

**INCIDENCE, PREDICTORS AND OUTCOMES OF PREGNANCY WITHIN TWO  
YEARS AFTER UNILATERAL SALPINGECTOMY FOR RUPTURED TUBAL  
ECTOPIC PREGNANCY: CASE COHORT STUDY.**

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FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF DEGREE OF  
MASTER OF MEDICINE IN OBSTETRICS AND GYNECOLOGY**

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**DECLARATION**

I hereby declare that this proposal is my original work.

I also declare that it was developed with the guidance of my supervisors.

It has not been submitted to any other university for any purpose.

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## **DEDICATION**

To my dearest husband Dr. Hassan for his love, companionship, support and encouragement throughout the program and life.

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## **LIST OF ABBREVIATIONS**

**ART**- Assisted Reproductive Technology.

**A&E** - Accident and Emergency.

**CS** - Cesarean Section.

**CBD** - Central Business District.

**EP** - Ectopic Pregnancy.

**GOPC** - Gynaecology Out-Patient Clinic.

**hCG** - Human Chorionic Gonadotropin.

**IUP** - Intra-Uterine Pregnancy.

**IVF** - In Vitro Fertilization.

**IUD** - Intra-Uterine Device.

**KNH** - Kenyatta National Hospital.

**LMP** - Last Menstrual Period.

**PID** - Pelvic Inflammatory Disease.

**POD** – Pouch of Douglas

**OR** - Odds Ratio

**STD** - Sexually Transmitted Diseases.

**TVS** -Trans-Vaginal Ultrasonography.

**WHO**-World health organization

## TABLE OF CONTENTS

DECLARATION .....	ii
CERTIFICATE OF AUTHENTICITY .....	iii
ACKNOWLEDGEMENT .....	iv
DEDICATION .....	v
LIST OF ABBREVIATIONS.....	vi
TABLE OF CONTENTS.....	vii
LIST OF TABLES .....	viii
LIST OF FIGURES .....	ix
ABSTRACT.....	x
INTRODUCTION .....	1
Ethical Considerations .....	27
Study limitations .....	27
RESULTS .....	27
Presentation at the time of ectopic pregnancy .....	29
Reproductive history.....	33
DISCUSSION.....	38
Incidence of pregnancy within two years of unilateral salpingectomy.....	38
Predictors of pregnancy within two years of unilateral salpingectomy .....	39
Outcomes of pregnancy within two years of unilateral salpingectomy .....	40
Strengths and limitations.....	40
Conclusions.....	41
Recommendations.....	41
Dissemination of results.....	42
REFERENCES .....	43
APPENDICES .....	46
APPENDIX I: CONSENT FORM.....	46
APPENDIX II: QUESTIONNAIRE.....	49
APPENDIX III: WORK PLAN .....	57
APPENDIX IV: BUDGET .....	58

## LIST OF TABLES

Table 1: Characteristics of women who underwent salpingectomy during previous ectopic pregnancy in KNH (N=276) .....	28
Table 2: Patient presentation and laboratory investigations of ectopic pregnancy in KNH .....	30
Table 3: Association between socio-demographic characteristics and conception within two years after unilateral salpingectomy .....	31
Table 4: Association between socio-economic characteristics and conception within two years after unilateral salpingectomy .....	32
Table 5: Association between menstrual history and conception within two years after unilateral salpingectomy .....	33
Table 6: Association between outcomes of previous pregnancies, history of STD and FP with conception within two years after unilateral salpingectomy .....	34
Table 7: Association between intra-operative findings and pregnancy .....	35
Table 8: Logistic regression for living with a partner, age and occupation .....	36
Table 9: Pregnancy outcomes among women who desire to be pregnant within two years after unilateral salpingectomy for ruptured ectopic pregnancy .....	37



## LIST OF FIGURES

- Figure 1: Schematic of the relationship between the variables and occurrence of pregnancy. .... 15
- Figure 2: Incidence of pregnancy among women who desired to be pregnant within two years after unilateral salpingectomy for ruptured ectopic pregnancy ..... 29

## **ABSTRACT.**

**Background:** An EP oftenly implants in the oviducts and accounts for 1-2% of all pregnancies. It leads to reproductive failure in affected women. Up to 40-60% women conceived after surgery in developed nations with varying outcomes and associated factors. These parameters are unknown in Kenya and Sub-Saharan Africa at large.

**Objective:** To determine incidence, predictors and outcomes of pregnancy among women who desired to conceive within 2 years after unilateral salpingectomy for ruptured tubal EP at KNH between 2011 and 2013.

### **Methodology**

**Study design:** A case cohort study was conducted among 276 women. Ninety two women (cases) conceived while 184 women (controls) did not conceive during study period.

**Study procedures:** A structured questionnaire was completed by the principal investigator via telephone administered interviews and participants' medical records.

**Data analysis:** Data analysis was conducted using SPSS version 21 using 95% CI.

**Results:** It was established that 92 (33.3%) got pregnant. The predictors of pregnancy included age, complications during previous pregnancies, absence of pelvic adhesions etc. Ninety percent of pregnancies were IUP and 10% were repeat EP.

**Conclusion:** The incidence of pregnancy was much lower (33%) when compared to elsewhere (60%). None of the predictors of pregnancy were in tandem with data from elsewhere. Rate of IUP was higher (90% versus 60%) while repeat EP was comparable (10% versus 19%) with estimates from literature.

## INTRODUCTION

An ectopic pregnancy is one that implants outside the endometrial cavity usually in the fallopian tubes (tubal pregnancy). In developed countries it accounts for approximately 1-2% (up to 4% with ART) of all pregnancies while its incidence in developing countries is variable ranging between 0.8% to 4%.<sup>1</sup> The actual prevalence of ectopic pregnancy in Sub-Saharan Africa, Kenya included is not documented but estimates obtained from a survey on '*extrapolation of incidence rate of ectopic pregnancy to different countries and regions*' indicate that the incidence of EP in Kenya is 0.003% (3cases/1000population).<sup>2</sup>

The incidence of ectopic pregnancy has increased primarily due to increased incidence of pelvic inflammatory diseases and progress in diagnostic modalities including the use of highly sensitive beta hCG assays and TVS that allows early diagnosis. Tubal pregnancies may rupture and cause intra-peritoneal hemorrhage making it the leading cause of early pregnancy deaths with 73% of early pregnancy maternal deaths and 5-6% of maternal deaths according to *World Health Organization 2007*.

Several risk factors are associated with EP including PID, contraceptive failure, tubal corrective surgeries for infertility, tubal damage from previous tubal pregnancy, tubal sterilization, ART with patent and damaged tubes, IUD use, prior abortion, prior cesarean section, tubal endosalpingitis, pelvic adhesions, among others.<sup>3</sup>

Ectopic pregnancy can be managed either surgically (laparoscopic or laparotomy), medically using methotrexate or expectantly.<sup>4,5</sup>

In Kenyatta National Hospital ruptured ectopic pregnancy is managed by laparotomy in which women undergo unilateral salpingectomy. Both ectopic pregnancy and its management may compromise a woman's health and future pregnancy prospects.

Globally EP is major issue in contemporary gynaecological practice. Apart from being a major cause of early pregnancy maternal deaths, importantly it has a poor prognosis in terms of fertility post EP management. In addition, adverse pregnancy outcomes are common in subsequent pregnancy. Future reproduction ability of women after EP is compromised although a 40-60% has been documented in developing countries. No documentation of pregnancy prospects after treatment of EP has been documented in Sub-Saharan Africa including Kenya.

KNH receives a large number of patients with EP (at least 2 patients per day) and all the patients are managed with open unilateral salpingectomy as the treatment of choice. There is therefore need for a study within this setting to determine the fate of these women in terms of pregnancy prospects after management of EP by providing baseline data to inform guidelines and policy formulations directed towards improved management of EP.

## **LITERATURE REVIEW**

### **General estimates of EP incidence**

Ectopic pregnancy (eccysis) is pregnancy implanted outside the endometrial cavity commonly in the fallopian tubes (tubal pregnancy).

Different countries have documented different incidence rates. In Europe the incidence is 1 in every 300 pregnancies in comparison with some African countries where the incidence is as high as 1 in every 20-50 pregnancies. The incidence in France where most studies on EP have documented the rate is 2% while in Finland the incidence is 2.8%. In USA the incidence is now at 2.2 % while it is 1.6% in England. In Saudi Arabia the incidence has been reported to be 1.2% while in India the reported incidence is 1 per 161 pregnancies (0.6%).

Incidence of EP has also been documented for some African states. In Yaounde, Cameroon the incidence was 0.8%, in Trankei, South Africa it was 1.1%, Madagascar 2.9%, Benin 4%, Gabon 2.3%, Guinea 1.5%, Nigeria incidence is up to 3.1%.<sup>1</sup>

This variable incidence in Africa could be due to the heterogeneity among studies conducted in different populations and settings. From these few reported incidences an inference of the real incidence of EP in Africa cannot be made because the estimates are from a handful of African countries and African states like Kenya are not included.

