Risk factors for ectopic pregnancy in a population of Cameroonian women: A case-control study

Yvette Audrey Assouni Mindjah[1]*, Félix Essiben[2], Pascal Foumane[2], Julius Sama Dohbit[2], Emile Telesphore Mboudou[2]

1 Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon,
2 Department of Obstetrics and Gynaecology, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon

* amyt.2017@gmail.com

Abstract

Objective

To identify the risk factors for ectopic pregnancy (EP) in a population of Cameroonian women.

Sample and methods

We performed a matched case-control study; 88 women with diagnosed EP (cases), and 176 women with first trimester intrauterine pregnancy (IUP) (controls), who underwent questionnaires. Odds Ratio (OR) and 95% confidence intervals (CIs) were calculated and adjusted for potential confounding factors via multivariate logistic regression analysis.

Results

Of the fifteen identified risk factors, 4 were independently associated with increased odds of EP: prior pelvic inflammatory disease (PID) (adjusted odds ratio [AOR] 13.18; 95% CI 6.19–27.42), followed by current use of levonorgestrel-only pills for emergency contraception (LNG-EC) (AOR 10.15; 95% CI 2.21–46.56), previous use of depot medroxyprogesterone acetate (DMPA) (AOR 3.01; 95% CI 1.04–8.69) and smoking at the time of conception (AOR 2.68; 95% CI 1.12–6.40).

Conclusion

The present study confirms the wide variety of EP's risk factors. Moreover, some new findings including current use of LNG-EC, previous use of DMPA, smoking at the time of conception are noteworthy. Thus, in our limited resources country where prevention remains the cornerstone for reducing EP chances of occurrence, clinicians should do enough counselling, especially to women with known risk factors. The necessity to facilitate access to more equipment to enable early diagnosis of EP is very crucial and should be seriously considered, in order to reduce the burden of EP in Cameroonian women.

Introduction

Ectopic pregnancy (EP) is the main cause of maternal death during the first trimester of pregnancy and accounts for approximately 10% of all pregnancy-related deaths [1,2]. In African developing countries, where most of the women tend to present at the rupture stage (with an unstable hemodynamic state), it is an important cause of maternal deaths, with a case fatality rates around 1–3%; 10 times higher than reported in industrialized countries [3–5]. In Ghana, 8.7% of maternal deaths were due to EP [5]. Recently in Cameroon, it was reported to be responsible for 12.5% of maternal deaths [6]. This could be explained by late diagnosis, due to the unavailability of diagnostic means in our context, although the early diagnosis of EP became possible with various examinations notably transvaginal ultrasonography and quantitative measurement of the β subunit of human chorionic gonadotropin (β-hCG) [5,7]. A delay in diagnosis most often leads to severe complications (rupture and hemoperitoneum) and consequently to surgical treatment by laparotomy with salpingectomy [5,8–11].

Over the last few decades, the incidence of EP has steadily increased around the world. In the Western countries, it varies between 1–2% [9]. Yet this incidence is higher in developing countries, especially in Cameroon where it reaches 4.23% [7,12,13]. Some Sweden studies have demonstrated that the increased in EP's incidence was strongly associated to a rise in the incidence of PID and some sexually transmitted infections (STIs) [14,15].

There are other risk factors that have been associated with EP including prior EP, previous tubal surgery, documented tubal pathology, history of infertility, cigarette smoking, assisted reproduction technologies (ARTs), multiple lifetime sexual partners, older maternal age, and in utero diethylstilbestrol (DES) exposure [16–20]. Some meta-analyses found that oral contraceptive pills (OCPs), intrauterine devices (IUDs), and female sterilization could increase the risk of EP to different degrees in cases of contraceptive failure [16,21]. The use of levonorgestrel-only pills for emergency contraception (LNG-EC) at the time of the conception has recently been identified as a risk factor for EP [19,20]. In Cameroon, where the era is for the promotion of family planning nationwide through the increased use of modern contraceptives, it would be important to evaluate their involvement and strength in EP's occurrence in our context.

Further, given that the mortality and morbidity associated with EP are related to the length of time required for diagnosis, increased awareness and knowledge on its risk could help by providing better prediction and prevention in at risk-women. Moreover, this could enable an early and accurate diagnosis prior to the rupture, resulting in a reduction in the need for surgery and some complications.

Materials and methods

This study was approved by the Institutional Ethical Review Board for Human Health, under the ethical clearance No 314/CIERSH/2016, and by the Institutional Ethical Review Board of the Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon under the ethical clearance No 166/CIER/2017. Administrative authorizations were obtained in both hospitals involved prior to the beginning of the study. A written informed consent was obtained from each participant before recruitment.

