Original Article

A Re-Evaluation of Ectopic Pregnancies in a Resource-Limited Setting: A Ten Year Review

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Abstract

Context: Ectopic pregnancy (EP) is a severe challenge in contemporary gynaecology, particularly in developing economies. Late presentation and diagnosis increase the associated morbidity and mortality. With the worldwide surge in incidence and varied presentation patterns, re-evaluation has become necessary. This study, therefore, aims at re-evaluating the risk factors and clinical patterns of EP cases in a tertiary health facility in a resource-limited setting. **Settings/Methods/Statistical Analysis:** All EP cases managed at the Teaching Hospital of the University of Nigeria (UNTH), Enugu, Nigeria, from January 1, 2008, to December 31, 2017, were retrospectively evaluated. The collected data was analyzed with the 23.0 edition of Statistical Package for the Social Sciences. Descriptive statistics was done for the qualitative variables. Cross-tabulation was done; the association levels were determined by Chi-square/Fisher's exact test and Student's *t*-test for the qualitative and quantitative variables. $P = 0.05$ was considered as the statistical significance level. **Results:** There were 6448 deliveries and 4129 gynaecological admissions. The mean age of the patients was 29 ± 3 years. Most (76.3%) of the participants (61) were multiparous, whereas only (2) 2.5% of the participants were grand-multiparous. The EP prevalence rate was 1.2% (80 out of 6448), and it constituted 1.9% (80 out of 4129) of all gynaecological admissions. All the patients presented with ruptured EP. The main presentation of EP among the participants was abdominal pain (69, [86.3%]), while the most presenting risk factor was a history of induced abortion (52, [65%]). **Conclusion:** We concluded that ectopic gestation remains a major gynaecological emergency in our environment. Most of our patients had ruptured EP, which could negatively impact our society, which places a high premium on childbearing.

Keywords: Ectopic pregnancy, evaluation, gynaecological emergencies, ruptured, unruptured

Introduction

Ectopic pregnancy (EP) is a critical problem in contemporary gynaecology, predominantly in the evolving society, due to adverse maternal outcomes.[1] An EP arises once a fertilized egg implants and develops outside the endometrium of the uterus.[1] EP could present as either ruptured or unruptured. Ruptured EP is a real surgical and life-threatening emergency.

It contributes to 9%–10% of all maternal demises and is a common contributor to pregnancy-related deaths in early pregnancy.[2] The adverse maternal outcomes are worse in developing countries because most of our patients present late with mainly ruptured ectopic pregnancies and associated hemodynamic compromise.[3] It is a major reason for fetal wastage, sub-fertility with associated recurrent rates of 10%–20%.[4]

The exact incidence of EP varies significantly from country to country. It differs even with different institutions in the same country, depending on the denominator (women of reproductive age, live births, and registered pregnancies) used in the computations and the tools accessible for the diagnosis.[2] At present, the incidence is increasing globally, yet the death rate per case has decreased in the last decade.[5,6] The increasing incidence globally might be related to a combination of factors such as a rise in the number of cases of pelvic inflammatory

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diseases (PID), increase use of ovulation induction agents, assisted reproductive techniques, and more tubal sterilization, while the reduction in the rate of death could be due to better diagnostic facilities and early intervention.[6]

This lethal condition's stated incidence differs from 2.2% in North America (USA), 2.0% in France, and 2.8% in Finland.[7] The frequency referred in Nigeria is 1.3% in Nnewi,[8] 2.1% in Abakiliki,[9] 1.5% in Sokoto,[10] 1% in Ilorin,[11] and 3.3% in Port Harcourt.[12]

Reported EP risk factors are multiple. They include PID, history of EP, history of pelvic surgeries, puerperal sepsis, and post-abortion sepsis. Others are endometriosis, congenital anomalies of the tubes, appendicitis, intrauterine contraceptive devices (IUCD), maternal ingestion of diethylstilbestrol, chromosomal malfunctions, and consumption of progestin-only medications. Cigarette smoking, pregnancies resulting from artificial reproductive technology, early intercourse, multiple sexual partners, race, and age >35 years are also known risk factors.[10-14] Nevertheless, EP can as well take place devoid of any apparent risk factor.[5,15]

