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Clinical profile of ectopic pregnancies in a national referral hospital in Bhutan: A two-year retrospective study

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ABSTRACT

Introduction: Ectopic pregnancy is an emergency and a life-threatening condition which is an important cause of major maternal morbidity and mortality. This study was designed to determine incidence, common identified risk factors, clinical presentations, management, morbidity and mortality due to ectopic pregnancy at the national referral hospital in Thimphu, Bhutan. **Methods:** This was a retrospective study of all cases of ectopic pregnancies for a period of two years from 1st January 2018 to 31st December 2019. Socio-demographic characteristics, risk factors, clinical presentations, investigations and mode of treatments were extracted. Simple descriptive statistics such as frequencies, percentages, mean and range were utilised. **Results:** There were 9603 pregnant women admitted for delivery, out of which 122 were ectopic pregnancies. The incidence of ectopic pregnancy was 12.7/1000 pregnancies. Majority of them were in the age group of 21-30 years and 32.69% of the affected were nulliparous. While Pelvic inflammatory disease was seen in 41.35%, 20.19% were unmarried. Abdominal pain, amenorrhea, and vaginal bleeding were the most common symptoms. Among the ectopic pregnancies, 99.5% were diagnosed with ultrasound. A total of 94.23% had undergone surgical intervention, of which only 1% had laparoscopic surgery. No maternal mortality had occurred. **Conclusions:** Women with past history of pelvic inflammatory disease, previous miscarriage, unmarried, and nulliparous presenting with history of amenorrhea, abdominal pain, vaginal bleeding should be a high index of suspicion for ectopic pregnancy. Timely diagnosis and intervention in the form of surgical or medical management will reduced the morbidity and mortality due to ectopic pregnancy.

Keywords: Ectopic pregnancy; incidence; laparoscopic surgery; pelvic inflammatory disease.

INTRODUCTION

Ectopic pregnancy is defined as a pregnancy that occurs outside of the uterine cavity. It is one of the important causes of maternal morbidity and mortality globally. Ectopic pregnancy presents as an acute emergency and a life-threatening event, especially in the first three months of pregnancy and accounting for 10 percent of maternal mortality and morbidity globally[1]. Approximately 1 to 2% of all pregnancies in developed and developing countries are ectopic pregnancies[2]. A study carried out in the United States from 2004 to 2008; the incidence of ectopic pregnancy is 14.7 per 1000 pregnancies[3,4]. In South East Asia Region, the incidence of ectopic pregnancy varies between 0.25 to 1.9 %[5, 6]. However, it is on the increasing trends[6]. This increase in the incidence has been attributed to increase in sexual transmitted disease rates, caesarean sections, assisted reproductive technologies (ART) and also due to improved diagnostic modalities and improvement in health facilities[6,7].

The etiology of ectopic pregnancy is multifactorial, and many risk factors like pelvic inflammatory disease, caesarean sections, tubal or pelvic surgeries intrauterine devices users, infertility, and miscarriages are associated with it but in 50% of women with ectopic pregnancies have no identifiable risks[8-11]. The mechanisms underlying the risk of extrauterine implantation remain unclear. The postulated mechanism includes, anatomic obstruction, abnormalities in tubal motility or ciliary function, abnormal conceptus, and chemotactic factors stimulating tubal implantation[7] 95% of ectopic pregnancies occur in the fallopian tube, followed by cornual site, the ovary, cervix, caesarean scar and abdomen[8].

The incidence and the severity of clinical presentations of ectopic pregnancy has relationship to the socio-demographic variables such as age, educational status, parity, marital status and also to risks factors like pelvic inflammatory disease, caesarean sections, tubal or pelvic surgeries intrauterine devices users, infertility, and miscarriages[8-11].

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The classic triad of symptoms of an ectopic pregnancy includes abdominal pain, bleeding per vaginum and amenorrhea [8]. These Classic presentations occurs at around 6 to 8 weeks of gestation but the clinical presentations can range from asymptomatic to secondary amenorrhea, abdominal pain, bleeding per vagina, syncope, vomiting and hypovolemic shock depending at the time of diagnosis and hospital admission[12-14]. Ectopic pregnancy is diagnosed by detailed history, proper clinical examination, and investigations such as urine pregnancy test, measurement of serum β-human chorionic gonadotropin level, trans-abdominal as well as trans-vaginal ultrasonography and in doubtful cases offering diagnostic laparoscopy[7,15,16]. Early diagnosis reduces the risk of tubal rupture, morbidity and mortality, allows more conservative management and preserves the future fertility. Management of the ectopic pregnancy is by expectant, medical, and surgical based on the clinical presentation and condition of woman[15,16].

