



Incidence, risk factors, clinical presentation and treatment of ectopic pregnancy in the Limbe and Buea Regional Hospitals in Cameroon



Atabong Emmanuel Njingu^{1,2}, Samuel Nambile Cumber^{3,4,5}, Meh Martin Geh^{1,6}, Mandeng Ma Linwa Edgar¹, Claude Ngwayu Nkfusai^{7,8}, John Palle Ngunde¹, Gregory Edie Halle-Ekane¹

¹Faculty of Health Sciences, University of Buea, Buea, Cameroon, ²Etoug Ebe Baptist Hospital, Yaounde, Cameroon, ³Postdoctoral Fellow, Centre for Health Systems Research & Development, University of the Free State, Bloemfontein, South Africa, ⁴Office of the Dean, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa, ⁵School of Health Systems and Public Health, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa, ⁶St Mary Soledad Catholic Hospital Bamenda, Bamenda, Cameroon, ⁷Cameroon Baptist Convention Health Services, Yaounde, Cameroon

⁸Corresponding author: Claude Ngwayu Nkfusai, Cameroon Baptist Convention Health Services, Yaounde, Cameroon

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Abstract

Introduction: ectopic pregnancy (EP) is the leading cause of maternal mortality in the first trimester of pregnancy in our environment. This study aimed at evaluating the incidence, risk factors, clinical presentation and treatment of ectopic pregnancy in the Limbe and Buea Regional Hospitals in Cameroon. **Methods:** this was a retrospective nested case control study carried out from December 2006 to December 2016. A ratio for control vs cases of 3:1 was obtained. Any pregnancy implanted outside the normal uterine cavity was considered as an ectopic pregnancy. Student's t-test was used to compare continuous variables and Pearson's Chi-square test for categorical variables. The association between EP and the demographical and clinical variables was estimated using logistic regression. Statistical significance was set at p-values < 0.05. **Results:** a total of 247 cases of EP were registered out of 17221 deliveries giving an incidence of 1.43% in ten years. History of pelvic inflammatory disease (OR = 3.10, CI (1.76-5.44), p < 0.001), previous EP (OR = 10.22, CI (2.61-14.82), p < 0.001), History of induced abortion (OR = 2.68, CI (3.32-9.73), p < 0.001), history of adnexa surgery (OR = 4.37, CI (2.17-10.32), p < 0.001) and history of appendectomy (OR = 2.16, CI (0.99-6.64) p < 0.001), were also found to be associated with increased risk of EP. More than five percent (5.52%) of the patients were in shock at presentation. Diagnosis was confirmed mainly by use of ultrasound (78.53%) and treatment was principally by laparotomy (97.55%) with salpingectomy (95.60%). Most (90.18%) of ectopic pregnancies were ruptured at presentation. Only 2.45% of cases were managed medically with the use of methotrexate. **Conclusion:** the incidence of ectopic pregnancy (EP) in our environment is within the global range (hospital-based incidence of 1.43%) and is rising. Late presentation, lack of modern diagnostic and management tools have made laparotomy with salpingectomy the principal method of management of ectopic pregnancy in our environment.

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Introduction

Ectopic pregnancy (EP) is a clinical condition that results from the implantation of a fertilized ovum outside the normal uterine cavity. It is a common cause of morbidity and mortality in women of reproductive age globally [1-3] and the most common cause of maternal mortality in the first trimester, it accounts for up to 12.5% of maternal mortality in Cameroon [4]. Apart from maternal morbidity and mortality, EP is also associated with foetal loss, repeat ectopic gestation and impairment of subsequent fertility [5-7]. The incidence of EP ranges from 1-2% globally [8]. In Cameroon, an incidence of 0.79% was found in the year 2000 at the Yaounde University Teaching Hospital [9], 2.3% incidence from 1998 to 2008 in the Bafoussam Regional Hospital [10] and 3.45% in the Sangmelima District Hospital in 2008 [11]. Case fatality rate of Ectopic pregnancy is 10 times higher in our environment compared to high income countries [12-15]. The goal of this research was to provide data that will serve as basis for interventional programs designed to prevent and decrease the morbidity and mortality due to ectopic pregnancy. This study will also go a long way to improve on quality of care of patients with EP and provide baseline data for future studies.

Methods

Study design, period and setting: this was a retrospective nested case control study carried out in the maternity of the Limbe and Buea Regional Hospitals (LRH and BRH respectively) from December 2006 to December 2016. These two hospitals are the main Referral Centers in the South West Region of Cameroon.