Participants and methods

This case-control study was carried out in the two main referral hospitals for gynaecologic and obstetric emergencies in the Yaoundé metropolis–Yaoundé Gynaeco-Obstetric and Pediatric Hospital (YGOPH), Principal Maternity of the Yaoundé Central Hospital (YCH)—from November 1st, 2016 to April 30, 2017. According to the American College of Obstetricians

and Gynecologists Practice Bulletin [22], the diagnosis and location of pregnancy were confirmed at operation for EP patients who underwent surgical treatment. Transvaginal ultrasonography combined to the measurement of serum β-HCG levels was used to confirm EP's diagnosis for patients who received medical treatment. During the study period, all women who had been diagnosed with EP in the inpatient department of gynaecology of each hospital were recruited in the case group (EP group). Women with a first trimester intrauterine pregnancy (IUP) at the prenatal clinic of these hospitals during this period, matched for age at a 1:2 ratio were included as controls (intrauterine pregnancy [IUP] group).

The investigator was responsible for data collection from the participants during an interview, by using a questionnaire. They were assured of confidentiality, as some of the questions were very private. All women who provided incomplete information were excluded. After excluding 6 participants, a total of 264 women were enrolled in the case-control study, including 88 cases (EP group) and 176 controls (IUP group); a response rate of 97.78%.

Information collected included sociodemographic characteristics (age, educational level, marital status, professional category, and smoking at the time of conception). The professional category was defined according to the Cameroonian Nomenclature of Trades, Jobs, and Professions [23]. There were questions included details about past relevant reproductive and gynaecologic histories (including previous miscarriage, prior induced abortion, parity, prior *Chlamydia Trachomatis* (CT) infection, prior PID, prior EP, previous infertility, documented tubal pathology, previous tubal surgery, age at sexual debut, lifetime's number of sexual partners) and about surgical history. Previous and current use of contraceptives (including intrauterine devices [IUDs], combined oral contraceptives [COCs], progestin-only pills [POPs], LNG-EC, progestin-only implants and progestin-only injectable of depot medroxyprogesterone acetate (DMPA). According to Cheng Li et al. [24], a woman was defined as a previous user of a given contraceptive method if she had used the method in the previous cycle and as a current user if she had used the method in the current cycle.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics software, version 23. The frequency of distribution of each variable was examined according to the case and control groups. Crude odds ratios (ORs) of each variable with their 95% confidence intervals (CIs) were calculated in the bivariate analysis. When we explored the association between risk of EP and prior CT infection, documented tubal pathology there were missing values; these were eliminated from the analysis. All *p values* were calculated using statistical Chi-Square and Fisher's exact tests when necessary. Values less than 0.05 were considered statistically significant. Variables significantly associated with EP by bivariate analysis were included as candidates in the multivariable logistic regression analysis to adjust for potential confounders and calculate the adjusted odds ratio (AOR) with the aim of identifying the independent risk factors for EP.

Results

During the study period, a total of 90 women with EP were enrolled. One hundred and eighty women with IUP were recruited to be included in the control group. After women providing incomplete information were excluded, 264 women with first trimester pregnancies were included in the study; with a total of 88 final cases (EP group) and 176 controls (IUP group).

Socio-demographic factors

Table 1 presents the sociodemographic characteristics between the two groups. EP women were more likely to have a high school educational level (p<0.001). Because of the matching

Table 1. Socio-demographic characteristics of enrolled participants.

Variables	Cases N = 88 n (%)	Controls N = 176 n (%)	OR (95%CI)	P value
Age (years)				
[18–23]	10 (11.4)	21 (11.9)	Reference	1.000
[23–28]	24 (27.3)	47 (26.7)	0.93 (0.37–2.29)	
[28–33]	35 (39.8)	70 (39.8)	0.95 (0.40–2.24)	
[33–38]	13 (14.6)	26 (14.6)	0.95 (0.34–2.60)	
[38–43]	5 (5.7)	10 (5.7)	0.95 (0.25–3.53)	
≥43	1 (1.1)	2 (1.1)	0.95 (0.07–11.78)	
Marital status				
Single	26 (29.5)	45 (25.6)		0.556
Married or living together	62 (70.5)	131 (74.4)	0.81 (0.46–1.44)	
Educational level				
Primary school	14 (15.9)	11 (6.4)	Reference	<0.001
Secondary school	54 (61.4)	85 (48.3)	2.00 (0.84–4.73)	
High school	20 (22.7)	80 (45.5)	5.35 (2.10–13.64)	
Professional category				
Professional and managerial occupations	3 (3.4)	11 (6.3)	Reference	0.125
Intermediates professions	12 (13.6)	32 (18.2)	0.72 (0.17–3.06)	
Services and sales staff	38 (43.2)	51(29.0)	0.36 (0.09–1.40)	
Unemployed	35 (39.8)	82 (46.6)	0.63 (0.16–2.43)	
Smoking				
Yes	21 (23.9)	18 (10.2)	2.75 (1.37–5.49)	0.003
No	67 (76.1)	158 (89.8)		

OR odds ratio, CI Confidence interval.