The actual incidence of EP in Kenya has not been documented although a survey from USA extrapolated the incidence of EP in Kenya to be 0.003%.<sup>2</sup>

The incidence is about 1-2% (10-20 cases/1000 pregnancies) of all pregnancies in the developed world with a prevalence of 6-16 %. Ectopic pregnancies are more common in black women (8 %) than in white women (4 %).<sup>3</sup>

The overall incidence of EP is on the increase in most countries based on the prevalent risk factors and locally available diagnostic modalities. Globally EP is an issue and the incidence has been increasing over the decades.

Maternal mortality from EP is 5-6% in developed countries according to *World Health Organization* while it is estimated to be 4-10% according to *UpToDate* but unknown in developing countries. In sub-Saharan Africa mortalities from ectopic pregnancies and abortions are recorded in female ward registers rather than maternity ward registers with deaths outside health facilities excluded from health service data. It is therefore highly likely that the contribution of EP to maternal ill-health is significantly underestimated. Based on the review of published literature conducted during the current search there were no data documenting the general incidence of EP in Kenya or its contribution to maternal mortality at the nationwide or regional levels representing a major gap in research evidence in the country and to an extent the wider Eastern Africa region.

### **Incidence of pregnancy after EP treatment**

The incidence of pregnancy after EP depends on the management approach adopted during treatment of EP among other factors. Management of ectopic pregnancy can either be surgical, medical or expectant.<sup>4,5</sup> During surgery open (laparotomy) or laparoscopy (gold standard) is done. Regardless of the method of entry into the abdominal cavity a salpingectomy (surgical removal of the fallopian tube) or a salpingotomy (surgical unblocking of the fallopian tube) is

done.<sup>6</sup> Medical management of EP is by using methotrexate in different schedules while in expectant management observation is used in women who fulfill a certain criteria.

Treatment of EP in Africa is peculiar since most states including Kenya lack modern diagnostic modalities for EP as well expertise and equipment for conservative management of EP. Late presentation further complicates management of EP with most of patients presenting with ruptured EP.

The focus of contemporary management of ectopic pregnancy is preserving a woman's optimal fertility for future pregnancy. Conservative surgical procedures (laparoscopy) seem to be the best in conserving future fertility when compared to radical methods (laparotomy). Laparoscopic procedures (salpingostomy or salpingectomy) have the advantage of shorter hospital stay, less intra-operative blood loss and lower analgesic requirement. Salpingostomy by itself also has the disadvantage of post-operative bleeding and persistent beta hCG.<sup>7</sup> Laparoscopic salpingectomy was also shown to be less successful in eliminating persistent beta hCG post-operatively when compared with laparotomy.<sup>8</sup>

Laparotomy on the other hand has the disadvantage of longer stay in hospital, more intra-operative blood loss and higher requirement of analgesia. Salpingectomy leaves a woman with one fallopian tube which may further compromise her future fertility prospects. Laparotomy has the advantages of complete elimination of EP and reduced incidence of post-operative bleeding.

A study done in France showed that conservative procedures were slightly better in preserving subsequent fertility in women who had previous infertility issues.<sup>9</sup> In Scotland, women with an EP pregnancy had increased chance of another pregnancy within two years compared with women who had a live birth. When compared with women whose first pregnancy was a

miscarriage, women who had an initial ectopic pregnancy had a lower chance of a second pregnancy unlike when compared with women whose pregnancy was a termination or induced abortion.<sup>10</sup> It was found in one study in France that spontaneous conception was 70.4% after laparoscopic surgery and only 53.2% when laparotomy was done.<sup>11</sup>

In conclusion, with regard to the incidence of pregnancy after EP management, evidence in literature shows that medical management of EP is the most effective in preserving fertility in women who meet the criteria for medical management while effect of expectant management has not been extensively studied. Chances of future pregnancy are higher if conservative methods were employed during management at the time of event. There is a scarcity of African studies on this area and no studies were retrieved during the literature review that reported incidence for pregnancy in the post EP management period in Kenyan women.

### **Risk factors /predictors associated with EP**

Studies in EP literature have documented risk factors that consistently occur in women with EP. These risk factors are important because they can predict the future fertility prospects of women who may require obstetric intervention to improve fertility.

In these studies, up to 6-fold increase in frequency of ectopic pregnancy has been reported due to its association with some risk factors like PID, contraceptive failure, tubal corrective surgeries for infertility, tubal damage from previous tubal pregnancy, tubal sterilization, ART with patent and damaged tubes, IUD use, prior abortion, prior cesarean section, tubal endosalpingitis, pelvic adhesions, among others.



### *Pelvic inflammatory disease*

PID occurs following sexually transmitted infection of the upper genital tract caused by either *Nisseria gonorrhoea* or *Chlamydia trachomatis* or both. PID increases the rate of EP by 6-fold. Several mechanisms through which PID could increase the risk of EP have been suggested. PID causes tubular cilia loss, narrowing of tubular lumen, pocket formation, pelvic and peritubular adhesions which lead to tubular kinking and angulation consequently leading to EP or infertility. Risk factors associated with PID include multiple sexual partners, young age (15-25years), unprotected intercourse, previous PID, among others.

### *Contraceptive failure*

Use of contraception generally lowers pregnancy rates including chance of getting an EP. If pregnancy does however occur, some methods increase the probability of getting EP. For example conception with an IUD will most often result in an EP in comparison with non-users of IUD. Mechanism of EP in IUD-users includes duration of IUD use, insertion of progesterone IUD and pelvic infection after IUD insertion. Progestin only pills also predispose to EP secondary to their effect of lowering tubal motility.

### *Age*

Risk of EP increases with advancing maternal age. Women older than 35years of age have a 3-fold risk of having an EP when compared with women younger than 25 years. This high risk of EP in older women is attributed to age related hormonal imbalances and also the dramatic drop in female fertility by this age.

### *Tubal operation*

Tubal operations are usually done to correct infertility-related issues like tubal strictures or hydrosalpinx. These tubal abnormalities can lead to EP. Surgery causes tubal scarring or strictures which jeopardize the process of implantation leading to EP.

### *History of previous EP*

There's strong association between EP and subsequent EP. Women with previous EP have an increased risk of a repeat EP. Risk of EP increases immensely with the number of previous EP.

### *Smoking*

Smoking has been shown to strongly increase the risk of EP through unknown mechanisms, though it is thought smoking impairs tubal function especially tubal motility.

Several different risk factors associated with reproductive outcomes following an EP have been identified in different populations except for one study that assessed fertility outcomes after EP and use of IUD at time of index EP in France. Intra-uterine device non-users were found to have a 10.5% of getting an EP and none (0%) of IUD users got pregnant after treatment of EP. Intra-uterine pregnancy rate decreased with increasing age and was even lower in women who had history of infertility and tubal damage.<sup>12</sup>

An Iranian study identified several risk factors associated with EP with varied associations. These factors include previous EP, prior PID, previous tubal surgery, abdominal surgery, tubal blockage, advanced maternal age, cigarette smoking, intrauterine device, prior abortions, gravidity and previous live birth, and history of subfertility.<sup>13</sup>

A study done in France found that previous history of infertility was the only factor associated with poor reproductive performance. Women less than 30 years of age had 61% cumulative IUP rate at one year while it was only 51% in women aged more than 30years.<sup>14</sup>

History of infertility, age >30years, previous obstetric performance were the only factors affecting fertility in a study done in Saudi Arabia. Sixty four per cent of women 30 years and below achieved a term pregnancy while only 38% of those above 30years achieved a term pregnancy.<sup>15</sup>

Age of than 35years, history of infertility and tubal damage were the factors contributing to future fertility after EP in another study from France. Older age was noted to significantly reduce the chance of IUP with one year (rate of 37% in women above 35years and 65% in those less than 24 years).<sup>16</sup>

Commonest risk factors of EP identified in study in Nigeria were multiple sexual partners, previous abortions and sexually transmitted diseases.<sup>17</sup>

The following risk factors were identified in women EP from an Iranian study, age, gravidity of >2, parity of 3or more, previous abortion and EP, history of PID, history of pelvic and abdominal surgery, infertility and its treatments, tubal ligation and IUD use were all associated with EP.<sup>18</sup>

Age, smoking habits, history of previous abortions, prior STDs, IUD use, ovulation induction with clomiphene and history of infertility were identified in one study in France as factors that increase the risk of EP. Oral contraceptive pills reduced the risk of EP. Women aged between 35years and 45 years were found to increase the risk of getting an EP.<sup>19</sup>

### *Other risk factors*

There are other documented although rarer risk factors for EP. A woman who undergoes ***assisted conception*** can get an ectopic pregnancy especially when embryos have been transferred. Assisted conception is still a nascent field in the vast majority of developing countries and this may not be considered a major risk factor at population level but should be noted among the subgroup of women who undergo these assisted conception procedures.

A second risk factor for EP under this group is ***gravity and previous history of live birth***.

***Prior abdominal surgeries*** like appendectomy also fall in this category.

### **Pregnancy outcomes after EP treatments**

The expected outcomes of pregnancy in women who were treated for EP regardless of the mode of treatment at the time of incident can either be conception with an intra-uterine pregnancy or repeat/recurrent ectopic pregnancy. The consequences of intra-uterine pregnancy can either be an ongoing pregnancy, term or preterm delivery, miscarriage or an induced abortion.