Participants and sampling: cases of EP with intraoperative findings not consistent with EP were excluded from the study. A ratio for control vs cases of 3:1 was obtained. The control

group was obtained by systematic random sampling. Incomplete files were used in the calculation of the incidence but were excluded from the final analysis.

Study procedures and variables: any pregnancy implanted outside the normal uterine cavity was considered as an ectopic pregnancy. Heterotopic pregnancies (simultaneous existence of combined intrauterine and extrauterine pregnancies) were also considered as ectopic. Ovarian cystectomy and tubo-ovarian abscess drainage were also identified as adnexal surgery. Files of patients who had EP were selected from patients' record stores in the maternity, theatre and emergency units. The demographic characteristics, obstetric history, gynecological history, surgical history, smoking habits, clinical presentation, treatment method, intraoperative details and patient outcome were extracted and used to fill a pretested data collection form. Diagnosis was made by visualization of products of conception within the fallopian tube or any other extrauterine site.

Data management and data analysis: data were entered and analysed using Epi info version 7. Student's t-test was used to compare continuous variables and Pearson's Chi-square test for categorical variables. The association between EP and the demographical and clinical variables was estimated using logistic regression. Statistical significance was set at p-values < 0.05.

Ethical considerations: ethical approval was obtained from the Institutional Review Board of the Faculty of Health Sciences of the University of Buea (approval number: 2017/003/UB/SG/IRB/FHS) and administrative authorization by the Regional Delegate of Public Health South West region and the directors of the LRH and BRH.

Results

Incidence: a total of 247 cases of ectopic pregnancies (EP) and 17221 deliveries were recorded during the study period. This gives a hospital-based incidence of 1.43% in 10 years. Figure 1 demonstrates a rising trend of ectopic pregnancy during the ten years study period. Of the 247 cases, only 163 case records had enough information that was used for the final analysis.

Socio-demographic and clinical characteristics: the age range for this study was 18-44 years, the mean age was 27.68 ± 5.50 years for patients with ectopic pregnancy (EP) and 27.10 ± 4.18 years for patients without EP. The mean gestational age at presentation was 8.42 ± 3.25 weeks. Abdominal pain (n=161, 98.77%), amenorrhoea (n=130, 79.75%) and vaginal bleeding (n=113, 69.33%) were the most common presenting complains. Abdominal tenderness (n=159, 97.55%) was the most common sign on physical examination. Other presentations included signs of peritoneal irritation (n=32, 19.63%), tachycardia (n=30, 18.40%) and abdominal mass (n=11, 6.75%). Nine (5.52%) of patients were in shock at the time of presentation. Most EP cases (n=155, 95.09%) were tubal. More than half (52.15%) were in the right fallopian tube and 41.10% in the left. The commonest sites were the ampulla (50.66%) and isthmus (14.47%), however, 34.87% were unspecified. Induced abortion, previous EP and pelvic inflammatory disease were found to be associated with ectopic pregnancy (Table 1). Previous adnexal surgery was strongly associated with EP.

Predictors of ectopic pregnancy (multivariable analysis): to detect predictive factors of EP, multiple logistic regression was used. Four factors were found to be associated with significant increase in the risk of ectopic pregnancy (Table 2).

Laboratory tests done in ectopic pregnancy: ultrasound was used in the diagnosis of 128 (78.53%) cases. Urine pregnancy test was positive in 32 (19.63%) of the cases, paracentesis and culdocentesis were diagnostic in 18 (11.04%) and 14 (8.59%) of patients respectively. In one case (0.61%), the diagnosis was made intraoperatively during supposed CS in which a termed intra-abdominal pregnancy was found intraoperatively.

Management of ectopic pregnancy and intraoperative findings: laparotomy was the principal method of management. Surgery was employed in the management of 159 (97.55%) cases and medical treatment with methotrexate in 4 (2.45%) cases. Of the cases managed surgically, salpingectomy was done in 152 (95.60%) and salpingostomy in 6 (3.77%) of cases. Nine in 10 ectopic pregnancies were ruptured at presentation. Hemoperitoneum was present in 148 (90.80%) cases. Intraoperatively 15 (9.38%) of patients had pelvic adhesions, 5 (3.13%) had a concomitant ovarian cyst, 3 (1.88%) had distended uterus (heterotopic pregnancy) and 5 (3.13%) had uterine fibroid. Two in 10 patients required at least 1 unit of blood transfusion to complete their management. No death from EP was recorded.