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criteria of cases and controls used in the study, there was no significant difference in age (p = 1.000). Regarding the marital status and the professional category, we did not found a significant difference in women with EP compared to those with IUP. Smoking at the time of conception was more found among in EP cases than controls (OR: 2.75, 95% CI: 1.37–5.49).

Reproductive factors

EP's women were more likely to have had previous induced abortion than IUP controls (OR: 2.08, 95% CI: 1.21–3.57) (Table 2).

Surgical factors

Previous tubal surgery appeared to be more frequent in cases than controls (OR:10.54, 95% CI:1.21–91.67).

Gynaecological factors

Prior CT infection (OR: 6.42, 95% CI: 2.77–10.38), prior PID (OR: 13.53, 95% CI: 7.24–25.26), previous infertility (OR: 2.57, 95% CI: 1.44–4.58) and documented tubal pathology (OR: 3.96, 95% CI: 1.21–12.89) were more likely among cases than controls (Table 2). Also, EP cases were more likely to have had prior EP compared to controls (OR: 6.36, 95% CI:1.25–32.22). (Table 2).

Table 2. Reproductive, gynaecological and surgical histories of enrolled participants.

Variables	Cases N = 88 n (%)	Controls N = 176 n (%)	OR (95%CI)	P value
Reproductive history				
Previous miscarriage				0.223
Yes	32 (36.4)	51 (29.0)	1.40 (0.81–2.41)	
No	50 (54.8)	129 (75.2)		
Prior induced abortion				
Yes	38 (43.2)	47 (26.7)	2.08 (1.21–3.57)	0.007
No	50 (56.8)	129 (73.3)		
Parity				
0	22 (25.0)	66 (37.5)	Reference	0.020
1	19 (21.6)	45 (25.6)	0.76 (0.36–1.59)	
2–3	35 (39.8)	51 (29.0)	0.38 (0.20–0.74)	
4 or more	12 (13.6)	14 (8.0)	0.34 (0.14–0.84)	
Surgical history				
Previous tubal surgery				
Yes	5 (5.7)	1 (0.6)	10.54 (1.21–91.67)	0.017
No	83 (94.3)	175 (99.4)		
Gynaecological history				
Prior CT infection				
Yes	50 (68.5)	44 (25.3)	6.42 (2.77–10.38)	<0.001
No	23 (31.5)	86 (48.9)		
Prior PID				
Yes	59 (67.0)	23 (13.1)	13.53 (7.24–25.26)	<0.001
No	29 (33.0)	153 (86.9)		
Prior EP				
Yes	6 (6.8)	2 (1,1)	6.36 (1.25–32.22)	0.018
No	82 (93.2)	174 (98.9)		
Previous infertility				
Yes	32 (36.4)	32 (18.2)	2.57 (1.44–4.58)	0.001
No	56 (63.6)	144 (81.8)		
Documented tubal pathology				
Yes	7 (38.9)	9 (13.8)	3.96 (1.21–12.89)	0.017
No	11 (61.1)	56 (86.2)		

OR odds ratio, CI confidence interval, CT *Chlamydia Trachomatis*, PID pelvic inflammatory disease, EP ectopic pregnancy.

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An age of sexual debut less than 16 years was more probable in EP women than in IUP ones (OR: 3.27, 95% CI: 1.70–6.28); as well as having had more than 5 lifetime sexual partners (OR: 4.00, 95% CI: 2.14–7.45). (Table 3).

Contraceptive factors

Previous use of progestin-only injectable DMPA was more likely in EP cases, than controls (OR: 2.88, 95% CI:1.19–6.99) (Table 3).

By contrast, current use of LNG-EC was significantly more probable among EP cases than controls (OR: 7.42, 95% CI: 1.96–28.01). We did not find any women who were taking progestin-only injectable or implant, COCs or POPs during the cycle of conception.

Table 3. Previous sexual history, previous and current use of contraceptives.

Variables	Cases N = 88 n (%)	Controls N = 176 n (%)	OR (95%CI)	P value
Previous sexual history				
Age at sexual debut (years)				
<16	26 (29.5)	20 (11.4)	3.27 (1.70–6.28)	<0.001
≥16	62 (70.5)	156 (88.6)	0.30 (0.15–0.58)	
Lifetime number of sexual partners				
>5	32 (36.4)	22 (12.5)	4.00 (2.14–7.45)	<0.001
≤5	56 (63.6)	154 (87.5)	0.25 (0.13–0.46)	
Previous use of contraceptives*				
IUD				
Yes	2 (3.00)	4 (3.1)	0.96 (0.17–5.43)	1.000
No	65 (97.0)	126 (96.9)		
LNG-EC				
Yes	22 (32.8)	31 (23.8)	1.56 (0.81–2.99)	0.178
No	45 (67.2)	99 (76.2)		
COCs				
Yes	3 (4.5)	5 (3.8)	1.17 (0.22–5.06)	1.000
No	64 (95.5)	125 (96.2)		
POPs				
Yes	6 (9.0)	5 (3.8)	2.45 (0.72–8.37)	0.189
No	61 (91.0)	125 (96.2)		
DMPA				
Yes	13 (19.4)	10 (7.7)	2.88 (1.19–6.99)	0.015
No	54 (80.6)	120 (92.3)		
Progestin-only implants				
Yes	2 (3.0)	8 (6.2)	0.46 (0.09–2.27)	0.499
No	65 (97.0)	122 (93.8)		
Current use of contraceptives*				
LNG-EC				
Yes	10 (14.9)	3 (2.3)	7.42 (1.96–28.01)	0.001
No	57 (85.1)	127 (97.7)		