EP could be considered a tragic event with regard to conception; it is a failure of reproduction in the affected women.

Generally the chance of conception after surgery for EP is 50-69% while the chance of recurrent EP is 19%. The studies reporting the chances for future conception following EP have been conducted in developed countries and may not be directly generalizable to developing countries due to the clear-cut health systems differences.

Two studies done in Denmark showed that cumulative pregnancy rates was 61% and 88% with salpingotomy and 56% and 66% with salpingectomy while the rates of repeat EP was found to be 8% with salpingotomy and 5% with salpingectomy.<sup>20,21</sup>

In United Kingdom, spontaneous IUP rate after expectant and surgical management was found 84% and 64% respectively but the risk of repeat EP was not statistically significant between the two groups, 8% in the expectant group and 12% in the surgical arm.<sup>22</sup>

An RCT in Netherlands found out that the cumulative ongoing pregnancy rate after salpingotomy was 61% and 56% after salpingectomy although salpingotomy had a higher rate of persistent beta hCG in comparison to salpingectomy (7% versus 1%). The rate of recurrent EP was 8 and 5% in salpingotomy and salpingectomy respectively.<sup>23</sup>

Two other studies in Netherlands gave contradicting results. The first study indicated higher 3 year cumulative pregnancy rates in women treated conservatively when compared with those treated surgically while the second study showed that there was no difference between the two groups with regard to subsequent fertility and even rate of repeat EP.<sup>8,23</sup>

Women whose first pregnancy was EP regardless of mode of treatment had a higher chance of a second pregnancy when compared with women whose first pregnancy was a termination or women whose first pregnancy ended up in live birth. In comparison with women who had miscarriage in their first pregnancy, those with EP had a lower chance for a second pregnancy. Those with EP had a higher chance of a recurrent EP when compared with their counterparts.<sup>24</sup>

Most of the following estimates of pregnancy outcomes have all been extracted from EP literature in France where extensive research on this topic has been conducted. The rate of spontaneous conception following laparoscopy was shown to be high (70%) when compared

with laparotomy (53%) in a one study. The rates of live births were 50% and 37% respectively indicating that laparoscopic treatment was superior to laparotomy.<sup>11</sup>

In women using IUD at the time of EP, spontaneous IUP was 87% and only 60% in those who were not using IUD at the time of EP.<sup>12</sup>

Similarly in another study, after treatment of EP with methotrexate 82% of women got pregnant spontaneously or via assisted conception. Most of these pregnancies were IUP (81%) and 19% were repeat EP. Cumulative IUP rate after one year was 58% and 24% after 2 years.<sup>14</sup>

No statistically significance difference was found in rate of conception and carrying pregnancy to term (50% in conservative group and 56% in radical group) in one study from Saudi Arabia. There was also no significant difference in the probability of IUP for both term and spontaneous abortions between the two groups (61% and 69% respectively). There was also no difference in rate of repeat EP (11% in both groups).<sup>15</sup>

Mean time before conception after treatment was found to be 5 months in one study in France with 66% becoming pregnant and cumulative pregnancy rate at one year was 66% and 81% in second year (85% were IUP and 10% were recurrent EP). Cumulative repeat EP rate was 13% at first year and 19% after 2 years.<sup>16</sup>

In the same setting but a different study, the 2-year cumulative intra-uterine pregnancy after salpingectomy was 67%, 76% with salpingotomy and 78% with medical management. The 2-year cumulative EP recurrence rate was 19% following salpingectomy and salpingotomy; while it was 26% after medical treatment.<sup>24</sup>

It is evident that ectopic pregnancy although accounting for only 1-2% of all pregnancies poses a significant physical and psychological trauma to affected women especially those who desire to get pregnant again but have risk factors like older age (35 years and above), history of infertility, history of IUD use, previous miscarriages, previous pelvic surgeries, PID among others.

In reproductive health older age (35 years and above) is significantly associated with fertility since at this age, female fertility dramatically drops with only 5% chance of getting pregnant per menstrual cycle in comparison to more than 20% of conceiving per cycle in younger women. Secondly older age by itself is a risk factor for EP.

As per the available evidence older age also had reduced chances of getting pregnant (37-51%) after treatment for EP compared with younger women (61-65%). Twenty two percent of pregnant women with EP are aged between 35-44 years while the rate is only 7% in those aged between 15-24years.

The burden of EP in Africa is high but its magnitude is not sufficiently documented, and therefore the fate of women desiring pregnancy after management of EP is not known. In KNH all patients are managed by open salpingectomy, a radical procedure leaving these women with only one fallopian tube which may further compromise their chance for future conception.

This study therefore will provide baseline data for assessing a very sensitive aspect of EP management which is pregnancy outcome after unilateral salpingectomy for ruptured tubal pregnancy in KNH particularly in women desiring to conceive again after treatment of EP. The data obtained after the study may also inform clinical guidelines, best practice and policy formulations directed towards improvement of management of EP.

## **CONCEPTUAL FRAMEWORK**

### **NARRATIVE**

Ectopic pregnancy is quite common and may be life threatening if not managed in good time as it is the leading cause of early pregnancy maternal deaths. It affects 1 in every 40 pregnancies and the affected women endure a frightening and distressing experience following the consequences of ectopic pregnancy that include quick, early and sad loss of their baby, invasive treatment of the ectopic pregnancy, risk of mortality from the ectopic pregnancy and the impact of ectopic pregnancy on future pregnancy.

Several risk factors determine the probability of conceiving again after an ectopic pregnancy.

Socio demographic factors like age affect probability of future pregnancy. Woman older than 35 years if they become pregnant have a 3-fold risk of getting an ectopic pregnancy in comparison with those younger than 25 years.

Contraceptives prevent pregnancy but if conception occurs with an IUD in situ or with use of progestin only pills it may lead to EP.

Women who have or have history of PID and endosalpingitis have increased risk of getting ectopic pregnancy due to pathology caused to the tubes and surrounding tissues.

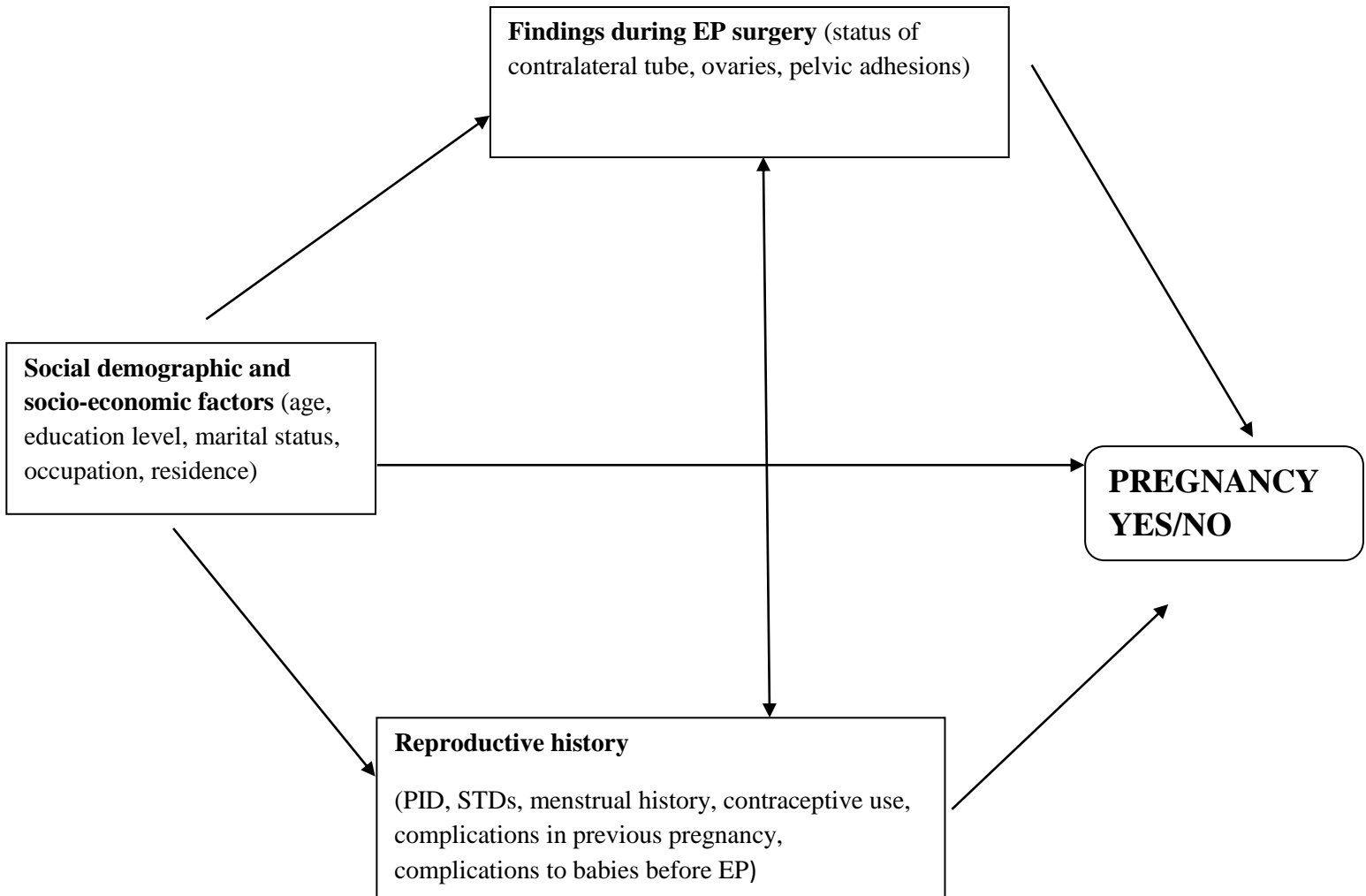
Tubal operations to improve fertility may also lead to EP due to poor cilia activity and poor conceptus transport.

