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Research Article

Ectopic pregnancy: a cause for maternal morbidity

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ABSTRACT

Background: Despite the scientific and technological advances maternal morbidity and mortality continue to occur across the globe with regional variation. Ectopic pregnancy is one such cause which contributes to devastating fate of pregnant ladies. Over a period of time there have been variations in the incidence, cause, clinical presentation and management of ectopic pregnancy. The objective is to observe variations with respect to incidence, cause, clinical presentation and management of ectopic pregnancy

Methods: The present study was a 1year prospective and 1 year retrospective study from Dec 2012 to Nov 2014 at a tertiary medical college in Karnataka. All diagnosed cases of ectopic pregnancy were enrolled in the study. Statistical methods employed in the present study were contingency table, chi-square test and contingency coefficient analysis (cross tabs procedure).

Results: 38 cases were studied during two year period out of which 94.8% were tubal pregnancies, 2.6% each were cervical pregnancy and pregnancy in the rudimentary horn of the uterus. Maximum incidence of tubal gestation was noticed between the age group of 21-30 years (60.1%). 55.2% were nulliparous and 29% were multiparas. Commonest mode of termination was rupture in 57.9% of the cases; tubal abortion was seen with haemoperitoneum in 26.3% of the cases.

Conclusions: Ectopic pregnancy remains a significant gynaecologic emergency, delay in diagnosis and treatment can be catastrophic, but early diagnosis and timely treatment can virtually eliminate need for surgical intervention.

Keywords: Ectopic, Pregnancy, Tubal

INTRODUCTION

Having an uneventful reproductive life is a blessing for any lady. Ectopic pregnancy is implantation of the fertilized zygote anywhere other than in the uterine cavity. It was first recognized by Busiere in 1693, when he was examining the body of a prisoner executed in Paris.¹ Lawson Tait first performed the documented operation for ruptured tubal pregnancy in 1884.² Tanaka and colleagues reported the first use of systemic methotrexate for an ectopic pregnancy in 1982.¹ Expectant management of ectopic pregnancy was extensively studied by Fernandez and associates in 1988.³ The management of ectopic pregnancy has changed over

the last two decades. In line with this shift in practice, there has been a fourfold decrease in the mortality rate; although the incidence of ectopic pregnancy has increased twofold over the last 25 years.⁴ Complacency would be inappropriate, however, because ectopic pregnancy remains the leading cause of maternal death in early pregnancy.⁵

METHODS

This study was undertaken at a tertiary care hospital in Southern India between December 2012 and November 2014. Total number of deliveries during the study period was 2681, live births were 2671 and we had 38 cases of

ectopic pregnancy, giving an occurrence of 1.4/1000 deliveries. All women in reproductive age group (15-45 years) presenting with a missed period, vaginal bleed or pelvic cramping, currently pregnant based on urinary or serum β -hCG level and excluding intrauterine pregnancy, were included in the study. Statistical methods employed in the present study were contingency table analysis, chi-square test and contingency coefficient analysis (cross tabs procedure).

All patients were evaluated with necessary investigations, sample of blood drawn for grouping and cross-matching to arrange for blood transfusion when needed. In acute cases with typical features of amenorrhoea, pain and bleeding the diagnosis was confirmed by ultrasonography, followed by laparotomy. Patients in shock were treated and taken up for surgery. In cases with doubtful diagnosis, patients were observed after hospitalization and laparotomy done subsequently, if necessary.

Patients who met the criteria for medical management (haemodynamically stable with the ectopic gestational sac of less than or equal to 3.5 cm with no cardiac activity, with normal blood count, normal results of liver and renal function test) were administered a single dose of 50 mg/m² of intramuscular methotrexate and followed up with serial serum β -hCG on day 1, 4 and 7 and ultrasonography. All the surgical interventions were performed under general anaesthesia, laparotomy or laparoscopy as the condition necessitated.