EP can present without symptoms, especially before it ruptures. When it ruptures, the symptoms could be life-threatening.[16] Patients with ruptured EP typically pose as an urgent situation with sudden onset of sharp lower abdominal pain, cessation of menses, with or without vaginal bleeding, dizziness, or fainting attacks.[5] However, the earliest symptom in unruptured EP is brownish vaginal discharge.[6]

An elevated suspicious index is essential in diagnosing EP when unruptured;[17] this is because the typical symptoms and signs are often absent.[18] However, in our environment, where most of the patients present late with significant haemoperitonium and hypovolemia, diagnosis is usually easier. It could be made clinically with laparotomy as the primary treatment option involving total or partial salpingectomy.[8-11,19,20]

The last appraisal for EP was done >10 years ago in the study centre. They found a prevalence of 2.2%[21] with young single ladies with a previous record of induced abortion and resultant pelvic infection being the most significant risk factor. There is currently increased awareness and utilization of ovulation stimulation agents, assisted reproductive technology, and hormonal contraception.[7,9,12] It is thus expected to increase the EP incidence reported in more developed economies.

Besides, most of the patients before now presented in emergencies as ruptured EP.[8-10] It is thus expected that with the availability of diagnostic tools in the last decade, for example, high-resolution ultrasound, diagnostic laparoscopy, and serum beta-human chorionic gonadotropin, most of the diagnosis ought to be made before rupture.

Consequently, the need for a periodic appraisal of this global challenge became necessary in our environment to determine if these expected epidemiological changes had manifested. The evidence generated from this study may be useful in reviewing policies on managing ectopic pregnancies in the study area and beyond. Hence, the work's main objective is to re-evaluate the risk factors and clinical pattern of ectopic pregnancies in a tertiary hospital in a resource-limited setting.

Materials and Methods

Study area

This report was performed in Enugu state, a mainland state in South-eastern Nigeria with a land area ~8727.1 km^2 (3369 mile^2) located within the West African semi-tropical rain forest belt.[22] Enugu state population is estimated to be 3,257,298 according to the 2006 population census. The female inhabitants constitute 50.1% of the population, and the community of women in their reproductive age (15–49 years) was estimated to be 716,600.[23]

Study design

This was a cross-sectional, retrospective compilation of all EP cases managed at the University of Nigeria Teaching Hospital Enugu, Nigeria, between January 1, 2008 and December 31, 2017.

Sample size determination

Applying the cross-sectional qualitative sample size formulae by Charan and Biswas,[24] the minimum sample size required to obtain 80% power of the study at 5% margin of error and 2.2% prevalence rate of ectopic gestation in a previous study[21] was 33 study participants. To enhance the research's power, we included all ectopic pregnant patients managed in the study centre. The ethical endorsement was acquired from the Health and Research Ethics Committee of the University of Nigeria Teaching Hospital, Enugu, with reference number NHREC/05/01/2008B-FWA00002458-1RB00002323.

The inclusion criteria were all cases of EP diagnosed and managed in the hospital at the specified period. In contrast, patients with incomplete information concerning EP in their folders were not included in the report. Patients' data were retrieved from the hospital's medical records department after identifying them from the documents at the gynecological ward, theater, and accident and emergency unit. The total gynaecological admissions and records of the total births within the period were also retrieved. The following data was obtained from the case notes: Sociodemographic characteristics (age, parity, educational status, marital status, and gestational age [GA] at presentation), history of contraception, sexually transmitted disease, PID, ovulation induction, prior history of surgeries/pelvic surgeries, clinical features at presentation, and types of treatment offered, estimated blood loss (EBL), and the necessities for transfusing blood. These were recorded in a prepared proforma.