Since future pregnancy cannot entirely depend on the aforementioned factors alone, the other factors (in the schematic) also act independently or synergistically leading to the occurrence of pregnancy regardless of whether it is intra-uterine or a recurrent ectopic pregnancy.



Figure 1: Schematic of the relationship between the variables and occurrence of pregnancy.

The **dependent variable** is pregnancy while the **independent variables** include socio-demographics, socio-economics, intra-operative findings during the EP and reproductive histories.



## **PROBLEM STATEMENT AND STUDY JUSTIFICATION**

### **Problem statement**

Ectopic pregnancy accounts for 1-2% of all pregnancy in the developed countries. The disease burden posed by EP in practice of gynecology is high in the developing countries including Kenya although there is no sufficient documentation of its magnitude, therefore the incidence, prevalence, risk factors, clinical presentation, modes of treatment and pregnancy prospects after management of EP is not known in Kenya.

Reasons as to why much is not known on contribution of EP to disease burden on practice of gynecology in developing countries (including Africa and Sub-Saharan Africa) include:

- At present more focus is directed towards causes of maternal morbidity and mortality from late pregnancy and puerperium rather than early pregnancy even though EP is the leading cause of early pregnancy deaths.
- All women presenting with EP are managed with radical surgery (open salpingectomy) as the treatment of choice since at that moment clinicians are overwhelmed by stabilizing the patient rather than her post-operative prospects for future pregnancy.
- The gold standard for management of EP is laparoscopy (salpingotomy or salpingectomy can be done) but in most developing countries radical management (open salpingectomy) is still being practiced due to lack of laparoscopic equipment and skill.
- After management these women are lost to follow up since they are probably seen only once for review in GOPC after which their future pregnancy prospects is unknown.

- **Justification**

Kenyatta National Hospital the setting for this study is one of the largest teaching and referral hospital in Kenya and it receives a bulk of patients presenting with EP (at least 2 patients daily). Most of these patients present as an emergency with ruptured EP and are managed with open unilateral salpingectomy as the treatment of choice, prospects for future pregnancy notwithstanding.

- There is need to understand the predictors of pregnancy in order to provide timely advice upon performance of unilateral salpingectomy.
- There is therefore need for a study within this setting to provide preliminary data on incidence, predictors and pregnancy outcomes after unilateral salpingectomy, to provide baseline data which in turn will inform guidelines, best practice and policy formulations to help improve management of EP.

## **RESEARCH QUESTION**

What is the incidence, predictors and outcomes of pregnancy among women who desired to conceive within two years after unilateral salpingectomy for ruptured ectopic pregnancy at KNH between 2011 and 2013?

## **HYPOTHESIS**

**NULL:** There is no association between known predictors of pregnancy and probability of pregnancy among women who desired to conceive within two years after unilateral salpingectomy for a ruptured ectopic pregnancy.

## **OBJECTIVES**

### **BROAD**

To determine the incidence, predictors and outcomes of pregnancy among women who desired to conceive within two years after unilateral salpingectomy for ruptured ectopic pregnancy in KNH between 2011 and 2013.

### **SPECIFIC**

1. To determine incidence of pregnancy among women who desired to conceive within 2 years after unilateral salpingectomy for ruptured ectopic pregnancy in KNH between 2011 and 2013.
2. To determine association between socio-demographics and socio-economic characteristics with pregnancy among women who desired to conceive within 2 years after unilateral salpingectomy for ruptured ectopic pregnancy in KNH between 2011 and 2013.

3. To determine the association between the reproductive history and intra-operative findings with pregnancy among women who desired to conceive within 2 years after unilateral salpingectomy for ruptured ectopic pregnancy in KNH between 2011 and 2013.
4. To determine the pregnancy outcomes among women who desire to conceive within 2 years after unilateral salpingectomy for ruptured ectopic pregnancy in KNH between 2011 and 2013.

## **METHODOLOGY**

### **Study design:**

This was a hospital-based case cohort study conducted in the Department of Reproductive health of KNH. Two hundred and seventy six consenting women who desired a pregnancy after unilateral salpingectomy for a ruptured tubal EP participated. Ninety two (cases) became pregnant and 184 (controls) did not. The predictors of pregnancy were compared among the cases and controls unlike the pregnancy outcomes which was determined only among the cases.

Case cohort study design was selected as a suitable design for this study because it allowed the reporting of incidence of pregnancy in a cohort of women following salpingectomy and also allowed the selection of a sample of cases and controls to be derived from same cohort of women to examine associated predictors of pregnancy among women who desired a pregnant within two years after unilateral salpingectomy for ruptured ectopic pregnancy. This design was also ideal because it can be used to study rare outcomes in data accumulated over time for example the data collected in KNH reproductive health department between 2011 and 2013. Case cohort study design also reduced the potential for both selection and information bias.

**Study site and setting:**

The study was conducted at Department of Reproductive Health of Kenyatta National Hospital (KNH), a national teaching and referral hospital. Kenyatta National hospital was suitable for this study because it receives a bulk of patients presenting with ruptured EP (at least 2 patients daily) who are managed with open unilateral salpingectomy and also retrieval of the participants' medical records was possible because the hospital's central registry is ISO-certified.

It is located in Nairobi 4 km west of the CBD and it's the main teaching hospital for the School of Medicine, University of Nairobi. It provides health services for patients from Nairobi and its environs as well as referrals from other hospitals countrywide including the greater Eastern Africa.

The Department of Reproductive Health has a labor ward, one elective gynecology cases ward (ward 1B), one acute gynecology ward (ward 1D), a triage room in the accident and emergency area (room 8), gynaecology theatre 2 in the main theatre, clinic 18 and clinic 66.

With regard to management of ectopic pregnancy, patients are first received in room 8 at A&E where history is taken and clinical examination is done, resuscitative measures instituted on the hemodynamically unstable patients, blood samples for confirmation of pregnancy, grouping and cross-matching are drawn, ultrasound scan requests are also ordered from here and preparation before surgery are all done here.

The patient is then transferred to theatre 2 where the open salpingectomy is done under general anaesthesia. After the operation the patient is wheeled to recovery room till full recovery from anaesthesia then admitted to ward 1D for post-operative care for 3 days after which the patient is discharged home through GOPC (clinic 18) if no post-operative complications.

The woman is then reviewed at GOPC after two weeks for any problems after discharge and status of wound healing assessed. If all is well the woman is then discharged from GOPC. Some clinicians address pregnancy prospects and advice the woman to wait for 3 months before trying to conceive again and return the moment she thinks she's pregnant again.

Care provision for patients with ectopic pregnancy is offered by a multidisciplinary team of service providers including consultants and specialists, senior registrars, residents, qualified nurses, medical and clinical officers together with nursing students.

### **Study population:**

Study participants were women admitted in KNH with ruptured tubal ectopic pregnancy between January 2011 and December 2013 and consequently managed with unilateral salpingectomy. The ectopic pregnancy was diagnosed using last menstrual period (LMP), positive pregnancy test and ultrasound scan confirming the ectopic pregnancy.

#### **INCLUSION CRITERIA**

- Women who desired to get pregnant again.
- Women who gave informed consent.
- Women with a ruptured index tubal ectopic pregnancy.

#### **EXCLUSION CRITERIA**

- Women with history of bilateral tubal ligation (BTL)
- Ectopic pregnancy outside the tubes.

## Sample size determination

(1) For determining the sample size for the incidence of pregnancy within 2 years after unilateral salpingectomy for ruptured ectopic pregnancy:

$$n = (Z^2 * pq) / d^2$$

n = sample size required: number of women who desired pregnancy after unilateral salpingectomy from a finite population of 500

$Z_{\alpha}$  = Normal standard deviate at 95% confidence level=1.96

P = percentage of women who desired pregnancy after unilateral salpingectomy and conceived=50 (Femke Mol et al, RCT)

$$Q=100-P=100-50=50$$

$$D=4$$

Based on a finite population of 500, the number of women who desired pregnancy =273

2. For determining the predictors of pregnancy within 2 years among women who desired pregnancy after unilateral salpingectomy, the sample size was obtained using the Fleiss formula below:

$$n_{cases-Fleiss} = \frac{\left[ z_{\alpha/2} \sqrt{(r+1) * p * (1-p)} + z_{1-\beta} \sqrt{r * p_0 * (1-p_0) + p_1 * (1-p_1)} \right]^2}{r * (p_0 - p_1)^2}$$

(Fleiss J.L. *Statistical Methods for Rates and Proportions*. John Wiley & Sons, 1981.