RESULTS

There were 38 cases of ectopic pregnancy during the two year study period against 2681 deliveries with the incidence of 1.4%. 23 were in the age group of 21-30 years (60.5%). Nulliparous women constituted 21 (55.1%) of these women and in twelve of them this was the first conception. Infertile women were 8 (21.1%) followed by those who had previous abortions 4 (10.5%) (Table 1). Multiple risk factors contributing in 4 (10.5%) (Figure 1). The typical triad of amenorrhoea, pain abdomen and bleeding was observed in 42.1% of the cases. Amenorrhoea and pain abdomen were the most

significant symptoms in 81.6% of cases. Other symptoms were either urinary disturbances or gastrointestinal (34%). The patients with ampullary pregnancy had typical triad of symptoms. Infundibular pregnancies had pain abdomen as main complaint. Undetermined cases had amenorrhoea as the major complaint (Table 2).

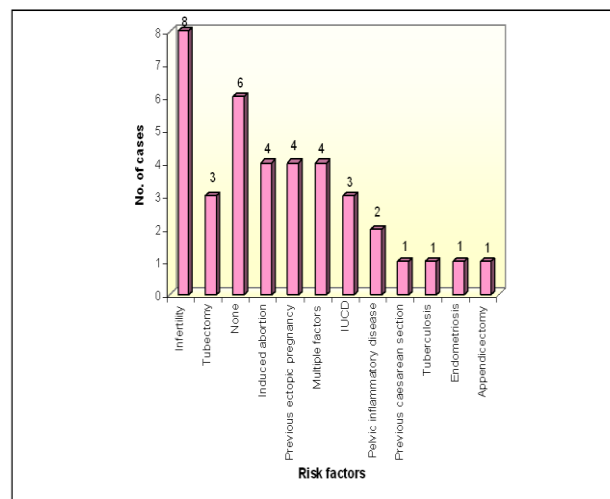


Figure 1: Risk factors in ectopic pregnancy.

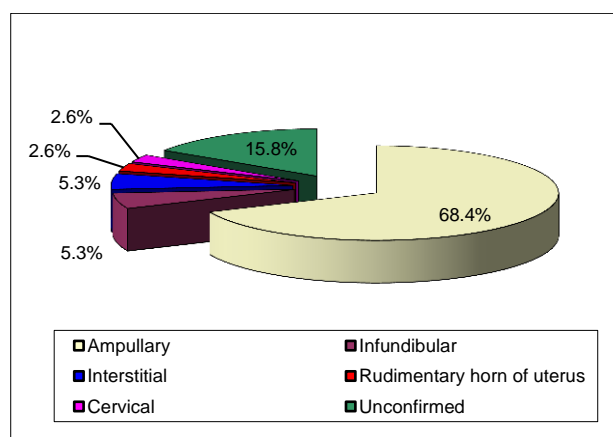


Figure 2: Site of ectopic pregnancy at treatment.

Table 1: Correlation of sample by age and parity.

Age group (years)	Parity				Total
	0	1	2	3	
15-20	4 (80.0%)	1 (20.0%)	-	-	5 (100.0%)
21-25	10 (83.3%)	2 (16.7%)	-	-	12 (100.0%)
26-30	6 (54.5%)	2 (18.2%)	2 (18.2%)	1 (9.1%)	11 (100.0%)
31-35	1 (14.2%)	1 (14.2%)	3 (42.9%)	2 (29.7%)	7 (100.0%)
36-40	-	-	-	2 (100.0%)	2 (100.0%)
41-45	-	-	1 (100.0%)	-	1 (100.0%)
Total	21 (55.2%)	6 (15.8%)	6 (15.8%)	5 (13.2%)	38 (100.0%)

$\chi^2 = 30.087, p = 0.012 (S)$

Table 2: Distribution of sample by site of ectopic pregnancy and mode of presentation.

