

# Clinical and Histopathological Findings of Ectopic Pregnancy Cases- A Retrospective Study from a Tertiary Care Hospital, Andhra Pradesh, India

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## ABSTRACT

**Introduction:** Ectopic Pregnancy (EP) is defined as a pregnancy that occurs in ectopic location, that is, outside the cavity of uterus. It is one of the leading causes of mortality in the first trimester of pregnancy and one of indication for emergency laparotomy. Timely diagnosis is extremely crucial as delay in diagnosis can lead to mortality. Diagnosing ectopic pregnancy is quiet challenging as there are many conditions which have similar presentation and may not require surgical management. Histopathology is required for confirmation of ectopic pregnancy by identifying trophoblastic tissue in ectopic location, since there are other conditions like haematosalpinx, ruptured haemorrhagic corpus luteum which can have similar presentation clinically.

**Aim:** To analyse the clinicopathological features of cases clinically diagnosed as ectopic pregnancy and estimate the percentage of cases which were confirmed on histopathology and assess the percentage of cases which were negative on histopathology.

**Materials and Methods:** This was a retrospective observational study conducted on three years data collected retrospectively between July 2017 to June 2020. Clinical details like age of the patient, parity, gestational age, previous history of any associated risk factors for ectopic pregnancy, were obtained from patient requisition forms and pathology records. Haematoxylin and Eosin (H&E) stained sections were reviewed. Descriptive analysis was done. Data entry was made in Microsoft (MS) excel sheet. Frequencies and percentages were calculated.

**Results:** Total of 128 cases (mean age 25.8±4.87 years) data was analysed in this study, most women were between 21-30 years 97 (75.7%), with mean age of 25.8 years and presented in 2<sup>nd</sup> pregnancy 40 (46.5%) out of 86 cases where details were known and in 6<sup>th</sup> week of gestation 28 (35.8%) out of 78 cases where details were known with mean gestational age of 7.2 weeks. Most common risk factors were previous abortions and previous caesarean section 36 (43.9%) out of 82 cases where details were known. Fallopian tube was the most common site 112 (99.1%) out of 113 cases. On histopathological examination, trophoblastic tissue was identified in 116 (90.6%) cases out of 128 cases. Total 12 (11.7%) cases showed no evidence of trophoblastic tissues, of these 3 (25%) cases showed ruptured corpus luteum, 7 (58.3%) showed haematosalpinx, and 2 (16.66%) cases showed chronic salpingitis changes.

**Conclusion:** Ectopic pregnancy was most frequent in women between 21-30 years, in 2<sup>nd</sup> pregnancy and in 6<sup>th</sup> week of gestation. Most common risk factors were previous abortions and previous caesarean section. Fallopian tube was the most common site. Ectopic pregnancy was confirmed on histopathological examination, 90.6% cases. A total of 11.7% cases which showed no evidence of trophoblastic tissues, were cases of haematosalpinx, ruptured haemorrhagic corpus luteum and chronic salpingitis and they presented clinically as ectopic pregnancy.

**Keywords:** Chronic salpingitis, Corpus luteum, Haematosalpinx, Ruptured haemorrhagic corpus luteum, Tubal abortion

## INTRODUCTION

Ectopic pregnancy is defined as pregnancy which occurs outside the uterine endometrial cavity [1]. It is one of the leading causes of mortality in the first trimester of pregnancy and one of indication for emergency laparotomy. Diagnosing ectopic pregnancy is quiet challenging as there are many conditions which have similar presentation, which may not require surgical management [2]. Timely diagnosis is extremely crucial as delay in diagnosis can lead to mortality. The incidence of ectopic pregnancy is increasing worldwide (1-2%), one of the reasons being early diagnosis and intervention due to advent of newer diagnostic modalities, which has reduced the mortality rate from as high as 7.1-3.5% [3] to near zero as per the recent studies from various parts of India [3-7]. Hence, the focus has shifted from reducing mortality rate to preserving fertility especially in cases which are being managed for infertility and assisted reproduction. There are many studies from India addressing the same issue, that is early identification of ectopic pregnancy but there are limited number

of studies on the conditions which might clinically present as ectopic pregnancy [3-9].

So, this study was undertaken to review all the cases submitted for histopathology with the diagnosis of ectopic pregnancy and estimate the percentage of confirmed cases based on histopathological examination and assess the percentage of other close mimics which present clinically as ectopic pregnancy; and to further analyse the clinicopathological features of all these cases.

