

Morbidity of Ectopic Pregnancy at Chris Hani Baragwanath Academic Hospital

Sbusiso Trevor Mndebele

0514059P

Research Report

Declaration

I, Sbusiso Trevor Mndebele declare that this work is original and contains no section copied in whole or in part from any other source, unless explicitly identified in quotation marks and with detailed, accurate referencing. I declare that this work has not been previously submitted to this university, or to any other university for the purpose of a postgraduate degree. It is being submitted for the Master of Medicine in Obstetrics and Gynaecology at the University of the Witwatersrand, Johannesburg.



(Signature)

09 day of **March** **2021** at **Johannesburg**

Dedication

I dedicate this research report to my family, friends and colleagues who helped me through this journey of compiling my research.

Presentations

23/10/2019: Poster presentation at the University of the Witwatersrand Research Day.

Abstract

Background: Ectopic pregnancy, is a high-risk condition in which a fertilized ovum implants outside the uterine cavity. The incidence is thought to be higher in developing countries, but specific numbers are not known. The morbidity related to ectopic pregnancy could mostly be avoided if the health service renders better quality care.

Objective: This study aimed to describe the demographics and risk factors of patients with ectopic pregnancy, as well as the presentation and condition severity. Furthermore, the purpose of this study was to describe the diagnostic modalities used, and the morbidity and management of ectopic pregnancy in our setting.

Methods: The study was a prospective audit carried out in the three gynaecology wards of Chris Hani Baragwanath Academic Hospital. The sample size was 200 admitted ectopic pregnancy patients, counting from the admission book over a 3-month period from August 2018 to October 2018. Demographic data, presenting symptoms and signs, risk factors, diagnostic modality, management, features of the ectopic pregnancy and morbidity were recorded on a Redcap data sheet.

Results: Signs of shock were present in 15% of patients and acute abdomen in 85.5% of patients. One hundred and seventy-four (87.0%) patients were diagnosed with ruptured ectopic pregnancies, while 25.0% of patients needed transfusions. One hundred and eighty-six laparotomies and 14 laparoscopies were performed during this study.

Conclusion: Most patients presented late with ruptured ectopic pregnancies while some required blood transfusions and intensive monitoring. There is need for comprehensive gynaecological services including contraception and early pregnancy evaluation, in order to improve the morbidity.

Acknowledgments

I would like to thank the Department of Obstetrics and Gynaecology at Chris Hani Baragwanath Academic Hospital for allowing me to collect data, as well as my supervisor for ongoing support and advice. I also want to thank my colleagues and family for their support in my career.

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Abbreviations

ART	Assisted Reproductive Technique
b-HCG	beta Human Chorionic Gonadotrophin
BP	Blood Pressure
CHBAH	Chris Hani Baragwanath Academic Hospital
EP	Ectopic Pregnancy
FFP	Fresh Frozen Plasma
HIV	Human Immunodeficiency Virus
ICU	Intensive Care Unit
IUCD	Intrauterine Contraceptive Device
LNMP	Last Normal Menstrual Period
PID	Pelvic Inflammatory Disease
RBC	Red Blood Cells
SA	South Africa
STI	Sexually Transmitted infection
TVU/S	Transvaginal Ultrasound

Morbidity of Ectopic Pregnancy at Chris Hani Baragwanath Academic Hospital

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1. Introduction

Ectopic pregnancy (EP) is a high-risk condition in which a fertilized ovum implants outside the uterine cavity, affecting 1 to 2% of all pregnancies and posing a significant threat to women of reproductive age¹. Although the true numbers are not known, developing countries are thought to have a higher incidence of EP than developed countries. Approximately 10% of women diagnosed with an EP will demise². The presentation of acute pelvic pain and vaginal bleeding are significant causes of morbidity related to EP². Long term sequelae also have significant effects on morbidity, leading to infertility². A change in certain risk factors have led to a rise in the incidence of EP along with the increasing availability and advancing diagnostic modalities³. Pelvic inflammatory disease (PID) is the most common risk factor of EP, which is mostly caused by sexually transmitted infections (STI), of which mainly chlamydia and gonorrhoea, while other factors associated with EP are post-abortion sepsis, puerperal sepsis, cigarette smoking, assisted reproductive techniques (ART), intrauterine contraceptive devices (IUCD) and fallopian tube surgery³. The diagnosis of EP should be considered in women of reproductive age who present with the common and typical symptoms of irregular vaginal bleeding, lower abdominal pain and amenorrhea⁴. A ruptured EP tends to have an acute presentation, while the un-ruptured are more likely sub-acute⁴. After significant rupture, the patient presents with features of shock, being pale, hypotensive and tachycardic with an acute abdomen due to blood loss⁴. Importantly, in some of the ruptured EP cases, presentation may be sub-acute with milder symptoms if the rupture occurs over time, and low-grade pyrexia which sometimes makes the diagnosis more difficult to establish⁴. Presentation is usually after six to ten weeks of amenorrhea and may be accompanied by gastro-intestinal symptoms, syncope, shoulder tip pain as well as adnexal tenderness or mass in some cases⁴.

Transvaginal ultrasound (TVU/S) is the diagnostic tool of choice for EP⁵. The EP should be positively identified, if possible, by visualising an adnexal mass that moves separate to the ovary⁵. TVU/S has reported sensitivities of 87.0 – 99.0% and specificities of 94.0 – 99.9% for the diagnosis of EP⁵. Early diagnosis, aggressive surgical management, and adequate blood replacement is instrumental in preventing maternal morbidity related to EP⁶. The most common EP location is in the fallopian tube, and as such usually within the ampullary region of the fallopian tube⁷. Ten percent of EP implant in the ovary, cervix, myometrium, interstitial portion of the fallopian tube, abdominal cavity or within a caesarean section scar⁷.

According to Moran, the provision of better-quality health care would reduce most of the morbidity and maternal deaths related to EP⁸. The outcome of women with EP is

compromised if the healthcare worker does not recognise the clinical picture or does not respond appropriately to the signs of worsening hypovolaemic shock by resuscitating the patient and arranging for surgery⁸. Laparoscopic surgery is superior to laparotomy in the surgical management of women with a ruptured EP⁹. Although the operating times are longer in laparoscopic surgery, the women report lower pain scores, have fewer blood transfusions, require a shorter period in hospital and need only a few days of recovery to be able to return to work⁹. The current standard of treatment in Africa, as a resource-poor region, is emergency laparotomy with salpingectomy of the involved fallopian tube. However, laparoscopic surgery has increased over the years¹⁰. Salpingectomy is the preferred surgical option if the contralateral tube is normal¹¹. A conservative surgical approach with either a salpingostomy or salpingotomy can be considered if future fertility is desired and the contralateral fallopian tube is abnormal¹¹. The objectives of the study were to describe the demographics and risk factors of patients with EP, as well as their presentation and severity, and also to describe the diagnostic modalities used, as well as the morbidity and management of EP in our setting.

2. Methods

The study was a prospective audit of EP patients recruited in the three gynaecology wards of Chris Hani Baragwanath Academic Hospital (CHBAH). Two hundred patients with EP were included in the study, counting from the patient admission book during a 3-month period from August 2018 to October 2018.

The data collection began once ethics approval was obtained. Data was collected from all female patients 18 years and older, admitted to the hospital diagnosed with an EP and who gave informed consent to participate in the research study. The patients were interviewed and relevant information to the study was obtained from the patient's files. A record of every patient screened, was kept. Critically ill patients were allowed to recover before gathering information. Follow up was carried out where necessary.