Site	Mode of presentation			
	Amenorrhoea	Pain abdomen	Bleeding	Others
Ampullary	19 (13.1%)	20 (32.8%)	18 (29.5%)	4 (6.5%)
Infundibular	1 (16.7%)	3 (50.0%)	2 (33.3%)	-
Interstitial	2 (50.0%)	-	2 (50.0%)	-
Rudimentary horn	1 (50.0%)	-	-	1 (50.0%)
Cervical	1 (50.0%)	-	1 (50.0%)	-
Undetermined	6 (42.8%)	4 (28.6%)	4 (28.6%)	-

$\chi^2 = 14.757$, $p = 0.469$ (NS)

Out of 38 patients, four were admitted in a state of shock, of which 3 had ruptured, ectopic, one had tubal abortion and one had rudimentary horn rupture. Pallor was significantly seen in 47.6% of the cases. 60.8% and 57.1% of ruptured ectopic and tubal abortion cases respectively presented with pallor. Blood transfusion was required in 57.9% of patients and more than three units transfusion was necessitated in 10.5% of the patients.

Table 3: Distribution based on details of management.

Management detail	No. of cases	Percentage
Unilateral salpingectomy	18	47.3
Salpingectomy with contralateral segmental resection of tube	1	2.6
Laparoscopy unilateral salpingectomy	3	7.9
Salpingostomy	2	5.3
Suction evacuation	1	2.6
Unilateral salpingectomy with ovarian cystectomy	2	5.3
Rudimentary horn excision with unilateral salpingectomy	1	2.6
Cornual repair	1	2.6
Medical management with methotrexate	6	15.8
Bilateral salpingectomy	1	2.6
Unilateral salpingo-oophorectomy	1	2.6
Hemoperitoneum evacuation	1	2.6
Total	36	100.0

$\chi^2 = 58.591$, $p = 0.000$ (HS)

Tenderness was significantly present in 81.5% of the cases. Distension and guarding were seen in about one third of the sample population. 15.8% of the patients were asymptomatic. At the time of treatment patient who had ruptured ectopic presented with typical symptomatic triad, whereas majority of patients with tubal abortion presented with pain abdomen. Patients with unruptured ectopic had different complaints in differing proportions. 65.8% of the cases had forniceal tenderness. Mass felt in

the fornix was significantly less. Tenderness on abdominal examination was elicited in 54% of ampullary, 50% of interstitial pregnancy significantly, while distension and guarding were observed in infundibular pregnancy. However, 13.4% of ampullary pregnancies and all of the ectopic gestation of unconfirmed site had no positive abdominal findings. Unconfirmed site of ectopic pregnancies have been presumed to be tubal ectopic pregnancies as suggested by ultrasonography. On abdominal examination, tenderness was commonly present in ruptured, unruptured and tubal abortions. But distension and guarding were exclusively present in ruptured ectopic gestation and in tubal abortions. 52.6% of patients had bleeding per vaginum on speculum examination, most of which were seen in ruptured ectopic gestation and tubal abortions. Most of the cases had normal uterine size, however six cases had enlarged uterus. Cervical movements are painful in 57.9% of the patients which with the history and typical triad of symptoms was of utmost help in arriving at the correct clinical diagnosis of ectopic gestation. Urine pregnancy test, the simple test relied on in diagnosing the pregnancy status had a positive predictive value of 0.95. In the present study, ectopic pregnancy was common on the right side.

Management of the cases was mainly surgical, followed by medical line of treatment. In case of ruptured tubal ectopic, decision for unilateral salpingectomy was made. Salpingectomy was considered in those who did not wish to conceive. The opposite site adnexa was conserved/salvaged based on the status of health of the tube. Those with medical management conservative procedure were advised for weekly follow up with β -hCG titre until it was <15 mIU/ml (Table 3).