Print.

Where:



n = size of cases

$Z\alpha$  = 95% level of significance = 1.96

$Z\beta$  = 80% power of the study = 0.84

$\bar{p}$  = average of  $(p_1+p_2)/2 = (7.6+20)/2=13.8$

$P_0$  = percentage of pregnant women who were 35 years and above=7.6 (Femke Mol et al, RCT)

$P_1$  = percentage of women who did not achieve a pregnancy who were 35 years and above =20(Femke Mol et al, RCT)

Odds ratio to be considered significant=0.33

Ratio of unexposed to exposed=1:2

$$\begin{aligned} n &= [1.960 \cdot \sqrt{((2+1) \cdot 13.8(100-13.8)+0.84 \sqrt{2 \cdot (7.6 \cdot (100-7.6)+20 \cdot 100-20)})^2} / \\ &(2(7.6-20))^2 = [1.96\sqrt{3 \cdot 13.8 \cdot 86.2+0.84\sqrt{2 \cdot 7.6 \cdot 92.4+20 \cdot 80)}}]^2 / (2(7.6-20))^2 \\ &= [1.96\sqrt{(3568.68) + 0.84 \sqrt{(1404.48+1600)}}]^2 / (2(7.6-20))^2 \\ &= [1.96 \cdot 59.7 + 0.84 \cdot 54.8]^2 / 307.5 = (117.0+46.0)^2 / 307.5 = 86 \end{aligned}$$

Minimum number of cases = 86; minimum number of controls=172

### **Sampling procedure and recruitment:**

Simple random sampling procedure was used to obtain the study sample from all the participants' files with diagnosis of laparotomy for ectopic pregnancy from January 2011 to December 2013. This was achieved by random selection from an obtained sampling frame and all the files in the frame were assigned identifiers based on sequential numbering. A computer generated random number sequence linked to identifiers was then generated and used to select 500 files randomly for the study. All the 500 files in the random sample were retrieved from the

hospital's main registry. The 500 files were retrieved to include the sample size, those who were not reached and replacement of those who declined participation. Participants' contacts were retrieved from their files, a telephone call was then made in presence of a witness (a colleague from the department) to thoroughly explain the purpose of the study and obtain a verbal consent to participate in the study. After a participant confirms to have understood and agreed to participate in the study, both the witness and principal investigator signed and dated the consent form and part I of the questionnaire was filled followed by completion of Part II of the questionnaire from the participant's medical records. If a participant declined participation she was excluded from the study and the next participant who consents recruited. Consecutive enrolment of participants was used. Minimum of 5 questionnaires was completed in a day of the 8 weeks of data collection. Those women who wished to conceive and conceived were chosen as cases while those who wished to conceive and did not conceive were the controls. The ratio of cases to controls was 1:2

## **Data variables:**

### **Independent variables:**

1. **Socio-demographic variables** - age, marital status, education level, occupation, residence.
2. **Reproductive history variables** – menarche, menstrual history, maternal, fetal and neonatal complications, history of contraceptive use, intra-operative findings and infection history.

### **Dependent variable:**

3. **Pregnancy and its outcome variables** – intra-uterine pregnancy with its consequences (delivery, ongoing, miscarriage) or repeat ectopic pregnancy.

## **Data collection and management**

A case cohort study was conducted involving women who desired a conception after unilateral salpingectomy for a ruptured EP. An estimated precision of 5% and the 95% confidence interval was used. A sample of 276 participants was used in the data collection process. Data was collected using a pretested questionnaire shown in appendix 3. The study instrument collected data on social demographics, social economics, reproductive history including conception and information on the index EP obtained from both telephone-administered interviews and participants' medical records. At least 5 participants were interviewed in a day depending on the availability of a witness to achieve the desired sample size of at least 276 women within the 2 months of data collection. The data was then entered into Microsoft excel data base with inbuilt

consistency and validation checks. Data was cleaned and stored in a password protected external storage device (USB) with accessibility to principal investigator, statistician and supervisors.

### **Reliability**

The questionnaire was pre-tested on a small number of randomly selected patients who recently had unilateral salpingectomy for ruptured tubal EP being reviewed in GOPC. The tool was then reassessed and necessary adjustments made.

### **Data Analysis and Statistical plans.**

Data was computerized using Microsoft Excel version 10 and analyzed using SPSS version 21 and presented in charts and tables. For demographic variables, the mean, mode and standard deviation were used. For categorical data, proportions and frequency distributions summarized data. Percentages were used to depict patient presentation and laboratory findings during the index EP. Cumulative incidence of pregnancy was determined by dividing number of women who got pregnant (92) over the total number of participants (276) recruited multiplied by 100. Odds ratio was the main measure of association between incidence of pregnancy and its predictors. Statistical significance was set at 5%. Univariate analysis was conducted using Pearson's chi square for independence while multivariable analysis with adjusted odds ratio was applied to determine independent predictors of pregnancy after unilateral salpingectomy following ruptured EP. The data was protected using passwords and backed up using external hard drive like flash disc. At the end of the study raw data was destroyed via shredding.

## **Ethical Considerations**

The principal investigator sought ethical approval from Kenyatta National Hospital-University of Nairobi Ethics and Research committee (Appendix 3). Verbal consent was sought from all participants recruited in the study. Information obtained from the participants' and their medical records was kept confidential and used for the purposes of the study alone. No names or any identifier of a participant was written on the data collection tool. Consent explanation and form is attached (Appendix 1).

## **Study limitations**

There was poor documentation of detailed history, clinical examination and intraoperative findings in the participants' medical records. Most of the participants shied away from revealing the infectious status.

## **RESULTS**

During the study conducted between June and July, 2016 a total of 276 women with a ruptured index ectopic pregnancy who had undergone unilateral salpingectomy and desired to get pregnant again were identified and participated in the study. The characteristics of the participants are summarized in table 1. The mean age of participants was 27.1 years ( $SD \pm 5.3$ ) with a range btw 16 and 44 years. The most frequent age groups were 25-29 years (43.1%) and 20-24 years (29.3%). Most participants had either primary (52.9%) or secondary (32.6%) level of education, 49.3 % were single and majority (97.8%) resided in Nairobi.

**Table 1: Characteristics of women who underwent salpingectomy during previous ectopic pregnancy in KNH (N=276)**

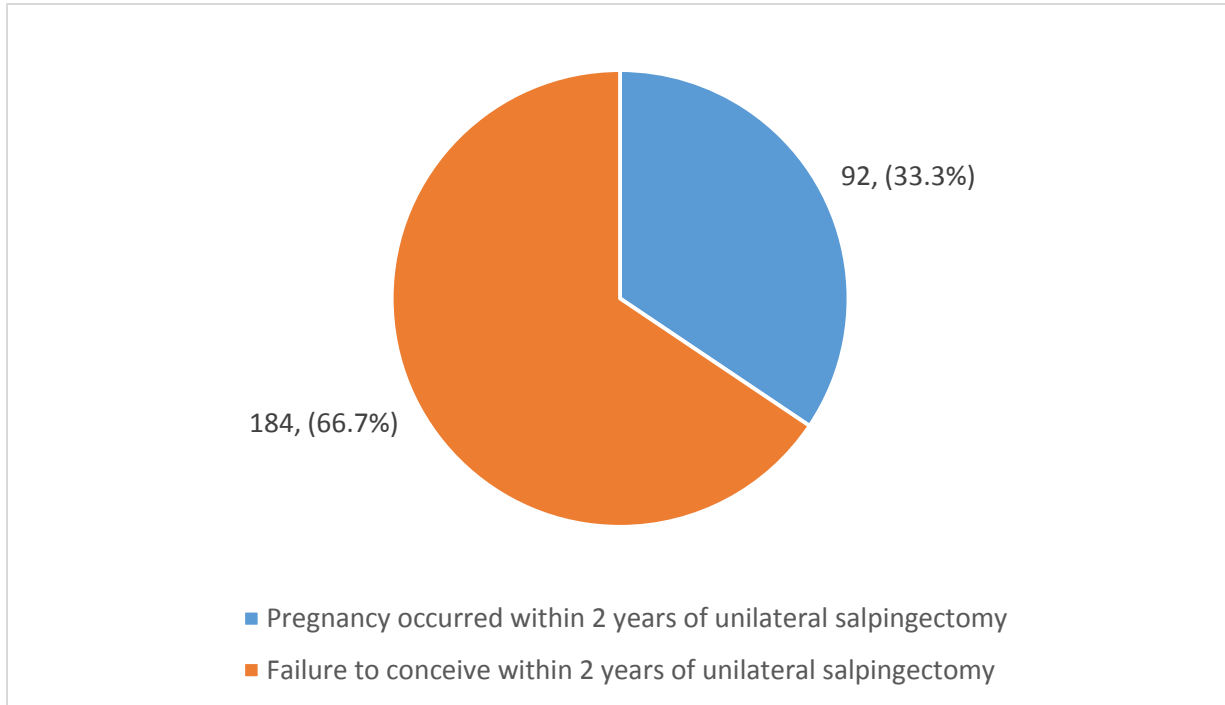
<b>Characteristic</b>	<b>Frequency (n=274)</b>	
<b>Percent (%)</b>		
<b>Age of participant</b>		
16-19	10	3.6
20-24	81	29.3
25-29	119	43.1
30-34	36	13
35-39	24	8.7
40-44	6	2.2
<b>Education level</b>		
Not educated	2	0.7
Primary	146	52.9
Secondary	90	32.6
College/university	38	13.8
<b>Marital status</b>		
Single	136	49.3
Married	99	35.9
Cohabiting		39
	14.1	
Separated	2	0.7
<b>Residence</b>		
Within Nairobi	270	97.8