OR odds ratio, CI confidence interval, IUD intra-uterine device, LNG-EC levonorgestrel-only pills for emergency contraception, COCs combined oral contraceptives, POPs progestin-only pills, DMPA depot medroxyprogesterone acetate

*Women who did not use contraceptives are not included here (n = 21 cases and n = 46 controls).

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The results of the multivariable logistic regression analysis are shown in Table 4. The model included smoking at the time of conception, prior PID, prior EP, prior induced abortion, prior tubal surgery, age at sexual debut, previous use of DMPA and current use of LNG-EC. Factors found to be independently associated to EP were: prior PID (AOR: 13.03; 95% CI 6.19–27.42), current use of LNG-EC (AOR: 10.15; 95% CI 2.21–46.56), previous use of DMPA (AOR: 3.01; 95% CI 1.04–8.69) and smoking at the time of conception (AOR: 2.68; 95% CI 1.12–6.40).

Discussion

This study found a strong independent association between prior PID and EP occurrence (Table 4). Our finding aligns with numerous studies which identified PID as a major risk

Table 4. Multivariable logistic regression analysis for independent risk factors of EP.

Variables*	AOR (95% Ci)	P value
Smoking at the time of conception		
Yes	2.68 (1.12–6.40)	0.026
No		
Prior PID		
Yes	13.03 (6.19–27.24)	<0.001
No		
Prior EP		
Yes	1.88 (0.21–16.80)	0.568
No		
Prior induced abortion		
Yes	1.79 (0.89–3.60)	0.101
No		
Prior tubal surgery		
Yes	0.99 (0.06–14.70)	0.997
No		
Age at sexual debut (years)		
<16	1.70 (0.73–3.94)	0.212
≥16		
Previous use of DMPA		
Yes	3.01 (1.04–8.69)	0.041
No		
Current use of LNG-EC		
Yes	10.15 (2.21–46.56)	0.003
No		

AOR adjusted odds ratio, CI confidence interval, EP ectopic pregnancy, PID pelvic inflammatory disease, DMPA depot medroxyprogesterone acetate, LNG-EC, levonorgestrel-only pills for emergency contraception

*All included variables had were statistically significant at $P < 0.05$

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factor for EP [19,25,26], because of scarring, resulting in tubal obstruction that interferes with egg's capture and migration, but also with spermatozoa migration [25]. Such finding could reflect an important rate of late diagnosis and untreated acute pelvic infections, in our country, probably due to poverty.

Consistent with previous studies [27–29], our study identified an independent significant connection between EP and the use of LNG-EC during the cycle of conception. It has been suggested that higher levels of progesterone could alter ciliary beat function and smooth muscles contractility of Fallopian Tubes (FTs), and the high serum peak of LNG observed after an administration of a single dose of LNG-EC could possibly result in a tubal motility decline; thus, increasing the risk of EP [29–31]. Thereby, if LNG-EC is taken at a time when it is ineffective in preventing pregnancy, the plasma concentration of LNG-EC might still remain high during the time of embryo-tubal transport due to its half-life of 24 h; therefore, the chance of embryo-tubal implantation increases with declined tubal motility [21].

Previous use of DMPA was also found to have an independent relationship with EP occurrence. It has been shown that during the menstrual cycle, level of Estradiol Receptors (ERs) -mostly localized on FT's ciliated, secretory epithelial and smooth muscles cells- fluctuate in response of high circulating Estradiol (E2) levels [32–34]. Adrenomedullin (ADM), a polypeptide structurally similar to calcitonin, expressed in epithelial cells of the human and rat FTs

increase and decrease along with circulating E2 levels during the menstrual cycle and increases ciliary beat frequency [35–36]. With these results, we suggest that by its antiestrogen activity (including inhibition of ERs, decreasing levels of circulating E2), DMPA could decrease ER's expression in FT cells, resulting in a loss of ADM expression and subsequent dysfunction in ciliary beat and tubal motility.

Such finding may also be due to a lack of barrier contraceptive use, such as condoms because, using a simple and safe contraceptive, women feel well protected from pregnancies. Yet with unprotected sex, there is a risk of STIs and subsequent PID.