DISCUSSION

The occurrence of ectopic pregnancy in the present study was 1.4 per 1000 deliveries. This study shows an increase in the incidence over the past one year to the current year. The incidence of ectopic pregnancy in various studies was 1.7%⁶, 1.5%⁷ and in the present study 1.5%. The rising incidence may be due to the increased incidence of sexually transmitted disease. This may also be due to the better diagnostic modalities available and heightened awareness.⁸ Majority of the cases belonged to 21-30 years

of age, but ectopic pregnancy can occur anytime in the reproductive age group. In the present study, maximum occurrence of ectopic gestation was seen in nulliparous. Some studies showed no specific relation to parity,⁹ but few reported that there is a decrease in the incidence of ectopic pregnancy with rising parity.⁷ In the ICMR multicentric case control study of ectopic pregnancy, majority of women were young and had low parity.¹⁰ In the present study, period of infertility ranged from 2 years to 9 years giving rise to 21% of the ectopic pregnancy. Significant incidence of prolonged infertility and its causal relationship to ectopic pregnancy has been observed by various authors. According to March Bank et al,¹¹ Savitha Devi et al⁶ and Rose et al.⁷ Positive history of infertility was reported as 2.9%, 48.07% and 15.1%.^{8,9,11} Infectious disease has been an associated risk factor with variable magnitude in different studies.^{8,9,11,12} PID following *Gonococcal*, *Chlamydial* and other bacterial infection contribute to four fold increased risk of ectopic pregnancy. Relative risk as per ICMR multicentric case control study was 6.4. Many cases of *Chlamydial salpingitis* are indolent, may go unrecognized causing tubal damage and subsequent tubal pregnancy. A strong association has been incriminated between chlamydia infection tests for ectopic gestation.¹³ History of abortion in the past 2 years was obtained in 10.5% of the cases. Tubal damage or dysfunction following the previous abortion appears to be a factor in some cases.⁷ 10.5% of the cases in present series have had previous ectopic gestation. Recurrent ectopic has been reported in various studies ranging between 3.2% to 20%. The risk of recurrent ectopic pregnancy was increasingly noted with history of surgery, history of live birth, and history of spontaneous miscarriage and not with a history of gonorrhoea, chlamydia, pelvic inflammatory disease, caesarean section, or pregnancy termination. In our study, there were 7 patients with previous abdominal operations, 3 of which was tubal ligation (7.9%), 2 were for ectopic gestation (5.4%), 1 was appendectomy (2.6%) and one was caesarean section (2.6%). In the current series, 7.9% of the patients used IUCD. March Banks quoted an incidence of 1.6% for ectopic pregnancy in patients using progestin only contraceptive. IUCD association was noted in 11.9%, 7.69% of ectopic pregnancy.^{6,11} Multiple factors like infertility previous abortions, malformation of uterus and previous ectopic were noticed in 10.5% of our cases. One case of tuberculosis (2.6%) on treatment was noted. Rose et al have reported tuberculosis as 3.2% of risk factors in their study. However, none of the risk factors could be associated in 15.9% of the patient in the present study. Rose et al reported no risk factors associated in 32.2%.

Most of the symptoms and signs were produced by ruptured ectopic pregnancies or by tubal abortion with haemorrhage into the peritoneal cavity. The typical triad of amenorrhoea, pain abdomen and bleeding was noticed in 42.1% of the current study. The incidence of the same seen in other studies was 66.0% and 35.2% respectively.^{7,15} None of the symptoms and signs is

