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Research Article

Factors Associated with Ectopic Pregnancy at Mbarara University Teaching Hospital in South Western Uganda

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Abstract

Background: Ectopic pregnancy (EP) is a life-threatening condition and a gynecological emergency which affects one in every 80-100 pregnancies. Risk factors for ectopic pregnancy identified in previous studies include low level of education, two or more lifetime sexual partners, smoking, prior history of vaginal discharge, previous use of intrauterine contraceptive device, tubal corrective surgery, tubal sterilization, previous history of induced abortion, early age of sexual debut, inconsistent condom use, multiple sexual partners, infertility, previous pelvic or abdominal surgery and previous genital infections.

Objective: We sought to identify/determine the factors associated with ectopic pregnancy at Mbarara Regional Referral Hospital (MRRH) Gynecological ward.

Methods: This was an unmatched case-control study carried out at MRRH involving 25 cases and 76 controls. Cases were women treated for ectopic pregnancy and the controls were women with normal intrauterine pregnancies from the antenatal clinic. Information on their socio-demographic, sexual and reproductive characteristics was obtained using a semi-structured questionnaire. Serological evidence of prior chlamydial infection was determined in both groups by testing for the presence of Chlamydia immunoglobulin G antibodies in their blood. Logistic regression was used to determine the factors associated with ectopic pregnancy. The significant level of <0.05 was used. Odds ratios and their corresponding 95% CIs were provided at both univariate and multivariate analysis.

Results: The factors associated with ectopic pregnancy included history of previous abdominal/pelvic surgery (aOR 6.9; CI: 1.47-32.98; p=0.000) being a single woman (aOR 12.0; 2.21-65.32; p=0.0026) and presence of Chlamydia antibodies with Odds ratio (O.R 4.9; CI: 1.15-21.29; p=0.002)

Conclusion: The factors associated with ectopic pregnancy included history of previous abdominal/pelvic surgery, being a single woman and prior *chlamydia trachomatis* infection.

Introduction

Ectopic pregnancy refers to implantation of a fertilized egg in a location outside of the uterine cavity [1]. The most common extra-uterine location is the fallopian tube, which account for 98% of all ectopic gestations. Other sites are ovary, cervix, corn of the uterus and abdominal cavity [2]. Ectopic pregnancy (EP) is a life-threatening condition and a gynecological emergency which affects one in every 80-100 pregnancies [3]. There is a fourfold increase in the incidence of ectopic pregnancy in the industrialized countries (from 0.3 to 1.2%) [4]. Such rise is mainly attributed to advanced techniques for diagnosing early ectopic pregnancy and increased prevalence of pelvic inflammatory disease [5]. The incidence of EP in Africa ranges between 0.5-3% [6,7]. Risk factors for ectopic pregnancy identified in previous studies include a strong association between prior Pelvic Inflammatory Diseases (PID) and EP with OR ranging from 2.0 to 10.1 [8]. The importance of infectious factors in ectopic pregnancy is well documented [9] There is probably a causal link. In Sweden, declining rates of Chlamydia infections, attributed to preventive policies, have been accompanied by a fall in the risk of ectopic pregnancy [10]. The other variables suggestive of a higher probability of exposure to sexually transmitted diseases (age at first intercourse and number of sexual partners) were associated with a risk of ectopic pregnancy in univariate analysis. Chlamydia trachomatis is the most common sexually bacterial infection in the world [11]. It is capable of infecting the genital organs of women and men. Generally, the infection does not produce symptoms or can produce mild symptoms [12].

Reinfection occurs easily if the partners do not receive treatment. Chlamydia prevalence and incidence is higher in individuals 16 to 19 years old [13]. Increase in the number of ectopic pregnancies is also attributed to increase in the incidence

