



## SPECTRUM OF HISTOPATHOLOGICAL CHANGES IN RUPTURED TUBAL ECTOPIC PREGNANCY AND ITS ASSOCIATION WITH TUBERCULOSIS

Khalida Depar<sup>1</sup>, Saima Gaffar<sup>2</sup>, Samreen Memon<sup>3</sup>, Pushpa Goswami<sup>4\*</sup>, Farhana Rajpar<sup>5</sup>, Barkha Goswami<sup>6</sup>

<sup>1</sup>Lecturer of Anatomy, Liaquat University of Medical & Health Sciences Jamshoro  
Email: khalida.depar@lumhs.edu.pk

<sup>2</sup>Assistant Professor of OBG. Liaquat University Hospital  
Email: saimagaffararain@yahoo.com

<sup>3</sup>Professor of Anatomy, Liaquat University of Medical & Health Sciences Jamshoro  
Email: Samreen.memon@lumhs.edu.pk

<sup>4\*</sup>Professor of Anatomy, Liaquat University of Medical & Health Sciences, Jamshoro  
Email: pushparamesh1998@gmail.com

<sup>5</sup>Associate Professor of Anatomy, Liaquat University of Medical & Health Sciences Jamshoro,  
Email: farhana.rajpar@lumhs.edu.pk

<sup>6</sup>House officer Liaquat University Hospital. Email: barkhagoswami9900@gmail.com

**\*Corresponding Author:** Pushpa Goswami

\*Professor of Anatomy, Liaquat University of Medical & Health Sciences, Jamshoro  
Email: pushparamesh1998@gmail.com

### Abstract

**Background:** Ectopic pregnancy significantly contributes in maternal morbidity and mortality. Fallopian tube is the commonest site of ectopic pregnancy. Genital tuberculosis, which manifest as chronic pelvic pain, pelvic inflammatory infection, infertility, or ectopic pregnancy, affects a significant number of women in underdeveloped countries where tuberculosis is still a serious health concern.

**Objective:** The aim of this study is to observe Histopathological changes in ruptured fallopian tube and association of tuberculosis in ruptured tubal pregnancy as an etiological factor for ectopic pregnancy.

**Method:** This descriptive study was conducted on 45 cases of ectopic tubal pregnancy admitted in the department of OBG during the study period. Slides were studied for various histological changes.

**Results:** Histopathological findings of ruptured fallopian tubes revealed ruptured ectopic products of conception and few chorionic villi in 16 cases, chorionic villi with decidual tissue and hemorrhage found in 12 cases, focal mucosal/intramural patches of necrosis seen in 13 cases while, TB granuloma in 04 cases. Tubal walls found invaded by chorionic villi up to serosa in 32 cases while tubal invasion was up to smooth muscle layer in 13 patients.

**Conclusion:** This study found non-significant association with tuberculosis in ruptured tubal ectopic pregnancy.

**Key Words:** Ectopic pregnancy, histopathological findings, ruptured fallopian tube, Tuberculosis

### **Introduction**

Ectopic pregnancy (EP) is the most fatal unexpected emergency in early maternity, with rising incidence during past 30 years across the world. Incidence is much higher in developing countries, around 1-3%. In Pakistan the reported incidence is about 1:112 to 1:130. The actual figures may be more than this due to lack of awareness and health facilities which fails to diagnosis and maintain statistical records. After post-abortal complications within the first three months of pregnancy, EP is the second most common cause of maternal demise [1, 2, 3].

The term EP comes from the Greek word "ektopos," which means "out of position. EP is defined as pregnancy that is implanted outside the uterine cavity, which is a site that by nature is not designed anatomically, and physiologically to accept the conception or to permit its growth and development [4, 5, 6].

EP is important cause of maternal morbidity and mortality especially in developing countries including Pakistan where majority of patients present late with rupture and hemodynamic compromise. The predisposing factors include pelvic inflammatory disease (tuberculosis), tubal deformities, endometriosis, previous surgery, and treatment for infertility. The spectrum of clinical findings in ectopic pregnancy ranges from completely asymptomatic to massive intra-abdominal bleeding and shock. The common symptoms of ectopic are triad of secondary amenorrhea, abdominal pain, and vaginal bleeding [7, 8, 9].

Pakistan in Tuberculosis (TB) ranks fifth among the twenty-two countries which are extremely burdened by TB. It is a major health problem in developing countries which can present as genital tuberculosis and responsible for affecting a number of women. TB presents as chronic pelvic pain, pelvic inflammatory disease, infertility and ectopic pregnancy. TB could be either primary that involve lungs, or intestine or secondary which may involve all organs and systems of body including genital tract. TB spreads either via blood, lymphatic, or directly from neighboring viscous. Frequency of involvement of genital organs is fallopian tubes 100%, endometrium 90%, ovaries 20%, cervix, vulva, and vagina 1% [10, 11, 12].

### **METHODOLOGY:**

This study was conducted in the Department of Anatomy, Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro in collaboration with Department of Obstetrics & Gynecology and Diagnostic and Research Laboratory Jamshoro/ Hyderabad after approval from Research Ethical Committee (REC), LUMHS. All eligible patients were fully explained with purpose of study in local language and enrolled after written informed consent either by patient or her attendant.

A total of 45 cases with ruptured ectopic pregnancy undergoing surgery/laparotomy were included in this study, detailed history was taken regarding age, educational level, obstetric history, last menstrual period, duration of marriage, gravidity, parity, amenorrhea, lower abdominal pain, vaginal spotting, syncope attack, history of previous tubal surgery, pelvic infection, ectopic pregnancy, use of IUCD, drug history of ovulation induction or contraception was recorded on predesigned proforma. All women with diagnosis of lower abdominal pain but not suspicious of ectopic pregnancy and ectopic pregnancies receiving medical treatment were excluded [13, 14, 15].