Data was collected on a Redcap data sheet. The answers on the sheet were either yes or no, or a value in case of a laboratory test measurement as well as written reports. Demographic data, presenting symptoms and signs, risk factors, diagnostic modality, management, features of the EP and morbidity were also recorded on the sheet. The statistical data analysis was done using Open EPI version 3.01 and Microsoft Office Excel. Information was analysed from the data collection sheet for each objective, employing descriptive methods. Categorical data in most objectives involved expression of mean, median, frequencies, percentages, and standard deviations. Statistical significance was accepted at $p < 0.05$. Permission to do the study was

granted by the Chief Executive Officer of CHBAH and the Human Research Ethics Committee of the University of the Witwatersrand: M180312.

3. Results

Two hundred patients were enrolled during the study period. There was a total of 232 major gynaecological emergency operations during the study period, which means EP surgery accounted for 86.2% of such operations at CHBAH.

Demographics and risk factors of EP are shown in Table 1. – The majority (33.5%) of patients were between 19 and 25 years old. Only 10.5% of patients were of advanced maternal age (>35 years). The mean age was 28.5 (SD 5.5) years and the median 27 years. Most (64.5%) of the patients were unemployed. The mean parity was 1.27 (SD 1.04) and the mean gravidity was 2.58 (SD 1.19). The majority of patients (59.0%) were at a gestation of 7 weeks to 8 weeks 6 days at presentation. Furthermore, most patients (92.5%) were not booked in any antenatal care at presentation, and most of them (74%) were referred to CHBAH from local clinics. Although the Human Immunodeficiency Virus (HIV) status was recorded at admission in 41.0% of patients the status was unknown.

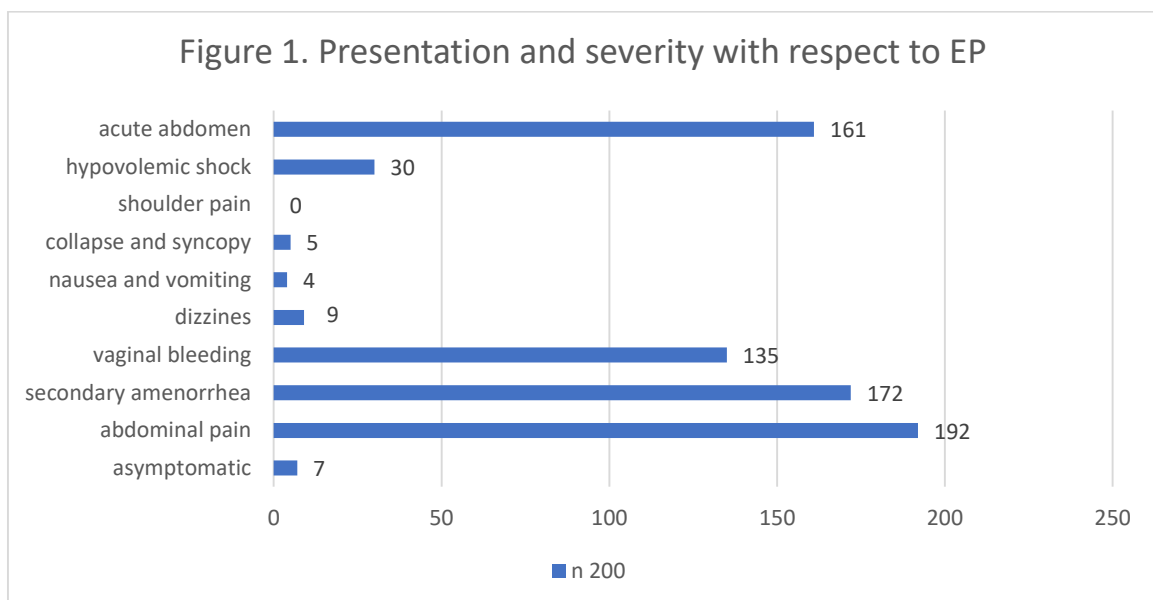
The risk factors considered in this study included previous tubal surgery unrelated to management of EP, previous tubal surgery related to management of EP, history of previous STI/PID, cigarette smoking, ART, IUCD and self-reported history of sepsis (septic miscarriage or puerperal sepsis). However, the risk factors were only identifiable in 36.0% of these EP patients.

Table 1. Demographics and risk factors of EP		
	200 (n)	%
Age (years)		
19 – 25	67	33.5
26 – 30	58	29.0
31 – 35	54	27.0
>35	21	10.5
Employment status		
Employed	71	35.5
Unemployed	129	64.5

Parity		
0	47	23.5
1	85	42.5
2	45	22.5
3	15	7.5
4	7	3.5
5	1	0.5
Gravidity		
1	36	18.0
2	68	34.0
3	59	29.5
4	23	11.5
5	9	4.5
6	5	2.5
Gestation by last known menstrual period (LNMP)		
< 3 weeks	0	0
3 weeks – 3 weeks 6 days	3	1.5
4 weeks – 4 weeks 6 days	5	2.5
5 weeks – 5 weeks 6 days	3	1.5
6 weeks – 6 weeks 6 days	27	13.5
7 weeks – 7 weeks 6 days	59	28.5
8 weeks – 8 weeks 6 days	61	30.5
9 weeks – 9 weeks 6 days	26	13.0
10 weeks – 10 weeks 6 days	8	4.0
11 weeks – 11 weeks 6 days	3	1.5
12 weeks – 12 weeks 6 days	5	2.5
>13 weeks	0	0
HIV status		
Positive	47	23.5
Negative	71	35.5
Unknown	82	41.0
Previous tubal surgery unrelated to management of EP	2	1.0
Previous tubal surgery related to management of EP	10	5.0

Previous STI/PID	41	20.5
Cigarette smoking	10	5.0
ART	0	0.0
Self- reported History of sepsis (septic miscarriage/ puerperal sepsis)	9	4.5
IUCD	0	0.0

The three most common symptoms at presentation were secondary amenorrhea, abdominal pain and vaginal bleeding. Hypovolemic shock (BP < 90/60 mmHg and pulse > 100bpm) and an acute abdomen (rigidity, guarding and rebound tenderness) were described in 30 (15.0%) and 161 (80.5%) of the patients, respectively. Only seven patients (3.5%) were asymptomatic, with the EP diagnosis made during their first antenatal visit.



Diagnostic modalities used in our setting to diagnose EP included ultrasound, both abdominal and transvaginal, where an empty uterus, presence of an adnexal mass and free fluid were searched for. Both urine and blood quantitative beta human chorionic gonadotrophin (b-HCG) tests were also performed (see Table 2). One patient had a negative urine pregnancy test; however, the qualitative b-HCG test was positive. In nine patients the record of a urine pregnancy test was missing from the file, but they were actually pregnant with EP. There were only 20 (10%) in-patients who had quantitative b-HCG as part of the work-up for medical management, but all 20 were eventually managed surgically because they did not meet the

criteria for medical management. Out-patients who were medically or conservatively managed were not included in the study as no in-patient records are available.

