FECUNDITY RATE AND PREGNANCY OUTCOME AFTER SURGICAL TREATMENT OF ECTOPIC PREGNANCY IN HOSPITAL KUALA LUMPUR

by

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Dr Azilah binti Husin

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LIST OF ABBREVIATIONS

B-hCG	Beta human chorionic gonadotrophin
COTDS	Computerised operating theatre documentation system
EP	Ectopic pregnancy
HKL	Hospital Kuala Lumpur
i.e.	*id est*, that is
IUP	Intrauterine pregnancy
IVF	In vitro fertilization
PUL	Pregnancy of unknown location
STI	Sexually transmitted illness
TVS	Trans vaginal ultrasound

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ABSTRAK

ABSTRAK

KADAR KESUBURAN DAN HASIL KEHAMILAN SELEPAS KEHAMILAN LUAR RAHIM YANG TELAH DIRAWAT SECARA PEMBEDAHAN DI HOSPITAL KUALA LUMPUR

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Pengenalan: Kehamilan luar rahim merupakan masalah genting dan kecemasan di dalam bidang sakit puan dan adalah punca utama morbiditi dan kematian di negara-negara membangun. Walaupun faktor risiko kehamilan ektopik telah ditentukan dalam kajian sebelum ini, faktor-faktor risiko utama kehamilan ektopik adalah berbeza di pelbagai negara kerana ciri-ciri budaya dan sosial yang berbeza. Morbiditi dan kematian yang berkaitan dengan masalah ini dapat dikurangkan sekiranya terdapat diagnosis awal dan rujukan segera. Dengan adanya diagnosis awal, rawatan perubatan dengan pemberian ubat methotrexate boleh ditawarkan dan risiko pembedahan boleh dielakkan. Namun, ini memerlukan pesakit supaya mengikut protokol yang diberikan untuk rawatan susulan. Bagi rawatan secara pembedahan pula, kebaikan dari segi kesuburan kehamilan akan datang di antara kaedah pembuangan keseluruhan tiub (salphingectomy) atau pemotongan di tiub (salphingostomy) tidak dapat dipastikan.

Kebiasaannya, bagi pesakit yang stabil keseluruhannya, pembedahan secara laparoskopi lebih digemari. Persoalannya, adakah faktor berkaitan pembedahan ini dan tahap pakar bedah yang melakukannya akan menjejaskan kesuburan pesakit tersebut dan hasil kehamilannya yang akan datang atau tidak.

Objektif: Untuk melihat kadar kesuburan selepas kehamilan luar rahim yang telah dirawat secara pembedahan di Hospital Kuala Lumpur.

Kaedah kajian: Satu kajian retrospektif telah dijalankan di Jabatan Obstetrik dan Ginekologi di Hospital Kuala Lumpur, dengan menggunakan data dari tahun 2006 hingga 2010. Seramai 120 orang pesakit yang mengalami kehamilan luar rahim dan dirawat secara pembedahan serta disahkan histologinya diambil secara rawak. Maklumat berkaitan pembedahan yang dilakukan diambil daripada rekod pesakit dan dianalisis perhubungannya. Kepentingan statistik telah diambil sebagai nilai p kurang daripada 0.05 ($p<0.05$).

Keputusan: Daripada 120 pesakit yang mengandung di luar rahim dan berkeinginan untuk hamil lagi, seramai 41 orang wanita berjaya mengandung semula dalam tempoh 5 tahun. Daripada jumlah wanita ini, seramai 29(70.7%) hamil di dalam rahim dan 12(29.3%) mendapat kandungan luar rahim berulang. Seramai 24(82.8%) yang mengandung ini telah melahirkan bayi lahir hidup dan 5(17.2%) mengalami keguguran. Waktu min dari waktu pembedahan hingga kehamilan yang berikutnya adalah 18.73±11.27 bulan. Ciri-ciri ibu berkaitan umur, status pariti dan status merokok tidak menyumbang kepada risiko kandungan luar rahim berulang. Faktor berkaitan

pembedahan dan doktor yang melakukan pembedahan juga tidak menunjukkan statistik yang signifikan untuk kadar kesuburan dan hasil kehamilan berikutnya.

Kesimpulan: Memandangkan bahawa sebarang cara dan jenis pembedahan yang dilakukan untuk kehamilan luar rahim tidak mempengaruhi kadar kesuburan dan kehamilan seterusnya, pilihan untuk pembedahan haruslah yang mempunyai lebih kurang komplikasinya. Oleh itu bagi pesakit yang stabil, pilihan pembedahan secara laparoskopi adalah digalakkan.

