

# Ectopic pregnancy and associated factors in a tertiary health facility: A comparative study

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## Abstract

**Background:** Ectopic pregnancy has remained a significant cause of maternal morbidity and mortality, especially in Sub-Saharan Africa. Despite its remarkably high incidence, there is yet a remarkable knowledge gap on the risk factors and clinical presentations of ectopic pregnancy in sub-Saharan countries, including Ethiopia. A better understanding of the illness will have an important impact on the prevention strategies. We have conducted a comparative study in a tertiary health facility in Ethiopia to assess the clinical presentation and risk factors of patients with ectopic pregnancy.

**Objectives:** The objective of the study is to describe clinical presentations and associated factors of ectopic pregnancy in a tertiary health facility in Ethiopia.

**Methods:** Unmatched case-control study design was employed to identify 100 ectopic pregnancy cases and 200 controls of women with intrauterine pregnancy on their second and third trimester of pregnancy who presented to St. Paul's Hospital Millennium Medical College during the study period. A structured questionnaire was used to collect sociodemographic data and clinical characteristics. Data was entered and analysed using IBM SPSS Statistics package version 20. A binary logistic regression model was fitted to identify independent predictors of ectopic pregnancy. The odds ratio and 95% confidence interval was calculated. A p-value of 0.05 was used as a cut-off to declare statistical significance.

**Results:** The incidence of ectopic pregnancy in our study was 1 per 90 live births. Similar to finding in other studies, the three common clinical presentation of patients with ectopic pregnancy were abdominal pain (97%), vaginal bleeding (72%) and missed period (33%). Both early initiation of sexual intercourse before the age of 18 and more than two lifetime sexual partner are found to be significantly associated with ectopic pregnancy ( $P < 0.5$ ). Use of levonorgestrel containing emergency hormonal contraception was not found to have no effect on the risk of ectopic pregnancy ( $P=0.26$ ).

**Conclusion:** Early initiation of sexual intercourse and having multiple sexual partners are important risk factors that should be considered when planning to reduce the incidence of ectopic pregnancy. Interventions need to be targeted in increasing awareness of the problem with possible prevention mechanisms, including sexual education and the use of barrier methods of contraceptives that can prevent sexually transmitted infections.

## Introduction

In Ethiopia, the lifetime risk of dying from pregnancy-related causes is 1 in 27, which is higher than the global figure of 1 in 92; Hence childbearing, which is a normal physiological process, can result in disability and death [1,2]. Over the past two decades, remarkable changes have happened, and maternal mortality has reduced from 708 per 100,000 live births in 1990 to 497 per 100,000 in 2013 [3]. Ectopic pregnancy is among the common causes of first-trimester maternal death in developed countries, including Ethiopia [3]. In addition to contributing to maternal mortality, it is also a significant cause of secondary infertility [4].

Several risk factors are attributed to ectopic pregnancy. History of pelvic inflammatory disease, previous pelvic surgery, previous ectopic pregnancy, and artificial reproductive technologies are some of risk factors described in the literature [4–6]. Infectious diseases like tuberculosis are also attributed as a cause in some settings [7]. In women with a previous history of ectopic pregnancy, the risk of recurrence can be as high as 15% [7]. Despite several evidences in developed countries, there is a significant knowledge gap on the risk factors of ectopic pregnancy in Ethiopia.

Different tubal and extra tubal sites were identified for Ectopic pregnancy. Only limited studies of large sample size have described specific sites of ectopic pregnancy [8,9]. Otherwise, studies on the site

of ectopic pregnancy are largely case reports and case series of few cases [10,11]. Among the tubal sites, ampulla is identified as the commonest site of implantation [12]. The site of implantation has an implication on the timing and severity of the clinical presentation as well as the outcome of subsequent pregnancy. So, it is critical to have studies that focus on the location of ectopic pregnancy implantation [12].