Table 2. Diagnostic modalities used in our setting to diagnose EP		
	200 (n)	%
TVU/S	198	99.0
Abdominal ultrasound	6	3.0
Empty uterus on ultrasound	197	98.5
Adnexal mass on ultrasound	122	61.0
Free fluid on ultrasound	177	88.5
Urine pregnancy test		
Positive	190	95.0
Negative	1	0.5
Not recorded	9	4.5
Quantitative b-HCG (mIU/ml)		
0 - 4999	10	5
5000 – 9999	6	3
>10000	4	2
Not done	180	90

The variables regarding the morbidity and management of EP (Table 3) were signs of rupture on arrival (presence of free fluid on ultrasound, hypovolemic shock, acute abdomen), the haemoglobin level at presentation, the number of transfusions, blood loss at surgery, high care admission, intensive care unit (ICU) admission, inotrope requirement and prolonged ventilation. A blood gas was performed in 89.5% of the patients to assess the severity of the disease. The majority of patients (92%) had a haemoglobin of more than 7g/dl.

The management was either laparotomy or laparoscopy, with laparotomy being the preferred route of entry used in our study (94%). Only two re-look laparotomies were performed due to suspicion of continuous bleeding. Two patients had an initial laparoscopy but in both cases it was converted to laparotomy due to inability to achieve haemostasis. The type of procedures were either salpingectomy, salpingostomy or salpingotomy, in which by far the most patients had a salpingectomy. In eight patients (4%) a salpingo-oophorectomy/adnexectomy was performed on the affected side due to suspected ovarian ectopic or extensive adnexal damage.

Most EP were on the right adnexa (66.5%). The contralateral tube appeared normal in 159 (79.5%) of the patients. The abnormal looking contralateral tube was recorded on the surgical notes as either hydrosalpinx or as absent. Seven (3.5%) patients had conservative surgical techniques (salpingotomy and salpingostomy) on the affected tube as the contralateral tube appeared to be abnormal.

Only two patients (1%) requested sterilisation before the procedure and tubal ligation was performed on the contralateral tube. Ninety-five percent of the patients desired future fertility after the procedure. The patient's contraception of choice after the procedure was noted. More patients chose injectable contraception (58%), than any other option. The site of the ectopic was most commonly the ampulla 127 (63.5%) followed by the isthmus 34 (17.0%). There were no maternal deaths in this cohort.

Table 3. Morbidity and management of EP.		
	200 (n)	%
Ruptured on arrival	174	87.0
Haemoglobin (g/dl)		
<7	16	8.0
7-11	107	53.5
>11	77	38.5
Mean 10.31(SD 2.18)		
Transfusions	50	25.0
Red blood cells (RBC)		
1 unit	7	3.5
2 units	21	10.5
3 units	9	4.5
4 units	10	5.0
5 units	3	1.5
Fresh frozen plasma (FFP)		
2 units	7	3.5
3 units	1	0.5
4 units	10	5.0
Cryoprecipitate		
4 units	1	0.5

5 units	2	1.0
6 units	1	0.5
10 units	2	1.0
Platelets		
1 unit	6	3.0
Total estimated blood loss (ml)		
0 – 499	96	48.0
500 – 999	64	32.0
1000 – 1499	19	9.5
1500 – 1999	2	1.0
2000 – 2499	15	7.5
2500 – 3000	4	2.0
Mean = 684.10 (SD 608.72)		
High care admission	9	4.5
Intensive care unit (ICU) admission	4	2.0
Required inotropes	3	1.5
Prolonged Ventilation (>2hours)	5	2.5
Laparotomy	188	94.0
Laparoscopy	14	7.0
Salpingectomy	193	96.5
Salpingotomy	2	1.0
Salpingostomy	5	2.5
Contralateral Tube		
Normal	159	79.5
Abnormal	41	20.5
Site of EP		
Ampulla	127	63.5
Isthmus	34	17.0
Fimbriae	21	10.5
Interstitial	13	6.5
Suspected Ovarian	3	1.5
Cervical	0	0.0
Abdominal	0	0.0

4. Discussion

In terms of demographics, the mean age of the patients in our study is similar to other studies^{3,4,9,10}. This implies that EP is a disease of middle reproductive ages, which rules out advanced maternal age (>35 years) as a risk factor for EP in our community ($p < 0.0001$). In one study the risk of EP was identified in patients with advanced maternal age and this hypothesis is based on the higher likelihood of exposure to most other risk factors with advanced maternal age, which include: increase in chromosomal abnormalities in trophoblastic tissue and age-related changes in tubal function delaying ovum transport, resulting in tubal implantation². The percentage of advanced maternal age patients (10.5%) in the study is similar to the advanced maternal age deliveries (11%) in the same period at CHBAH (Professor Adam, Head of Department of Obstetrics and Gynaecology, CHBAH, personal communication).

The unemployment rate is similar to other studies done in Zimbabwe and in South Africa^{4,10}. Most patients were parity of one and gravidity of two, which is similar to other studies^{3,4,10}. There is no obvious reason for EP to be more common in these multigravida patients, but one study had a theory that it is probably due to previous miscarriages and infections resulting in tubal damage³. Most patients were between seven to eight weeks gestation, and presented when the EP has ruptured, which is the gestation at which ampullary and isthmic EP usually rupture^{4,6}. There was a higher rate of known HIV positive patients (39.8%), than known HIV negative patients, which correlates with a study done in Mozambique¹². This might conclude a link between HIV and EP, but further studies need to be done to confirm the association.

Interestingly, in most patients no risk factors could be identified, which is similar to findings in other studies^{2,5,7}. However, some studies found a significant reported risk factor of previous PID and previous tubal surgery due to EP, which are noted risk factors in our study^{1,2,7}. The exact mechanism of this association is not understood but it has been proposed that in addition to distortion of tubal architecture, it may be due to an effect on the tubal microenvironment².

The three classic symptoms of EP presentation are secondary amenorrhea, vaginal bleeding and abdominal pain which are common and in keeping with most studies^{1-4,10}. Signs of shock were present in 15%, and acute abdomen in 80.5% of patients in our study, which is similar to other studies^{2-4,10}. Diagnosis of EP was made with TVU/S, which is the gold standard of diagnosing EP^{1,2,5,7}. A combination of TVU/S and quantitative b-HCG is used to decide on

patient management, which is in keeping with the accepted protocol to determine whether medical or surgical management is most appropriate^{1,2,5,7}.

The majority of patients were diagnosed with ruptured EP, which is similar to other studies done in SA and in India^{3,10}. South African authors believe that this is mainly due to poor contraception services, high numbers of unintended pregnancies, few early pregnancy confirmation visits, late consultation, and a poor means of investigation, compared to developed countries¹⁰. The mean haemoglobin of 10.3g/dl is slightly higher than the 9.0g/dl reported in a study in Zimbabwe⁴. Transfusions were needed in a quarter (25.0%) of the patients in the study, which is similar to reports in other studies done in SA^{9,10}, but is low in comparison to 77% of patients transfused in a study from Zimbabwe⁴. Most patients in the current study requiring transfusions, received two or more units of RBC (21.5%), which is lower than that reported in a study in Zimbabwe (67.5%) and a study in SA (67.7%)^{4,10}, but also similar to another study in SA (20.4%)⁹. Of the 30 (15%) patients who were in hypovolemic shock, 29 (97%) required transfusion/s. Of the 171 (85%) patients who were not in hypovolemic shock, only 21 (12.2%) required transfusion/s. This shows that almost all patients in hypovolemic shock from EP require transfusion/s ($p < 0.001$). Although there were no auto-transfusions during our study, Moran's⁸ opinion is that a patient with ruptured EP is the ideal candidate to benefit from auto-transfusion through red cell-saving techniques, which reduce or eliminate the need for blood from a blood bank⁸. Where cell-saving machines are available, they should always be used for a laparotomy for a ruptured EP. The mean blood loss at surgery was 684.10ml which is less than reported in other studies done in SA and Zimbabwe^{4,10}.