Prof. Madya Dr. Adibah Ibrahim: Supervisor

Dr Noor Haliza Yusoff: Co-Supervisor

ABSTRACT

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FECUNDITY RATE AND PREGNANCY OUTCOME AFTER SURGICAL TREATMENT OF ECTOPIC PREGNANCY IN HOSPITAL KUALA LUMPUR

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Introduction: Ectopic pregnancy is a gynaecological emergency and is an important cause of morbidity and mortality in developing countries. Although the risk factors of ectopic pregnancy have been determined in previous studies, the main risk factors of ectopic pregnancy are different in various countries due to different cultural and social characteristics. Early diagnosis and referral may reduced the morbidity and mortality associated with this life threatening condition. With earlier diagnosis, medical therapy with methotrexate can be offered and surgical management may be avoided. However, this will need a protocol for patient follow up for medical or expectant management of ectopic pregnancy. In the surgical management of ectopic pregnancy, the benefits of salphingectomy over salphingostomy in predicting the future fertility are uncertained. Laparoscopy procedure is generally more favored over laparotomy. However, it depends on the stability of the patient's haemodynamic status. However, whether these

surgical factors and surgeon's expertise will affect the subsequent pregnancy and its outcome is questionable.

Objectives: To determine the fertility rate and pregnancy outcome after ectopic pregnancy that has been managed surgically in Hospital Kuala Lumpur.

Patients and Methods: A retrospective study was carried out in the Department of Obstetrics and Gynaecology in Hospital Kuala Lumpur, utilizing the data from the year 2006 to 2010. This comprised of randomly 120 patients that presented for ectopic pregnancy managed surgically and also confirmed histology. The surgical approach and the level of surgeon data were determined from patient's case notes and analyzed for the associations and significance. Statistical significance was taken as p value of less than 0.05 ($p<0.05$).

Results: From 120 patients of ectopic pregnancy during the study period, 41 patients were able to conceive within 5 years after the ectopic pregnancy. Out of this subsequent pregnancy, there were 29(70.7%) intrauterine pregnancies and 12(29.3%) recurrent ectopic pregnancies. Out of the intrauterine pregnancies, 24(82.8%) had live birth babies and another 5(17.2%) had miscarriages. The mean time to next pregnancy for patient to get pregnant was 18.73±11.267 months. The maternal characteristics (age, parity and smoking status) do not contributed to the risk of recurrent ectopic pregnancy. The surgical approach and the surgeon's level also do not have any statistically significant for the fecundity rate and the subsequent pregnancy outcome.

Conclusion: In view that any surgical approach and type of surgery done for the ectopic pregnancy does not influence the fecundity rate in subsequent pregnancy, the choice for surgical management in a stable patient should be the one that has less surgical complications, therefore laparoscopy procedure should be encouraged.

Assoc. Prof. Dr. Adibah Ibrahim: Supervisor

Dr Noor Haliza Yusoff: Co-Supervisor

INTRODUCTION

1.0: Introduction

Ectopic pregnancy is a serious condition which affects the general and reproductive health of a woman and is a potentially life threatening condition. It is a pregnancy which embryonic implantation occurs outside the normal uterine cavity. About 95% of the ectopic pregnancy occurs in the fallopian tube. Rarely, it occurs in the ovary, rudimentary horn of a bicornuate uterus and the cervix. Lately, ectopic pregnancy over the caesarean scar also has been reported.

Some ectopic pregnancies are never been diagnosed, as the fertilized ovum dies and is slowly absorbed. On the other hand, fetus may continue to grow in the fallopian tube and can lead to tubal rupture and abdominal bleeding. The clinical presentation of ectopic pregnancy varies from being asymptomatic to severe internal bleeding, which may lead to death. However the number of death related to ectopic pregnancy has decreasing dramatically because of earlier diagnosis and treatment.

Both maternal and embryonic factor are thought to contribute to the development of aetiology of ectopic pregnancy. This may involve with abnormalities of tubal function and ovum quality. Embryo transfer can be disrupted by damage of the mucosal portion of the

fallopian tube. Any scarring due to infection or trauma could lead to trapping of conceptus in the fallopian tube.

The risk factors are thought to include previous ectopic pregnancy, pelvic infection, smoking, previous pelvic surgery and the use of certain types of intrauterine contraceptives devices. In women whose age is more than 35 years old, there appears to be a decrease in fertility an increase rate of pregnancy complications, including spontaneous abortions and ectopic pregnancy. Changes in tubal function resulting in impaired ovum transport could be a possible factor for age-related ectopic pregnancy.

Infertility alone or in combination with treatment is a risk factor for ectopic pregnancy. The treatment for infertility involves fertility drugs for ovulation induction. There has been concern for possible association between in vitro fertilization (IVF) and ectopic pregnancy as well.

Once diagnosed as ectopic pregnancy, it may be managed surgically, medically or expectantly. Expectant and medical management need patient to come for a proper follow up protocol. Surgical option includes salpingectomy or salpingostomy, approach via laparotomy or laparoscopy. Indications for surgical treatment of ectopic pregnancy include hemodynamically unstable patient, not suitable for or failed medical therapy. Laparotomy is done for a hemodynamically not stable patient, extensive intraperitoneal bleeding or need to convert from laparoscopy technique in view of poor visualization. It is also indicated in

places where laparoscopic skill is limited and difficult laparoscopic operative access such as when dense adhesion or massive haemoperitoneum is present.

