati maita sarudzo yekupinda muchirongwa munofanirwa kunzwisisa chinangwa chechirongwa, zvamungangowana kana zvakaipa zvingangoitika nekuve muchirongwa. Ndizvo zvinonzi informed consent muchirungu.

CHINANGWA CHECHIRONGWA
i. Kutsvaga uwandu hwedambudzikpo rekuita nhumbu muchubhu pazvipatara zve Harare ne Parirenyatwa.
ii. Kuda kuona zvinokonzera nezvingangowedzera cuti muite dambudziko irori.
iii. Kuda kuona hudzamu hwechirwere nekuwanda kwevanorasikirwa neupenyu nekuda kwechirwere ichi.

ZVICHAITWA MUCHIRONGWA
Tichatora mhorowondo yepamuviri penyu pazvino uye nezveutano hwenyu hwapabonde. Zvichaitwa muchipatara mushure mekurapwa kwenyu, pakavanzi.

KUSAGADZIKANA KANA NJODZI
Hapana njodzi inotarisirwa sezvo pasina mamwe matesiti kana marapirwo mamwe kunze kwemarapirwo amunenge matoitwa muchipatara.

ZVAMUNGANGOWANA
Hapana zvamungangowana ikozvino, asi zvichabuda muchirongwa ichi zvichabatsira mamwe madzimai nemiwo. Vachadzidza nezveutano hwemadzimai (women’s reproductive health).

Initials__________

KUBUDA MUCHIRONGWA
Munogona kuita sarudzo yekusapinda muchirongwa kana kubuda panguva ipi zvayo musingaraskirwe nezvamanga muchawana pakurapwa kwenyu.

**KUCHENGETEDZWA KWEZVINYORWA**


**MIBVUNZO**

Munogona kubvunza mibvunzo yamunayo ikozvino. Kana mukazoita mimwe mubvunzo panguva inotevera munogona kuridza nhare kuna Dr. Marere panhamba 0773361701. Kana mune mubvunzo nezve kodzero yenyu semunhu ari muchidzidzo ridzai nhare kui Medical Research Council yeZimbabwe (MRCZ) panhamba 791792 kana ku Joint Parirenyatwa Hospital and College of Health Sciences Research Ethics Committee panhamba 791631 ext 2241

**MVUMO**

Nekusaina gwaro rino, murikubvuma kuti chidzidzo chatsanangurwa nemutauro wamunonzwisisa, uye kuti mapindurwa mibvunzo yamabvunza mukagutsikana.


Ndinobvuma kuve muchidzidzo

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<th>Saini yemurwere</th>
<th>Zuva ranhisi</th>
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Zita remurwere

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<th>Zuva ranhasi</th>
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**APPENDIX 3**
QUESTIONNAIRE

Study number: ..............................................

DEMOGRAPHY

a) Date of birth: ........../........../............... 

b) Age (in years): ...........................................

c) Marital Status
   1. Single/never married/not cohabiting
   2. Single/never married/cohabiting
   3. Married/monogamous
   4. Married/polygamous
   5. Widowed
   6. Divorced
   7. Separated

d) Occupation
   1. Housewife
   2. Unemployed
   3. Trader/hawker/semi-skilled
   4. Professional
   5. Subsistence farmer

e) Monthly income per month ...$............... 

f) Level of education (# of years) .................

g) Residence (stay > 6 months in a year)
   1. Urban
   2. Rural
   3. Farm
   4. Resettlement area/peri-urban

h) Health insurance/Medical Aid
   1. No medical aid
   2. Basic cover medical aid
   3. Comprehensive cover med/aid

i) Religion
   1. Christian
   2. Moslem
   3. Traditional
   4. Other

OBSTETRIC, GYNAECOLOGICAL & REPRODUCTIVE HISTORY
a) Parity
   1. Nulliparous (para 0)
   2. Para 1
   3. Para 2
   4. Para 3
   5. Para 4 and above

b) Age at first intercourse
   1. < 16 years
   2. 16-18 years
   3. >18 years

c) Number of partners you have had intercourse with to date
   1. 1 partner
   2. 2 partners
   3. 3 partners and more

d) Previous history of sexually transmitted infections
   1. 0 episodes
   2. 1 episode
   3. 2 episodes
   4. 3 or more episodes

