Ectopic Pregnancy : A Prospective Descriptive Study of 376 Cases

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Abstract: *This is a prospective study of 376 consecutive cases of ectopic pregnancies at Chiang Mai University Hospital from June 1988 to August 1992. The incidence was 12.5 per 1,000 live births. Common presenting symptoms were abdominal pain (98.4%), amenorrhea (83%) and vaginal bleeding (67.3%). Pelvic examination revealed enlarged uterus in 47.2%, adnexal mass in 42.2% and bulging cul-de-sac in 47.2%. Urine pregnancy and serum β-hCG tests were positive in 66% and 99.2% respectively.*

The most common site of tubal pregnancy was ampulla, followed by isthmus, fimbria and interstitial. Tubal rupture was found in 52%. More than half had normal pelvis; 31.7% had peritubal or pelvic adhesion. Salpingectomy was performed in 76.6% and salpingo-oophorectomy in 10%. Incidental appendectomy was done in 27.9% without any increase in morbidity. Literature on ectopic pregnancies was briefly reviewed. (Thai J Obstet Gynaecol 1995;7:95-104)

Short title: Prospective study of ectopic pregnancy.

Key words: ectopic pregnancy, signs and symptoms, incidental appendectomy.

Ectopic pregnancy is a life-threatening condition, that may cause maternal mortality and compromise future fertility. Its incidence has been increasing during the past decade and may be related to the rising incidence of pelvic inflammatory diseases, liberal use of tuboplasty, or the dramatic improvement in modern diagnostic measures such as laparoscopy, sensitive β-hCG and ultrasonographic technique.[1] Many previous studies on ectopic pregnancy were done by retrospective review of available medical records. Thus the data was, incomplete. In this report, we conducted

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a prospective descriptive study of ectopic pregnancy pattern in our university hospital in Northern Thailand.

Materials and Methods

Three hundred and seventy six consecutive patients who were confirmed surgically and pathologically as having ectopic pregnancies at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand, were interviewed during their postoperative hospitalization from June 1, 1988 to August 31, 1992. Information was obtained on patients' presenting signs and symptoms, contraceptive practices, past obstetrical, gynecological, medical and surgical history. Findings on general physical examination and pelvic examination as well as results from laboratory investigations, ultrasound reports, operative findings, and operative procedures were recorded on a standardized form. Further information, if needed, was obtained by direct contact with surgeons who performed the operations. All information was obtained as soon as possible in the immediate post operative period (within 24-72 hours after surgery) when both the patients and surgeons still have a fresh memory of the episodes. All patients' records were collected and reviewed by the investigators.

Statistical analyses were performed with two tailed t-test, chi-square and Fisher's exact tests where appropriate. For all analyses statistical significance was assumed at the $p < 0.05$ level.

Results

During the four year period from June 1, 1988 to August 31, 1992 we had 30,080 deliveries and altogether 376 cases of ectopic pregnancy, giving an overall incidence of 12.5 ectopic pregnancies per 1,000 deliveries. The yearly incidences were 10.62, 9.39, 15.68 and 13.48 per 1,000 deliveries respectively. The mean age of the patients (± SD) was 28.2 ± 5.2 years (range 16-41 years). Most of them

Table 1 *Occupation of patients*

Occupation	No.	(%)
Employees	147	(39.1%)
Farmers	75	(20.0%)
Merchants	58	(15.4%)
Housewives	46	(12.2%)
Civil servants	32	(8.5%)
Students	16	(4.3%)
Prostitutes	2	(0.5%)
Total	376	(100)

were employees or farmers (Table 1).

Ninety two per cent were married, 7.4% were single and 0.6% were divorced. Twenty two per cent of patients reported of having multiple sexual partners. Their mean duration of sexual exposure before the occurrence of ectopic pregnancies was 6.1 ± 5.2 years. Nearly half (47.7%) were primigravidas, 33.6% were second gravidas and 14.1% were having their third pregnancies when the ectopic pregnancy occurred. One hundred and thirty six cases (36.2%) had one or more previous abortion, of which 54 cases were induced abortions. The methods of induced abortions commonly used were dilatation and curettage and menstrual extraction (Table 2)

Table 2 ***Methods of induced abortions***

Methods	No.	(%)
Dilatation and curettage	18	33.3
Menstrual extraction	17	31.5
Forceful uterine massage	6	11.1
Oral medication	4	7.4
Injectable medication	3	5.5
Hypertonic saline	1	1.9
Combination of 2 above methods	2	3.7
Unknown	3	5.6
Total	54	100.0

Sixty one cases (16.2%) had a history of salpingitis, 74 cases (19.7%) had previous pelvic operation and 28 cases (7.4%) had one or more previous ectopic pregnancy. Two cases of ectopic pregnancy in this study resulted from in vitro fertilization and embryo transfer (IVF & ET). The majority of cases (73.3%) were not currently using any contraceptive methods and, in fact, 39.3% of them had been Attempted to conceive for more than one year. Those who practised contraception (26.7%) were using the following methods : combined pills (41 cases), tubal sterilization (16 cases), condom (12 cases), postcoital pills (11 cases), IUDs (10 cases), DMPA (7 cases) and rhythm method (3 cases).