of pelvic infections. Chlamydia trachomatis is responsible for the most common sexually transmitted bacterial infection. In 2008, an estimated 106 million new cases of urogenital chlamydia among adults occurred globally, the largest burden being in low income countries [14]. In 2010 WHO estimated 10 million new infections of chlamydia in Africa [15]. Additionally, previous studies [16] have found that, among all the possible risk factors of EP, the strongest evidence is for an association between previous EP and sequent EP. Barnhart et al 2006 indicated that the risk of facing a repeat EP increases intensely with the number of prior EP (OR=2.98 for one prior EP and OR=16.04 for 2 or more). Other research studies also estimated the risk of facing a repeat EP to be between 2.4 and 25.0 [17]. Furthermore, it has been reported that previous tubal surgery is a major risk factor for EP with an estimated OR of 4.7 (2.4-9.5) according to a meta-analysis. It is uncertain whether the increased risk is arising from a surgical procedure or from the underlying problem. Also, previous studies have reported different results about the association between non-tubal abdominal or pelvic surgery and subsequent EP from no association to OR ranging from 2.4 to 5.0 [18]. Previous studies found that the risk of EP increases with advancing maternal age [9]. Based on some results, the average maternal age was significantly higher for women with EP than controls. Furthermore, compared with women aged ≤26 years, the risk of EP for women aged 27-32 and aged 33-38 were 3.9 and 4.3 times higher respectively, while women aged ≥39 years approximately had a 9-fold risk of EP [19]. Existing evidence on how advanced maternal age has an effect on EP risk remains unclear. It is improbable that the higher risk of EP in older age cohorts is due to chromosomal abnormalities in the trophoblastic tissue [9]. Some researchers attributed it to some age-related factors, such as: Possible tubal scarring from PID, major gonococcal and chlamydial epidemics and changes in tubal function leading to delay in ovum transport and tubal implantation [20]. However, these hypotheses need to be investigated.

Several studies have reported a strong association between tobacco use and EP. In a meta-analysis, smoking patients demonstrated significantly higher odds of EP (OR=15.69, 95% CI2.87-85.76). Studies have also found that there is an association between spouse's cigarette smoking and EP with an OR of 1.7 (95% CI: 1.05-2.85). [21,22]. Although, the reason why smoking causes EP remains unknown, animals studies have shown that inhalation of cigarette smoke may impair fallopian tube function by affecting ciliary beat frequency and smooth muscle contraction [19]. Early studies on risk factors of EP indicated that OR greater than one belonged to current IUD use [21]. Although the exact mechanism by which implantation is occurring outside the uterus is not well understood, it is thought that IUD-induced inflammation may result in deciliation of the endosalpinx and this delays ovum transport, which leads to EP [23]. In a case-control study comparing 243 women using an IUD and suffering from EP to 140 IUD users with an intrauterine pregnancy, studies have also described that progesterone IUD, duration of IUD use, and pelvic pain after the insertion of the IUD are the factors increasing the risk of EP in IUD users. In addition, other influencing factors associated with decreasing risk of EP are the displacement of the IUD and use of anti-inflammatory drugs before the pregnancy.

The results concerning EP after spontaneous abortion differ among studies. Spontaneous abortions may have a causal effect, possibly mediated by infection. However, there may also be common risk factors for ectopic pregnancy and spontaneous abortions, such as chromosomal abnormalities or hormonal factor [23]. The available evidence suggests that the chromosomal abnormalities may be ruled out, but hormonal factors require further study, together with other factors including immunologic factors. Multiple studies have produced conflicting results regarding the association between EP and a history of induced abortions [9]. However, a large case–control study including 803 cases of EP showed an increased risk of EP for women with a history of two or more prior induced abortion with an adjusted OR of 1.9 (95% CI=1.0-3.8) [16]. Therefore, our study sought to identify and determine the factors associated with ectopic pregnancy at Mbarara University Teaching Hospital in Southwestern Uganda.

Materials and Methods

This was an unmatched case-control study i.e. (1:3 ratio of cases to controls) carried out at Mbarara Regional Referral Hospital between September 2016 to January 2017. Consecutive sampling method was used to enrol all mothers who met the inclusion criteria until the sample size was achieved.The cases were 25 consecutive women with a diagnosis of ectopic pregnancy during the study period. The control group was made up of women with confirmed uncomplicated intrauterine pregnancy, attending the antenatal clinic of MRRH. Each case of ectopic pregnancy was followed by pregnant controls attending the antenatal clinic. The sample size for this study was calculated using the Kelsey et al (1996) formula for calculating sample size for unmatched case-control studies. After computing for the expected 10% attrition, the sample size was calculated to be 25 cases and 76 controls giving a total sample size of 101. All patients who had laparotomy for tubal ectopic pregnancy, who consented to this study and satisfied the inclusion and exclusion criteria, were recruited until the minimum sample size was obtained. The approval to conduct the study was obtained from the Department of Obstetrics and Gynecology, Faculty of Medicine Research Committee (DMS 6), MUST Research Ethics Committee (No. 21/7-16) and the Uganda National Council of Science and Technology (HS 2146). Informed consent was obtained from all respondents and confidentiality was ensured. Study participants were identified by study codes and not their names, for issues of confidentiality. In addition, authority was sought from the office of the hospital director of MRRH to conduct the study in this institution.

