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Clinical study of ectopic pregnancy in a tertiary care centre in Andhra Pradesh

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Abstract
Background: If not detected early, ectopic pregnancy can result in a gynaecological emergency with significant abdominal bleeding, hypovolemic shock, and maternal death. The main objectives of this study are to find out the incidence of ectopic pregnancy, demographic profile of the women, risk factors and to study the clinical presentation, treatment modalities and outcome in our hospital.
Methods: This prospective observational study was conducted in the department of obstetrics and Gynaecology, at a tertiary care centre, Andhra Pradesh from January 2021 to December 2022. A total of 62 cases of ectopic pregnancy were analysed for parameters like demographic characteristics, gravidity, risk factors, clinical presentation, treatment modalities and outcome.
Results: The incidence of ectopic pregnancy in present study was 9.7 per thousand deliveries. Majority of cases belonged to age group of 21-25 years (67.7%) and were gravida 3 and above (49.1%). Commonest risk factors identified were tubal ligation (29%) and history of previous abortions (19.3%). The frequent presenting symptoms were abdominal pain (87%) and amenorrhea (38.7%). Most of the patients required surgical management (91.9%), medical management was done in 4 cases and expectant management was done in 1 case. Tubal ectopic pregnancy (87%) is more common. Anaemia was seen in 64.5% of cases that required multiple blood transfusions (72.5%) for resuscitation. There was no maternal mortality in the current study.
Conclusions: Ectopic pregnancy is an emergency in which timely intervention will reduce the maternal morbidity and mortality. Clinical presentation varies from case to case and still there is a chance of missing the diagnosis in a small proportion of patients even with the availability of advanced imaging techniques. For early diagnosis a clinician should be aware about the various presentations and associated risk factors of ectopic pregnancy.

Keywords: Ectopic pregnancy, hemoperitoneum, risk factors, expectant management

Introduction

In ectopic pregnancy the fertilized ovum implants outside the endometrial cavity of the uterus. In the first trimester of pregnancy, rupture ectopic pregnancy continues to be the leading cause of maternal death [1].

If not detected early, it can result in a gynaecological emergency with significant abdominal bleeding, hypovolemic shock, and maternal death [2]. Most hospital-based research in developing nations have found that ectopic pregnancy case-fatality rates range from 1% to 3%, which is ten times greater than that seen in developed nations [3].

The main causes of these deaths are due to wrong diagnosis, delayed diagnosis and late admissions with severe hypovolemic shock. Ruptured ectopic pregnancies with severe intra-abdominal bleed may present with gastrointestinal symptoms like nausea, vomiting, diarrhoea and poses a great challenge in correct diagnosis [4].

The most common extra uterine pregnancy is the tubal pregnancy in which a fertilized ovum implants in the fallopian tubes, predominantly the ampulla. Tubal pregnancies account for 98% of all ectopic gestations. Other sites include ovary, cervix, horn of the uterus, caesarean scar, abdominal cavity and heterotopic pregnancy [5].

The fallopian tube serves as a highly regulated environment for the movement of oocytes, fertilisation, and early embryo migration to the uterus for implantation [6]. Tubal ectopic pregnancy results from atypical embryo transit as well as a change in the tubal environment, which permits atypical implantation to take place [7].

Almost 50% of cases have no identifiable risk factors. Prior damage to the fallopian tubes, resulting from previous ectopic pregnancy and previous tubal surgeries to treat infertility or for sterilisation, pelvic inflammatory disease, prior pelvic surgeries, endometriosis, Intrauterine contraceptive devices, smoking and assisted reproductive techniques are some of risk factors for ectopic pregnancy that clinician need to be aware of [8-11].

Any pregnant woman who experiences vaginal bleeding or lower abdominal pain when intrauterine pregnancy has not yet been confirmed should be evaluated for ectopic pregnancy. Due to the sloughing of decidual endometrium, vaginal bleeding in women with ectopic pregnancies can range from spotting to menstruation-like levels. Even with ectopic implantation, this endometrial decidual response takes place [12].

Ectopic pregnancy pain can vary in type, location, and intensity. As the fallopian tube distends during pregnancy, it frequently starts as a colicky abdomen or pelvic discomfort that is localised to one side. Once the tube bursts and hemoperitoneum forms, the discomfort could spread to other areas of the body [13].