Another independent factor found to be associated with EP in our study was smoking at the time of the conception. This has been demonstrated in other countries [37,38]; but to our knowledge, none in Cameroon. Shaw et al. [38] reported that cotinine (the most abundant metabolite of nicotine) increased the expression of prokineticin receptor-1 (PROKR1), a regulator of smooth muscle contractility and genes that are important in implantation, in the FT. In this sense, they hypothesized that smoking predisposes women to EP by altering tubal PROKR1 expression resulting in changes in FT function. Therefore, awareness of women on smoking dangers and encouraging them on smoking avoidance and cessation is necessary.

Other variables were significantly associated with EP occurrence, but not independently after the multivariable logistic regression analysis; probably due to confounding variable effect, such as STDs. STDs could have been the confounder increasing the relationship between these factors and EP occurrence. However, it would be important to pay attention to these variables in order to enhance prevention in our resource-limited country.

In our findings, prior CT infection, previous infertility, documented tubal pathology and prior EP were found to increase EP risk. These results are consistent with those of previous studies, which indicated that EP risk was higher in women with prior CT infection [19,25,26], as well as previous infertility, documented tubal pathology [17,20] and prior EP [20,39]. The healing process that follows *C. Trachomatis* infection can result in alterations of tubal mucosa and limit tubal motility [19]. This could lead to PID and subsequently, interfere with the egg's capture or with spermatozoa's migration [19]. Infertility may result from these tubal damages. The association between prior EP and the new EP may reflect persistent exposure to pre-existent risk factors, especially those that cause tubal dysfunction.

The study also revealed a significant connection between prior induced abortion and EP occurrence. This finding seem**s** to be different from those in countries where abortions are legalized [40,41]. In Cameroon, as in most African countries where abortions are not legalized, most abortions are illegal and usually occur in poor aseptic conditions [42]. Thus, increasing post-abortion sepsis risk and subsequent PID. There are others African publications reporting a relationship between prior induced abortions and EP [25,42]. Clearly, this is an area deserving further attention because such finding may reflect potential inadequacies of the national family planning policy in our country. This thus evokes an increased need for a popularization of modern contraceptives use among Cameroonian women, in order to prevent unwanted pregnancies, which motivate the decision to have an abortion. On the other hand, it suggests that there should be more training medical staff on post-abortion care in primary and secondary hospitals, to improve the management of abortions related complications.

We found a significant relationship between previous tubal surgery and EP. Our results are in line with those of a meta-analysis including 27 case-control studies and 9 cohort studies, which reported previous tubal surgery to be strongly associated with the occurrence of EP [17].

Have had first sexual intercourse at less than 16 years was significantly associated with EP occurrence, and having more than 5 lifetime's sexual partners. The early age at sexual debut has long been identified as a determinant for STDs, notably bacterial infections for both

behavioral and biological factors [43]. In line with this, Cates asserted that the earlier sexual activity is started, the longer the time of exposure to different sexual partners because, for adolescents, adolescence represents a time for sexual experimentation [44]. Concerning this, Aral has suggested that the risk of STDs in women having cumulated several sexual partners was associated to the fact that they tend to have large number of current partners [45]. In Cameroon, Nkwabong et al. in their cross sectional descriptive study including 70 patients diagnosed with acute PID of 1344 women who were seen for gynaecologic problems, 45 (64.3%) had many sexual partners; the reason, being probably the fact that they depend on their partners due to underemployment and poverty in Cameroon [46]. We believe that reducing the costs in genital infections examinations for adolescents at least in health services, might help improve the early diagnosis and treatment of STDs in order to reduce subsequent sequelae such as PID, infertility, and EP.

No significant association was found between previous use of LNG-EC, COCs, POPs and EP. Probably the number of the studied participants was too small for any meaningful deductions. In fact, in Cameroon, modern contraceptives are used by a minority of population. According to the Demographic and Health survey and multiple indicators realized in Cameroon [47], among non-pregnant women aged between 15–49 years, 16% were using at least one contraceptive method. The injectable use rate was 2%, that of pills 2% and for other modern contraceptives, less than 1%. This could be linked to prejudices, socioeconomic and cultural barriers, lack of information and ignorance of some Cameroonians, which are abord key obstacles to adoption of contraception. This suggest**s** a need for increasing access to and changing social norms about modern contraception.

Conclusions

The major risk factor identified in this study is prior PID. In order to control these infections, a strengthening of health education in Cameroonian women of childbearing age, by encouraging them to reduce risky sexual behaviours (such as having multiple sex partners or unprotected sex without regular screening for STIs) is essential. Furthermore, policies on reducing the cost of screening and treatment of STIs should be put in place, especially for adolescents to promote timely access to healthcare for reducing chances of PID and subsequent EP.