Results

Majority of the participants were Banyankole, had at least primary level of education and were residents of Mbarara. Mean age of the cases was 27.8±4.3 and 25.2±5.9 for controls. There were significantly more [12(48.0%)] single women among the cases population with ectopic pregnancy than the controls

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[5(6.58%)] [p < 0.01]. (Table1). Table 2 shows sexual behaviour of the participants. The cases engaged in sexual intercourse at a significantly younger age than the controls (p<0.01). There were more cases participants with multiple sexual partners compared to the control group. Previous history of pelvic inflammatory disease was obtained in 24(96.00%) among the cases. This was significantly more than 8(10.53%) among the controls (p=0.02). The cases group had significantly more surgeries 13(52.00%) compared to only 6(7.89%) among the control group. Table 3 shows that prior chlamydia trachomatis infection, single women and a history of previous pelvic / abdominal surgery are independently associated with ectopic pregnancy at Mbarara Regional Referral Hospital. Logistic regression model analysis of risk factors for ectopic pregnancy showed a four-fold increase in the risk of ectopic pregnancy in those with C. trachomatis antibodies when controlling for previous history of pelvic inflammatory disease (O.R 4.9; 95% CI 1.15-21.29). Controlling for the effects of sociodemographic characteristics, previous history of pelvic inflammatory disease, marital status, number of sexual partners showed that single women (OR 12.0; 95% CI 2.21-65.32) and having a history of previous abdominal/pelvic surgery (OR 6.9; 95% CI 1.47-32.98) were shown to be more likely to be associated with ectopic pregnancy as well.

Table 1: Sociodemographic Characteristics (N=101)

Characteristic	Controls n (%)	Cases n (%)	P-value
Age in years			
16-19	12(15.79)	1(4.00)	
20-24	38(50.00)	6(24.00)	
25-34	21(27.63)	14(56.00)	0.011
35-42	5(6.58)	4(16.00)	
Mean age	27.8±4.3	25.2±5.9	
District			
Mbarara	68(90.67)	20(80.00)	
Greater Bushenyi	4(5.33)	4(16.00)	0.234
Others	4(4.00)	1(4.00)	
Residence type			
Rural	38(50.00)	13(52.00)	0.862
Urban	38(50.00)	12(48.00)	
Tribe			
Banyankore	59(77.63)	20(80.00)	
Baganda	5(6.58)	3(12.00)	
Bakiga	7(9.21)	2(8.00)	0.496
Others	5(6.58)	0(0.00)	
Level of education			
No formal education	2(2.63)	0(0.00)	
Primary education	38(50.00)	6(24.00)	
Secondary education	24(31.58)	11(44.00)	0.075
Tertiary education	12(15.79)	8(32.00)	
Marital status			
Single	5(6.58)	12(48.00)	0
Married	68(89.47)	12(48.00)	
Separated	3(3.95)	1(4.00)	
Religion			
Christian	44(57.89)	14(56.00)	0.868
Moslem	32(42.11)	11(44.00)	
Occupation			
Unemployed	13(17.33)	1(4.00)	
Peasant	35(46.67)	3(12.00)	
Business	21(28.00)	15(60.00)	0.001
Professional	6(8.00)	6(24.00)	
Income in Uganda shs			
<90,000/=	24(31.58)	24(96.00)	0
>90,000/=	52(68.42)	1(4.00)	

Table 2: Sexual and Reproductive Characteristics (N=101)

Characteristic	Controls n (%)	Cases n (%)	p-value
Parity			
1	41(53.95)	1(4.00)	
2	22(28.95)	21(84.00)	0
>3	13(17.11)	3(12.00)	
Menarche			
<12 years	2(2.67)	1(4.00)	
12-14 years	37(49.33)	21(84.00)	0.006
>14 years	36(48.00)	3(12.00)	
Coitarche			
<19 years	46(60.00)	25(100.00)	0

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>19 years	30(40.00)	0(0.00)	
Multiple sexual partners			
No		11(44.00)	
Yes		14(56.00)	0.004
Induced abortion			
None	74(97.37)	20(80.00)	
01-Apr	2(2.63)	5(20.00)	0.003
History of previous PID			
No		1(4.00)	
Yes		24(96.00)	0.002
History of puerperal /postabortal sepsis			
No	75(98.68)	24(96.00)	
Yes	1(1.32)	1(4.00)	0.403
History of abdominal/pelvic surgery			
No		12(48.00)	
Yes		13(52.00)	0
History of IUCD usage			
No	73(97.33)	24(96.00)	
Yes	2(2.67)	1(4.00)	0.735

Table 3: Factors associated with ectopic pregnancy at Multivariate Analysis.