When an ectopic pregnancy has ruptured and there is hemoperitoneum, the physical examination can detect indicators of hemodynamic instability (such as hypotension and tachycardia). Cervical motion or adnexal tenderness are frequent symptoms of unruptured ectopic pregnancy in patients [14].

Definitive diagnosis of ectopic pregnancy can be made with ultrasound visualization of a yolk sac and/or embryo in the adnexa. However, most ectopic pregnancies do not reach this stage. More often, patient symptoms combined with serial ultrasonography and trends in beta human chorionic gonadotropin levels are used to make the diagnosis.

The rate of increase in β-hCG levels, typically measured every 48 hours, can aid in distinguishing normal from abnormal early pregnancy. In a viable intrauterine pregnancy with an initial β-hCG level less than 1,500 mIU per mL (1,500 IU per L), there is a 99% chance that the β-hCG level will increase by at least 49% over 48 hours. A slower-than-expected rate of increase or a decrease in β-hCG levels suggests ectopic pregnancy or early pregnancy loss [15].

To make a final diagnosis of ectopic pregnancy, the patient history is frequently supplemented with serial quantitative hCG levels, sequential ultrasonography, and occasionally, uterine aspiration. Recurrence and impairment of subsequent fertility are the most important concerns [16].

The main objectives of this study are to find out the incidence of ectopic pregnancy, to know age group, gravidity and risk factors and to study the clinical presentation, treatment modalities and outcome of all cases of ectopic pregnancy in our hospital.

Methods

This prospective observational study was conducted in the department of obstetrics and Gynaecology, at a tertiary care centre, Andhra Pradesh from January 2021 to December 2022. A total of 62 cases of ectopic pregnancy were analysed for parameters like demographic characteristics, gravidity, gestational age, risk factors, clinical presentation and treatment modalities as well as morbidity and mortality.

Inclusion criteria

All patients with clinical, biochemical and/or radiological diagnosis of ectopic pregnancy.

Exclusion criteria

There are no exclusion criteria.

Thorough clinical examination was done after taking proper history. Following that, hemodynamically unstable patients had a urine pregnancy test done, and stable patients had USG done in addition to UPT. With a tentative diagnosis of a ruptured ectopic pregnancy, emergency laparotomies were then performed on patients with hemodynamic instability. In stable cases, expectant or medical management was done according to qualifying criteria.

Statistical Analysis

Data were entered in MS excel spreadsheet and analysed using SPSS software version 23.0. For categorical variables, data were compiled as frequency and percent. For continuous variables, data were calculated as mean ± SD.

Results

The total number of deliveries during study period was 6357 and number of ectopic pregnancies was 62. So, the calculated incidence of ectopic pregnancy in present study was 9.7 per thousand deliveries. Table 1 shows the age distribution of subjects. Out of 62 cases, majority of cases belonged to age group of 21-30 years (67.7%). This can be attributed to the peak fertile age with higher incidence of associated risk factors.

Table 1: Age Distribution

Age group	N = 62	Percentage (%)
≤20	4	6.4%
21-25	23	37%
26-30	19	30.6%
31-35	9	14.5%
>35	7	11.3%

Distribution of subjects according to gravidity is shown in table 2. It was observed that 41.9% of cases were gravida 3 and above, which constitutes the majority. This can be due to greater association of risk factors like history of sterilization, secondary infertility and abortions in the patients.

Table 2: Gravidity

Gravidity	N = 62	Percentage (%)
G1	16	25.8%
G2	20	32.2%
≥G3	26	41.9%

In our study, 30.6% of cases have no known risk factors, some patients had multiple risk factors as shown in table 3. The most common associated risk factors were tubal ligation (29%), history of previous abortions (19.3%) and pelvic inflammatory disease (12.5%) which was derived from prior diagnosis and untreated symptoms, 4.8% of cases had association with endometriosis, 6.4% of cases had IUCD in-situ, infertility was a risk factor in 8% and history of previous ectopic pregnancy was seen in 3.1% of cases.