Besides, findings of current use of LNG-EC, previous use of DMPA and smoking at the time of conception as risk factors, are newly identified in our context. All this highlights that physicians should pay attention to women's counselling about EP (in the face of this multiplicity of risk factors reflecting increased susceptibility to EPs nowadays in our country). In addition, an increased need for easier access to equipment and skills for earlier diagnosis of EP is emerging, in a view of managing EPs, with less implication on fertility of Cameroonian women.

Strengths and limitations

The study was carried out across the two main referral hospitals for gynecologic and obstetric emergencies in Yaoundé; well representing the urban and rural population. The cases and controls were from the same source of population, which makes this comparison valid and the findings are generalizable to all EP in our context. However, as a hospital-based case-control study we acknowledge for recall and selection bias.

Supporting information

S1 Table. Dataset.
(XLS)

Acknowledgments

Author Contributions

Conceptualization: Yvette Audrey Assouni Mindjah, Félix Essiben, Pascal Foumane, Julius Sama Dohbit, Emile Telesphore Mboudou.

Data curation: Yvette Audrey Assouni Mindjah, Félix Essiben, Pascal Foumane.

Formal analysis: Yvette Audrey Assouni Mindjah, Félix Essiben, Pascal Foumane.

Investigation: Yvette Audrey Assouni Mindjah.

Methodology: Yvette Audrey Assouni Mindjah, Félix Essiben, Pascal Foumane, Julius Sama Dohbit, Emile Telesphore Mboudou.

Project administration: Félix Essiben, Pascal Foumane, Emile Telesphore Mboudou.

Resources: Yvette Audrey Assouni Mindjah.

Supervision: Félix Essiben, Pascal Foumane, Julius Sama Dohbit.

Validation: Pascal Foumane, Julius Sama Dohbit, Emile Telesphore Mboudou.

Writing – original draft: Yvette Audrey Assouni Mindjah, Julius Sama Dohbit.

Writing – review & editing: Yvette Audrey Assouni Mindjah, Pascal Foumane, Julius Sama Dohbit, Emile Telesphore Mboudou.

References

1. Farquhar CM. Ectopic pregnancy. Lancet. 2005 Aug 13; 366(9485):583–91. https://doi.org/10.1016/S0140-6736(05)67103-6 PMID: 16099295

2. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller A, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health. 2014 Jun 5; 2(6):323–33.

3. Panti A, Ikechukwu N, Lukman O, Yakubu A, Egondo S, Tanko B. Ectopic pregnancy at Usmanu Danfodiyo University Teaching Hospital Sokoto: a ten year review. Ann Niger Med. 2012 Dec; 6(2):87–91.

4. Omokanye LO, Balogun OR, Salaudeen AG, Olatinwo AW, Saidu R. Ectopic pregnancy in Ilorin, Nigeria: a four year review. Niger Postgrad Med J. 2013 Dec; 20(4):341–5. PMID: 24633280

5. Goyaux N, Leke R, Keita N, Thonneau P. Ectopic pregnancy in African developing countries. Acta Obstet Gynecol Scand. 2003 Apr; 82(4):305–12. PMID: 12716313

6. Der EM, Moyer C, Gyasi RK, Akosa AB, Tettey Y, Akakpo PK, et al. Pregnancy Related Causes of Deaths in Ghana: A 5-Year Retrospective Study. Ghana Med J. 2013 Dec; 47(4):158–63. PMID: 24669020

7. Tebeu P, Halle-Ekane G, Da Itambi M, Enow Mbu R, Mawamba Y, Fomulu J. Maternal mortality in Cameroon: a university teaching hospital report. Pan Afr Med J. 2015 May 7; 21(16).

8. Foumane P, Mboudou ET, Mbakop S, Dohbit JS, Belinga E, Doh AS. La place du traitement peu ou non invasif dans la prise en charge de la grossesse extra-utérine à l'hôpital gynéco-obstétrique et pédiatrique de Yaoundé: une analyse rétrospective sur cinq ans. Clin Mother Child Health. 2010 Jan 1; 7(1).

9. Gervaise A, Fernandez H. Prise en charge diagnostique et thérapeutique des grossesses extra-utérines. J Gynécologie Obstétrique Biol Reprod. 2010 May; 39(3S):17–24

10. Ikeme AC, Ezegwui HU. Morbidity and mortality following tubal ectopic pregnancies in Enugu, Nigeria. J Obstet Gynaecol. 2005 Aug; 25(6):596–8

11. Bhuria V, Nanda S, Chauhan M, Malhotra V. A retrospective analysis of ectopic pregnancy at a tertiary centre: one year study. Int J Reprod Contracept Obstet Gynecol. 2016 Jul; 5(7):2224–7.

12. Centers for Disease Control and Prevention (CDC). Ectopic pregnancy—United States, 1990–1992. MMWR Morb Mortal Wkly Rep. 1995 Jan 27; 44(3):46–8.