## MATERIALS AND METHODS

This was a hospital based retrospective observational study done at Department of Pathology, Guntur Medical College, Guntur, Andhra Pradesh, India. The data collected from July 2017 to June 2020, was retrospectively analysed in February and March 2021, after obtaining approval from the Institutional Ethics Committee (IEC application no GMC/IEC/03/2021).

**Inclusion criteria:** All the specimens submitted to Department of Pathology, Guntur Medical College, Guntur, Andhra Pradesh, India, with the diagnosis of ectopic pregnancy were included in the study.

**Exclusion criteria:** Specimens of uterine gestation like missed abortions, spontaneous abortions and retained products of conception and those cases who had not given consent for using their material for research were excluded from the study.

**Sample size calculation:** The estimated minimum sample size required, with incidence rate of ectopic pregnancy in population as 0.9% [3], with 95% confidence interval and 5% precision was 14 cases. A total of 128 cases were included in the study by convenience sampling.

## Study Procedure

The clinical details like age of the patient, parity, gestational age, previous history of any associated risk factors for ectopic pregnancy, were obtained from patient requisition forms and pathology records. Patient consent was routinely obtained while they submit the specimen for histopathological examination. Haematoxylin and Eosin (H&E) slides of all these cases were reviewed and the presence or absence of trophoblastic tissue in ectopic location, site of ectopic gestation, presence or absence of rupture of fallopian tube, additional pathological findings if any like salpingitis in fallopian tube, corpus luteum in ovary were recorded.

## STATISTICAL ANALYSIS

All the collected data was entered in Microsoft excel sheet, version 2201. Frequencies and percentages were calculated. Mean was calculated for continuous variables.

## RESULTS

There were a total of 128 samples which were submitted with a clinical diagnosis of EP, during the study period of three years. The age range was between 18-40 years with the mean and SD (standard deviation) of  $25.8 \pm 4.87$  years. Most of the women (75.7%), were between 21-30 years. The details of parity were known in 86 cases. Most women 40 (46.5%) out of 86 presented in second pregnancy [Table/Fig-1]. Most of the women (35.8%) presented in sixth week of gestation and 28.2% of women presented after eighth weeks of gestation [Table/Fig-1]. The mean gestational age was 7.2 weeks. The details of risk factors were available in 82 cases. The most frequently identified risk factors were history of abortions and previous caesarean section 36 (43.9%) out of 82 followed by history of tubectomy and history of infertility or assisted reproduction (6% each) [Table/Fig-1].

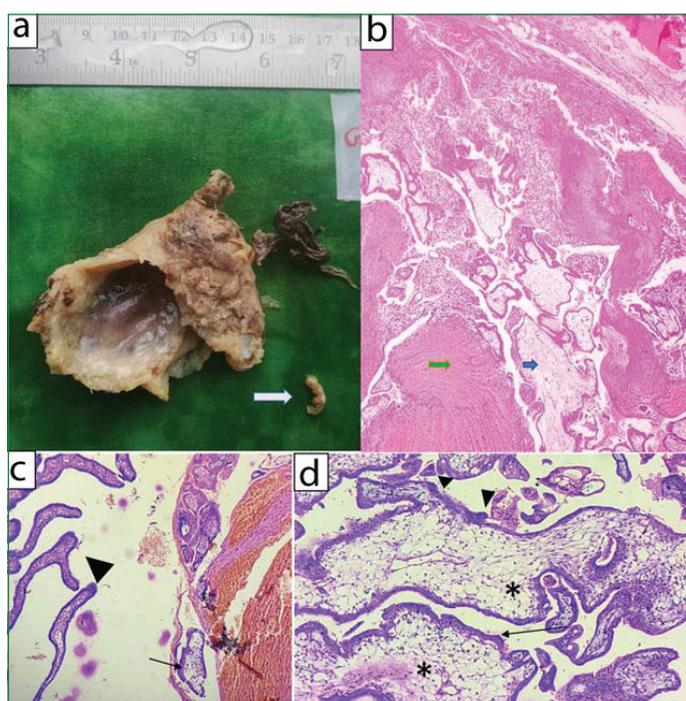
The Fallopian tube was the most common site of ectopic pregnancy 112 (99.1%) out of 113, right tube was more commonly involved than left tube and in one case, the site for ectopic was cornua [Table/Fig-1]. In three cases where ectopic pregnancy was suspected in ovary, products of conception were not identified on histopathology. The fallopian tube was ruptured in 67 (59.3%) cases and unruptured in 46 (40.7%) cases, [Table/Fig-1].