Table 3: Risk Factors

Risk factors	N = 62	Percentage (%)
No risk factors	19	30.6%
Tubal ligation	18	29%
Pelvic inflammatory disease	9	14.5%
Previous Abortions	12	19.3%
Endometriosis	3	4.8%
IUCD in-situ	4	6.4%
Previous ectopic	1	1.6%
Infertility	5	8%

Table 4 shows the clinical symptoms, with abdominal pain (87%) being the most frequent complaint, followed by amenorrhea (38.7%) and vaginal bleeding (19.3%). Vomiting was seen in 4 cases, loose stools in 1 case.

Table 4: Clinical symptoms

Clinical symptoms	N = 62	Percentage (%)
Abdominal pain	54	87%
Amenorrhea	24	38.7%
Bleeding per vaginum	12	19.3%
Vomiting	4	6.4%
Loose stools	1	1.6%

On examination, 22.6% of cases had pallor and 11.3% were presented with shock at time of admission that required immediate resuscitation as shown in table 5. Abdominal tenderness was elicited in 58% of cases, 27.4% had vaginal bleeding on per speculum examination, 35.4% of cases had adnexal tenderness and 19.3% of cases had cervical motion tenderness.

Table 5: Clinical signs

Clinical signs	N = 62	Percentage (%)
Pallor	14	22.6%
Shock (at admission)	7	11.3%
Abdominal tenderness	36	58%
Vaginal bleeding	17	27.4%
Adnexal tenderness	22	35.4%
Cervical motion tenderness	12	19.3%

Table 6 shows USG findings like empty uterus (91.9%) with adnexal mass (88.7%) and free fluid in pouch of Douglas (54.8%). Presence of foetal cardiac activity was noted in 19.3% of cases. UPT was done in all cases and 91.9% of cases had positive UPT.

Table 6: Ultrasonography findings

USG findings	N = 62	Percentage (%)
Empty uterus	57	91.9%
Adnexal mass	55	88.7%
Free fluid in POD	34	54.8%
Foetal cardiac activity present	12	19.3%

After clinical and radiological evaluation, most of the patients required surgical management (91.9%) and medical management was done successfully in 4 cases (6.4%) after qualifying for criteria.

The criteria used for medical management were those who were hemodynamically stable, had gestational sac diameter <=3.5 cm, with low initial serum βhCG < 5000 mIU/ml, no free fluid in pelvis, no contraindications for methotrexate and those who are willing for regular follow-up.

Watchful and expectant management was successfully done in 1 case with meticulous follow-up till βhCG levels became undetectable. Patients with ectopic pregnancy and serum hCG levels less than 200 mIU/mL and falling (although this is not clearly defined) are prospective candidates for expectant care, according to the American College of Obstetricians and Gynecologists.

In exploratory laparotomy, unilateral salpingectomy was the most common surgical procedure (51.6%), followed by bilateral salpingectomy (17.7%) as shown in table 7.

Table 7: Mode of management

Mode of management	N = 62	Percentage (%)
Expectant	1	1.6%
Medical	4	6.4%
Surgical	57	91.9%
Unilateral Salpingectomy	32	51.6%
Unilateral Salpingoophorectomy	5	8%
Unilateral Salpingoophorectomy with contralateral salpingectomy	4	6.4%
Bilateral Salpingectomy	11	17.7%
Ovarian Ectopic Excision	3	4.8%
Cornual resection	2	3.2%

Hemoperitoneum was detected in 39 cases of which 23 cases (59%) had blood volume of more than 500 ml as shown in table 8.

Table 8: Hemoperitoneum

Hemoperitoneum	N = 39	Percentage (%)
≥500ml	23	59%
<500ml	14	35.9%

In our study, tubal ectopic pregnancy (87%) was more common. Ovarian ectopic pregnancy was seen in 12.9% of cases. Most frequent site observed in our study was ampullary (61.3%), followed by isthmic (20.9%) as shown in table 9.

Table 9: Site of ectopic

Site of ectopic	N = 62	Percentage (%)
Fallopian tube	54	87%
Ampullary	38	61.3%
Isthmic	13	20.9%
Interstitial	2	3.2%
Fimbrial	1	1.6%
Ovarian	8	12.9%

Our study reported 79% of ectopic pregnancies as ruptured and unruptured tubal ectopic was seen in 21%, as shown in table 10.