	Univariable		**Multivariable**	
Variable Chlamydia IgG Antibodies	OR[95% CI]	P value	aOR[95% CI]	P value
No	1	0.0019	1	0.0019
Yes	4.4[1.70-11.48]		4.9[1.15-21.29]	
Marital status				
Single	13.6[4.05-45.62]	0	12.0[2.21-65.32]	0.0026
Married	1		1	
Separated	1.8[0.18-19.70]		0.6[0.04 -8.48]	
Parity				
1	1		1	
2	39.1[4.92-310.73]		24.9[1.47-205.98]	
>3	9.4[0.90-98.96]	0	6.9[1.47-32.98]	0.3752
Menarche				
<12 years	1		1	
12-14 years	1.1[0.09-13.27]	0.0031	3.4[0.77-14.82]	0.2796
>14 years	0.1[0.01-2.41]		1.1[0.11-11.50]	
Coitarche				
<19 years	0.6[0.02-0.34]	0	0.9[0.37-2.28]	0.8622
>19 years	1		1	
Multiple sexual partners				
No	1		1	
Yes	3.8[1.48-9.82]	0.0051	3.1[0.18-11.88]	0.4376
Induced abortion				

None	1		1	
01-Apr	9.2[1.66-51.27]	0.0067	7.0[0.43-46.68]	0.8681
History of Abdominal /pelvic surgery				
No	1		1	
Yes	12.6[4.02-39.71]	0.0001	6.9[1.47-32.98]	0
History of previous PID				
No	1		1	
Yes	104[24.23 -171.5]		85[33.14-169.4]	0.5689

Discussion

Our study found that women with ectopic pregnancy were more likely to be single, corroborating the findings in another Nigerian study [24]. This can be explained by the fact that single women are more likely to have multiple sexual partners than married women. In examining the risk factors for Chlamydia infection among patients with ectopic pregnancy and normal pregnancy this study looked at the sexual and reproductive characteristics of both groups. The results of univariate analysis showed that women with ectopic pregnancy engaged in sexual intercourse at a significantly younger age than women with intra uterine pregnancy. This finding is in keeping with previous studies which linked early coitarche with Chlamydia trachomatis infection [8]. Adolescents are prone to sexually transmitted disease (STD) because of high risk sexual behaviour. Biologically, the adolescent is particularly at risk of STD because the columnar epithelium, which is susceptible to Chlamydia and gonococcal organisms extend from the endocervical canal to the ectocervix making it fully exposed to pathogens. They also have difficulties using barrier methods of contraception and may have less access to STD care because of limited facilities, negative peer pressure, concealment and restrictive policies especially in the developing countries [9]. Previous history of pelvic inflammatory disease was significantly higher in patients with ectopic pregnancy when compared with women with normal pregnant controls. This agrees with the findings of previous studies in this regard [25].

In contrast to other studies [25], this study found that induced abortions were relatively low in women with ectopic pregnancy and did not have any association with ectopic pregnancy. This could be explained by the small number of participants in this study who had a history of induced abortions and therefore it was difficult to assess statistical difference with such a small number. In our study previous history of abdominal/ pelvic surgery was associated with ectopic pregnancy and this compares with studies done in other areas [15].This could be explained by the fact that previous surgery in the pelvic area or on the tubes can cause adhesions and impede the egg's movement causing implantation in the tubes and other sites. However, when these were subjected to logistic regression model (multivariate) analysis, patients with Chlamydia antibodies showed a four-fold increase in the risk of ectopic pregnancy when controlling for previous history of pelvic inflammatory disease. In addition, the multivariate analysis revealed that women with history of previous abdominal/pelvic surgery and those that were single were significantly associated with ectopic pregnancy.

Conclusion

This study has shown that being single and having a history of previous abdominal/pelvic surgery were positively associated with ectopic pregnancy. Furthermore, a greater proportion of women with ectopic pregnancy had serological evidence of prior *C. trachomatis* infection than women with intrauterine pregnancy. It also demonstrated a four-fold risk association between prior *C. trachomatis* infection and ectopic pregnancy.

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