specifically pathognomonic of ectopic pregnancy, but combination of various findings is slightly suggestive of the condition. Presence of shock was seen in 9.5% of the patients. 9.7% of the cases series have said to have presented in shock.⁷ More acute the condition, more clear is the clinical picture. Therefore, undisturbed ectopic gestation is likely to be missed in most of the cases because of vague clinical features. Acute pain in the lower abdomen was the common presenting features in 81.6% of the cases with 40% of tubal rupture cases. Pain was absent in 24.2% of the patients may be due to the undisturbed ectopic or individual difference in the pain threshold. Amenorrhoea was present in 81.6% of the cases which is comparable to those reports of an incidence of 78.5% and 73% in their study.^{7,15} Absence of amenorrhoea in 23% of their cases was as conspicuous as 21% in the current study. Comparable reports of symptoms and signs of ectopic pregnancy in various studies are represented in the table below (Table 4). Vaginal bleeding of different patterns was noticed in 60.5% of the cases which was comparable to other studies. Other symptoms were giddiness in 7.3%, retention of urine in 2.6% of the patients, nausea and vomiting in 6 patients (15.7%), loose stools in 2.6% and dysuria in 6 patients (15.7%). Oumachigui reported shoulder pain in 8%, fainting attacks in 18%, vomiting in 31% and urinary symptoms in 12.5%. The classical sign of cervical movement tenderness was present in 57.9% of the patients. Ectopic nidation outside the fallopian tube is rare, 2.6% cervical in the present study and 2.6% in the rudimentary horn of uterus. A case series reported 1.4% of abdominal, 0.15% of ovarian and 0.15% cervical pregnancies. Bouyer et al¹⁶ reported 95% of tubal pregnancies in their study, others being ovarian (3.2%), abdominal (1.3%) and cervical (<1%). It's been shown in an original study that 66% of the cases were diagnosed by ultrasonography as a complex adnexal mass and free fluid of 62%.⁷ But, on laparotomy haemoperitoneum was reported in 88% of the patients. In the present study 73.7% of the cases had haemoperitoneum with 57.9% of ruptured ectopic and 15.8% of the cases with tubal abortion. Since majority of our patients were referred from outside with established signs of ruptured ectopic pregnancy, they needed surgical radical approach as treatment. However, those diagnosed at an earlier period (15.8%) with conditions having met were treated by medical management with single dose of methotrexate administration systemically. 10.6% of them were treated conservatively surgically. Gupta et al reported 1% of medical management in their series. However 1 of the 6 patients treated by medical methotrexate administration was failure as an immediate outcome. One more patient had recurrent ectopic on the same side after 10 months of previous treatment. When appropriately selected non-surgical treatment is an effective and safe alternative to surgical method for unruptured ectopic pregnancy, more so important for nontubal ectopic pregnancies: interstitial, cervical and caesarean section scar pregnancies. Currently the initial human chorionic gonadotropin level probably remains the single most important predictor of

success.¹⁷ Concern for long-term reproductive performance should not be a factor in selecting between any of these four commonly used treatments for unruptured ectopic pregnancy.¹⁸ There was one post-operative morbidity with the wound infection. She was treated and discharged in good condition later on. Blood transfusion was necessitated in 57.9% of the patients intraoperatively and or post operatively.

Table 4: Risk factors for ectopic pregnancy.

Risk factor	March Banks et al ¹¹	Savitha Devi et al ⁶	Rose et al ⁷	Present study
None	-	-	32.2%	15.9%
OCP	1.6%	-	-	-
Tubectomy	5.6%	13.4%	5.4%	7.9%
Induced abortion	2.5%	1.9%	45.1%	10.5%
IUCD	11.9%	4.69%	21.5%	7.9%
Previous ectopic	-	-	3.2%	10.5%
Infertility	2.9%	48.0%	15.1%	21.0%
Multiple factors	-	-	-	10.5%
Appendicectomy	-	-	-	2.6%
Prior caesarean	-	-	7.5%	2.6%
PID	4%	25%	34.4%	5.4%
Tuberculosis	-	-	3.2%	2.6%
Endometriosis	-	-	-	2.6%

CONCLUSIONS

While there is an increased incidence of ectopic pregnancy, mortality has dropped precipitously because of improved diagnostic and management modalities. Diagnosis rests on maintaining a high suspicion for women with symptomatic complaints in the first trimester or women without complaints but with risk factors. Most of our patients had surgical emergencies, as they were brought late with established diagnosis of ruptured ectopic pregnancies. Few of the patients diagnosed at earlier stage were given medical therapy. Ectopic pregnancy remains a significant gynaecologic emergency, delay in diagnosis and treatment can be catastrophic, but early diagnosis and timely treatment can virtually eliminate need for surgical intervention.

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