### **Incidence of pregnancy after unilateral salpingectomy**

Out of the 276 women who had undergone unilateral salpingectomy and wished to conceive within 2 years of the operation, a total of 92 had a pregnancy within two years. Thus, the cumulative incidence of pregnancy among women who desired to be pregnant within two years

after unilateral salpingectomy for ruptured ectopic pregnancy was 33.3% (95% CI 28.8 % – 40.4%), Figure 2.

**Figure 2: Incidence of pregnancy among women who desired to be pregnant within two years after unilateral salpingectomy for ruptured ectopic pregnancy**



### **Presentation at the time of ectopic pregnancy**

Among the 276 patients presenting at KNH with ruptured index ectopic pregnancies 65.2% were referrals from other health facilities. Table 2 presents the clinical features of patients on presentation with the ruptured index ectopic pregnancy. About 3% of the patients were resuscitated during admission. There were close to 100%, 97%, 76% and 50% women who presented with amenorrhea, abdominal pain, vaginal bleeding, and a positive paracentesis respectively. Out of the 94% whose hemoglobin levels were estimated close to 61% had anemia with hemoglobin level < 11g/dl. Most had positive beta hCG.

**Table 2: Patient presentation and laboratory investigations of ectopic pregnancy in KNH**

<b>Presentation</b>	<b>Frequency (n=276)</b>
<b>Percent (%)</b>	
Amenorrhea	276
100	
Abdominal pain	268
97.1	
Vaginal bleeding	210
76.1	
Cold extremities	5
1.8	
Paracentesis positive	139
50.4	
Resuscitation done	8
2.9	
<b>Laboratory investigation</b>	
Hemogram done	259
93.8	
Hemoglobin <11g/dl	159
61.4	
Leucocyte <4000cells/ml	6
2.3	
Hematocrit<40%	174
67.2	
Hematocrit>40%	85
32.8	
Beta hCG positive	209
75.7	
Beta hCG	3
1.1	



The odds of conception within two years after unilateral salpingectomy was significantly higher (33%) in women aged 30-34 years but lower (21%) in older women aged 35-39 years when compared to the younger women (24%) aged 20-24 years. (OR 26.8;  $p < 0.0001$ ). (Table 3). Women with secondary (26%) and tertiary (12%) were less likely to conceive compared to 61% with primary education. The participants who reported that they were cohabiting (8%) were less likely to conceive when compared to those who were single or married women (57% versus 33%). (Table 3)

**Table 3: Association between socio-demographic characteristics and conception within two years after unilateral salpingectomy**

Characteristic	Conception within 2 years		OR (95% CI)	P value
	Yes	No		
<b>Age</b>				
16-19 years	3(3.3)	7(3.8)	1.15(0.27-4.84)	0.85
20-24 years	22(23.9)	59(32.1)	Ref	
25-29 years	14(15.2)	107(58.2)	0.36(0.17-0.74)	0.006
30-34 years	30(32.6)	3(1.6)	26.8(7.43-96.83)	<0.0001
35-39 years	19(20.7)	5(2.7)	10.2(3.39-30.62)	<0.0001
40-44 years	4(4.3)	3(1.6)	3.58(0.74-17.27)	0.113
<b>Level of education</b>				
Not educated	1(1.1)	1(0.5)	1.55(0.10-24.35)	0.757
Primary	56(60.9)	87(47.3)	Ref	
Secondary	24(26.1)	69(37.5)	0.68(0.39-1.18)	0.171
College/university	11(12.0)	27(14.7)	0.64(0.29-1.39)	0.260
<b>Marital status</b>				
Single	53(57.6)	83(45.1)	Ref	
Married	30(32.6)	69(37.5)	0.78(0.46-1.35)	0.376
Cohabiting	7(7.6)	32(17.4)	0.34(0.14-0.83)	0.018
Separated	2(2.2)	0(0.0)	NA	
<b>Residence</b>				
Nairobi	91(98.9)	176(95.7)	Ref	
Outside Nairobi	1(1.1)	8(4.3)	0.24(0.03-1.96)	0.184

The occupation of respondents including spousal occupation showed a significant association with conception after unilateral salpingectomy within 2 years (Table 4). Women who were self-employed (46%) were more likely to conceive compared to unemployed (20%) women OR = 6.59; 3.35-12.96,  $p < 0.001$ . Women in salaried employment were also more likely to conceive within two years OR = 3.16; 1.62-6.16,  $p = 0.007$ .

**Table 4: Association between socio-economic characteristics and conception within two years after unilateral salpingectomy**

Characteristic	Conception within 2 years		OR (95% CI)	P value
	Yes (n=92)	No (n=184)		
<b>Employment status</b>				
Unemployed			Ref	
Self employed	18(19.5)	96(52.2)	6.59(3.35-12.96)	<0.0001
Salaried employment	42(45.7)	34(18.5)	3.16(1.62-6.16)	0.0007
<b>Spouse's employment status</b>	32(34.8)	54(29.3)	NA	
Unemployment	0(0.0)	1(100.0)	Ref	
Self employed	42(45.7)	119(64.7)	6.93(3.24-14.81)	0.0001
Salaried employment	50(54.3)	64(34.8)		

## Reproductive history

Among the factors related to maternal reproductive history age at menarche, complication in previous pregnancy, complication to the baby before the EP and absent pelvic adhesions intra-operatively were significantly associated with conception within two years following unilateral salpingectomy (Table 5, 6 and 7).

The mean age at menarche in women who conceived within two years was  $14.2 \pm 2$  years compared to a mean age of  $15.1 \pm 2$  years in those who did not conceive ( $p = 0.001$ ) Table 5.

**Table 5: Association between menstrual history and conception within two years after unilateral salpingectomy**

	Conception within 2 years			
	Yes (n=92)	No (184)	OR(95% CI)	P value
<b>Menstrual history</b>				
Mean age at menarche (years) $\pm$ SD	$14.2 \pm 2$	$15.1 \pm 2$	NA	0.001
<b>Length of menstrual cycle</b>				
<28 days	1(1.1)	4(2.2)	0.517(0.057-4.71)	0.559
28 days	73(79.3)	151(82.1)	Ref	
>28 days	18(19.6)	29(15.7)	1.28(0.67-2.46)	0.452
<b>Menses associated with pain</b>				
Yes	42(45.7)	87(47.3)	Ref	
No	50(54.3)	97(52.7)	0.753(0.46-1.24)	0.269
<b>Number of soaked menstrual towel/day during menses</b>				
1-3	14(15.2)	17(9.2)	1.79(0.84-3.81)	0.165
3-6	77(83.7)	167(90.8)	Ref	
>7	1(1.1)	0(0.0)	6.48(0.26-161.0)	0.254

History of any complication in a previous pregnancy or complication to babies before the EP were significantly associated with conception (OR 27.5 and 0.009 respectively) compared to history of STI/D and neonatal complications. FP use was not associated with conception. Table 6

**Table 6: Association between outcomes of previous pregnancies, history of STD and FP with conception within two years after unilateral salpingectomy**

	Conception within 2 years		OR (95% CI)	P value
	Yes (n=92)	No (n=184)		
<b>Previous pregnancy outcomes, STD and FP history</b>				
<b>Complication in previous pregnancy</b>			27.5(3.5-214.7)	0.002
Yes	12(92.3)	1(7.7)	Ref	
No	80(50.0)	183(50.0)		
<b>Any complication to baby before EP</b>			0.009(0.001-0.065)	<0.0001
Yes	1(1.1)	102(55.4)	Ref	
No	91(98.9)	82(44.6)		
<b>Neonatal complications before EP</b>			0.06(0.07-6.46)	0.724
Yes	1(1.1)	3(1.6)	Ref	
No	91(98.9)	181(98.4)	NA	
<b>History of STDs</b>			Ref	
Yes	0(0.0)	1(0.5)	1.20(0.28-5.14)	0.806
No	89(96.7)	178(96.7)		
Don't know	3(3.3)	5(2.7)	NA	
<b>History of PID</b>			Ref	
Yes	1(1.1)	1(0.5)	1.30(0.54-3.13)	0.557
No	82(89.1)	166(90.2)		
Don't know	3(3.3)	14(7.6)	1.00(0.59-1.17)	1.000
<b>Contraceptive use before EP</b>			Ref	
Yes	62(67.4)	124(67.4)		
No	30(32.6)	60(32.6)		