Many studies have discussed regarding the reproductive outcomes following the two surgical techniques. Area discuss were regarding patient selection, surgical techniques and follow up times (Mol *et al.*, 1998; Bangsgaard *et al.*, 2003; Barnhart, 2009). In a patient who wishes to preserve the fertility, salphingostomy is offered. However, if the patient has completed the family and no more desire for fertility, has history of previous ectopic in the same tube or severely damaged tube, salpingectomy is preferred. Studies had shown that there was no difference in the chance of having subsequent intrauterine pregnancy in the operation was performed either laparoscopically or laparotomy, or salpingostomy or salpingectomy. Around 60% of women affected by ectopic pregnancy will go on to have viable intrauterine pregnancy and about 5-20% risk of recurrence ectopic pregnancy. However, further determination of other associated factors such as patient's characteristics (age, parity, and previous miscarriages), history of previous affected tubes (previous surgery or infection), condition of the tubes (ipsilateral and contralateral), the location and size of the pregnancy may help to counsel the patient with regards to their subsequent pregnancy potential and outcome.

Patient who came to HKL was from a different population and different socioeconomic background. Sometimes, patient that came to HKL is not a permanent residence of Kuala Lumpur, thus make a medical or expectant management of ectopic pregnancy rather

difficult as the patient need to come for a proper follow up, which could be difficult for them. This management was not practiced in HKL. Therefore, most standard treatment of ectopic pregnancy in HKL is surgical management either by laparotomy or laparoscopy approach. HKL is not just a national referral centre for obstetrics and gynaecology in the country; it also serves as education and continuing professional development for all level of staff. Since HKL is a training centre for medical officers, registrars and nurses, there are different levels of surgeon managing the case. There is no study for ectopic pregnancy done before in HKL. The data produced from this study could be quoted as information for the patient on fertility outcomes after the surgical treatment of ectopic pregnancy.

LITERATURE REVIEW

2.0: Literature review

2.1 Incidence of ectopic pregnancy

There has been an increasing number of ectopic pregnancy detected. In Malaysia, there were not many study published regarding review of the ectopic pregnancy. Sivalingam in 1981 stated the crude incidence of ectopic pregnancy was 1 in 358 deliveries in Johor Bahru, Malaysia (Sivalingam, 1981). However, a later study by Wan Zahanim in 1997, which was done in University Science of Malaysia (HUSM) had stated a higher incidence of 1 in 198 pregnancies (Wan Zahanim, 1997). The crude incidence of ectopic pregnancy in Hospital Kuala Lumpur was even higher from year 2006-2010, i.e. 1 in 75 deliveries. The raised of the incidence could be due to many factors such as, pelvic inflammatory disease and smoking in women of reproductive age, the increase use of assisted reproductive technology (ART) and earlier diagnosis and management with the developing of early pregnancy assessment unit (EPAU)(Sivalingam *et al.*, 2011).

Some of the ectopic pregnancy may be managed as outpatient therefore it may be not included in hospital data. It is possible that the data in ectopic pregnancy rate were rising and falling in previous decades. They noted that the overall ectopic pregnancy rate decreased by 2% from 1992 to 2002. However, the ectopic pregnancy 'reproductive failure' increase by 17% and contraceptive failure' was increase by 29%(Coste *et al.*, 2004). This could be due to rising Chlamydia infection followed by prevention and treating

the condition, change of the use of intrauterine devices or the rising intervention of Assisted Reproductive Technique (ART) (Zane *et al.*, 2002; Coste *et al.*, 2004).

The population characteristics were different between each country. Socio-economic disparities may contribute to the incidence rate of ectopic pregnancy. Patient factors (poverty rate, insurance status, employment rate and population size including age and parity), hospital factors (hospital type and characteristics) and hospital service volume were all included in the study for the relationship of socio-economic status with complications outcome of ectopic pregnancy(Stulberg *et al.*, 2011).

It was noted that hospital factors are significantly that contribute to complication outcome of the ectopic pregnancy. Private hospitals had lower odds of complications as compared to public (OR 0.39, 95% CI 0.25-0.61) and total length of stay of less than 2 days are more in private hospital (OR 0.57, 95% CI 0.42-0.76) (Stulberg *et al.*, 2011). The study also mentioned that the adverse outcomes were more likely to occur in those patients with non insurance coverage, those with other co-morbidities and admitted to public or religious hospitals.