Ectopic pregnancy is an important cause of hospital admission resulting in morbidity and mortality among Bhutanese women. At present there is minimal information on the ectopic pregnancy diseases burden, common risk factors, clinical presentation and management of ectopic pregnancies in our setup and also no data on ectopic pregnancies in the country. This study was undertaken with the aim to report the incidence, presence or absence of common risk factors, clinical presentation and management of ectopic pregnancy admitted in the National referral hospital. This study will help build up strategies for improvement of diagnosis, clinical management and prevention of ectopic pregnancies.

METHODS

Study design and study setting

This was a retrospective descriptive study. The medical record of patients diagnosed with ectopic pregnancy admitted between January 2018 to December 2019 at the National Referral Hospital were retrieved and reviewed. Ethical clearance was sort from Resear Ethics Borad of Health (No REBH/approval/2020/038 dated 05/09/2020).

Data collection

The patient information dating from January 2018 to December 2019 for a period of two years were compiled and organized as per the study objective. All the ectopic pregnancies admitted from 1st January 2018 to 31st December 2019 were included in this study.

Data were extracted from medical records, admission registers, operation theater registers and transferred onto the structured data pro-forma forms. There were a total of 122 ectopic pregnant women admitted and managed in the hospital as per the admission and operation theater registers. We could retrieve only 104 medical records and 18 medical records were not traceable and were missing.

Data entry and Analysis

The collected data were double entered in Epidata and analyzed using Epi-analysis version V2.2.2.182. For categorical variables, data was compiled as frequencies and percentage. For continuous variables, data was calculated as Mean and standard error or standard deviation. Range was also calculated.

RESULTS

Demographic characteristics and Incidence

A total of 9603 pregnant women admitted, of these 122 were ectopic pregnancies. The incidence risk of ectopic pregnancy was 12.7 per 1000 pregnancies at the National Referral Hospital. The mean age of the patient was 29.35 years±.51SE (Standard Error) and majority were in the age group of 21 to 30 years (Table 1). Over20 % of unmarried women and 2% women in live-in relationship had the ectopic pregnancies. About 33% of ectopic pregnancies were in nulliparous women (Table 1).

Risk Factors

Among the seven known risk factors assessed, pelvic inflammatory disease accounted for 41.35 % of the risk factor for ectopic pregnancies followed by previous miscarriage and previous

Table 1. Socio-demographic characteristics of women with ectopic pregnancies at National Referral Hospital, Thimphu, Bhutan in 2018-2019

Characteristics	Frequency	Total
	n (104)	*n* (Percent)
Age group (in years)		
Mean age 29.35, SE (0.511) 95% CI (28.34-30.37)		
Age range (18 – 40 years)		
18-20	5	4.81
21-30	59	56.73
31-40	40	38.46
≥40	0	0.00
Education level		
Graduate/postgraduate	0	0.00
Graduate	12	11.54
Secondary	39	37.50
Primary	44	42.31
Illiterate	9	8.65
Marital status		
Married	78	75.00
Unmarried	21	20.19
Live-in relationship	2	1.92
Divorce	3	2.88
Obstetrics Gravida		
1	34	32.69
2	30	28.85
3	29	27.88
4	8	7.69
5	2	1.92
6	1	0.96

n(%), number and percentage of women.SE = Standard Error, CI= confidence Interval

Table 2. Risk factors of ectopic pregnancies among women at National Referral Hospital, Thimphu, Bhutan in 2018-2019

Risk factors	Frequency	Percent
	n (104)	(%)
Previous ectopic pregnancy	10	9.62
Previous miscarriage	10	9.62
Pelvic inflammatory diseases	43	41.35
Pelvic surgeries	9	8.65
IUD*	1	0.96
Tubal sterilization	1	0.96
Infertility	7	6.73
Ectopic pregnancy without the above risk factors	23	22.12

n(%), number and percentage of women
**IUD Intrauterine devices*

Table 4. Distribution of ectopic pregnancies according to the site at National Referral Hospital, Thimphu, Bhutan in 2018-19

Characteristics	Frequency	Percent
	n (104)	(%)
Types of ectopic pregnancy		
Tubal ectopic pregnancy	98	94.23
Ovarian	3	2.88
Cornual	2	1.92
Cervical	1	0.96
Abdominal	0	0.00
Caesarean scar	0	0.00
Types of tubal ectopic pregnancy	**Frequency**	**Percent**
	n (98)	(%)
Ampullary	49	50.00
Isthmial	16	16.32
Fimbrial	25	25.51
Isthoampullary	8	8.16

n (%), number and percentage of women

ectopic pregnancy. In 22.12% of the ectopic women, none of the seven known risk factors assessed were present (Table 2).