Absence of intra-operative pelvic adhesions (OR 2.74, p 0.023) was significantly associated with pregnancy within two years of unilateral salpingectomy when compared with status of the ovaries and contralateral tube. Table 7

**Table 7: Association between intra-operative findings and pregnancy**

	Conception within 2 years		OR (95% CI)	P value
	Yes (n=92)	No (n=184)		
<b>Intra-operative findings</b>				
<b>Ovaries</b>			1.56(0.84-2.90)	0.157
Normal	22(23.9)	37(20.1)	3.84(1.77-8.34)	0.853
Abnormal	19(20.7)	13(7.1)	Ref	
Not indicated	51(55.4)	134(72.8)		
<b>Contralateral tube</b>			1.47(0.84-2.56)	0.178
Normal	31(33.7)	47(25.5)	0.92(0.36-2.34)	0.853
Abnormal	7(7.6)	2(1.1)	Ref	
Not indicated	54(58.7)	17(9.2)		
<b>Pelvic adhesions</b>		120(65.2)	0.53(0.17-1.63)	0.266
Present	4(4.3)		2.74(1.15-6.53)	0.023
Absent	13(14.1)	16(8.7)	Ref	
Not indicated	75(81.5)	10(5.4)		
		158(85.9)		

Table 8 shows the results of logistic regression analysis of predictors of conception within two years of unilateral salpingectomy. Living with a partner/ husband, participant age and occupation were the independent predictors of conception after logistic regression adjustment for the effect of education, history of family planning use, pelvic adhesions and status of ovaries.

Women who were aged 30-34 years (OR = 70.8, 95% CI 18.26-274.5) and 35-39 years (OR = 26.22, 95% CI 7.47-91.9) were significantly more likely to conceive within two years compared to those aged less than 20 years. The participants who lived with a partner/ spouse on a daily basis were more likely to conceive within two years (OR = 0.37, 0.09) compared to those who did not live with a partner or spouse. Women in employment (OR = 6.98-13.8) were approximately more than seven times likely to conceive within two years of salpingectomy compared to those who were not in employment and salaried employment.

**Table 8: Logistic regression for living with a partner, age and occupation**

VARIABLE	ADJUSTED* OR (95% CI)	P-VALUE
<b>Marital status</b>		
Single	1	
Married	0.370 (0.118-1.158)	0.088
Cohabiting	0.093 (0.013-0.693)	0.020
<b>Age</b>		
16-19 years	0.965 (0.164-5.689)	0.969
20-24 years	1	
25-29 years	0.113 (0.056-0.226)	0.000
30-34 years	70.822 (18.269-274.546)	0.000
35-39 years	26.227 (7.477-91.996)	0.000
40-44 years	26.227 (7.477-91.996)	0.039
<b>Employment status</b>		
Unemployed	1	
Self employed	13.832 (5.571-34.341)	0.000
Salaried employment	6.986 (2.593-18.820)	0.000

\*Adjusted for effect of education, history of contraceptive use, pelvic adhesion, and status of the ovaries

P < 0.05 indicates a statistically significant difference between several groups for example, there was a statistically significant difference between mothers who were single and those who were living with a partner (cohabiting) when comparing to conceiving within two years or not.

**Pregnancy outcomes after unilateral salpingectomy (N=92)**

**Table 9: Pregnancy outcomes among women who desire to be pregnant within two years after unilateral salpingectomy for ruptured ectopic pregnancy**

<b>Pregnancy outcomes</b>	<b>Frequency (n=92)</b>	<b>Percent</b>
Intrauterine pregnancy	83	90.2%
Repeat ectopic pregnancy	9	9.8%
<b>Outcome of intrauterine pregnancy</b>		
Miscarriage	4	4.3%
Delivered:	65	70.7%
Term	61	93.8%
Preterm	3	4.7%
Still birth	1	1.5%
Pregnancy is ongoing	14	15.2%

Most women who become pregnant had IUP (90%) with 10% repeat EP.

## **DISCUSSION**

### **Incidence of pregnancy within two years of unilateral salpingectomy**

In the current study one in every three women undergoing unilateral salpingectomy in KNH for EP management and desiring future pregnancy conceived within two years of the surgical procedure yielding a cumulative incidence of 33.3 per 100 cases during a 2-year period. To the best of our knowledge and based on an extensive review of both published and unpublished literature this estimate represents the first documented incidence of pregnancy after EP management in Kenya.

Despite the absence of data from Kenyan or sub-Saharan Africa studies, the incidence reported in KNH was lower than the range reported in existing studies on fertility outcomes following EP management. A French study showed that spontaneous conception was 53% after laparotomy for ectopic pregnancy<sup>(11)</sup> The mean time to pregnancy following salpingectomy has been reported to be 5 months.<sup>(16)</sup> The two-year period of time covered by the current study sets a baseline for assessment of pregnancy outcomes among women desiring pregnancy following management of ruptured tubal ectopic pregnancies. There are several possible explanations for the higher incidences in those studies compared to the present study. Firstly, the baseline prognosis for fertility varies considerably between study centers. Secondly, there is evidence from literature that conservative forms of surgery are associated with higher incidences of fertility compared to radical surgical procedure and this might reflect practice within different centers.<sup>(9,10,11)</sup> Thirdly, differences in study designs can give different findings with prospective studies reporting higher incidence of fertility compared to retrospective studies possibly due to the differences in monitoring and reporting for the two study designs. Lastly, comparisons of incidence of pregnancy are hampered by both varying duration of follow up and outcome definitions (intrauterine pregnancies, or both intrauterine and ectopic pregnancies). All these considerations



notwithstanding the incidence of pregnancy following EP management in KNH appeared to be in the lower range of reports appearing in current literature.

### **Predictors of pregnancy within two years of unilateral salpingectomy**

Of the factors examined in this study, living with a spouse, participant's age, occupation, complications during a previous pregnancy, complication of the baby before EP and absence of intra-operative adhesions predicted incidence of pregnancy within two years of unilateral salpingectomy.

In literature among the established and strong predictors of pregnancy following salpingectomy included upper genital tract infections, pelvic surgeries, contraceptive failure, intrauterine device use, assisted reproductive technologies, pelvic adhesions, smoking and previous history of infertility.

An unexpected finding in the current study was that status of the ovaries, status of contralateral tube and history of contraception use did not predict pregnancy following EP as in other literature.

Similarly, history of sexually transmitted diseases (STD) and pelvic inflammatory disease (PID) were not associated with conception. It is important to note the following while interpreting these findings. Firstly, STD and PID occurred very rarely in this study hence there was limited statistical power to demonstrate the effect of these events on the occurrence of future pregnancy probably because participants shied away from revealing their infectious status. Secondly, the assessment of status of ovaries, contralateral tube and presence of pelvic adhesions was based on documentations within intraoperative notes. For a significant number of EP patients these features were not documented within notes hence there was significant possibility of patient misclassification in this part of the analysis.

### **Outcomes of pregnancy within two years of unilateral salpingectomy**

Most (90%) women who conceived within two years had intrauterine pregnancies, a figure way higher than literature reports likely due to the study's small sample size but the rate of repeat EP was about 10% which was comparable to estimates reported in literature. Between 11 and 19% of participants in previous studies had repeat EP. Among the potential explanations of repeat EP include abnormal contralateral tube and pelvic adhesions after surgical management of EP.

### **Strengths and limitations**

The main strengths of the study are the efficiency of case-cohort design in which only a subpopulation of the parent cohort were used in detailed analysis of predictors of pregnancy outcomes. This study is subject to the limitations of retrospective observational study designs including information and classification biases. However, it is noteworthy that sampling of cases and controls from the same population (parent cohort) reduced the potential for selection bias and secondly, information bias was reduced by the fact that risk factor exposure assessment was conducted by an investigator blind to case status. Despite these advantages of the case cohort design that reduce selection and information biases, prospective studies of pregnancy outcomes are needed to validate the findings reported in the present study.

The main limitation of the results are the fact that patient recruitment was conducted within a single, tertiary level hospital that might not be representative of the facilities attended by most Kenyan women. This could lead to limited external validity of the findings.

## **Conclusions**

This study conducted at KNH has determined that pregnancy occurs within two years in 33% of women presenting with EP and undergoing unilateral salpingectomy and desired a conception. The factors that independently predicted pregnancy incidence at two years are participant's age, living with a spouse, absence of pelvic adhesions, complications in previous pregnancies and occupation, which could be a proxy for socio-economic status that influences access to healthcare. Most mothers conceiving within two years of salpingectomy had intrauterine pregnancy with live term deliveries but repeat EP occur in approximately one out of every 10 pregnancies.