Racial disparity may be the cause of high adverse outcome from ectopic pregnancy, but this was not shown to have a relationship in the study by Butts et al in 2010, however their study also concluded that low socio-economic status was statistically significant

contributed to the adverse outcome and failure of medical treatment of ectopic pregnancy. In another study done in Hospital of the University of Pennsylvania also look into the race and socio-economic status with the response of medical treatment of ectopic pregnancy (Butts *et al.*, 2010). Since there is little study comparing outcome of treatment of ectopic pregnancy, therefore, studying the ectopic pregnancy at the population level is warranted.

2.2 Risk factors of ectopic pregnancy

Many studies (Bouyer *et al.*, 2003; Coste *et al.*, 2004; Parashi *et al.*, 2014) identified the risk factors for ectopic pregnancy were that one third are associated with tubal damage cause by infection or surgery, another third with smoking and another third risk couldn't be established. Another study done in a population of Iranian woman published in 2014, noted that there was no statistically significant relation between ectopic pregnancy and prior tubal surgery, tubal pathology, prior infertility, assisted reproductive technology ($p>0.05$). However, there was a significant association between prior ectopic pregnancy, prior tubal ligation, use of intrauterine device and prior abdominal/pelvic surgery with ectopic pregnancy ($p<0.05$)(Parashi *et al.*, 2014).

The incidence of ectopic pregnancy is much higher in patient undergone fertility treatment compared with spontaneous pregnancy, particularly in those patient who had tubal factor infertility such as tubal infection or previous tubal surgery (salpingostomy or salpingectomy) from previous ectopic pregnancy (Patil, 2012). Other than that, endometriosis that may lead to tubal and pelvic adhesions and abnormal tubal function was

also identified as a risk factor for ectopic pregnancy (Refaat *et al.*, 2008). Determination of main risk factors in a population may assist in the prevention, early detection and appropriate management of the ectopic pregnancy.

2.3 Presentation and diagnosis of the ectopic pregnancy

Commonly patient may present with amenorrhea, lower abdominal pain and vaginal bleeding. Patient who presented with shoulder tip pain, syncope and shock may reflect significant severe hemoperitoneum. Occasionally, ectopic pregnancy may be diagnosed before the patient having the symptoms, since there is availability of transvaginal (TVS) scan and using the radioimmunoassay of serum B-hCG. Ultrasound may aid to localize the gestation sac as intrauterine or ectopic. TVS scan is useful diagnostic tool when there is positive visualization of the ectopic mass with or without yolk sac or fetal echo extra-uterine. It is preferable than transabdominal ultrasound because the transvaginal view allows for direct visualization. By 5.5 weeks gestation, an intrauterine pregnancy should be identifiable by TVS as we can see the yolk sac (Gurel *et al.*, 2007). Visualizing the product of conception within the uterus will rules out ectopic pregnancy, given the incidence of heterotropic pregnancy is one in 4000 spontaneous conception in general population (Ory, 1992).

When an initial TVS is able to directly visualize the gestational sac or fetal echo in an ectopic location, the treatment for the ectopic pregnancy should be initiated. An early treatment may reduce the morbidity from ruptured ectopic pregnancy. The challenges arise

when the TVS cannot identify the pregnancy as intrauterine (viable or failing) or extrauterine resulting the diagnosis as pregnancy of unknown location (PUL).

Usually diagnosis can be made from the patient's history, physical examination and TVS. However, if the diagnosis is still not achieved, using beta subunit of human chorionic gonadotrophin (B-hCG) levels might be helpful. If the level of B-hCG is beyond the discriminatory level, it may suggest an ectopic pregnancy. The discriminatory level of B-hCG is defined as B-hCG above level that the TVS should detect and intrauterine pregnancy. In general, an intrauterine gestational is expected to be visualizes when B-hCG is 1000 mIU/mL (Second International Standard) or 2000 mIU/mL (International Reference Preparation). Occasionally not just single level B-hCG is used, but serial levels can be done to detect changes and can be used to evaluate the PUL. 99% of viable intrauterine pregnancy has 50% increase of serial B-hCG within 48 hours and failure to increase within this rate may suggest an ectopic pregnancy or failing intrauterine pregnancy (Barnhart *et al.*, 2004). However, there is still 20% of ectopic pregnancy increase by more than 50% within 48 hours (Barnhart, 2009). Therefore, serial ultrasound and B-hCG is needed in evaluating and managing pregnancy of unknown location. The falling levels of B-hCG may indicate an ectopic pregnancy or failing intrauterine pregnancy. An undetectable level of B-hCG is the only way to confirm complete resolution of the pregnancy.

The diagnosis of EP also can be done surgically. Laparoscopically, there may be hemoperitoneum and distended fallopian tube. There will be sign of rupture of the

fallopian tube as well. However sometimes, the size of the ectopic is too small that cannot be seen during laparoscope.

2.4 Various management of ectopic pregnancy

Treatment of ectopic pregnancy can be either expectant management, medical or surgical (RCOG Guideline No. 21). Expectant management is an option for a patient who is stable, only has minimal clinical sign and the pregnancy is of unknown location.