Table 10: Condition of ectopic

Condition	N = 62	Percentage (%)
Ruptured	49	79%
Unruptured	13	21%

One of most common morbidities seen in 64.5% of cases is anaemia that required multiple blood transfusions (72.5%) for resuscitation, as shown in table 11. Fever was seen in 9.6% of cases, ICU admission was required in 17.7% of cases and suture site infection was seen in 2 cases. No maternal mortality was observed in our study.

Table 11: Post-op Complications

Post-op complications	N=62	Percentage (%)
Anaemia	40	64.5%
Blood transfusion	45	72.5%
Fever	6	9.6%
ICU admission	11	17.7%
Suture site Infection	2	3.2%
Maternal mortality	0	0%

Discussion

In the present study, the incidence of ectopic pregnancy was 9.7 per 1000 deliveries. Various studies reported incidence rate variability like Shetty S *et al.* [17] (5.6/1000), Jayati Nath *et al.* [18] (2.9/1000) and Behera A *et al.* [19] (18/1000). The incidence rate variability in different studies is due to varied clinic socio demographic profile of study population.

The mean age in our study is 26.8±4.8 years. Majority of the patients (67.7%) were in the age group of 21 to 30 years in our study. Similar results were found by Samantaray SR *et al.* [20] (73.6%), Shetty S *et al.* [17] (74.2%), Panda SR *et al.* [21] (70%) and Gaddagi *et al.* [22] (70.2%). This corresponds to the age of peak sexual activity and reproduction.

In our study multigravida (53.1%) were found to be more prone to have an ectopic pregnancy, followed by second gravida (28.1%). This result was similar to other studies conducted by Shetty S *et al.* [17] and Samantaray SR *et al.* [20]. This can be attributed to increased sexual life, pelvic inflammatory diseases, usage of intrauterine contraceptive devices and opting for tubal ligation in those who completed childbearing. In contrast, the higher incidence of ectopic pregnancy in primigravida was reported by Tahmina S *et al.* [23] and Attri P *et al.* [24]

Most of cases had no identifiable risk factors (37.5%) whereas some cases had multiple risk factors. Tubal ligation (29%) and Previous abortions (19.3%) were some of commonly identified risk factors in our study. Malacova E *et al.* [25] found that women undergoing tubal sterilization at a young age are at particular risk for subsequent ectopic pregnancy. The risk among younger women doubled between 5 and 15 years after sterilization. Laparoscopic electrodestruction and partial salpingectomy carried the highest risk of ectopic pregnancy. Similar observations were reported by Samantaray SR *et al.* [20] and Tahmina S *et al.* [23]

In recent times, studies [26] suggest that ectopic pregnancy may be associated with endometriosis due to altered tubo-ovarian anatomy. Inflammation, a hallmark of endometriosis, is induced by tubal endometriosis and may contribute to fallopian tube dysfunction and ectopic pregnancy. Tubal endometriosis may be associated with tubal ligation, since endometrialisation of the tubal mucosa has been observed following this procedure.

Yong PJ *et al.* [27] reported in their meta-analysis that endometriosis was associated with an increased risk of ectopic pregnancy (odds ratio [OR] 2.16 to 2.66, 95% CI 1.67-2.79 and 1.14-6.21); however, there was high heterogeneity among studies. It is vital to note that women with endometriosis are often treated because of infertility with assisted reproduction techniques (ART), which itself is a highly relevant risk factor for ectopic pregnancy.

Few studies like Panda SR *et al.* [21] and Raman S *et al.* [28] reported increased incidence of pelvic inflammatory disease as major risk factor for ectopic pregnancy. Pelvic infection (e.g., nonspecific salpingitis, chlamydia, gonorrhoea), especially recurrent infection, is a major cause of tubal pathology and, therefore, increases the risk of ectopic pregnancy. Pelvic infection may alter tubal function and may also cause tubal obstruction and pelvic adhesive disease. Some data suggest that a history of chlamydial infection results in the production of a protein (PROKR2) that makes a pregnancy more likely to implant in the tubes [29].