On gross examination, the tube was ruptured and haemorrhagic in 67 cases and occasionally showed grossly identifiable villi and foetus [Table/Fig-2(a)]. On histopathological examination, of the 128 cases, trophoblastic tissue was identified in 116 (90.6%) cases [Table/Fig-2(a-d)], of these two cases showed changes of molar pregnancy [Table/Fig-3]. Total 12 (11.7%) cases showed no evidence of trophoblastic tissues, of these, 3 (25%) showed ruptured corpus luteum, 7 (58.33%) showed haematosalpinx, and 2 (16.66%) cases showed chronic salpingitis changes.

Of these 12 cases, where ruptured ectopic was suspected clinically and no trophoblastic tissue was identified microscopically,  $\beta$ -hCG (beta-Human Chorionic Gonadotropin) levels were not done

Patient characteristics	Frequency (percentage)
<b>Age distribution (n=128) (years)</b>	
≤20	12 (9.3%)
21-30	97 (75.7%)
31-40	19 (14.8%)
Mean age-25.8 years	
<b>Parity (n=86)</b>	
0	23 (26.7%)
1	10 (11.6%)
2	40 (46.5%)
3 and >3	13 (15.1%)
<b>Gestational age (n=78)</b>	
5 weeks	7 (8.9%)
6	28 (35.8%)
7	7 (8.9%)
8	14 (17.9%)
>8 weeks	22 (28.2%)
Mean gestational age-7.2 weeks	
<b>Risk factors (n=82)</b>	
History of abortion	36 (43.9%)
History of previous caesarean section	36 (43.9%)
History of tubectomy	5 (6%)
History of infertility or assisted pregnancy or IVF	5 (6%)
<b>Location of ectopic gestation (n=113)</b>	
Fallopian tube	112 (99.1%)
Right	59 (52.2%)
Left	53 (46.9%)
Cornual	1 (0.88%)
<b>Whether ruptured or not (n=113)</b>	
Ruptured	67 (59.3%)
Unruptured	46 (40.7%)

**[Table/Fig-1]:** frequency distribution of patient characteristics.  
IVF: In-vitro fertilisation



**[Table/Fig-2]:** a) Gross picture showing ruptured tube with dilated lumen along with blood clot and foetus (arrow); b) Fallopian tube with intra luminal chorionic villi (blue arrow) and hemorrhage (green arrow) (H&E, 100X); c) Showing tubal plicae on the left side (arrow head), and chorionic villi on the right side (thin arrow) (H&E, 100X); d) Chorionic villi with central loose myxoid stroma (\*) lined by cytotrophoblasts (thin arrow) and syncytiotrophoblasts (arrow head) (H&E, 400X).

Histopathological diagnosis	Frequency (percentage)
<b>Trophoblastic tissue seen (n=116, 90.6%)</b>	
Tubal ectopic gestation	114 (98.27%)
Tubal molar pregnancy	2 (1.72%)
<b>Trophoblastic tissue not seen (n=12, 11.7%)</b>	
Chronic salpingitis with foreign body giant cell reaction	2 (16.66%)
Haematosalpinx with rupture	7 (58.33%)
Ruptured corpus luteum	3 (25%)

**[Table/Fig-3]:** Showing histopathological diagnosis.

prior to the surgery in five cases. These cases on histopathology showed haemorrhage and ruptured fallopian tube suggestive of ruptured haematosalpinx, nevertheless, tubal abortions could not be excluded in these cases. In two cases, where urine pregnancy test was positive, histopathology showed only haemorrhage with no trophoblastic tissue; the same differential diagnosis discussed above can be applied in these two cases as well. In two cases, where fallopian tube showed chronic salpingitis changes with no evidence of trophoblastic tissue, one case had corpus luteum and follicular cyst.

In three cases, where ovarian ectopic was suspected extensive sampling was done and entire tissue submitted was processed but no trophoblastic tissue could be identified; nonetheless there was ruptured corpus luteum in all three cases.

## DISCUSSION

The incidence of ectopic pregnancy seems to be on rise probably owing to the availability of better diagnostic modalities [6]. With early diagnosis and prompt management, the mortality rate has reduced significantly to near zero as can be seen from data published from latest studies from various parts of India [3-7]. The common age group in most of the studies including the present study is 21-30 years, details shown in [Table/Fig-4] [3-7]. Most women in the present study presented in second pregnancy similar to Shrivastava M et al study [5]. However, there is a wide variation in presentation in relation to parity amongst various studies as can be seen in though ectopic pregnancy can occur at any pregnancy, multiparous women appear to be more at risk than primi pregnant women [Table/Fig-4] [3-7].

Most women presented in sixth week of gestation in the present study and majority of them were below eight weeks which is similar to Barik S et al., study [4]. The mean gestational age was 7.2 weeks in the present study, which is similar to other studies [4,7].