There were 9 (4.5%) high care admissions, 4 (2%) ICU admissions, 3 (1.5%) patients who required inotropes and 5 (2.5%) with prolonged ventilation (>2 hours). This was lower than shown in studies in India and Zimbabwe^{3,4}, resulting in a lower morbidity in our setting than in other 3rd world countries. The number of laparotomies (188; 94%) performed in the current study, is similar to the numbers recorded in other developing countries⁴. Few laparoscopies are performed, probably due to the nature of presentation in our setting, resources and training. Laparoscopic surgery is shown to be superior to laparotomy in the surgical management of women with ruptured EP, due to lower pain scores, shorter hospital stay, less blood loss and fewer blood transfusions as reported in a number of studies^{2,5,7,9}. This is also shown in our study as all patients who required transfusion/s, had a laparotomy, while none of those patients who had laparoscopy needed transfusion/s ($p < 0.001$). Most patients (193; 96.5%) had salpingectomy, which is the preferred option where the contralateral tube is

normal^{2,5,7}. Thirty-five (17.0%) patients in the study had a salpingectomy performed on the affected tube even though the contralateral tube was abnormal, rather than potentially fertility preserving surgical techniques such as a salpingotomy or salpingostomy. In patients with tubal factors adversely affecting fertility such as previous PID, previous EP and damaged tubes, there is a higher rate of intrauterine pregnancy in the next gestation if a salpingotomy or salpingostomy was previously performed⁵. The site of the EP is no different to that reported in most studies^{2,4,5,7,10}.

5. Conclusion

The prevalence and complications of EP remain high in our environment as it accounts for 86.6% of the major gynaecological emergency operations at CHBAH. It is a common cause of maternal morbidity in the first trimester of pregnancy. In our study, most patients presented late with ruptured EP and some required blood transfusions and intensive monitoring post-surgery. Most patients were managed by laparotomy, which is adequate, but in modern medicine, laparoscopy should be considered in stable patients who do not meet the medical management criteria.

To improve the EP morbidity, there is a need for comprehensive gynaecological services including contraception and early pregnancy evaluation of patients with risk factors, as well as ongoing education to increase the awareness of sexually active women about safe sexual practices and the consequences of STI/PID. Improvement in laparoscopic surgery training and access to equipment is essential to decrease EP morbidity. Further studies are needed to determine the most effective interventions and management of EP in developing countries.

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Appendix A: Ethics Clearance

 UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
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Office of the Deputy Vice-Chancellor (Research & Post Graduate Affairs)

TO: Dr ST Mdebele
School of Clinical Medicine
Department of Obstetrics and Gynaecology
Chris Hani Baragwanath Academic Hospital

E-mail: sbura02@gmail.com

CC: Supervisor: Dr A Wise <amyjulietwise@yahoo.co.uk>
and <HREC-Medical.ResearchOffice@wits.ac.za>

FROM: Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 30/07/2018

REF: R14/49

PROTOCOL NO: **M180312** (*This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study*)

PROJECT TITLE: *Morbidity of ectopic pregnancy at Chris Hani Baragwanath Academic Hospital*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.



MSWorks2000/Iain0007/Clearscan.wps



R14/49 Dr ST Mndebele

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M180312

NAME: Dr ST Mndebele
(Principal Investigator)
DEPARTMENT: School of Clinical Medicine
Department of Obstetrics and Gynaecology
Chris Hani Baragwanath Academic Hospital

PROJECT TITLE: Morbidity of ectopic pregnancy at Chris Hani
Baragwanath Academic Hospital

DATE CONSIDERED: 06/04/2018

DECISION: Approved unconditionally

CONDITIONS:

SUPERVISOR: Dr A Wise

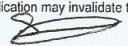
APPROVED BY:

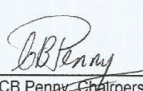
DATE OF APPROVAL: 30/07/2018
Professor CB Penny, Chairperson, HREC (Medical)

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on 3rd floor, Phillip V Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/We fully understand the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to resubmit to the Committee. I agree to submit a yearly progress report. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in March and will therefore be due in the month of March each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).


Principal Investigator Signature


31/07/2018
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Author Guidelines (SAJOG)

Original articles not exceeding 3 000 words, with up to 6 tables or illustrations, are usually observations or research of relevance to Obstetrics and Gynaecology. References should preferably be limited to no more than 15. Please provide a structured abstract not exceeding 250 words, with the following recommended headings: *Background, Objectives, Methods, Results, and Conclusion.*

Manuscripts must be provided in UK English. Qualification, affiliation and contact details of ALL authors must be provided in the manuscript and in the online submission process.

Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.

Scientific measurements must be expressed in SI units except blood pressure (mmHg) and haemoglobin (g/dl). Litres is denoted with a lowercase 'l' e.g. 'ml' for millilitres). Units should be preceded by a space (except for %), e.g. '40 kg' and '20 cm' but '50%'. Greater/smaller than signs (> and 40 years of age'. The same applies to $\pm$ and $^{\circ}$, i.e. '35 $\pm$ 6' and '19 $^{\circ}$ C'.

Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160...

Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'

Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.

General formatting The manuscript must be in Microsoft Word or RTF document format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes, with the exception of Tables).

ILLUSTRATIONS AND TABLES If tables or illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.

Tables may be embedded in the manuscript file or provided as 'supplementary files'. They must be numbered in Arabic numerals (1,2,3...) and referred to consecutively in the text (e.g. 'Table 1'). Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged. Tables must be cell-based (i.e. not constructed with text boxes or tabs) and accompanied by a concise title and column headings. Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'. Figure legends: Fig. 1. 'Title...' All illustrations/figures/graphs must be of high resolution/quality: 300 dpi or more is preferable, but images must not be resized to increase resolution. Unformatted and uncompressed images must be attached as 'supplementary files' upon submission (not embedded in the accompanying manuscript). TIFF and PNG formats are preferable; JPEG and PDF formats are accepted, but authors must be wary of image compression. Illustrations and graphs prepared in Microsoft PowerPoint or Excel must be accompanied by the original workbook.

REFERENCES Authors must verify references from the original sources. *Only complete, correctly formatted reference lists will be accepted.* Reference lists must be generated manually and not with the use of reference manager software. Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization and others.

All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order). Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus. Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al. First and last page, volume and issue numbers should be given.

Wherever possible, references must be accompanied by a digital object identifier (DOI) link and PubMed ID (PMID)/PubMed Central ID (PMCID). Authors are encouraged to use the DOI lookup service offered by [CrossRef](#).

Journal references: Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. *Stat Med* 1998;289(1):350-355. [<http://dx.doi.org/10.1000/hgjr.182>] [PMID: 2764753]

Book references: Jeffcoate N. *Principles of Gynaecology*. 4th ed. London: Butterworth, 1975:96-101. *Chapter/section in a book:* Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA jun, Sodeman WA, eds. *Pathologic Physiology: Mechanisms of Disease*. Philadelphia: WB Saunders, 1974:457-472.

Internet references: World Health Organization. *The World Health Report 2002 - Reducing Risks, Promoting Healthy Life*. Geneva: World Health Organization, 2002. <http://www.who.int/whr/2002> (accessed 16 January 2010).