## **Recommendations**

Based on the analysis reported above the study recommends that:

- Multicenter center study should be done to determine the exact incidence, associated predictors and pregnancy outcomes after treatment of EP and the other remaining facets of EP at the national level since this study is just a preliminary and can't be generalized.
- Improvement in documentation of clients' medical records by care providers.
- Establishment of a data base to follow up all patients who present with ectopic pregnancy within the facility and nationally to avail data for further studies on any aspect of EP both.
- The ministry of health in conjunction with Kenyatta National Hospital to procure more laparoscopic equipment for the management of all EPs and also train more staff on skills to handle these equipment and clientele.

**Dissemination of results**

By sharing these research findings, the study may stimulate studies on other uninvestigated aspects of EP. The study will have a direct impact on improvement of care of EP in KNH.

For the study findings to be useful to stakeholders, dissemination should be action-oriented by recognizing the study outcomes making recommendations incorporating the study's or other approaches to improve care to clients with EP in KNH.

The findings will be presented to the department, KNH/UoN research department and for research publications.

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## **APPENDICES**

### **APPENDIX I: CONSENT FORM**

**STUDY TITLE:** INCIDENCE, PREDICTORS, AND OUTCOME OF PREGNANCY WITHIN TWO YEARS AFTER UNILATERAL SALPINGECTOMY FOR RUPTURED ECTOPIC PREGNANCY AT KENYATTA NATIONAL HOSPITAL.

#### **Principal Investigator**

I am Dr Mariam Umar, a postgraduate student in the Department of Obstetrics and Gynaecology in the University of Nairobi. I am carrying out a study as part of the requirement for Master of Medicine in Obstetrics and Gynaecology. My contact is 0737831090

#### **Supervisors:**

1. Prof. P.M. Ndavi, Associate Professor of Obstetrics and Gynaecology, Department of Obstetrics and Gynaecology, University of Nairobi.
2. Dr Frank Kagema, Consultant Obstetrician and Gynaecologist, Department of Reproductive Health, KNH.

**Study introduction:** Up to 2% of all pregnancies are ectopic. EP implants outside the endometrial cavity and is a life threatening condition in affected women. It is the leading cause of first trimester maternal deaths and is a form of reproductive failure in the affected women. In KNH all affected women are managed with open surgery where the affected tube is removed (unilateral salpingectomy). The fate of these women with regard to future conception after treatment of EP is not known.



**Purpose Of Study:** To determine the incidence, predictors and outcomes of pregnancy within two years after unilateral salpingectomy for ruptured ectopic pregnancy at KNH.

**Study Procedure:** Telephone administered interviews will be conducted by the principal investigator in the presence of a witness (a colleague within the department) to partly complete a structured questionnaire. The remaining data will be obtained from participant's medical records.

**Benefits:** The study will confer no benefits to the participant but it will provide baseline data on incidence, predictors and pregnancy outcomes after unilateral salpingectomy, which in turn will inform guidelines and policy formulations to help improve management of EP.

**Risks:** This study carries no extra risks or costs to the participant.

**Compensation:** There will be no any form of compensation for participating in this study.

**Participation:** Participation in the study will be purely voluntary, you may choose not to participate or withdraw at any point of questionnaire filling. You will not be penalized or intimidated in any way if you wish to withdraw your participation from the study.

**Confidentialiy:** All information provided by the participant will be completely anonymous. The information collected will be treated and kept confidential and in the custody of principal investigator and used only for the purpose of the study.

Study approval has been given by the Kenyatta National Hospital Administration and Kenyatta National Hospital/University of Nairobi ethics committee {KNH/UON-ERC}.

I am requesting your participation in this study.

Your agreement to participate in the study will be taken as a voluntary consent to participate in this study.

**For Further Information Please Contact:**

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**CONSENT FORM**

I have fully understood the information provided in the consent form above and have been given opportunity to ask questions. I give my voluntary consent to participate.

Witness's signature..... Date.....

Investigator's signature..... Date.....

## **APPENDIX II: QUESTIONNAIRE**

### **INCIDENCE ASSOCIATED PREDICTORS AND OUTCOME OF PREGNANCY AFTER UNILATERAL SALPINGECTOMY FOR RUPTURED TUBAL ECTOPIC PREGNANCY IN KNH.**

#### **PART 1: RESPONSE FROM PARTICIPANTS**

Date ..... /..... /.....

Participant's code.....

1. What's your age? ..... years
2. What is your education level?
  - a) not educated (none)
  - b) Primary:     standard.....
  - c) Secondary:   form.....
  - d) college/ university
  - e) Other
3. What is your marital status?
  - a) Single
  - b) Married
  - c) Cohabiting
  - d) Separated
  - e) Divorced
4. Where do you live?
  - a) Nairobi
  - b) Outside Nairobi

5. What is your occupation?

- a) Unemployed (housewife)
- b) Self employed
- c) Salaried employment
- d) Other (specify)

6. What is your spouse's/partner's occupation?

- a) Unemployed
- b) Self employed
- c) Salaried employment
- d) Other( specify)

7. What was your age at menarche? .....years

8. What is the length of your cycle?

- i. <28days
- ii. 28days
- iii. >28days

9. Are your menses associated with pains?

- i. yes
- ii. no

10. How many soaked sanitary towels do you use per day during your menses?

- i. 1-3

- ii. 3-6
- iii. >7

11. What is the duration of your menstrual flow?

- i. <3 days
- ii. 3-6 days
- iii. >7 days

12. Did you have any complications in your previous pregnancies?

- i. Yes
- ii. No

13. Were there any complications to the baby?

- i. Yes
- ii. No

14. Were there any complications within the first 28 days after delivery?

- i. Yes
- ii. No

15. Previously, have you been on any method of family planning?

- a) Yes
- b) No

16. Have you had any history of sexually transmitted diseases (STDs)?

- a) Yes
- b) No
- c) Don't know

17. Have you had any history of pelvic inflammatory disease (PID)?

- a) Yes
- b) No
- c) Don't know

18. After the ectopic pregnancy, have you become pregnant again?

- i.
- ii. Yes
- iii. If yes above (i), was that pregnancy an intrauterine pregnancy?
  - a. Yes
  - b. b No
- iv. If no above (iii), was it a repeat ectopic pregnancy?
  - a. Yes
  - b. No

19. What was the outcome of the intrauterine pregnancies?

- i. Miscarriage?
  - a. Yes
  - b. No

- i. Delivered a live birth?
  - a. Yes
  - b. No
  - c. If yes above (3), was it
    - i. Term
    - ii. Preterm

- ii. Delivered a still birth?
  - a. Yes
  - b. No

- iii. Is the pregnancy ongoing?
  - a) Yes
  - b) No

**PART 2: RESPONSES FROM PARTICIPANTS' RECORDS.**

Date ...../...../.....

Participant's code.....

20. Date of admission ...../...../.....

21. Referral?

- i. Yes
- ii. No

22. Presenting findings at admission

- i. Abdominal pains
  - a. Present
  - b. Absent
- ii. Amenorrhea
  - a. <8weeks
  - b. >8weeks
- iii. vaginal bleeding
  - a. Present
  - b. Absent
- iv. Paracentesis
  - Positive
  - Negative

### 23. Resuscitation

- a. Yes
- b. No

### 24. Laboratory tests

- a. Haemogram
  - i. Hb level
    - a) <11g/dl
    - b) >11g/dl
  - ii. leucocyte count



a) <4000cells/mcL

b) >4000cells/mcL

iii. haematocrit count

a) <40%

b) >40%

b. beta hCG result

i. positive

ii. negative

#### 25. Haemoperitoneum

i. Present

ii. Absent

#### 26. Status of contralateral tube

i. normal

ii. abnormal

iii. not recorded

#### 27. Pelvic adhesions

i. present

ii. absent

iii. not recorded

28. Status of the ovaries

- i. normal
- ii. abnormal
- iii. not recorded

29. Transfusion during operation

- i. Transfused
- ii. Not transfused

30. Transfusion requirement post-operatively

- i. Transfused
- ii. Not transfused

### APPENDIX III: WORK PLAN

Activities	Nov 2015	Dec 2015	Jan 2016	Feb 2016	Mar 2016	Jun 2016	Jul 2016	Aug 2016	Sept 2016	Oct 2016	Nov 2016
KNH/UON ERC proposal review and approval											
Data collection											
Data analysis											
Drafting report and corrections from supervisors											
Final draft											
Binding and submission											

## APPENDIX IV: BUDGET



	<b>Unit of Measure</b>	<b>Duration/ Number</b>	<b>Cost (kshs)</b>	<b>Components</b>
Statistician	Pax	1		30,000
Final Report	1 copy	70 pages	10.00	700
Photocopying				
Consent Form	258 forms	3 pages	3.00	2,322
Assent Form				
Questionnaires	258 forms	9pages	3.00	6,966
Final Report	5 copies	70pages	3.00	1,050
Final Report Binding	6 copies		500.00	3,000
ERC Fees				2,000
Access to records				1,500
Calls willing participants	276 pax	15 minutes	4.00	16,560
Calls unwilling participants	150 pax	5 minutes	4.00	3,000
Total				67,098.00

- Source of funds-KNH
- No funds were given for participation.