Discussion

The objective of this study was to evaluate the epidemiological, clinical and therapeutic features of ectopic pregnancy in two regional hospitals in Cameroon. The incidence of EP was found to be 1.43% and a rising trend was demonstrated from 2010 to 2016. The incidence of ectopic pregnancy has followed a rising trend during the last three decades globally [1,13-18]. A rising trend was also noted in this study. Globally, the reasons for the rising trend are thought to include: increase incidence of sexually transmissible infections (STI), tubal surgeries, smoking in women of reproductive age, increase use of assisted reproductive techniques and earlier diagnosis of cases that would otherwise have resolved due to

availability of more sensitive methods of diagnosis. The incidence of 1.43% noted in this study is similar to studies by Belley Priso *et al.* [19] in Douala and Udigwe *et al.* [14] in Nigeria, where the incidence of ectopic pregnancy was reported to be 1.1% and 1.3% respectively. This is however higher than the reported 0.79% by Leke and colleagues [20] in Yaounde. This discrepancy in finding could be attributed to the fact that, the study by Leke *et al.* was a population-based study. The study considered the total number of deliveries in the population including centers without an operating theatre, whereas this study was a hospital-based study in two referral centers with high number of operative cases.

Similar to other studies [6,21,22], previous ectopic pregnancy was found to have the strongest association with development of subsequent EP, our study demonstrated that the risk of EP was 10 times higher for women with history of previous EP compared to women who have never had EP (OR = 10.22, 95% CI = 2.61-14.82). In an analysis of 255 cases and 375 controls in 2006, Karaer and colleagues also demonstrated that prior EP was the most important risk factor for ectopic pregnancy (OR = 13.1) [23]. In a nested case-control study by Barnhart *et al.* [21] involving more than 2000 women, it was estimated that, the likelihood of facing a repeat EP increased with the number of prior EP (1 prior event: 2.98; ≥ 2 prior events: 16.04) [21]. Overall, the risk of repeat EP have been shown by most studies to be between 2.4 and 25.0 [6,21-23]. These findings implies that, recurrent ectopic pregnancies likely reflect persistence in tubal pathology and tubal dysfunction [21]. While nontubal pelvic surgeries have been shown to have no significant association with ectopic pregnancy [22]. Tubal surgeries on the other hand increases the risk of EP by about 5 (2.4-9.5) times according to previous studies [6,24], in the same like, we observed in this study that adnexal surgeries involving the fallopian tubes were strongly associated with EP (OR=4.37, 95% CI =.17-10.32).

It is unclear whether the increased risk is due to the tubal surgery or the preexisting tubal disorder that warranted the surgery [6]. Another finding of this study was that, the risk of EP increased as maternal age increases. Our analysis showed that women aged 35-39 and ≥ 40 years were more likely to be diagnosed with ectopic pregnancy than those aged 20-24 years. This is consistent to findings by Moini *et al.* and Jacob *et al.* [6,22]. The exact mechanism by which increased maternal age increases the risk of EP remains unclear; it has been suggested that, tubal scarring from PID and progressive decrease in tubal motility with age could result to delay in ovum transport and tubal implantation [6,24,25]. Women with history of previous pelvic inflammatory disease were found to be 3 times more likely to develop EP compared to controls. This is similar to reports by Bouyer and colleagues who showed that prior pelvic infection was associated with 3-4 fold increase in the risk of EP [25]. Karaer *et al.* later corroborated these findings in their 2006 study which stated that prior PID was the second most important risk factor for EP [23]. On the one hand, our study failed to find an association between ectopic pregnancy and previous spontaneous abortion. Similar to our study, Bouyer *et al.* and Honoré *et al.* also failed to find an association between EP and prior spontaneous abortion [25,26].

In contrast, Moini and colleagues found significant increase in the risk of EP in patients with prior spontaneous abortion. These studies suggested that infection, hormonal imbalance or immunologic factors could be the cause of the increased risk of EP. On the other hand, we observed a strong association between EP and prior induced abortion, similar to some studies [24,25,27] and contrary to other studies [6,28]. Some researchers have described a strong association between EP and prior nontubal abdominal surgeries with odd ratio ranging from 2-5 [6,21,29,30]. In the same like, we observed that women with prior appendectomy were more likely to develop ectopic pregnancy compared to controls. Ruptured appendicitis have been implicated as a cause of tubal scarring

which can lead to subfertility and EP [31-33]. Multiple studies have reported use of IUD, infertility and parity each as risk factors for EP [6,21,27,34]. In this study, the small number of recorded cases for each of the above-mentioned variables made it difficult to truly assess their relationship with EP. Abdominal pain, amenorrhoea and vaginal bleeding were the most common presenting symptoms and these are similar to the findings of other studies [11,13,14] within the sub region. The abdominal pain in EP is due to peritoneal irritation secondary to rupture. Most of the patients in this study (90.18%) presented with ruptured ectopic pregnancy, unlike in the developed countries where the unruptured cases are more common [2,35,36].