Other references (e.g. reports) should follow the same format: Author(s). Title. Publisher place: publisher name, year; pages. Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'. Unpublished observations and personal communications in the text must not appear in the reference list. The full name of the source person must be provided for personal communications e.g. (Prof. Michael Jones, personal communication)'.

PROOFS A PDF proof of an article may be sent to the corresponding author before publication to resolve remaining queries. At that stage, only typographical changes are permitted; the corresponding author is required, having conferred with his/her co-authors, to reply within 2 working days in order for the article to be published in the issue for which it has been scheduled.

Appendix C: Plagiarism Form

University of the Witwatersrand, Johannesburg

School of Clinical Medicine

SENATE PLAGIARISM POLICY

Declaration by Students

I Sbusiso Trevor Mndebele (Student number: 0514059P) am a student registered for
MMED (Obstetrics and Gynaecology) in the year 2020. I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that ALL the work submitted for assessment for the above course is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.

Signature: _____



Date: 03/02/2020

Appendix D: Turnitin Report

Appendix E: Protocol

Morbidity of Ectopic pregnancy at Chris Hani Baragwanath Academic Hospital

Dr S T Mndebele

Student no: 0514059P

MMed (Obstetrics and Gynaecology)

Supervisor: Dr A Wise

MBChB (Wits), FCOG (SA), MMed (O&G) (Wits), HIVDip (SA), ACHM (FPD), Cert
(Maternal and Fetal Medicine)

Senior Consultant at Rahima Moosa Mother and Child Hospital

List of abbreviations

EP – Ectopic Pregnancy

β -hCG – Beta Human Chorionic Gonadotrophin

SA – South Africa

CHBAH = Chris Hani Baragwanath Academic Hospital

TVU – Transvaginal Ultrasound

NHRD - National Health Research Database

RCOG – Royal College of Obstetrician and Gynaecologist

1. Introduction

Ectopic pregnancy is defined as a condition where a fertilized ovum implants outside the normal uterine cavity^{1,8}. It remains the commonest life-threatening surgical emergency in gynaecology especially in the tropics where most patients present with the ruptured variety. Hence, it is an important cause of maternal morbidity and mortality in the first trimester of pregnancy, accounting for almost 10% of all maternal deaths^{1,9,10}. Responsible for thousands of hospital admissions, surgical interventions and blood transfusions. Worldwide, EP complicates 0.25-2.0% of all pregnancies^{7,14}. In the developing world, however, data are few and often out of date. Nonetheless, EP accounted for 11/1000 live births in Africa from the 1960s to the mid-1980s⁷. In a study in Pakistan the institutional setting EP accounted for 1% of total pregnancies and more than half of all women with EP presented with acute abdomen and required emergency laparotomy¹. In a Nigerian study the incidence is a bit higher, 2.01%³. It is common in the developing countries probably due to the high rates of pelvic infections, unsafe abortions and puerperal sepsis⁴.

In a study in India 71.66% patients were in the age group of 21-30 years, this may be because in this time-period is the maximum fertile period and use of contraception is infrequent and occasional⁵. Also, a study in Nigeria the mean age of the patients was 27 ± 2 years³. Therefore, the age group is similar in the two studies done. EP were common in multiparous women than primigravida (18.42%) in India and other studies found a similar pattern².

Over the past few decades, the management of EP has been revolutionized. This is the result of the emergence of several non-surgical options to what had once been thought to be a solely surgically treatable condition. An earlier diagnosis can be made with transvaginal ultrasound and quantitative beta human chorionic gonadotrophin. This increases the chances of success of medical treatment and minimizes the morbidity, mortality and financial burden created by this health problem⁴. Above the discriminatory zone of 1,500 mIU/mL - 2,500 mIU/mL, a normal intrauterine pregnancy should be visible by TVU with 100% sensitivity, the absence of such implies an abnormally implanted gestation¹².

The aetiology of EP most of the time remains uncertain although multiple risk factors have been attributed to its occurrence. It is observed that the frequency of EP has been on the increase during the last few decades owing to the increased incidence of venereal diseases, puerperal sepsis, post abortion sepsis, previous tubal surgery, cigarette smoking, increased usage of contraceptives, short birth spacing interval and increased usage of assisted reproductive techniques^{3,13}. Risk factors were found in 33% of cases in a study in Pakistan⁶.

In an Indian study, previous abdominal/pelvic surgery/lower segment Caesarean section (32.69%), previous abortion/medical termination of pregnancy (32.69%), pelvic inflammatory disease (25%) and ovulation induction (23.07%) were major contributing factors responsible for incidence of EP⁷.

EP are classified by the site at which they are found. They can be tubal (more than 95%), cervical, ovarian, abdominal, intra-ligamentous or over a caesarean scar. In the fallopian tube the ectopic gestation can be in the ampulla (70%), isthmic (12%), fimbria (11%), interstitial or cornual (2%)^{12,14}. The right fallopian tube was observed to be the most common site of occurrence of EP in India¹¹. The natural progression of a tubal pregnancy is that it can be unruptured early on, later it may rupture as the trophoblast invades the thin anti-mesenteric border of the tubal wall usually. There can be spontaneous involution with death of the conceptus at an early stage. Complete tubal miscarriage, incomplete tubal miscarriage or a tubal blood mole may be the result of an ectopic pregnancy. The time of rupture varies according to the anatomy of the different parts of the tube affected. The isthmic variant ruptures early at 6-8 weeks' gestation as it is the narrowest in diameter. The ampullary ectopic may rupture at 8-12 weeks as it has the widest diameter and the interstitial variant may rupture even later at 12-14 weeks because the surrounding myometrium can hypertrophy to accommodate the enlarging conceptus¹⁴.

Patients usually presents with secondary amenorrhoea, abdominal pain and irregular vaginal bleeding but some may be asymptomatic. The presentation may be acute or subacute and depends on whether rupture has occurred or not. Dizziness, and/or syncope are present and represent advanced stages of intra-peritoneal haemorrhage following rupture. Ruptured EP leads to the acute onset of abdominal pains and cardiovascular collapse, and without prompt intervention, can lead to death. Clinical findings of ruptured ectopic are shock, cervical motion tenderness, adnexal mass/tenderness, fullness of pouch of Douglas, acute abdomen and abdominal distension. A Nigerian study found that majority presented with ruptured EP (92.4%); abdominal pain (92.4%) and amenorrhoea (91.2%)⁹. The typical history of amenorrhea and abdominal pain was also found in an Indian study in 77% of women, 38% were in a state of shock¹⁰. To decrease maternal mortality and morbidity due to EP, there is a need for early diagnosis. However, the situation in the developing countries is quite different with morbidity remaining high due to delay in presentation. Patients present after rupture, require massive blood transfusions, are offered radical surgery and are hospitalized for some days³.

The morbidity was significant with 87.3% presenting after rupture, 38.8% being attended with signs of shock, 11.1% requiring intensive care admission and 77% being transfused with blood, and the mean hospital stay was five days following salpingectomy via laparotomy in Zimbabwe¹⁴. This demonstrates the high morbidity in developing countries. In a literature review, it was found that ruptured EP is associated with significant morbidity, around 20% will require transfusion and most will spend six to seven days in hospital or even more¹².