An expectant management is appropriate when B-hCG levels are low or declining and the pregnancy is of unknown location. This option is for clinically stable patient and has minimal symptoms. The women should be managed expectantly with 48-72 hours of follow up. However, immediate active intervention should be taken if the symptoms of ectopic pregnancy is increasing, and the B-hCG level has rise above the discriminatory level or start to plateau (Elson *et al.*, 2004). Majority of pregnancy of unknown location is abnormal and many resolved spontaneously, where small ectopic pregnancy were spontaneously absorbed or resolved by tubal abortion (Banerjee *et al.*, 1999). Women that were selected for expectant management should be educated and counselled for the need of close observations and risk of tubal rupture.

Medical management using intramuscular methotrexate is commonly used. This option is good as it is cost-effective and may avoid the risk of morbidity associated with surgery and

anaesthesia. However, these women need to be informed the adverse effects following the treatment and possible further treatment surgically and they must be able to return for assessment easily at any time. Therefore patient selection is important and it is done in a unit that has proper follow up protocols.

There is no absolute cut off level of B-hCG for the medical treatment of EP, but it was suggested that B-hCG level of more than 2000mIU/L should be offered for surgical rather than medical treatment (Sagiv *et al.*, 2012). B-hCG levels are the predictive or either successful or failure of treatment.

Intramuscular Methotrexate is used to treat the ectopic pregnancy. Patient must be screened for the suitability to proceed with the treatment. Further test should look for any evidence of organ (liver or kidney) damage or immune compromise. Patient must be hemodynamically stable and may comply to follow up surveillance. There are several regimens protocols for methotrexate therapy, either multi-dose or single-dose regimen. Once the declining level of B-hCG has already achieved, it is monitored weekly until complete resolution of B-hCG to zero.

Single dose or multi-dose regimens are named for the intended number of doses. In a single dose regimen, it has lower adverse effects, does not require folinic acid rescue and is cost effective (Stovall and Ling, 1993), but it has higher failure rate compare to multi-dose treatment. In a meta-analysis review comparing single dose and multi-dose regimens of

methotrexate noted a multi-dose regimens is more effective but have more side effect (Barnhart *et al.*, 2003).

Before surgical treatment was used, the mortality rate from ectopic pregnancy was as high as more than 60%. However, since the first successful surgical treatment was introduced by a British surgeon Robert Lawson Tait in 1883, the mortality rate has been reduced significantly.

Surgical therapy may be provided as laparotomy or laparoscopic procedure. Laparoscopic approach should be offered to women who are hemodynamically stable (Lundorff *et al.*, 1991). It is associated with less blood loss, reduced need for analgesia, reduced cost and need for hospitalization. There is no role for medical management in a patient shows sign of hypovolaemic shock. Laparoscopic management of tubal ectopic pregnancy has less surgical morbidity (operative time, blood loss and complications), compared to that of open laparotomy, (Ding *et al.*, 2008). Patients with hemodynamic instability caused by ruptured ectopic pregnancy require laparotomy and salphingectomy of the involved fallopian tube. There is a retrospective study that identified the risk factors for the conversion to laparotomy during laparoscope management of an ectopic pregnancy. Laparotomy should be considered in cases include multiple prior surgeries, pelvic adhesions, skills of the surgeon and staff, availability of the equipment and condition of the patient (Takacs *et al.*, 2005).

There was a study done in general hospital in Paris whereby the surgeons were still in training. Most of the cases were done laparoscopically, 70% salpingectomy and 19% salpingostomy. Complications of the laparoscopic procedure were rare. They concluded that the laparoscopic surgery for ectopic pregnancy can be done by a young inexperienced surgeon, provided supervised by the experienced gynaecologist (Aharoni *et al.*, 1993).

2.5 Fertility after tubal pregnancy

Over past decades, the incidence and management of ectopic pregnancy have changed. There are progress of earlier diagnosis, initial management, less invasive treatment and medical and expectant management. This changes in management may lead to preservation of the fallopian tube, thus could lower the infertility and recurrence rates. Several factors have been associated with infertility and high recurrence rates, such as older age, previous EP and previous sterility, prior tubal damage and type of surgery (Sherman *et al.*, 1982; Ory, 1992).

2.5.1 Intrauterine pregnancy

A conception rate of 56.7% within 5 years post surgical management of ectopic pregnancy was found at King Khalid University Hospital. 75% of these pregnancies resulted in live birth, another 22.1% ended in abortion, whereas 2.9% were repeat ectopic pregnancies. It was noted that history of pelvic inflammatory disease, infertility and the presence of post operative complications were important determinants for the outcome of subsequent

pregnancy (Al-Nuaim *et al.*, 1995a). An earlier study by Job-Spira *et a.l* in 1996 had described a mean time to pregnancy from a surgically managed EP was 4.8 months, with the one year cumulative intrauterine pregnancy of 70% (Job-Spira *et al.*, 1996). Age of less than 30 years, high educational level with no prior tubal damage was found to be the determinants for successful pregnancy.