Diagnosis of ectopic pregnancy depends on a clinical presentation together with serum beta-human chorionic Gonadotropin ( $\beta$ -HCG) measurement and imaging using ultrasound [13]. The most critical step in the diagnosis of ectopic pregnancy is exclusion of viable intrauterine pregnancy [13]. In some cases, trans-vaginal ultrasound may fail to localize the location of the pregnancy, putting the clinician in dilemma. Such pregnancies are approached as pregnancies of unknown location [10,14].

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Early diagnosis and prompt treatment help in averting the complications related with ruptured ectopic pregnancy. Unfortunately, in some circumstances, the patient may or may not be aware that she is pregnant at the time of evaluation at the emergency department [15].

In such cases, patients may present with a life-threatening emergency requiring a lifesaving surgery [2]. Early arrival of patients coupled with an increased ability of clinicians in diagnosing ectopic pregnancy improves outcome and preserves future fertility [16].

Risk factors and clinical presentation of ectopic pregnancy are not widely studied in Ethiopia. Thus, the objective of the study was to determine ectopic pregnancy and associated factors at Saint Paul's Hospital Millennium Medical College (SPHMMC) in the capital city, Addis Ababa, Ethiopia.

## Materials and method

We conducted an unmatched case-control study at Saint Paul's Hospital Millennium medical college (SPHMMC) in Addis Ababa, Ethiopia, between February 1, 2015, to January 31, 2016. All cases of ectopic pregnancies which fulfil the operational definitions were identified and interviewed for inclusion into the study. Unmatched controls of pregnant women in their 2<sup>nd</sup> and 3<sup>rd</sup> trimester pregnancies who were attending antenatal care in the hospital were selected and interviewed. Considering the low recruitment rate for ectopic pregnancy, we took a ratio of 1:2. Exclusion criteria for controls were those with age less than 18, not willing to give consent, and previous history of ectopic pregnancy.

Data collection procedures: Data was collected by three trained nurses working in the gynecology ward and gynecology outpatient department. A five day training was provided on the data collection instrument. Data for the ectopic cases were collected at the time of discharge from the hospital.

Additional data was collected regarding; Age at first sexual intercourse, number of lifetime sexual partners, prior history of treatment for STD, prior history of induced abortion and use of emergency hormonal contraceptives.

## Operational definitions

- Ectopic pregnancy is defined as implantation of the fertilized ovum outside the endometrial cavity lining proper. (cornual, tubal, ovarian, abdominal, and other rare sites.) Empty uterus with a discriminatory zone of serum b-HCG of 1500 mi/ml and 6500 miu/ml for trans-vaginal and trans-abdominal ultrasound respectively, is regarded as ectopic. Cases that are managed as ectopic pregnancies by the managing team will be taken as diagnostic.
- Heterotopic pregnancy is a condition in which extra-uterine (ectopic pregnancy) and intrauterine pregnancy occur simultaneously, and it was counted as ectopic in this study. Pregnancy of unknown origin (before reaching the serum b-HCG to the discriminatory zone) was not counted as ectopic.
- Prior history of induced abortion includes both medical and surgical abortion.
- Treatment for sexually transmitted diseases includes both medical and surgical management.

## Statistical analysis

Data was entered and analysed using SPSS version 20. Descriptive statistics were presented using frequency tables, means, and

proportions. A binary logistic regression model was fitted to identify independent predictors of ectopic pregnancy. A *p*-value of 0.2 was used to select variables for multivariate logistic regression analysis. A crude and adjusted Odds Ratio and 95% confidence interval was calculated. A *p*-value of 0.05 was used to declare statistical significance.

## Ethical consideration

Ethical clearance was obtained from the institutional ethical review board. In addition, a support letter was received to conduct the study from the department of obstetrics and gynecology at St. Paul's Hospital Millennium Medical College. Individual subjects were provided information about the objective of the study, and they provided both verbal and written consent to participate.

## Results

During the study period between February 1, 2015, to January 31, 2016, there were 100 cases of ectopic pregnancies. The total number of live births during that period in the hospital was 8972, making the incidence of ectopic pregnancy 1 per 90 live births. More than half of cases of ectopic pregnancy were from Addis Ababa (Table 1). The mean age at the diagnosis for ectopic pregnancy is 27 years.