EP can be managed expectantly, medically or surgically. Over the years the management has evolved from being a surgical emergency to more conservative medical management. The treatment option is influenced by the clinical state of the patient, site of the ectopic gestation, reproductive wish of the patient as well as the availability of facilities and technological expertise. When the EP has ruptured, surgery is usually performed. This can be achieved by either laparotomy or laparoscopy the former being the preferred method in haemodynamically unstable patients to achieve immediate haemostasis. These patients should be resuscitated first, intravenous access secured, blood sent for a full blood count and four units of blood cross matched in preparation for theatre. Surgery can be radical or conservative^{14,18}. One recent study in South Africa found that laparoscopic surgery is superior to laparotomy in the surgical management of women with ruptured EP, resulting in lower pain scores, fewer blood transfusions, shorter hospital stays and fewer days needed for convalescence, allowing women to return to work sooner at the cost of longer operating times¹⁶. Salpingectomy is the radical form of surgery where the affected tube is resected. It is usually performed, particularly if¹⁴:

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

In a study in India of 52 patients, 35 (70%) patients were managed by laparotomy, 12 patients underwent laparoscopy, 17 patients had less than 1000 ml, 22 patients had hemoperitoneum of 1000-2000 ml and 4 patients had >2000 ml of hemoperitoneum intraoperatively¹².

Salpingectomy was the most common surgical procedure performed in Indian study (82.86%) and 85.71% women received blood transfusion¹³.

Conservative surgery is when a salpingostomy or salpingotomy are done to save the affected tube. When evaluated in terms of reproductive outcome, conservative surgery is associated with higher subsequent intra-uterine pregnancy and higher recurrent ectopic rates when compared with radical surgery⁸. In the presence of a healthy contralateral tube there is no clear evidence that salpingotomy or salpingostomy should be used in preference to salpingectomy¹⁰.

Medical management with Methotrexate can be used to treat unruptured ectopic pregnancy in properly selected patients. Success is greatest if gestation is <6 weeks, there is no foetal heartbeat, the tubal mass is <3.5cm in diameter and β -hCG is <10 000IU/L¹⁸.

Conservative expectant management is offered to a small group of carefully selected cases of unruptured ectopic pregnancy. In the guidelines for management of tubal pregnancy, the Royal College of Obstetricians and Gynaecologists concluded that success was likely in women clinically stable, with a baseline β -hCG less than 1000IU/L, a hemoperitoneum less than 100ml, a tubal mass less than 2cm and no foetal parts on ultrasound¹⁷.

The above studies show that EP should be considered a relevant public health indicator, responsible for thousands of hospital admissions, surgical interventions and blood transfusions. Accounts for a sizeable proportion of infertility and ectopic recurrences. Most studies were done in India which apply to only one region of the world and few in Africa.

2. Aim

The aim of my study is to describe the morbidity related to EP in a tertiary institution recently. I also want to find out about the type of patients presenting at Chris Hani Baragwanath Academic Hospital in terms of demographics, presenting symptoms and signs, risk factors, severity of disease at presentation. Furthermore, I aim to describe how we diagnose and manage these patients at CHBAH. This will help us compare the above variables to other studies done.

3. Study Objectives

1. To describe the demographics and risk factors of patients with EP
2. To describe the presentation and severity with respect to EP
3. To describe the diagnostic modalities used in our setting to diagnose EP

4. To describe the morbidity, management and outcome of EP

4. Methods

4.1 Type

This will be a prospective audit study.

4.2 Site

The site of the study will be at CHBAH in the three gynaecology wards 59, 60 and 61 in SA. CHBAH is the 3rd largest hospital in the world with approximately 3200 beds and about 6'760 staff members. The gynaecology wards bed occupancy is 96 beds. There are 5300 gynaecology admissions per year with 3100 emergencies. There are +- 40 emergency laparotomies done for EP per month from theatre registers.

4.3 Inclusion criteria

All female patients 18 years and above admitted to the hospital diagnosed with EP at gynaecology wards and informed consent given.

4.4 Exclusion criteria

All patients who are treated as outpatients and patients who do not give informed consent to the study. Patients which pass away before getting information for the study. Patients less than 18 years of age.

4.5 Sample size

The estimated sample size is 200 patients from counting from admission books in a 3 months period.

4.6 Data collection

The data collection will begin as soon as after full ethics approval from April 2018 to June 2018. The patients will be interviewed in the gynaecology wards and relevant information to the study will be taken from patient files. A record of every patient screened, and number of patients excluded with reasons will be kept. Critically ill patients will be allowed to recover then information gathered after when stable. Follow up may be necessary in certain cases. The above is relevant to my study as this will allow time to gather the information from patients themselves directly. Data will be collected in a Redcap data sheet. The answers on the sheet

will be either yes or no or a value in case of a lab test and written reports. Demographic data, presenting symptoms and signs (e.g. hypovolemic shock which is low blood pressure of less than 90/60mmHg and pulse of more than 100b/min, also worst blood gas as in metabolic acidosis, etc), risk factors, diagnostic modality, management, features of ectopic and morbidity will be recorded on the sheet. Please refer to data collection sheet (attached).

4.7 Bias

Selection bias will occur because the patient studied are only in inpatient setting and only one hospital is involved. Some aspects of the objectives may not be included if information has not been recorded by the health care workers involved.

5. Data Analysis

The study overall will be a prospective cohort study. The data analysis will be done using Stata version 14.1/Statistica version 13.2 software. Information will be analysed from data collecting sheet for each objective employing descriptive methods. Descriptive methods in all objectives will involve expression of mean, range, frequencies and percentages, with 95 percent confidence interval. Statistical significance will be accepted at $p < 0.05$.

6. Ethics

Ethics clearance will be required as this involves human participants. The age of patients in the study will be 18 and above, so no minor will be involved in the study. Patient names and file numbers will be recorded in a separate data sheet and all identifiers will be removed prior to analysis and dissemination of the results. Ethics submission will be done as soon as the proposal has been accepted. The research will be registered on the National Health Research Database and institutional permission obtained via NHRD.

7. Timing

	Sept 2017	Oct 2017	Nov 2017	Dec 2017	Jan 2018	Feb 2018	Mar 2018	April 2018	May 2018	June 2018	July 2018	Aug 2019	Sept 2019	Oct 2019	Nov 2019	Dec 2019	Jan 2020	Feb 2020	Mar 2020
Literature review																			
Preparing protocol																			

Protocol assessment																			
Ethics application																			
Collecting data																			
Data analysis																			
Writing up																			
Submission																			

8. Funding

Transport	Available, will be working at CHBAH during the data collection
Photocopying	Own photocopying machine, paper and ink available from my own budget
Stationery	Available (pens, paper)
Laptop and internet	Available, own home laptop and Wi-Fi available at home and wits medical school

9. Problems

I don't expect any problems during data collection but expect to have the information available on patient files unless the files are lost or if patients are too sick to consent.