Clinical Presentation

The most common clinical presentations were abdominal pain (94.2%) followed by period of amenorrhea and vaginal bleeding. Nearly 20% presented with symptoms of hypovolemic shock (Table 3). Urine pregnancy test was advised in 101 patients (97.12%). Over 99% ectopic pregnancies were diagnosed by ultrasound scan (Table 3).

Site of ectopic pregnancy

The most common site was tubal (94.23%) and the ampulla was the site mostly involved part of the tubal pregnancy (50%). There

Table 3. Clinical presentations and investigations of women with ectopic pregnancies at National Referral Hospital, Thimphu, Bhutan in 2018-2019

Characteristics	Frequency	Percent
	n (104)	(%)
Clinical presentations		
Period of amenorrhea	74	71.15
Abdominal pain	98	94.23
Vagina bleeding/spotting	71	68.7
Hypovolemic shock	21	20.19
Investigations		
Urine pregnancy test	101	97.12
Serum β hCG test*	85	81.73
Ultrasound	103	99.04

n(%), number and percentage of women
**βhCG Beta human chorionic Gonadotropin*

Table 5. Type of Clinical management of women with ectopic pregnancies at National Referral Hospital, Thimphu, Bhutan in 2018-19

Characteristics	Frequency	Percent
	n	(%)
Type of clinical management		
Expectant	4	3.85
Medical	2	1.92
Surgical	98	94.23
Blood transfusion	54	51.92
Types of surgical management		
Partial Salpingectomy	1	1.02
Total Salpingectomy	86	87.76
Salpingo-opherectomy	9	9.18
Cornual resection	1	1.02
Laparoscopic partial/ total Salpingectomy	1	1.02
Laparoscopic Salpingostomy	0	0.00

n (%), number and percentage of women

was only one case of cervical ectopic pregnancy during this period and was managed medically (Table 4).

Management of patients.

94% of the ectopic pregnancies were offered surgical treatment and only 1% was operated by laparoscope. Nearly 88 % of women had undergone unilateral salpingectomy. Four women with β-hCG level less than 1500 IU/ml and haemodynamically stable were observed and managed expectantly. Four women were managed medically and two women had medical treatment failure and had to undergo surgery. Nearly, 52% of the ectopic pregnancies had blood transfusion (Table 5). There was no maternal mortality.

DISCUSSION

The incidence of ectopic pregnancy was 1.27% or 12.7/1000 pregnancies[17,18]. This incidence is comparable to many of the studies from the developing and developed countries[1,4-8]. The highest frequency of ectopic pregnancies was seen in the age group of 21 to 30 years at 56.73%. In many studies, the peak incidence was seen after 25 years which is similar to this study[1,5-7].

This finding corresponds to the age of peak sexual activity; reproduction and high-risk sexual behavior and among the Bhutanese women could be due to early age of marriage as the mean age of first marriage among Bhutanese women is 22 years[5,7,19].

In this study, 20% of ectopic pregnant women were unmarried, whereas study by Cheng Li reported only 14% and Ranji GG study had only 2% unmarried women[5,10]. This high proportion of ectopic pregnancies among the unmarried women in this study could be attributed to unprotected sexual activities thereby increased risk of sexually transmitted disease and Pelvic inflammatory disease which increases the risk of tubal damage[20]. This gives a strong reason to suspect ectopic pregnancy in a woman of reproductive age group irrespective of marital status.

Some of the risk factors for ectopic pregnancy were previous ectopic pregnancy, miscarriage, pelvic inflammatory disease, pelvis surgeries including caesarean section, and tubal sterilization. Pelvic inflammatory disease was the commonest risk factor (41%) identified among these ectopic pregnant women. This is similar to other studies where pelvic inflammatory disease as risk factor ranges from 15 to 40%[7-10,13, 14]. The higher occurrence of ectopic pregnancy in pelvic inflammatory disease was due to pelvic infections causing pelvic adhesions, mucosa damage and disruption of ciliary action causing implantation at tubal site[11,14]. Future studies need to be carried out to find out the commonest causative organisms for pelvic inflammatory disease and health education on safe sexual practices should be undertaken to prevent ectopic pregnancies among women of these reproductive age group.