13. Rongières C, Kattygnarath V. Grossesse extra-utérine: conséquences pour la fertilité ultérieure et facteurs décisionnels d'une prise en charge en assistance médicale à la procréation: J Gynécologie Obstétrique Biol Reprod. 2003; 32(S7):83–92.

14. Kamwendo F, Forslin L, Bodin L, Danielson D. Epidemiology of ectopic pregnancy during a 28 year period and the role of pelvic inflammatory disease. Sex Trans Inf. 2000 Feb; 76(1):28–32.

15. Bjartling C, Osser S, Persson K. The frequency of salpingitis and ectopic pregnancy as epidemiologic markers of Chlamydia trachomatis. Acta Obstet Gynecol Scand. 2000 Feb; 79(2):123–8. PMID: 10696960

16. Bray Madoue G, Saleh A, Serge R I, Tchari A, Kolombo D. Grossesse extra-utérine: Aspects épidémiologiques et Pronostic maternel à l'Hôpital de district de N'djamena sud (Tchad). Kisangani Méd. 2016 Jui; 6(1):111–6.

17. Ankum WM, Mol BW, Van der Veen F, Bossuyt P. M. Risk factors for ectopic pregnancy: a meta-analysis. Fertil Steril. 1996 Jun; 65(6):1093–9. PMID: 8641479

18. Saraiya M, Berg CJ, Kendrick JS, Strauss LT, Atrash HK, Ahn YW. Cigarette smoking as a risk factor for ectopic pregnancy. Am J Obstet Gynecol. 1998 Mar; 178(3):493–8. PMID: 9539515

19. Bouyer J, Coste J, Shojaei T, Pouly J-L, Fernandez H, Gerbaud L, et al. Risk factors for ectopic pregnancy: a comprehensive analysis based on a large case-control, population-based study in France. Am J Epidemiol. 2003 Feb 1; 157(3):185–94. PMID: 12543617

20. Li C, Zhao W-H, Zhu Q, Cao S-J, Ping H, Xi X, et al. Risk factors for ectopic pregnancy: a multi-center case-control study. BMC Pregnancy Childbirth. 2015 Aug 22; 15:187. https://doi.org/10.1186/s12884-015-0613-1 PMID: 26296545

21. Zhang J, Li C, Zhao W, Xi X, Cao S, Ping H, et al. Association between levonorgestrel emergency contraception and the risk of ectopic pregnancy: a multicenter case-control study. Sci Rep. 2015 Feb 12; 5:8487. https://doi.org/10.1038/srep08487 PMID: 25674909

22. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 94: Medical management of ectopic pregnancy. Obstet Gynecol. 2008 Jun; 111(6):1479–85. https://doi.org/10.1097/AOG.0b013e31817d201e PMID: 18515537

23. Institut National de la Statistique (INS). Nomenclature Camerounaise des Métiers, Emplois et Professions. Yaounde; Sept 2013.

24. Li C, Zhao W-H, Meng C-X, Ping H, Qin G-J, Cao S-J, et al. Contraceptive Use and the Risk of Ectopic Pregnancy: A Multi-Center Case-Control Study. PLoS ONE. 2014 Dec 10; 9(12).

25. Adewunmi A, Orekoya O, Rabiu K, Ottun T. The Association between Chlamydia trachomatis and Ectopic Pregnancy in Lagos,Nigeria-A Case Control Study. Open J Obstet Gynecol. 2015; 5:115–22.

26. Agholor K, Omo-Aghoja L, Okonofua F. Association of anti-Chlamydia antibodies with ectopic pregnancy in Benin city, Nigeria: a case-control study. Afr Health Sci. 2013 Jun; 13(2):430–40. https://doi.org/10.4314/ahs.v13i2.33 PMID: 24235946

27. Sheffer-Mimouni G, Pauzner D, Maslovitch S, Lessing JB, Gamzu R. Ectopic pregnancies following emergency levonorgestrel contraception. Contraception. 2003 Apr; 67(4):267–9. PMID: 12684145

28. Ghosh B, Dadhwal V, Deka D, Ramesan CK, Mittal S. Ectopic pregnancy following levonorgestrel emergency contraception: a case report. Contraception. 2009 Feb; 79(2):155–7. https://doi.org/10.1016/j.contraception.2008.08.006 PMID: 19135575

29. Paltieli Y, Eibschitz I, Ziskind G, Ohel G, Silbermann M, Weichselbaum A. High progesterone levels and ciliary dysfunction—a possible cause of ectopic pregnancy. J Assist Reprod Genet. 2000 Feb; 17(2):103–6. https://doi.org/10.1023/A:1009465900824 PMID: 10806589

30. Wånggren K, Stavreus-Evers A, Olsson C, Andersson E, Gemzell-Danielsson K. Regulation of muscular contractions in the human Fallopian tube through prostaglandins and progestagens. Hum Reprod Oxf Engl. 2008 Oct; 23(10):2359–68.