10. References

1. Mahboob U, Mazaar SB. Management of ectopic pregnancy: a two-year study. JAMCA. 2006;18(4): 34–37. Available: <https://www.ncbi.nlm.nih.gov/pubmed/17591007/>. [Accessed 02/09/2017].
2. Sudha VS, Thangaraj DS. A retrospective study on ectopic pregnancy: a two-year study. IJRCOG. 2016;5(12): 4365-4368. doi: <http://dx.doi.org/10.18203/2320-1770.ijrcog20164344>. [Accessed 02/09/2017].
3. Lawani OL, Anozie OB, Ezeonu PO. Ectopic pregnancy: a life-threatening gynecological emergency. IJWH. 2013;5: 515–521. doi: <https://doi.org/10.2147/IJWH.S49672>. [Accessed 01/09/2017].
4. Brucker R, Bui T, Kwan-Gett T, Stewart L, Hall AJ, Kinzer MH. Ectopic Pregnancy Mortality — Florida 2009–2010. MMWR. 2012;61(6): 106–110. Available: <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6106a2.htm>. [Accessed 02/09/2017].
5. Panchal D, Vaishnav G, Solanki K. Study of Management in Patient with Ectopic Pregnancy. NJIRM. 2011;2(3): 91–93. Available: <https://www.ejmanager.com/mnstemps/18/18-1312693204.pdf>. {Accessed 01/09/2017].
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8. Mufti S, Rather S, Mufti S, Rangrez RA, Wasiqa, Khalida. Ectopic Pregnancy: An Analysis of 114 Cases. JK-Practitioner. 2012;17(4): 20-23. Available: https://www.researchgate.net/publication/289363301_Ectopic_pregnancy_An_analysis_of_114_cases. [Accessed 02/09/2017].
9. Iklaki CU, Emechebe CI, Njoku CO, Ago BU, Ugwu B. Review of Ectopic Pregnancy as a Cause of Maternal Morbidity and Mortality in a Developing Country. IOSR-JDMS. 2015;14(8): 86-91. doi: 10.9790/0853-14868691. [Accessed 04/09/2019].
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11. Shaikh BS, Jampala S, Devi SS, Mallika M. A Study of Ectopic pregnancy in a Tertiary Care Teaching Hospital. IJOGR. 2016;3(2): 132–136. doi: 10.5958/2394-2754.2016.00036.9. [Accessed 02/09/2017].
12. Prasanna B, Jhansi CB, Swathi K, Shaik VM. A Study on Management, Morbidity and Mortality of Ectopic Pregnancy Attending a Tertiary Care Centre. AWCH. 2015;1(1): a10-a13. doi: 10.21276/awch. [Accessed 03/09/2017].
13. Rakhi, Mital P, Hooja N, Anuradha A, Priyanka M, Andleeb F. Ectopic Pregnancy: A Devastating Catastrophe. Sch. J. App. Med. Sci. 2014;2(3A): 903-907. Available: <http://saspublisher.com/wp-content/uploads/2014/06/SJAMS-23A903-907.pdf>. [Accessed 04/09/2017].
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18. Edridge WW, Guidozzi F, Buchmann EJ, Frank K. Wits Gynaecology Protocol. University of the Witwatersrand. 2017. 18-21.

Appendix F: Data Collection Sheet

Informed Consent Obtained

Yes	
Date	
Time	

Demographic Data

Age (years)				
Occupation (employed/unemployed)				
Residence	Soweto			
	Lenasia			
	Orange farm			
	Johannesburg			
	Elsewhere (specify)			
Parity (number)				
Gravidity (number)				
Gestation at Diagnosis (LNMP)	LNMP date			
	Gestation			
Booked or Un-booked				
RH	Positive			
	Negative	Antibody negative	Anti D given (mcg)	
			Anti D not given	
		Antibody positive		
		Antibody not done		
	Not known			
RPR	Positive	Bicillin given (no of doses)		
		Bicillin not given		

	Negative				
	Not done				
HIV	Positive	CD4	Cells/mm3		
			Not done		
		VL	Copies/ml		
			Not done		
		On treatment (drug combination)			
		Not on treatment			
	Negative				
	Unknown				

Presenting Symptoms and Signs

First presentation	Date	
	Time	
	Referred from (Self, GP, Clinic, Hospital Level)	
Any previous presentation during current pregnancy (yes or no, if yes diagnoses and management)		
Asymptomatic (yes/no)		
Abdominal Pain (yes/no, if yes duration)		
Secondary Amenorrhea (yes/no)		
Per Vaginal Bleeding (yes/no, if yes duration)		
Vitals	Blood Pressure	
	Pulse	
	Temperature	
	Respiratory rate	
	Saturation in room air	
Other symptoms or signs (name and duration)		

Haemoglobin (value on arrival)		
Worst blood gas	PH	
	PCO ₂ (mmHg)	
	PO ₂ (mmHg)	
	Base excess (mmol/L)	
	HCO ₃ (mmol/L)	
	Lactate (mmol/L)	
	Not done	
Diagnoses of EP	Date	
	Time	

Risk Factors

Previous Tubal Surgery	Sterilisation (type)		
	Previous salpingectomy (side)		
	Previous salpingostomy/salpingotomy (side)		
	Reversal of sterilisation		
	No		
Previous EP	Salpingectomy (side)		
	Salpingotomy/salpingostomy (side)		
	Fimbriectomy (side)		
	No		
History of Pelvic Inflammatory Disease/ Sexually Transmitted Infections anytime in her life		Yes (number of times)	
		No	
Cigarette Smoking	Years		
	No per day		

	Not smoking	
Assisted Reproductive Techniques in this pregnancy (yes or no, if yes type)		
History of Sepsis (puerperal/post-abortion)		

Diagnostic Modality

Transvaginal Ultrasound	Uterus empty	
	Adnexal mass (size)	
	Free fluid	
	Not done	
Abdominal Ultrasound	Uterus empty	
	Adnexal mass (size)	
	Free fluid	
	Not done	
Urine Pregnancy Test (positive or negative)		
Serum Beta Human Chorionic Gonadotrophin (value)		

Morbidity

Ruptured on arrival (yes/no)			
Transfusion (number)	Red blood concentrate		
	Fresh frozen plasma		
	Cryoprecipitate		
	Platelets		
	Cell saver used(ml)		
	None		
Surgery	Yes	Date	

		Time	
	No		
Blood loss intra-op	Documented(ml)		
	Not documented		
Oophorectomy (unilateral/bilateral/wedge/not done)			
Salpingectomy (unilateral/bilateral/not done)			
Salpingostomy/salpingotomy (unilateral/bilateral/not done)			
Contralateral Tube (normal or abnormal)			
Contralateral Tube (ligated or not)			
Adhesions (yes or no)			
High Care admission (yes or no, if yes duration in hours)			
Intensive care unit admission (yes/no, if yes duration in hours)			
Required inotropes (yes/no)			
Prolonged ventilation (yes/no, if yes duration in hours)			
Negative Laparotomy/ Laparoscopy (yes or no)			
Hysterectomy (yes or no)			
Relook Laparotomy (yes or no, if yes date and time)			

Management

Laparoscopy	Yes	Date	
		Time	
		Duration	
	No		
Laparotomy	Yes	Date	
		Time	
		Duration	
	No		

Site of Ectopic

Ampulla (yes/no)	
Isthmus (yes/no)	
Fimbria (yes/no)	
Interstitial (yes/no)	
Ovarian (yes/no)	
Cervical (yes/no)	
Abdomen (yes/no)	
Caesarean Section Scar (yes/no)	
Not specified	

Future Contraception (yes/no)

Barrier	
Oral	
Injectables	
Implants	
Intrauterine device	
Sterilisation	
Decline	
Undecided	

Outcome

Demised	Yes	Date	
		Time	

	No	
--	----	--

Appendix G: Patient Consent Form

University of Witwatersrand (Faculty of Health Sciences)

Informed Consent Form for Research Involving Human Subjects

Title: Morbidity of Ectopic Pregnancy at Chris Hani Baragwanath Academic Hospital

Investigator: Dr S T Mndebele

Department: Obstetrics and Gynaecology

In this consent form, “you” always means the study subject and “me/I” as the investigator.