Symptoms and signs: The presenting symptoms and signs are shown in Table 3.

Abdominal pain was experienced in almost all cases. The pain was unilateral in 60.4% of cases, bilateral in 29.5%, localized in the lower midline in 9.8% and epigastric in location in 0.3%. The pain was found to be on the same sides with ectopic pregnancies in 91.6% of patients and on the contralateral sides in 8.4%. The majority of them also

Table 3 ***Presenting symptoms and signs****

	No./Total cases	Percentages
Symptoms		
Abdominal pain	369/375	98.4
Amenorrhea 308/371	83.0	
Vaginal bleeding	253/376	67.3
Symptoms of pregnancy	182/374	48.7
Fainting or syncope	175/375	46.7
Symptoms of shock	106/376	28.2
Shoulder pain	79.371	21.3
Signs		
Fever > 37.5 c	33/376	8.8
Palpable adnexal mass	158.374	42.2
Uterus: Normal size	191.362	52.8
Enlarged	171.362	47.2
Cul-de-sac: Normal	191.362	52.8
Bulging	171.362	47.2

* Data missing in some cases for the following reasons: one hilltribe patient could not communicate in Tahi, some patients were unsure or gave equivocal responses when asked about certain symptoms, some pelvic findings such as uterine size and bulging of cul-de-sac were difficult to assess in some cases.

had amenorrhea, with a mean duration (± SD) of 59 ± 21.4 days. Shoulder pain was reported in only one fifth of patients, of these 51.9% were bilateral.

Laboratory findings: Urine pregnancy test using latex agglutination inhibition (Planosec, Organon, sensitivity 2,000 IU/L 1st IRP) was done in 256 out of the 376 patients, with positive results in 169 cases (66%). Serum β-hCG (radioimmunoassay method, sensitivity 5 IU/L, 1st IRP) was performed in 258 cases, with positive results in 256 (99.2%). In the two cases with negative results, pathological reports described exhausted villi. Initial hemoglobin levels were below 10 g/dl in 29.5% of patients ; low hemoglobin levels were seen more often in patients with ruptured ectopic pregnancy (42.6%) than in the group with unruptured ectopic pregnancy (16.5%). In this study, leukocytosis (defined as white cell count > 10,000/ml.) was noted in 57.6% of patients.

Culdocentesis : needle aspiration of blood from cul-de-sac was done in 250 patients, yielding non clotted blood (positive culdocentesis) in 234 (93.6%). Dry tap (no blood or fluid) was obtained in 15 cases (6%). In one case with abdominal pregnancy, clotted blood was obtained, presumably from aspiration of blood from the placental site. Culdocentesis was positive in 134 out of 140 cases with bulging cul-de-sac, which was not

significantly different from 94 out of 103 patients who were recorded as having normal cul-de-sac on initial pelvic examination (status of cul-de-sac was not recorded in 6 cases with positive culdocentesis). The least amount of hemoperitoneum that could give a positive culdocentesis in this study was 30 ml. On the contrary, six out of 91 cases (6.6%), who had culdocentesis performed and were later found to have > 1,000 ml of blood in the peritoneal cavity, were reported to have dry tap.

Laparoscopy : Diagnostic laparoscopy was performed in 34 out of 376 cases (9%). Because of its invasive nature, the procedure was done only in selected cases with minimal signs and symptoms. Laparoscopy confirmed the presence of ectopic pregnancy in 29 cases (85.3%). In three patients (8.8%), the diagnosis was missed and in the other two patients (5.9%) laparoscopy was not helpful because visualization of adnexal structures was not possible due to marked pelvic adhesion.

Ultrasonography : Pelvic ultrasonography is a non invasive diagnostic tool and was, therefore, liberally performed in 166 out of 376 cases (44.1%) in this study. It confirmed the diagnosis of ectopic pregnancy in 156 cases (94%). Ectopic pregnancy was missed in 10 cases, who were incorrectly diagnosed as follows ovarian cysts (3 cases), tubo-ovarian abscess (3 cases), normal pelvic organ (1 case), intrauterine pregnancy (1 case), incomplete abortion (1 case) and missed abortion (1 case).