2.5.2 Recurrence of ectopic pregnancy

Age and prior ectopic pregnancy are important determinants in pregnancy rates after an ectopic pregnancy. The risk of second ectopic pregnancy was related to the age but not to the parity. Repeat ectopic pregnancy is increased as the age of the patient increased and decreased as the parity increase (Al-Nuaim *et al.*, 1995a; Sobande, 2000). On the other hand, Lee *et al.* in 1991 showed a contradicting result where they found similar risk of repeat EP among parous and nulliparous women (Lee *et al.*, 1991). It is thought that risk of recurrence of EP was 5-20% with one previous EP and increased to 32% or more if more than one previous EP (Sivalingam *et al.*, 2011). This is true for a patient who had bilateral salpingectomy done for the EP, there is risk of recurrence EP in the interstitial tube or tubal remnants following IVF.

2.5.3 Effects of different treatments on fertility after ectopic pregnancy

Fertility outcome after ectopic pregnancy is an issue. There is lack of randomized trials on looking at management of ectopic pregnancy that specifically focusing on recurrence rate

and impact on future fertility. Mostly it was an observational studies or cohort studies and case series.

Some studies discussed the subsequent fertility outcome of ectopic pregnancies based on the surgical techniques used either laparoscopy versus laparotomy and salpingostomy versus salpingectomy. The decision for salpingectomy or salpingostomy was usually made intra operatively depending on the patient's history, wishes for the future fertility and the surgeon's skills. Reproductive outcome after laparoscopy and laparotomy has been compared with few studies (Sowter and Frappell, 2002). It was noted that intrauterine pregnancy rate was 61% after laparoscopy surgery and 52% after laparotomy. Apart from that in a patient with intact contra-lateral tube and no past history of tubal disease, there was no significant in difference surgical method whether the treatment was radical or conservative, the fertility results were similar (Lee *et al.*, 1991; Dubuisson *et al.*, 1996; Kjellberg *et al.*, 1999). The recurrent ectopic pregnancy rate was 7% after laparoscopy and 14% after laparotomy. There is no statistical significant in this difference and the reproductive outcome also seems to be similar.

An observational studies indicated that among women treated with different type of treatment used (laparoscopy; radical and conservative and medical treatment), noted that pregnancy rate was higher by doing salpingostomy (50-76%) in compare to salpingectomy (38-67%) (Mol *et al.*, 1998; de Bennetot *et al.*, 2012). However, it was not statistically significant in the multivariate analysis. The 2-year cumulative rate of recurrence was 18.5%

after salphingostomy or salphingectomy and 25.5% after medical treatment (de Bennetot *et al.*, 2012).

A recent published randomized DEMETER trial 2013, study the affect of subsequent spontaneous fertility from different treatment for the resolution of ectopic pregnancy. There were not significantly different between medical treatment and conservative surgery, and the 2 year rates of IUP were 67% after medical treatment and 71% after conservative surgery. On the other hand, the fertility outcomes also were not statistically different between conservative and radical surgery (Fernandez *et al.*, 2013).

OBJECTIVES

3.0: Objectives of the study

1. To determine the 5 years fecundity after surgical treatment for ectopic pregnancy.

2. To determine the pregnancy outcome after surgical treatment for ectopic pregnancy.

3. To determine the associated factors affecting the conception and successful intrauterine pregnancy within 5 years of surgically treated ectopic pregnancy.

Justification and benefit of the study:

With the result of this study, we hope to create a local data based on current surgical option of treating ectopic pregnancy and its relationship to future fertility outcome for the patients.

METHODOLOGY

4.0: Methodology

4.1 Study design

This is a case series study via retrospective record review carried out in Hospital Kuala Lumpur. It covered 5 years period from 2006 to 2010. Over the 5 years duration, there were 912 cases of ectopic pregnancy admitted in HKL. Those who had undergone surgical treatment were registered in COTDS, the in ward registration book and in the operation theatre. These records were reviewed for sample recruitment for this study. 120 patients were randomised to be included into this study. The randomisation was done using the computer generated clock of 5.

The patient's records were traced from the record office. The patient's performa was entered as shown in Appendix 1. Duplicate or incomplete records were excluded.

Since this is a retrospective review, further information depends on whether the same patient came back to the same hospital later after their ectopic pregnancy episode. Therefore, for those patients that have no further follow up in HKL, they were called up by phone to complete further questions and consented verbally.

4.2 Sample size determination

Determination of the sample size was based on the assumption that 56.7% conception rate occurred after an episode of ectopic pregnancy (al-Nuaim *et al.*, 1995d).