31. Shao R, Feng Y, Zou S, Weijdegård B, Wu G, Brännström M, et al. The role of estrogen in the pathophysiology of tubal ectopic pregnancy. Am J Transl Res. 2012 Jul 20; 4(3):269–78. PMID: 22937205

32. Hinson JP, Kapas S, Smith DM. Adrenomedullin, a multifunctional regulatory peptide. Endocr Rev. 2000 Apr; 21(2):138–67. https://doi.org/10.1210/edrv.21.2.0396 PMID: 10782362

33. Li HWR, Liao SB, Chiu PCN, Tam WW, Ho JC, Ng EHY, et al. Expression of adrenomedullin in human oviduct, its regulation by the hormonal cycle and contact with spermatozoa, and its effect on ciliary beat frequency of the oviductal epithelium. J Clin Endocrinol Metab. 2010 Sep; 95(9): E18–25. https://doi.org/10.1210/jc.2010-0273 PMID: 20534761

34. Li Y-Y, Li L, Hwang IS-S, Tang F, O W-S. Coexpression of adrenomedullin and its receptors in the reproductive system of the rat: effects on steroid secretion in rat ovary. Biol Reprod. 2008 Aug; 79 (2):200–8. https://doi.org/10.1095/biolreprod.107.064022 PMID: 18401014

35. Marinoni E, Di Iorio R, Letizia C, Lucchini C, Alò P, Cosmi EV. Changes in plasma adrenomedullin levels during the menstrual cycle. Regul Pept. 2000 Feb 8; 87(1–3):15–8. PMID: 10710283

36. Chiu PCN, Liao S, Lam KKW, Tang F, Ho JCM, Ho PC, et al. Adrenomedullin regulates sperm motility and oviductal ciliary beat via cyclic adenosine 5'-monophosphate/protein kinase A and nitric oxide. Endocrinology. 2010 Jul; 151(7):3336–47. https://doi.org/10.1210/en.2010-0077 PMID: 20444935

37. Bouyer J, Coste J, Fernandez H, Job-Spira N. [Tobacco and ectopic pregnancy. Arguments in favor of a causal relation]. Rev Epidemiol Sante Publique. 1998 Mar; 46(2):93–9. PMID: 9592851

38. Shaw L, Oliver E, Lee K, Critchley H, Horne A. Cotinine Exposure Increases Fallopian Tube PROKR1 Expression via Nicotinic AChR-7 A Potential Mechanism Explaining the Link between Smoking and Tubal Ectopic Pregnancy. Am J Pathol. 2010 Nov; 177(5):2509–15. https://doi.org/10.2353/ajpath.2010.100243 PMID: 20864676

39. Barnhart KT, Sammel M, Gracia C, Chittams J, Hummel A, Shaunik A. Risk factors for ectopic pregnancy in women with symptomatic first-trimester pregnancies. Fertil Steril. 2006 Jul; 86(1):36–43. https://doi.org/10.1016/j.fertnstert.2005.12.023 PMID: 16730724

40. Atrash HK, Strauss LT, Kendrick JS, Skjeldestad FE, Ahn YW. The relation between induced abortion and ectopic pregnancy. Obstet Gynecol. 1997 Apr; 89(4):512–8. PMID: 9083304

41. Ahman E, Shah I. Unsafe abortion: global and regional estimates of incidence of unsafe abortion and associated mortality in 2000. Geneva: World Health Organization; 2004 p. 13–7. Report No.: 4.

42. Anorlu RI, Oluwole A, Abudu OO, Adebajo S. Risk factors for ectopic pregnancy in Lagos, Nigeria. Acta Obstet Gynecol Scand. 2005 Feb; 84(2):184–8. https://doi.org/10.1111/j.0001-6349.2005.00684.x PMID: 15683381

43. CDC, Premarital sexual experience among adolescent women, United States, 1970–1988. MMWR 1990; 39 (51,52); 929–32.

44. Cates W Jr. The epidemiology and control of sexually transmitted diseases in adolescents. In: Adolescent medicine: State of the art reviews. Philadelphia: Hanley and Belfuy. 1990; 1 (3)

45. Aral SO. Sexual behaviour as risk factor for sexually transmitted diseases. Reproductive Tract Infections: Global Impact and Priorities for Women's Reproductive Health. Plenum Press. New York: Germaine A, Holmes KK, Piot P, Wasserheit JN; 1992. p. 185–91.

46. Nkwabong E, Dingom MA. Acute Pelvic Inflammatory Disease in Cameroon: A Cross Sectional Descriptive Study. Afr J Reprod Health. 2015 Dec; 19 (4):87–91. PMID: 27337857

47. Institut National de la Statistique (INS), ICF International. Enquête Démographique et de Santé et à Indicateurs Multiples du Cameroun 2011. Calverton, Maryland, USA; 2012 p. 103–5. Report No.: 5.