e) Previous history of pelvic inflammatory disease
   1. 0 episodes
   2. 1 episode
   3. 2 episodes
   4. 3 or more episodes

f) HIV status
   1. Unknown
   2. Positive
   3. Negative

g) Method of contraception recently used
   1. Hormonal (pills) ......COC / POP
   2. Hormonal (injectables/implants)
   3. Intrauterine device (IUD)
   4. Bilateral tubal ligation
   5. Barrier methods
   6. None

h) Treatments for sub-fertility
   1. Not applicable
2. Fertility drugs (pills/ injections)
3. Tubal corrective surgery
4. Traditional methods

i) History of any abdominal/pelvic surgery
   1. None
   2. Abdominal surgery
   3. Previous ectopic pregnancy
   4. Pelvic abscess
   5. Previous caesarian section

j) Cigarette smoking
   1. Yes
   2. No

k) History of previous abortion
   1. Yes
   2. No

HISTORY OF CURRENT GYNAECOLOGICAL PROBLEM

a) Date of last normal menstrual period: ........../........./.............

b) Date of onset of symptoms: ........../........./.............

c) Date of Admission: ........../........./.............

d) Period of amenorrhea .................days

e) History of abnormal vaginal bleeding
   1. Yes
   2. No

f) History of lower abdominal/pelvic pain
   1. Yes
   2. No

g) Lower back pain
   1. Yes
   2. No

h) Recent dyspareunia
   1. Yes
   2. No

i) duration of lower abdominal pain if it was present
   1. up to 1 week
2. more than 1 week

j) pregnancy test
   1. unknown status
   2. not done
   3. positive test result
   4. negative result

k) pregnancy booking status (current)
   1. booked
   2. unbooked

l) use of ultrasound scan in aiding diagnosis
   1. not done
   2. suggestive of ectopic
   3. negative result

m) Primary health care giver
   1. Local clinic
   2. General practitioner
   3. Private hospital
   4. Government hospital
   5. none of the above

MANAGEMENT OF PATIENT AT THE CENTRAL HOSPITAL

a) Attended/admitted with signs of shock (raised pulse, low blood pressure)
   1. Yes
   2. No

b) Pulse rate on admission ...............beats/minute

c) Systolic blood pressure on admission ..................mmHg

d) Diastolic blood pressure on admission ..................mmHg

e) Volume of crystalloid given before operation .............mls

f) Pre-treatment or pre-operative Hemoglobin .............g/dl

g) Interval time to surgery/intervention in hours .............

h) Primary intervention
   1. Laparatomy
   2. Laparascopy
   3. Medical treatment with methotrexate
   4. Expectant management

i) If surgical intervention
   1. Salpingectomy
2. Salpingo-oophrectomy
3. Salpingostomy
4. Salpingotomy
5. Other ......................

j) Surgeon performing the surgery
   1. SRMO
   2. Junior registrar
   3. Senior registrar
   4. Consultant

k) Intra-operative findings
   1. Ruptured ectopic
   2. Unruptured ectopic
   3. No ectopic
   4. Ovarian cyst
   5. Other ......................

l) State of pelvis at laparotomy
   1. Normal anatomy
   2. Pelvic adhesions/diseased contra-lateral tube
   3. Not documented
   4. Absent tube

m) Site of Tubal Ectopic pregnancy:
   1. Ampullary
   2. Isthmic
   3. Fimbrial
   4. Corneal
   5. Not tubal ectopic
   6. Not ectopic pregnancy

n) Tube affected
   1. Right
   2. Left
   3. Not documented

o) Estimated blood loss ....................mls

p) Blood transfusion
   1. Not transfused
   2. No of units ...................

q) Post- operative admission
   1. General gynaecological ward
2. High care unit
3. Intensive care unit

r) HIV status (test result)
   1. Positive
   2. Negative
   3. Not known

s) Date of Hospital discharge: …………/………../…………

t) Length of Hospital stay ………….days

u) Complications
   1. Anaemia
   2. Wound site sepsis
   3. Urinary tract infection
   4. Pyrexia
   5. Death
   6. None
   7. Other ……………

v) Discharge bill: ………………………………………………………………………

APPENDIX 4 Algorithm for management of a woman with suspected ectopic pregnancy
REFERENCES


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