Based on formula for single proportion study;

$n= (z/\Delta)^2 p(1-p)$

n=required sample size

z= value for standard normal distribution

p=expected proportion for fertility rate

Δ = precision at 0.1

$N= (1.96/0.1)^2 0.56 (1-0.56)$

N= (384.16) 0.56 (0.46)

N=98.9 → 99 patients

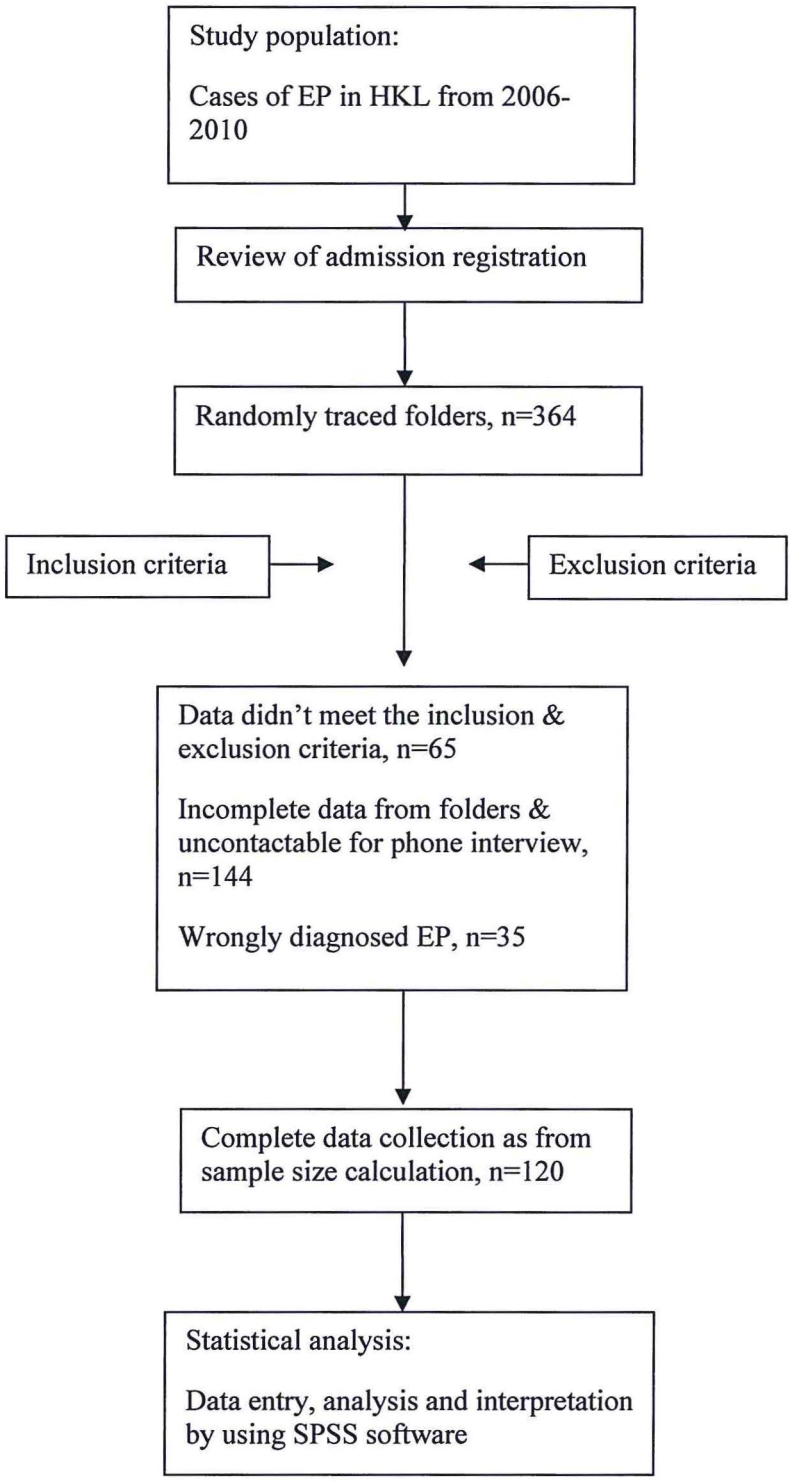
20% drop out rate is considered; therefore

N= 99+ 20% (99)

N= 118.6

N= 120 patients

4.3 Study Flow Chart



4.4 Inclusion and Exclusion Criteria

Inclusion criteria:

1. The pregnancy is a spontaneous conception.

2. The previous ectopic pregnancy must be confirmed histopathologically (HPE).

3. The management of the previous ectopic pregnancy must be treated surgically either laparoscopy or laparotomy.

4. Patient is still married during the study period.

5. Patient has desire for future fertility.

6. Age more than 18 years old during the onset of the ectopic pregnancy.

7. Patients not on any contraception.

Exclusion criteria

1. Unmarried patients or divorcee during the study period.

2. Ectopic pregnancy occured after Assisted Reproductive Technology (ART).

3. Patient that received medical treatment or conservative management of ectopic pregnancy.

4. Patients that undergone permanent sterilization technique during the intervention of the ectopic pregnancy, either tubal ligation or hysterectomy.