In this study 20% had no known risk factors identified, this could be due to subclinical infections or malformation of tubes or other unidentified risk factors and studies had shown that 50% the ectopic pregnancies have no identifiable risk factors[8]. The presence of known risk factors may increase the degree of suspicion, but the absence of these factors does not reduce this risk of ectopic pregnancy. Acute abdominal pain was the most common clinical presentation seen in 95% of the ectopic pregnant women followed by secondary amenorrhea and vaginal bleeding. This finding was similar to other studies[7,8,12,14]. Any woman of reproductive age group irrespective of marital status presenting with acute abdominal pain, ectopic pregnancy needs to be rule out. Nearly one fifth of women were admitted with features of hypovolemic shock which was higher compared to the other study where the percentage was about 8 to 16 % [7, 8]. This was due to ruptured tubal ectopic pregnancies with haemoperitoneum and could be due to late presentation to the hospital due to referral from other health centers and also this study was conducted in the tertiary hospital which is a referral center.

The urine pregnancy test, serum β-human chorionic gonadotropin and ultrasound were the diagnostic tools used for diagnosis of suspected ectopic pregnancy. In this study ultrasound was most popular diagnostic tool used for the diagnosis of ectopic pregnancy as it was done in 99% of the ectopic pregnancies and majority had ruptured tubal pregnancies. Extra uterine gestational sac, hemoperitoneum and adnexal mass were some of the features noted by ultrasound. Data from literature show that ultrasound was able to diagnose 80% to 90% of the cases[5,14].

Women with amenorrhea, vaginal bleeding, and abdominal pain must be subjected to early ultrasonography to confirm the location of pregnancy to prevent late diagnosis. Ultrasonography services is the mainstay for evaluating ectopic pregnancies, therefore, it should be made available in all health centers.

Tubal pregnancy was the commonest type of ectopic pregnancy seen in this study and was probably due to the tubal damage leading to abnormal site implantation. This also explains pelvic inflammatory disease as commonest risk factor identified with ectopic pregnancy causing tubal damage as reported in this study and in numerous other studies[5,7,8,14]. In this study, 84% of tubal ectopic pregnancies had undergone unilateral salpingectomy as a result of ruptured tubal ectopic pregnancies. Therefore, mechanisms to early diagnosis must be emphasized.

Women with ectopic pregnancy were offered expectant, medical and surgical management depending upon the clinical presentation and clinical criteria. The success rate of medical treatment in this study was 50%, which was lower compared to other studies at 65 to 95%[16,21]. This was due to improper selection of the cases. In this study 92.31% of the ectopic pregnancies had surgery done due to ruptured tubal ectopic pregnancies with haemoperitoneum which was similar to many other studies where surgery was done in 86 to 94% of the cases[7,8,14]. Laparoscopic surgical approach is preferable over an open approach considering numerous advantages, such as, shorter hospital stay, less analgesia requirement, reduced morbidity and better future reproductive outcome. In our study only 1% of the ectopic pregnancy had undergone laparoscopic surgeries, compared to most of the studies where 4.2 % to 7% ectopic pregnancies had undergone laparoscopic surgeries due to availability of facilities for laparoscopic surgery and early presentation of patients who were hemodynamically stable[7,8,14,21,22]. This discrepancy with our study was due to late presentation or late diagnosis and also limited exposure of the surgeon to laparoscopic techniques.

There was no maternal mortality due to ectopic pregnancy during this study period.

STRENGTHS AND LIMITATIONS

This was the first hospital-based study conducted on ectopic pregnancies. This study provides base line information like

incidence, risk factors, clinical presentation and management. The study was not without limitations, as the study involved extraction of data from routinely collected clinical records, and not all information could be completely retrieved. In addition, it was not possible to determine the causes of late presentation and number of missed diagnosis.

CONCLUSIONS

Women with past history of pelvic inflammatory disease, previous miscarriage, unmarried, young nulliparous and presenting with history of amenorrhea, abdominal pain, vaginal bleeding in the reproductive age should be considered as a high index of suspicion for ectopic pregnancy. Early diagnosis and intervention in the form of surgical or medical management will reduced the morbidity and mortality due to ectopic pregnancy. Health awareness on diagnosis and prevention of ectopic pregnancies needs to be created among women of reproductive. If ectopic pregnancy is diagnosed early, open surgery can be avoided by offering laparoscopic surgery.

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AUTHORS CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

SG: Concept, design, data collection and analysis, manuscript writing and review.

KT: Concept, Design, data collection and analysis, manuscript writing and review

TC: Design, data collection, manuscript writing and review

KL: Design, data collection, manuscript writing and review

TO: Design, data collection and analysis, manuscript writing and review

Author agree to be accountable for all respects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

None

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