Statistical analysis

We evaluated the data using the Statistical Package for the Social Sciences, software version 23.0 (Chicago, IL, USA). Categorical parameters were shown as frequency and

percentages, whereas continuous variables were reported as means and standard deviations. The relationship between the categorical variables was done using the Chi-square/Fisher exact test, whereas Student's *t*-test and ANOVA were used for the quantitative variables. A significant level was set at a $P = 0.05$.

Table 1: Sociodemographic characteristics of participants

	Frequency (%)
Age group	
≤20	5 (6.3)
21-25	17 (21.3)
26-30	20 (25.0)
31-35	32 (40.0)
36-40	4 (5.0)
>40	2 (2.5)
Tribe	
Igbo	77 (96.3)
Others	3 (3.8)
Occupation	
Student	20 (25.0)
Professional	14 (17.5)
Civil servant	8 (10.0)
Trader	24 (30.0)
Housewife	10 (12.5)
Farmer	4 (5.0)
Educational level	
Primary	8 (10.0)
Secondary	42 (52.5)
Tertiary	30 (37.5)
Marital status	
Married	58 (72.5)
Single	22 (27.5)
Parity	
0	5 (6.3)
1	12 (15.0)
2	20 (25.0)
3	30 (37.5)
4	11 (13.8)
≥5	2 (2.5)

Results

In this report, there were 6448 deliveries and 4129 gynaecological admissions. There were 83 cases of EP, of which 80 patients (96.4%) had complete data in the file for analysis. The prevalence of ectopic gestation was 1.2% (80 of 6448) which also constituted 1.9% (80 of 4129) of all admissions in gynecology.

The mean age was 30.3 years. A significant proportion of women (62.5%) were multiparous, and 15.0% were nulliparous, only 2.5% were grand-multiparous. Most women were married 72.5% and mainly traders 30.0%. Only 3.8% were non-Igbos. All were Christians and 52.5% had secondary education. The details of the participant's sociodemographic characteristics are in Table 1. While the yearly trend of ectopic pregnancy among participants is shown in Table 2.

The clinical presentations of the participants included abdominal pain (86.3%), vaginal bleeding (80.0%), amenorrhea (65.0%), dizziness (37.5%), and shock (15.0%). All the patients with a period of amenorrhea and 65.0% of the participants presented at ≤12 weeks GA [Table 3]. Some risk factors for EP identified among the participants were a history of induced abortion (68.0%), PID (46.3%), use of ovulation induction (17.5%), previous abdominopelvic surgery (7.5%), puerperal sepsis (6.3%), and IUCD use (5.0%). The details of the clinical presentations and risk factors are in Table 3.

The age, parity, and GA were significantly associated with the tubal site ($P < 0.001$). Patients aged 35 years and below were more plausible to have EP at the ampulla tubal site. Multiparous patients and women at seven weeks gestation or less were more likely to have EP at the ampulla tubal site. Details are shown in Table 4.

The EBL was significantly higher when EP occurred in the cornual site ($F = 15.199$, $P < 0.001$). Transfusion was significantly lower when EP occurred at the Ampulla site ($F = 3.533$, $P = 0.034$). However, the Duncan multiple comparison tests indicate that EBL did not substantially alter between the Ampulla and the isthmus. Simultaneously, the

Table 2: Yearly trend of ectopic pregnancy among participants

Years	Number of deliveries	Number of gynecological admissions	Number of ectopic pregnancies	Incidence of ectopic pregnancies (%)	Percentages of gynecological infections (%)
2008	512	518	7	1.4	1.4
2009	408	482	9	2.2	1.9
2010	569	508	8	1.4	1.6
2011	775	518	10	1.3	1.9
2012	894	339	10	1.1	2.9
2013	951	418	14	1.5	3.3
2014	708	270	7	1.0	2.6
2015	489	315	7	1.4	2.3
2016	707	441	9	1.3	2.0
2017	435	320	2	0.5	0.6
Total	6448	4129	83	1.2	1.9