The signs noted on physical examination (abdominal tenderness, cervical motion tenderness, tachycardia, hypotension and shock) followed the trend of examination findings in other studies in the sub region [10,11,13]. Abdominal ultrasound was the main method of diagnosis in this study, urine pregnancy test and clinical diagnosis were also employed. This is similar to findings in other studies in low income countries [10,37,38], in contrast to studies [2,36,39] in high income countries modern diagnostic techniques such as serum β -hCG assay, serum progesterone titres and laparoscopy were non-existent in the study centers during the period of the study. Management of ectopic pregnancy in this study was essentially by laparotomy (97.55%) with salpingectomy (95.60%). Medical therapy was only utilized in 2.45% of the cases. This concurs with findings in other studies in Cameroon and Nigeria [10-12]. However, higher use of non-invasive management techniques was reported by Foumane *et al.* [40] in Yaounde and Belley Priso *et al.* in Douala. In these studies, non-invasive methods of management were used in the management of 21% and 3.99% of patients respectively. This is due to the fact that, these studies were carried out in specialized centers with appropriate tools to diagnose and manage cases of EP using these methods that were totally unavailable in our center of study. No death from EP was

recorded in this study. Other studies in Africa reported case fatality rates ranging from 0.79 to 1.4% [13,20,41]. The absence of death in this study could be due to the presence of effective blood bank and qualified trained personnel in the centers of this study.

Conclusion

The incidence of ectopic pregnancy (EP) in our environment is within the global range (hospital-based incidence of 1.43%) and is rising. Although many risk factors for EP have been clearly established, the cause of a large proportion of EP remains uncertain. Late presentation, lack of modern diagnostic and management tools have made laparotomy with salpingectomy the principal method of management of ectopic pregnancy in our environment. This study should serve as an alert for prompt diagnosis and management of EP. The main limitation of this study was missing information in patient records. To overcome this problem, 84 case files were left out of the final analysis because they lacked basic patient information (gestational age, signs and symptoms at presentation, and intraoperative findings) needed for the final analysis.

What is known about the topic

- Previous studies in Cameroon showed that the incidence of ectopic pregnancy (EP) ranges from 0.79-3.45% and mortality was at 12.5%;
- In studies carried out in other countries, smoking and use of intrauterine device (IUD) were found to be associated with ectopic pregnancy;
- Laparoscopic surgery and medical management with methotrexate consisted more than 70% of treatment of EP in developed countries.

What this study adds

- This is the first study on ectopic pregnancy in the southwest region of Cameroon to best of our knowledge and literature search. Previous studies in other regions in Cameroon showed varying results for different regions of the country -Our study found and incidence of 1.43% which different from the findings in other studies in others regions of the country;
- Tobacco and IUD use were not found to be associated with EP in this study, mainly due to the small number of reported usages - Tobacco and IUD use could hence be of minimal importance when designing measures to curb EP;
- This study shows that though more invasive and with more side effects, laparotomy with salpingectomy remains the main method of management of EP in resource limited settings and it is effective in preventing deaths due to EP.

Competing interests

The authors declare no competing interests.

Authors' contributions

This work was carried out in collaboration with all authors. AEN, GEHE, MMLE, SNC, CNN, MMG and JPN did the study design and wrote the protocol. AEN and GEHE did the literature search, cross-checked the statistical analysis and made important inputs in the drafting of the manuscript. cross-checked the data entry while AEN and MMLE analysed the data. GEHE supervised the study. AEN wrote the first draft manuscript. SNC, CNN, JPN, MMLE and MMG revised the

manuscript. All the authors have read and agreed to the final manuscript.