You are being asked to take part voluntarily in the research project described above. Before agreeing to take part in this research study, it is important that you read the consent form that describes the study. Please ask me to explain any words or information that you do not clearly understand. If you decide to enrol in this study, your involvement will last about 30 minutes. If you agree to take part in this study, I will ask questionnaire and review information in your file pertaining the study.

There are no known risks associated with this research. There will be no direct benefits to you for taking part in this study. You have the option not to take part in this study. If you choose to take part, you have the right to stop at any time. There will be no penalties involved if you choose not to take part in this study or stopping. Your part in this study is confidential. None of the information will identify you by name. Your personal information may be disclosed if required by law.

The results of this research study may be presented at meetings or in publications. You may ask any questions you have now. If you have questions later call Dr S T Mndebele 0714746972.

This proposal has been reviewed and approved by HUMAN RESEARCH ETHICS COMMITTEE: (MEDICAL) of the University of Witwatersrand, which is a committee whose task it is to make sure that research participants are protected from harm. If you wish to find about more about the HREC (MEDICAL), contact Ms Zanele Ndlovu 011 717 1252/2700/1234/2656. Ethics clearance certificate no. M180312.

I have read each page of this paper about the study (or it was read to me). I know that being in this study is voluntary and I choose to be in this study. I have had the opportunity to ask questions about it and any questions that I asked to have been answered to my satisfaction.

I consent voluntarily to participate as a participant in this research.

Participant Name: _____ Date: _____

Participant Signature: _____ Time: _____

Consent form explained by Investigator: Signature _____

Printed name: _____

Date: _____ Time: _____

A copy of this ICF has been provided to the participant.

Appendix H: Patient Information Sheet

Study title: Morbidity of Ectopic pregnancy at Chris Hani Baragwanath Academic Hospital

Greeting: Good day

Introduction: I *Dr ST Mndebele* am doing a research on Morbidity of Ectopic pregnancy at Chris Hani Baragwanath Academic Hospital. Ectopic pregnancy is defined as a condition where a fertilized ovum implants outside the normal uterine cavity. Research is just the process to learn the answer to a question. In this study we want to learn about the morbidity related to Ectopic pregnancy in a tertiary institution. I also want to assess the type of patients presenting at Chris Hani Baragwanath Academic Hospital in terms of demographics, presenting symptoms and signs, risk factors, severity of disease at presentation. Furthermore, I aim to describe how we diagnose and manage these patients at the hospital.

Invitation to participate: I am asking / inviting you to take part in a research study because you were admitted for the condition in the research.

What is involved in the study: You will be interviewed in the gynecology wards and relevant information to the study will be taken from your file if you consent to the study. If you are critically ill, you will be allowed to recover before gathering information. Data will be collected in a Redcap data sheet. The answers on the sheet will be either yes or no or a value in case of a lab test and written reports. Demographic data (age, occupation, residence, number of children and pregnancies, booking at clinic and HIV status), presenting symptoms and signs (e.g. hypovolemic shock which is low blood pressure of less than 90/60mmHg and pulse of more than 100b/min, also worst blood gas as in metabolic acidosis, etc), risk factors, diagnostic modality, management, features of ectopic, future contraception and morbidity. This will take about 30 minutes of your time. There will be no procedures or bloods done during the collection of data. The data collected will be stored safely and it will be destroyed after 2 years if the results are published, alternatively after 6 years if no publication.

Benefits: There will be no direct benefits to you for taking part in this study

You will be given pertinent information on the study while involved in the project and after the results are available.

Participation is voluntary: You have the option not to take part in this study. If you choose to take part, you have the right to stop at any time. There will be no penalties involved if you choose not to take part in this study or stopping.

Reimbursements: You will not be paid for taking part in this research study.

Confidentiality: Efforts will be made to keep personal information confidential. None of the information will identify you by name. Absolute confidentiality cannot be guaranteed. Personal information may be disclosed if required by law. The results of this research study may be presented at meetings or in publications; however, your identity will not be disclosed in those presentations. This research has been reviewed and approved by HUMAN RESEARCH ETHICS COMMITTEE: (MEDICAL) of the University of Witwatersrand, which is a committee whose task it is to make sure that research participants are protected from harm.

Ethics clearance certificate no. M180312.

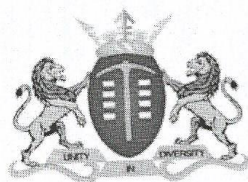
Contact details of researcher: Dr ST Mndebele. Cell no 0714746972. Email address sbura02@gmail.com.

Contact details of supervisor: Dr A Wise. Cell no. 0731527513.

Email address: amyjulietwise@yahoo.co.uk.

Contact details of REC administrator and chair: If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Appendix I: Permission to Conduct Research from Hospital



GAUTENG PROVINCE

HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE
CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 15 Dec 2017

TITLE OF PROJECT: Morbidity of ectopic pregnancy at Chris Hani Baragwanath Academic Hospital

UNIVERSITY: Witwatersrand

Principal Investigator: ST Mndebele

Department: Obstetrics and Gynaecology

Supervisor (If relevant): A Wise

Permission Head Department (where research conducted): Yes

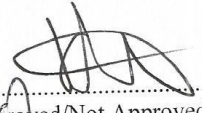
Date of start of proposed study: Dec 2017

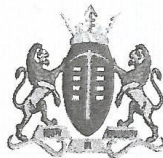
Date of completion of data collection: Dec 2019

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Hospital. The CEO /management of Chris Hani Baragwanath Hospital is accordingly informed and the study is subject to:-

- Permission having been granted by the Human Research Ethics Committee of the University of the Witwatersrand.
- the Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- the MAC will be informed of any serious adverse events as soon as they occur
- permission is granted for the duration of the Ethics Committee approval.


.....
Recommended
(On behalf of the MAC)
Date: 15 December 2017


.....
Approved/Not Approved
Hospital Management
Date: 15/12/17



GAUTENG PROVINCE

HEALTH
REPUBLIC OF SOUTH AFRICA

PERMISSION TO CONDUCT RESEARCH AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PRINCIPAL RESEARCHER:

FULL NAME

Sibusiso Trevor Mudebele

DESIGNATION

Registrar (O&G)

CONTACT NUMBER

0714746972

EMAIL

sbura02@gmail.com

NAME OF SUPERVISOR

Dr A. Wise

TITLE OF RESEARCH

Morbidity of Ectopic
Pregnancy at Chris Hani Baragwanath
Academic Hospital

STUDY SITE/S Chris Hani Baragwanath Academic Hospital

BRIEF OUTLINE OF METHODOLOGY

Prospective Cohort Study
The Patients will be interviewed in the
wards and information related to the study
gathered from Patients files

PROTOCOL Accepted

DATA SHEET Accepted

EXPECTED START DATE 01/05/2018 EXPECTED DURATION 3 months

ETHICS CLEARANCE? Y / N / DEPENDING

CONFLICT OF INTEREST? Y / ☒ N DETAILS

COST TO HOSPITAL AND OR PATIENTS? Y / ☒ N

SOURCE OF FUNDING Self

APPROVAL OF HOD Y/N

[Signature]

HOD

gadam

08/12/2017

SIGNATURE

NAME IN PRINT+ DESIGNATION

OFFICIAL STAMP+ DATE