Several studies like Li C *et al.* [30] reported that incidence of ectopic pregnancy is approximately two- to three-fold higher in patients with infertility. This could also reflect the increased incidence of tubal factor infertility in this group of patients.

Compared with spontaneously conceived pregnancies, pregnancies resulting from *in vitro* fertilization (IVF) treatments are associated with an increased risk of an ectopic implantation. Karadağ C *et al.* [31] found that day five or six blastocyst transfer may decrease ectopic pregnancy rates when compared with day three transfer. Even though 8% and 4.8% of cases had infertility and endometriosis respectively in present study, ART as risk factor was not reported as it is dealt in other centres.

In general, the use of the IUD as a contraceptive reduces the risk of an ectopic pregnancy, but if the IUD fails, resulting in a pregnancy with an in-situ IUD, it can increase the risk of an ectopic pregnancy. Li C *et al.* [30] concluded that women of reproductive age who used intrauterine contraceptives previously for a long time would increase their risk of developing an ectopic pregnancy, even though the intrauterine contraceptive device had been removed.

The most frequent presenting complaints were abdominal pain (87%), followed by amenorrhea (38.7%) and vaginal bleeding (19.3%). The symptomology is on concordance with Samantaray SR *et al.* [20] Based on symptomology alone 88.7% of cases were clinically diagnosed, which were supported by a positive UPT (91.9%) and ultrasonography in hemodynamically stable patients.

In our study, tubal ectopic constituted 87% of cases, predominantly in the ampulla (61.3%). Similar findings were reported by Samantaray SR *et al.* [20], Bouyer *et al.* [32] and Gaddagi RA *et al.* [22] The abnormalities in the contraction of the fallopian tube muscles are influenced by oestrogens (produce a sphincter-like response) and progestins (relax), predominantly in the ampullary-isthmic and utero-tubal junction of the salpinx. This explains ampulla being the most frequent site of tubal ectopic, followed by isthmic.

At the time of diagnosis, 79% of ectopic had ruptured, with 59% of patients having hemoperitoneum more than 500 ml. Similar findings were reported by many studies. [17, 20, 33, 34] The high rate of rupture could be due to late recognition and delayed referral to our hospital.

After thorough evaluation, 1 case was managed expectantly. According to studies [5], stable and well counselled women with ectopic pregnancy and serum -hCG levels between 175-200 mIU/mL and declining qualify for expectant care. Medical

management was done successfully in 4 cases with single dose of methotrexate after qualifying for criteria. Appropriate baseline investigations were done, and patient was counselled about the probability of outcome.

Rest of the cases (91.9%) were managed surgically, most of them needing emergency laparotomy due to hemodynamic instability. Unilateral salpingectomy (51.6%) was the most performed surgical procedure followed by bilateral salpingectomy (17.7%). Surgical management as primary mode of management was reported by many studies [19, 20, 23, 24]. This could be attributed to high rupture rate due to late referral to tertiary care centres in developing countries. This can be addressed by the establishment of Early Pregnancy Assessment Units (EPAU), where ectopic pregnancy is likely to be identified at an early stage when medical management is still feasible [35].

Major postoperative morbidity included varying degrees of anaemia (64.5%) requiring blood transfusion. ICU admission was required in 17.7% of cases and 9.6% of cases had an episode of febrile illness. No maternal mortality was observed in our study. Similar findings were reported by Samantary SR *et al*. [20] and Tahmina S *et al*. [23]. Dvash S *et al*. [36] has shown that factors affecting patients' access to healthcare, such as the COVID-19 delay the timely diagnosis of ectopic pregnancy.

Some of the areas that need improvement to enhance outcomes in ectopic pregnancy include lack of awareness of early pregnancy, late reporting by women to healthcare facilities when aware of pregnancy, and failure of healthcare personnel to use diagnostic aids for detecting ectopic pregnancy.

Conclusion

Ectopic pregnancy is an emergency in which timely intervention will reduce the maternal mortality and morbidity. Clinical presentation varies from case to case and still there is a chance of missing the diagnosis in a small proportion of patients even with the availability of advanced imaging techniques. For early diagnosis a clinician should be aware about the various presentations and associated risk factors of ectopic pregnancy.

Conflict of interest

None to declare

Ethical Issues

None

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None

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