Tables and figure

Table 1: ectopic pregnancy and surgical, gynaecologic and obstetric history

Table 2: backward logistic regression analysis predictive factors for EP

Figure 1: trend of incidence Ectopic pregnancy

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Table 1: ectopic pregnancy and surgical, gynaecologic and obstetric history

	Study group (n = 163) (%)	Control group (n = 655) (%)	OR	95% CI	P value
History of spontaneous abortion					
No	129 (79.14)	551 (84.12)	Reference		
Yes	34 (20.86)	104 (15.88)	1.20	0.91-2.15	0.1286
History of PID					
No	140 (85.89)	622 (94.96)	Reference		
Yes	23 (14.11)	33 (5.04)	3.10	1.76-5.44	< 0.001
History of IUD					
No	163 (100)	652 (99.54)	Reference		
Yes	0 (0)	3 (0.46)	0.00	Undefined	0.387
History of infertility					
No	161 (98.77)	648 (98.93)	Reference		
Yes	2 (1.23)	7 (1.07)	1.15	0.24-5.59	0.562
Previous EP					
No	150 (92.02)	646 (98.63)	Reference		
Yes	13 (7.98)	8 (1.37)	10.22	2.61-14.82	< 0.001
History of induced abortion					
No	130 (79.75)	627 (95.73)	Reference		
Yes	33 (20.25)	28 (4.27)	2.68	3.32-9.73	< 0.001
History of abdominal surgery					
No	124 (76.07)	541 (82.60)	Reference		
Yes	39 (23.93)	114 (17.40)	1.49	0.99-2.25	0.0560
Specific surgery types					
Adnexal surgery	14 (8.59)	8 (1.22)	4.37	2.17-10.32	< 0.001
Appendectomy	7 (4.29)	12 (1.83)	2.16	0.99-6.64	
Caesarean section	17 (10.43)	80 (12.21)	0.93	0.53-1.63	
Laparotomy	1 (0.61)	5 (0.76)	0.88	0.10-7.59	

OR=Odds ratio; CI=Confidence interval; PID=Pelvic inflammatory disease; EP=Ectopic pregnancy

Table 2: Backward logistic regression analysis predictive factors for EP			
Variables	OR	CI	P value
Adnexal surgery	2.16	1.20-8.35	< 0.001
Induced abortion	1.47	3.20-9.69	0.030
PID	1.98	1.60-5.32	0.009
Appendectomy	1.56	1.20-8.35	0.020

OR=Odds ratio, CI=Confidence interval, PID=Pelvic inflammatory disease

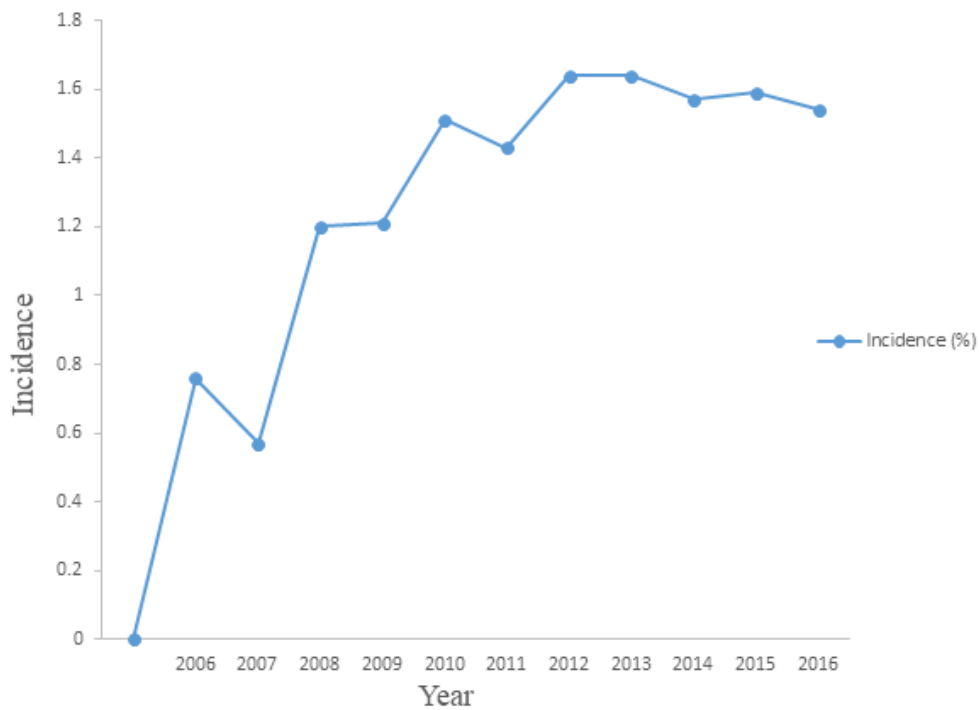


Figure 1: trend of incidence ectopic pregnancy