Table 3: Clinical presentation and risk factors of ectopic pregnancy

Variable	Frequency (%)
Clinical presentation	
Abdominal p]ain	69 (86.3)
Vaginal bleeding	64 (80.0)
Amenorrhea	52 (65.0)
Dizziness	30 (37.5)
Shock	12 (15.0)
Diarrhea	8 (10.0)
GA at presentation (weeks)	
≤7	23 (28.8)
8-12	57 (71.2)
>12	0 (0.0)
Sites of ectopic tubal rupture	
Ampulla	59 (76.0)
Isthmus	8 (10.0)
Interstitial/corneal	11 (14.0)
Risk factors found in patients	
Previous abortion	52 (65.0)
Pelvic inflammatory disease	37 (46.3)
Ovulation induction	14 (17.5)
Previous abdominopelvic surgery	6 (7.4)
Puerperal sepsis	5 (6.3)
IUCD use	4 (5.0)
Previous ectopic pregnancy	0 (0.0)

IUCD: Intrauterine contraceptive device, GA: Gestational age

Table 4: Association between age, parity, GA and tubal site

	Tubal Sites				*P*
	Ampullar *n* (%)	Isthmus *n* (%)	Cornual *n* (%)		
Age group					
< 20	5 (100.0)	0 (0.0)	0 (0.0)	59.195	< 0.001
21 - 25	17 (100.0)	0 (0.0)	0 (0.0)		
26 - 30	20 (100.0)	0 (0.0)	0 (0.0)		
31 - 35	19 (59.4)	8 (25.0)	5 (15.6)		
36 - 40	0 (0.0)	0 (0.0)	4 (100.0)		
>40	0 (0.0)	0 (0.0)	2 (100.0)		
Parity					
0	5 (100.0)	0 (0.0)	0 (0.0)	77.440	< 0.001
1	12 (100.0)	0 (0.0)	0 (0.0)		
2	20 (100.0)	0 (0.0)	0 (0.0)		
3	24 (80.0)	6 (20.0)	0 (0.0)		
4	24 (80.0)	2 (18.2)	9 (81.8)		
≥5	24 (80.0)	24 (80.0)	2 (100.0)		
GA presentation					
< 7 weeks	57 (100.0)	0 (0.0)	0 (0.0)	61.753	< 0.001
8 - 12 weeks	4 (17.4)	8 (34.8)	11 (47.8)		

transfusion rate did not appreciably differ irrespective of whether ectopic occurred at the isthmus or the cornu. The EBL and transfusion were also significantly higher at GA 8 and above ($P < 0.001$). Details of the association of EBL and tubal site of ectopic and GA at presentation of the participants are shown in Table 5.

Discussion

This study re-emphasized that EP contributes significantly to gynaecological admissions in our centre made worse, probably due to patients' poor health-seeking behavior. During the study period, the incidence of EP was 1.2%. It corroborates 1.0% and 1.5% reported in Ilorin and Sokoto.[11,25] It was lower than a study in the same centre that found an incidence of 2.2% in 2003.[21] This could be explained based on the assumption of an increase in the awareness of emergency contraception in our environment with a consequent reduction in unwanted pregnancies and abortions or that most cases of EP are diagnosed before rupture. Thus, they presented and got treated as elective cases in private hospitals. In addition, with the proliferation of *in vitro* fertilization technology and ovulation induction globally, it is expected that EP cases would be on the rise. Our findings, however, are at variance with this assumption, probably because most of the cases of an EP might have presented and got treated as unruptured cases in private hospitals.