The typical presentation of ectopic pregnancy is abdominal pain accounting for 97% of the cases, followed by vaginal bleeding (72%), and amenorrhea (33%). Of the total cases of ectopic pregnancy, 96% were managed surgically with laparotomy, while 4% were managed medically with methotrexate. About 98% of the ectopic pregnancies were tubal. Most of the tubal ectopic pregnancies (89%) have tubal rupture with hemoperitoneum upon presentation. Of the surgically managed cases, 96.5% had salpingectomy, and 3.5% had salpingostomy. Eight percent of patients with ectopic pregnancies had a previous history of ectopic pregnancies. Thirty-eight percent of the cases presented with a hemoglobin level of <10 gm/dl, of which 26% required blood transfusion.

There was a statically non-significant positive correlation between the use of emergency levonorgestrel hormonal contraceptive (post-pill) and development of ectopic pregnancy (OR=1.568 with 95 % CI 0.681-2.857). History of sexually transmitted disease (STD) was also found to have a positive correlation with ectopic pregnancy compared to the control groups with an (OR= 1.76, 95% CI 0.575-5.383). Prior history of induced abortion was also more common among the ectopic cases compared to the control group (OR=1.66, 95% CI, 0.899-3.078). Controlling confounders, Age at first sexual intercourse of less than 18, and having more than two lifetime sexual partners were significantly associated with ectopic pregnancy with a *p*-value of 0.001 and < 0.031, respectively (Table 2).

## Discussion

The incidence of ectopic from our study was comparable to other studies done in the same city with a similar setting [2]. Similarly, the clinical presentation of patients with ectopic pregnancy were mainly abdominal pain, vaginal spotting, and amenorrhea, which is consistent with other studies conducted in similar and different settings. Most importantly, more than 35% of the cases of ectopic pregnancy patients had anemia (hemoglobin level of <10 gm/dl) at presentation to the hospital, and about 26% of them had significant intraperitoneal bleeding and required blood transfusion due to mainly the late arrival to the hospital. This finding of a significant proportion of severe anemia requiring transfusion is much higher than reported in other studies [10]. The repeat tubal ectopic rate is 8% from the overall cases, and

**Table 1.** Comparison of sociodemographic and obstetric characteristics of cases and controls from February 1, 2015, to January 31, 2016. \*TVT: Technical and vocational training, \*\* Non-governmental organization.

Age(years)	Ectopic cases	Controls	Total
15-19	7 (7%)	4 (2%)	11 (3.7%)
20-24	29 (29%)	54 (27%)	83 (27.7%)
25-29	34 (34%)	87 (43.5%)	161 (40.3%)
30-34	20 (20%)	43 (21.5%)	63 (21.0%)
>35	10 (10%)	12 (6%)	22 (7.3%)
<b>Place of residence</b>			
Addis Ababa	52(52%)	169(84.5%)	221(74%)
Outside Addis Ababa	48(48%)	31(15.5%)	79(26%)
<b>Educational level</b>			
Illiterate	23 (23%)	26(13%)	49 (16.3%)
Able to write and read	1 (1%)	3 (1.5%)	4 (1.3%)
Primary 1-4	9 (9%)	20(10%)	29 (9.7%)
Primary 5-8	13 (13%)	61(30.5%)	74 (24.7%)
Secondary	7 (7%)	31(15.5%)	38 (12.7%)
TVT*	41 (41%)	43(21.5%)	84 (28%)
Degree and above	6 (6%)	16(8%)	22 (7.3%)
<b>Occupation</b>			
Farmer	16 (16%)	0 (0%)	16 (5.3%)
Housewife	29 (29%)	130 (65%)	159 (53%)
Daily laborer	11 (11%)	18 (9%)	29 (9.7%)
Government employer	7 (7%)	24 (12%)	31(10.3%)
NGO** employer	12 (12%)	2 (1%)	14 (4.7%)
Trader	15 (15%)	14 (7%)	29 (9.7%)
Student	5 (5%)	2 (2%)	7 (2.3%)
Others	5 (5%)	10 (5%)	15(5%)
<b>Parity</b>			
0	43 (43%)	79 (39.5%)	122 (40.7%)
1-4	57 (57%)	121 (60.5%)	178 (59.3%)
<b>Marital status</b>			
Married	83 (83%)	196 (98%)	279 (93%)
Single	15 (15%)	4 (2%)	19 (6.3%)
Divorced	2 (2%)	0 (0%)	2 (0.7%)