Ultrasonography revealed the presence of adnexal masses in 84.5%, pseudosac in uterine cavity in 7.2%, free fluid in cul-de-sac in 76.9%. Uterus was noted to be normal in 69.8%

Operative findings : Laparotomy was performed in all patients. The location of ectopic pregnancies was as follows tubal 366 cases, ovarian 1 case, abdominal 3 cases, rudimentary horn 3 cases and unknown in 3 cases (conceptive products were seen intra-abdominally at operation and it was not possible to identify the primary sites, gestational ages of these three cases were 34, 75 and 105 days from the first days of the last menstrual periods respectively). Tubal pregnancy occurred on the right side in 187 patients (51.1%) and on the left side in 179 (48.9%). Tubal pregnancy was located most commonly in the ampulla (64.1%), followed by isthmus (21.3%), fimbria (12.3%) and interstitial (2.3%) respectively. The average dimeter (± S.D.) of tubal gestation was 3.5 ± 1.8 cm. Rupture of tubal pregnancy was seen at the time of operation in 196 cases (53.6%). The percentage of patients with ruptured tubal pregnancy remained relatively constant over the five-year period in this study (55.3%, 60%, 51.9%, 50% and 47% respectively), Corpus luteum was noted to be present in 210 out of 376 cases (55.9%). Their location was on the same side as ectopic gestation

in 69.5% and on the contralateral side in 30.5%

There was no other pelvic pathology in 198 patients (52.7%) with ectopic pregnancy. Peritubal adhesion was seen in 56 cases (14.9%); pelvic adhesion in 63 cases (16.8), ovarian cysts in 23 cases (6.1%), pelvic endometriosis in 5 cases (1.3%) and myoma uteri in 3 cases (0.8%)

Operative procedures : The most common operation was unilateral salpingectomy (76.6%), followed by unilateral salpingo-oophorectomy (10.1%), salpingotomy (7.4%), hysterectomy (2.1%) and miscellaneous i.e. removal of abdominal pregnancy, ovarian wedge resection, etc ; in 3.8%). Incidental appendectomy was performed in 105 cases (27.9%). When compared with patients who did not have incidental appendectomy, we found that operative time was significantly longer in the group with incidental appendectomy (79.4 ± 27.9 minutes vs 61.8 ± 20.7 minutes, $p < 0.001$, t-test), but there was no difference in febrile morbidity ($p = 0.237$, Chisquare test) or wound infection rates ($p = 0.4265$, Fisher's exact test) among the two groups. The overall mean operative time (± S.D) was 70.2 ± 26.4 minutes. There were 191 (50.8%) patients who required blood transfusion for an average volume (± S.D.) of 977.1 ± 511.2 ml.

There were six patients (1.6%) who had wound infection. Urinary tract infection occurred in 1 case. Thrombocytopenia was diagnosed in 1 patient, who had ruptured uterine horn and required 8 units of blood transfusion. There was no maternal mortality in this study.

Discussion

The incidence of ectopic pregnancy can be calculated in at least three different ways.[2] First, one can use reproductive age women (15-44 yars old) as the denominator but such calculation will be less helpful in determining risk factors because women are included regardless of their sexual exposures.[3] Total pregnancies can also be used as the denominator and, as such, will theoretically reflect the true proportion of pregnancies that are ectopic in location. In practice, however, spontaneous and illegal abortions are usually under reported and will, therefore, result in an over estimation of ectopic pregnancy rate. In this study, we calculated the incidence of ectopic pregnancy by using live-birth as the denominator. This has the advantage in that it allows us to compare our data with that reported from other hospitals.

Our data agreed with other reports[4-7] in that ectopic pregnancy can occur in any woman of reproductive age and that it shoud be suspected in patients with a history of infertility, preious abortion or previous ectopic pregnancy, previous history of plevic inflammatory disease, tuboplasty or other pelvic operations. It is interesting to note that 26.7% of ectopic pregnancy

in our study occurred in women who were practising contraception. Of these, 59% were using hormonal contraception, 16% were cases of sterilization failure and 10% were IUD failures. It has been hypothesized that progesterone in contraceptive pills can inhibit oviductal propulsion at the ampullary isthmic junction and, therefore, ovum trapping may result.[8] According to Tatum and Schmidt,[9] the incidence of ectopic pregnancy after elective tubal sterilization is approximately 16%. It may result from the development of tuboperitoneal fistula after failure of sterilization, allowing sperm to pass into the distal segment of the oviduct and fertilize the egg. Ory,[10] in a collaborative multicenter case-control study of the incidence of ectopic pregnancy in the United States from 1965 through 1977, showed that IUD did not play a significant role in the increased incidence of ectopic pregnancy. However, pregnancy during IUD wearing was more likely to cause tubal pregnancy because IUD acted preferentially to impair intrauterine implantation.