The most common risk factor identified in this study was previous history of abortions and caesarean sections [Table/Fig-5] [3-7]. Shrivastava M et al., also identified these factors as most common risk factors in their study [5]. Barik S et al., also identified previous caesarean section as risk factor in more than quarter of their patients [4]. Similar observations were made by Rajni GG et al., and Wakankar R in their studies [10,11].

The fallopian tube was the most common site for ectopic pregnancy in the present study as in most other studies [3-7] [Table/Fig-6]; for some unknown reason, the involvement of right fallopian tube was slightly more than left right fallopian tube in the present study, similar observations were made by Barik S et al., Shrivastava M et al., and Rajni GG et al., [4,5,10]. The fallopian tube was ruptured in 59.3% of cases, these observations were similar to the findings of Barik S et al., and Murugesan A et al., [4,6].

In present study, ectopic trophoblastic tissue could be identified in 90.6% of cases on histopathological examination. Trophoblastic tissue is histologically identified by presence of chorionic villi and decidual changes. Present study positivity rate was slightly less than Rajni GG et al., study; they have studied 925 cases, and found trophoblastic tissue in 881 cases with a positivity rate of 95.2% [10].

Parameters compared	Present study (n=128)	Barik S et al., study [4] (n=280)	Tahmina S et al., study [3] (n=72)	Shrivastava M et al., study [5] (n=47)	Murugesan A et al., study [6] (n=82)	Pranathi L and Madhavi Y study [7] (n=45)
<b>Age distribution (n=128) (years)</b>						
≤20	12 (9.3%)	14 (5%)	2 (2.7%)	-	1 (1.2%)	1 (2.2%)
21-30	97 (75.7%)	202 (72.14%)	37 (51.4%)	-	58 (70.7%)	26 (57.8%)
31-40	19 (14.8%)	36 (16.43 (31-35)	29 (40.3%)	-	14 (17.1%)	16 (35.6%)
>40	0	18 (6.43%) (>35 years)	4 (5.6%)	-	0	2 (4.4%)
Mean age	25.8 years	-	-	27.4 years	-	-
<b>Parity (n=86)</b>						
0	23 (26.7%)	57 (20.71%)	20 (27.8%)	8 (17%)	-	13 (28.9%)
1	10 (11.6%)	98 (35%)	25 (34.7%)	11 (2.4%)	-	16 (35.6%)
2	40 (46.5%)	79 (28.2%)	23 (31.9%)	23 (48.9%)	-	14 (31.1%)
3 and >3	13 (15.1%)	46 (16.43%)	4 (5.6%)	8 (17%)	-	2 (4.4%)
<b>Gestational age (n=78) (weeks)</b>						
5	7 (8.9%)	58.9% (<8 weeks)	-	-	-	-
6	28 (35.8%)	-	-	-	-	-
7	7 (8.9%)	-	-	-	-	-
8	14 (17.9%)	-	-	-	-	-
>8	22 (28.2%)	41.1%	-	-	-	-
Mean gestational age	7.2 weeks	-	7.1 weeks	-	-	7.3 weeks

**[Table/Fig-4]:** Patient characteristics of present study in comparison to other studies [3-7].

Clinical history and risk factors	Present study	Barik S et al., study [4]	Tahmina S et al., study [3]	Shrivastava M et al., study [5]	Murugesan A et al., study [6]	Pranathi L and Madhavi Y study [7]
History of abortion	36 (43.9%)	28 (10%)	26 (36.1%)	8 (17%)	14 (19.7%)	14 (30.95%)
History of previous caesarean section	36 (43.9%)	73 (26.07%)	27 (37.5% (pelvic surgeries)	6 (12.8%)	-	-
History of tubectomy	5 (6.1%)	39 (14.11%)	-	3 (6.4%)	21 (28.76%)	15 (33.33%)
History of infertility or Assisted pregnancy or IVF	5 (6.1%)	29 (10.36%)	13(18.1%)	4 (8.5%)	8 (10.96%)	7 (16.66%)

**[Table/Fig-5]:** Distribution of patients according to risk factors (n=82) in comparison to other studies [3-7].

Ectopic molar pregnancy was identified in two cases in present study. Ectopic molar pregnancy is extremely uncommon with reported incidence of approximately 1.5 in every 1,000,000 pregnancies, with only few reported cases in literature [12-17].