4.5 Ethical approval

Approval from local ethical committee in USM (The Human Research Comittee, Universiti Sains Malaysia) (FWA Reg. No: 00007718; IRB Reg. No: 00004494) dated 21st October 2013 (Appendix 2) and Medical Research & Ethics Committee (NMRR-13-1076-15209) dated 20th December 2013 obtained to conduct the study (Appendix 3).

4.6 Data collection

The basic information collected for each woman include: age, parity, race, nationality and smoking habits. The operative findings data are the level of the surgeon, operating approach via laparoscopy or laparotomy, the ectopic pregnancy findings and definite surgical treatment for the ectopic. For the follow up cases, almost all patients were called up by telephone for an interview to complete the data. They were asked about their desire or not for the new pregnancy, the achievement of pregnancy after the ectopic pregnancy, time to pregnancy (if pregnancy occurred), number of pregnancy, and obstetric outcome (if the pregnancy occurred).

4.7 Data analysis

In order to evaluate the results of the survey, statistical computer software Statistical Package for Social Sciences (SPSS) version 22 were used. The Kolmogorov-Smirnov test was used to determine whether the variables were distributed normally. The comparison of two independent scale variables was carried out by a parametric and non parametric t test.

A p value is used to indicate if the differences between two particular groups that were in this study are statistically significant (where $p<0.05$ is considered statistically significant at the 95% confidence interval).

RESULTS

5.0: Results

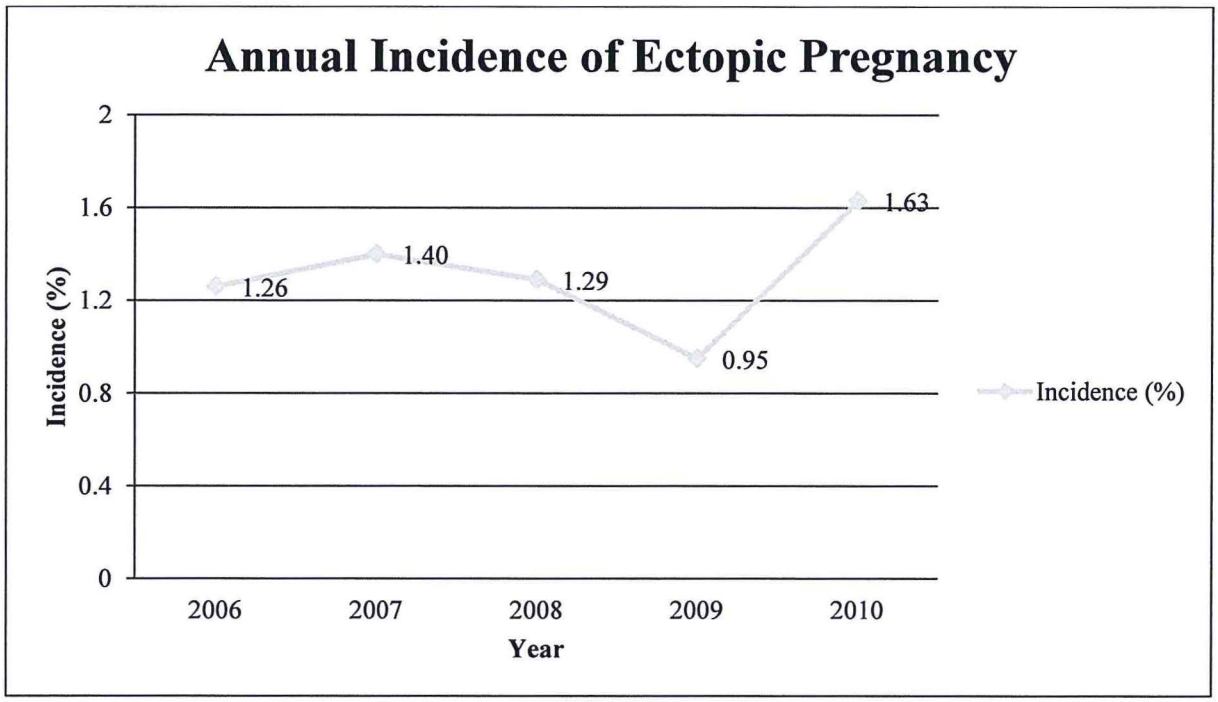


Figure 1: Annual incidence of ectopic pregnancy in HKL from 2006 to 2010

Annual incidence of ectopic pregnancy in HKL from year 2006 to 2010 was ranges from 0.95% to 1.63%.