Like other studies,[4,11] the most common presenting symptoms in our patients were pain, amenorrhea and vaginal bleeding. Other significant clues for diagnosis included symptoms of pregnancy, fainting or syncope and palpable adnexal mass. Urine pregnancy (latex hemagglutination inhibition) test is imprecise and gives a positive result in only 66% of patients with ectopic pregnancy. This is so because the hCG level in ectopic pregnancy is often lower than the sensitivity of conventional urine pregnancy tests. The current availability of a very sensitive and accurate serum pregnancy test has resulted in an increased use of this method in the detection of ectopic pregnancy. In our hands, serum β-hCG a sensitivity of 10 mIU/ml is almost always (99.2%) positive, which agrees with the experience of others.[8,12]

Romero et al[13] reported positive culdocentesis in 83.5% of patients with ectopic pregnancy. The present study gives a higher positive rate of 94% and confirms that culdocentesis is a valuable diagnostic procedure despite its invasive nature. We feel that a positive culdocentesis in conjunction with a clinical history and physical examination suggestive of ectopic pregnancy warrants an immediate laparotomy.

Pelvic ultrasound is a noninvasive procedure that is helpful in localizing the site of pregnancy. The use of β-hCG combined with endovaginal ultrasound will assist the physician in making an early diagnosis of this condition.[14,15] Laparoscopy is useful in suspected cases of unruptred ectopic pregnancy, who have minimal signs and symptoms. It allows precise visualization of the entire female reproductive tract and has limited the need for laparotomy.[8] Nevertheless, laparoscopy has limitation in cases where adnexal pathology is obscured by marked pelvic adhesion as were

seen in 5.9% of our patients. In three cases, no lesion was seen during laparoscopy, presumably due to the small size of very early ectopic gestations and the relative inexperience of the involved laparoscopist.

As in other studies,[1-4,8,11] tubal pregnancy is the most common type of ectopic pregnancy ; the most common site of which is located in the ampullar part, followed by the isthmic, fimbria and interstitial part respectively. Despite the availability of sensitive β-hCG test and vaginal ultrasound in our institution, the incidence of ruptured tubal pregnancy was still very high. This may be due to the fact that many patients were misdiagnosed and had been treated elsewhere, by local practitioners and traditional healers, without improvement before they were referred to out center.

Insunza et al.[16] reported that about one in every four tubal pregnancies, the corpus luteum is on the opposite ovary, which agrees well with our data (30.5%). This finding supports the theory of transperitoneal migration of fertilized ovum.[17]

Although many options exist, operative measure is still the milestone of treatment for ectopic pregnancy. In our report, salpingectomy was the treatment of choice for most cases of tubal pregnancy. Salpingotomy was done in selected cases with small, unruptured tubal pregnancy, in whom clinical condition was stable and future fertility was desired. However, some authorities[18-19] would advocate medical treatment with either methotrexate or RU-486 rather than surgery for such patients. Recently, laparoscopic surgery has been introduced for both conservative and radical treatment of ectopic pregnancy with very good results.[20-21] Unfortunately, facilities for operative laparoscopy were not available in our hospital at the time of this study.

There is no concensus regarding incidental appendectomy at the time of surgery for ectopic pregnancy. According to a recent ACOG Technical Bulletin,[22] incidental appendectomy is not advised and any ancillary surgical procedures should best be limited to simple lysis of adhesion. The primary concern is that bacterial contamination of tubal wound and free blood in the peritoneal cavity can occur during appendectomy. Thompson[23] believes that the prognosis for subsequent pregnancy is so dismal after operation for ectopic pregnancy that any additional insult such as elective appendectomy should be avoided. On the contrary, many studies[23-26] demonstrate that incidental appendectomy at surgery for ectopic pregnancy does not place the patients at increased operative risk and even spares them from the possible subsequent development of acute appendicitis. Our study also reveals that the added procedure carries no increased risk in morbidity or mortality rates. However, to maintain this low level of risk, incidental appendectomy should only be done when the patient's condition

is satisfactorily near the end of the operation and the appendix is easily located and accessible.

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