Trophoblastic tissue could not be identified in 10.4% of the present study cases. There are case reports and cohort studies of histologically negative ectopic pregnancy [8,9]. In Farahani L et al.,

Site	Present study	Barik S et al., study [4]	Tahmina et al., study [3]	Shrivastava et al., Study [5]	Murugesan et al study [6]	Pranathi and Madhavi study [7]
Fallopian tube	112 (99.1%)	271 (97%)	68 (94.4%)	46 (91.5%)	71 (97.26%)	44 (97.62%)
Right	59 (52.2%)	148 (52.86%)	-	31 (61.7%)	-	-
Left	53 (47%)	132 (47.14%)	-	18 (36.2%)	-	-
Cornual	1 (0.88%)	6 (2%)	1(1.4%)	-	2 (2.82%)	1 (2.38%)
Ruptured	67 (59.3%)	196 (70%)			45 (61.64%)	
Unruptured	46 (40.7%)	60 (21.43%)			10 (13.7%)	

**[Table/Fig-6]:** Distribution of patients according to site of Ectopic Pregnancy (EP) (n=113) in comparison to other studies [3-7].

study, the incidence of negative histology for ectopic pregnancy was below 5% [8].

There could be several reasons for absence of trophoblastic tissue microscopically, ranging from sampling error, misdiagnosis to tubal abortion [8]. The tubal abortion is expulsion of products into abdominal cavity through fimbria [18]. The natural course of ectopic pregnancy could be; 1) asymptomatic with spontaneous absorption; 2) symptomatic but unruptured; 3) symptomatic and ruptured and 4) tubal abortion either complete or incomplete [19]. A positive pregnancy test either by a serum  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) levels or urinary pregnancy tests, in the absence of trophoblastic tissue should raise the suspicion of tubal abortions [20]. In present study, in five cases where  $\beta$ -hCG levels were not done prior to the surgery, histopathology was suggestive of ruptured haematosalpinx, nevertheless, tubal abortions could not be excluded in these cases. Similarly, in two cases, where urine pregnancy test was positive, histopathology showed only haemorrhage; tubal abortion cannot be excluded in these two cases as well.

In two cases of chronic salpingitis in present study, one case had corpus luteum and follicular cyst which might have mislead the diagnosis on ultrasound. The other case might as well be a case of complete tubal abortion. Ravindra S et al., have identified chronic salpingitis in 20 (22%) out of 90 among the cases studied. However, they regarded chronic salpingitis as an additional risk factor in their study and they considered that it is involved in etiopathogenesis of ectopic pregnancy. Meyur R et al., also identified chronic salpingitis in 23 (31.5%) cases of the cases studied [22].

In present study, three cases where ovarian ectopic was suspected, histopathology showed ruptured corpus luteum which is known to present as acute abdomen due to hemoperitoneum and can clinically mimic ectopic pregnancy [23]. Although, presence of adnexal mass which can appear as a sac-like ring, solid or complex along with pelvic free fluid suggestive of hemoperitoneum. Such cases have a positive predictive value of 93% for diagnosing ectopic pregnancy on ultrasound, a corpus luteum can also have similar "ring of fire". The echogenic mass can be seen in both ovarian mass and ectopic pregnancy; similarly, hemoperitoneum can also be seen in the rupture of both ectopic pregnancy and haemorrhagic cyst [24]. The ruptured corpus luteum management varies according to the clinical presentation and laboratory investigation findings and ranges from simple observation to emergency laparotomy. That is why, ruptured corpus luteum should also be entertained in the differential diagnosis along with ectopic pregnancy in acute abdomen in early pregnancy [23].

In addition, many other ovarian cysts can be seen in pregnancy apart from corpus luteum like follicular cyst, haemorrhagic and endometriotic cysts which can undergo torsion, haemorrhage or rupture and present as acute abdomen [25].

### Limitation(s)

The radiological correlation could not be done due to non availability of the data. Beta HCG levels were not available in few cases which were negative for trophoblastic tissue on histopathology. So, tubal abortion and missed abortions cannot be excluded in these cases.

### CONCLUSION(S)

Ectopic pregnancy was most common in 21-30 years age group multiparous women with mean gestational age of 7.2 weeks. Previous abortions and caesarean section were common risk factors identified and right fallopian tube was the most common site. Haematosalpinx and ruptured haemorrhagic corpus luteum were close mimics and presented clinically as ectopic pregnancy.

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**PLAGIARISM CHECKING METHODS:** <sup>[Jain H et al.]</sup>

- Plagiarism X-checker: Oct 05, 2021
- Manual Googling: Mar 09, 2022
- iThenticate Software: Apr 09, 2022 (7%)

**ETYMOLOGY:** Author Origin**AUTHOR DECLARATION:**

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Oct 03, 2021**Date of Peer Review: **Feb 09, 2022**Date of Acceptance: **Mar 21, 2022**Date of Publishing: **Jul 01, 2022**