**Table 2.** Multivariate logistic regression analysis of predictors of ectopic pregnancy.

	Cases	Controls	Adjusted Odds Ratio	95% CI	P-value
Post pill	23 (23%)	32 (16%)	1.568	0.681-2.857	0.259
Induced abortion	22 (22%)	29 (14.5%)	1.66	0.899-3.078	0.309
Coitarche at <18yrs	68(68%)	57 (28.5%)	5.33	3.168-8.971	<0.001
STD	6 (6%)	7 (3.5%)	1.76	0.575-5.383	0.876
Sexual partners >2	15 (15%)	11 (5.5%)	3.03	-	0.031

most of them ended up with salpingectomy on the remaining fallopian tube, constraining their future fertility. Early detection and medical management of ectopic pregnancy could have prevented not only unnecessary invasive surgery that compromises future fertility but also surgery-related morbidity for the patient.

In line with other studies, early initiation of sexual intercourse and having multiple numbers of sexual partners were found to be significantly associated with ectopic pregnancy [17]. The high incidence of sexually transmitted diseases in a developing country like Ethiopia the burden of ectopic pregnancy due to tubal damage is likely to be higher when compared to the developed countries [18,19]. The importance of safe sexual practice education as one possible way of preventing unwanted pregnancy and sexually transmitted infections is suggested in researches [18].

The association of ectopic pregnancy with the use of emergency levonorgestrel containing contraceptives and history of STD has shown a positive correlation with ectopic pregnancy, but the association was not significant enough to make a conclusion. This could be due to confounders like recall bias and subclinical infections in the case of STD. So, we should encourage women to have a safe sexual practice and use regular contraceptive drugs rather than relying on post pills as a primary means of contraception. In addition, further studies are needed to determine the contributions of asymptomatic sexual transmitted infections, which is an important cause of tubal scarring and damage.

## Conclusion

Ectopic pregnancy carries significant morbidity among pregnant individuals. Unlike the finding from other studies, a significant proportion of patients with ectopic pregnancy in our study required blood transfusion upon presentation. Preventive strategies should focus on avoidable determinants, including comprehensive sexual education and early detection of ectopic pregnancy. Remarkably high rate of patients with the previous ectopic presented with ruptured ectopic pregnancy underscoring the need to improve counselling upon discharge to encourage early diagnosis of ectopic and possible conservative managements. The medical treatment of ectopic pregnancy is encouraging, but it needs a longitudinal follow-up study to see for short term and long-term outcomes.

**Recommendations:** Ectopic pregnancy should be considered in a reproductive age woman with lower abdominal pain to prevent maternal morbidity and near-miss cases in the first trimester of pregnancy. We need to build the knowledge of ectopic pregnancy in lower and middle health care providers. The use of first-trimester ultrasound scanning should be done for selected cases, mainly with a previous history of ectopic pregnancy, to prevent late presentation and rupture with subsequent loss of the remaining fallopian tube. Women of reproductive age should be counselled to have safe sexual intercourse practice, including delaying the age to initiate sexual intercourse to minimize the chance of ectopic pregnancies.

We should advise women in the reproductive age group to use regular contraceptive methods for the prevention of pregnancy. The use of post pills (levonorgestrel containing emergency hormonal contraceptive) as primary means of contraception can have a high chance of failure and may increase the likelihood of ectopic pregnancy if the method fails.

We recommend further matched adequately powered cases control studies, including the use of laboratory tests for chlamydial antibody titer to establish a strong correlation of ectopic pregnancy and sexually transmitted diseases and infections.

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