Major risk factors for our patients included a history of criminal termination of pregnancy and PID. It could be due to the increasing liberal coital activity in our clime, poor awareness and utilization of contraception, and sepsis from illegal abortions procured from quacks and proliferation and use of substandard antibiotics to treat PID.[20] These findings are like the significant risk factors in previous studies from our centre[21] and across Nigeria.[3,25]

In this study, ruptured EP cases were either acute or subacute. The diagnosis was mainly based on history, physical examination, and abdominal paracentesis. A pregnancy test was done as a supportive diagnostic investigation. Transvaginal/transabdominal ultrasound confirmed the diagnosis. The availability of high-resolution ultrasound should have made EP diagnosis much earlier, but our study's finding was different. This is because of our patients' poor health-seeking behavior. Second, it is probable that the majority of the unruptured cases presented and got treated at private hospitals. The most typical EP site from our work was the fallopian tubes ampullar. This is like reports from other studies.[9,11,21] None of the patients had expectant or medical management as all presented with ruptured EP and therefore had surgical treatment.

Patients that present in shock should be operated on immediately after resuscitation; it is both diagnostic and therapeutic. An acute presentation with massive blood loss affects the cardiovascular system and is life-threatening. This condition requires immediate resuscitation with intravenous fluids and blood. Definitive treatment is emergency laparotomy with salpingectomy and ovarian conservation. The benchmark for the diagnosis and care of unruptured ectopic gestation is laparoscopy.[25] However, this was not used for our patients as they all presented with ruptured EP. We removed the damaged tubes in many of the cases as a life-saving surgical procedure.

Table 5: Comparison of mean estimated blood loss and transfusion across tubal sites of ectopic pregnancy; and the mean estimated blood loss and transfusion across gestational age

	Tubal sites of ectopic pregnancy, mean±SD			*F*	*P*
	Ampulla	Isthmus	Cornual		
EBL	671.31±242.12*	856.25±400.39*	1181.81±414.89	15.199	<0.001
Transfusion	1.72±0.45	2.00±0.01*	2.00±0.01*	3.533	0.034
	GA at presentation (weeks), mean±SD			*T*	*P*
	<7	8-12			
EBL	637.72±211.56	1063.04±393.19		6.256	<0.001
Transfusion	1.70±0.46	2.00±0.01		3.087	<0.001

*Duncan multiple comparison tests indicating means not significantly different. EBL: Estimated blood loss, SD: Standard deviation, GA: gestational age

Moreover, in agreement with the National Institute of Clinical Excellence guideline, women with such an EP presentation should have salpingectomy.[18]

Most of the patients came with moderate anemia from blood loss. However, few had blood transfusion due to cardiovascular compromise. Projected blood loss was substantially greater in the cornual area with a considerably higher blood transfusion rate. This situation could be explained due to the increased vascularity around the cornual region with difficulty securing haemostasis. Blood transfusion was also higher when patients presented at eight weeks or more gestation. The blood transfusions as well placed an extra responsibility on the previously constrained health reserves in our centre and the country but was a life-saving intervention. As published by numerous hospital-based studies in Africa, the maternal mortality rate in ectopic gestation is between 1% and 3%.[21] This figure may not be the actual representation; maternal deaths are often under-reported, especially for deaths before arrival. Interestingly, there was no recorded case fatality in our study.

The study's strength lies in the fact that it compared associations between variables EBL and transfusion across tubal sites of ectopic. Unlike previous studies, the EBL and transfusion across GA were evaluated.

Limitations of the study

However, the limitations of the study remain that it was a single-centre, retrospective study, and the sample size was relatively small. It also did not report the clinical outcome (morbidity) of the EP patients. However, we intend to tackle these limitations in our next appraisal of EP by using a prospective design in multiple centre using a larger sample size.

Conclusion

This study strengthened the known fact that EP remains a major contributor to gynaecological admissions in our environment. Most of the patients presented with ruptured EP. This scenario harms a society that places a high premium on childbearing. Prompt diagnosis, recognizing risk factors, and appropriate intervention will reduce ectopic adverse effects.

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Conflicts of interest

There are no conflicts of interest.

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