After surgery/laparotomy the ruptured segment of fallopian tubes was observed for length, diameter, and color, products of conception, tortuosity of tube, blood clot, site of rupture and any adnexal mass [16, 17].

After gross examination, the tissue section of ruptured tubal ectopic pregnancy were processed with histopathological technique then features were studied on hematoxylin and eosin which include, lumen (intact/ruptured), histological architecture, invasion of tubal wall by syncytiotrophoblast and

cytotrophoblast, hemorrhagic spots, necrosis, presence of tuberculosis granuloma for confirmation /presence of tuberculosis [18].

The data was entered and analyzed using SPSS-23. Mean standard deviation was calculated for continuous variables like age, gestational age, parity and duration of symptoms. Frequencies and percentages were calculated for categorical variables, like tubal rupture lumen, histological architecture and invasion of tubal wall. Stratification were done with regards to age, gestational age, parity and duration of symptoms to see the effect of these on outcomes via chi-square test and p-value of <0.05 considered as significant [19].

## RESULTS:

In this study total 45 women of ruptured ectopic tubal pregnancy were enrolled. Mean age of study population was 29.95 years  $\pm$  6.24; while, Mean  $\pm$  SD of gravidity, parity and gestation age were 3.4 $\pm$ 2.0, 1.1 $\pm$ 1.02 and 3.6week $\pm$ 1.0 respectively. The risk factors and clinical presentations are depicted in table 1. Histopathological changes in table 2 and 3 with photomicrograph (1,2,3) while associations were depicted in table 4 and 5 with chi square.

**Table 1:** Risk Factors and clinical presentation in study population (n=45)

<b>Risk factors</b>	<b>No. of cases</b>	<b>Percentage (%)</b>
Previous CS	20	44.5 %
PID	06	13.3 %
H/O previous ectopic pregnancy	04	8.9 %
Previous abortions	04	8.9 %
Infertility	02	4.4 %
Bilateral Tubectomy	01	2 %
Unknown	08	17.7 %
<b>Presenting complain</b>	<b>No. of cases</b>	<b>Percentage (%)</b>
Amenorrhea	40	88.8%
Lower abdominal pain	41	91%
Vaginal bleeding/ spotting	20	44.5%
All three	17	37.8%
Vomiting	05	11%

**Table 2:** Histological findings in the lumen of ruptured fallopian tube (n=45)

	<b>Frequency</b>	<b>Percent</b>	<b>Cumulative Percent</b>
<b>Ruptured ectopic products of conception and few chorionic villi</b>	16	35.6	35.6
<b>Chorionic villi decidual tissue and areas of necrosis</b>	12	26.7	62.2
<b>Focal mucosal or intramural patches of necrosis</b>	13	28.9	91.1
<b>TB Granuloma</b>	04	8.9	100.0
<b>Total</b>	45	100.0	100.0

**Table No. 3:** Tubal wall invasion by chorionic villi (n=45)

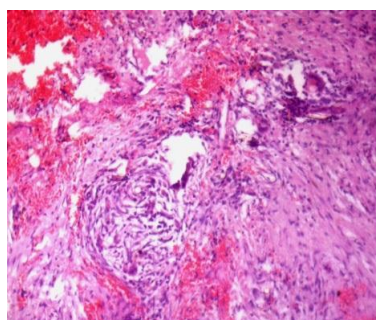
<b>Tubal Invasion by chorionic villi</b>	<b>Frequency</b>	<b>Percent</b>	<b>Cumulative Percent</b>
<b>Up to smooth muscle</b>	13	28.1 %	28.9
<b>Up to serosa</b>	32	71.1 %	100.0
<b>Total</b>	45	100.0 %	

**Table 4:** Association of Histopathological changes in ruptured tubal pregnancy with age

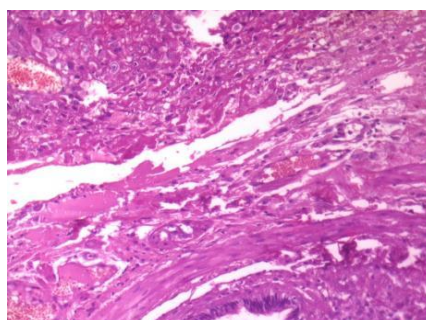
Lumen of ruptured fallopian tube	Age groups			Total
	18 to 25 years	26 to 35 years	>35 years	
Ruptured ectopic products of conception & chorionic villi	05(11.1%)	04(8.9%)	07(15.6%)	16(35.6%)
Chorionic villi decidual tissue and areas of hemorrhage	8(17.8%)	3(6.7%)	1(2.2%)	12(26.7%)
Focal mucosal/ intramural patches of necrosis	5(11.1%)	6(13.3%)	2(4.4%)	13(28.9%)
TB granuloma	00	04 (8.9%)	00	04 (8.9%)

**Table 5:** Association of Histopathological changes in ruptured tubal pregnancy with past history of surgery and presence of tuberculosis

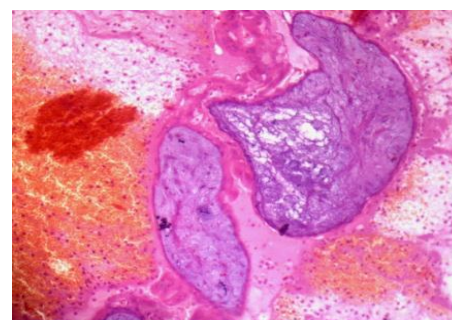
Lumen of ruptured fallopian tube	Past history of surgery		Presence of tuberculosis	
	Yes	No	Yes	No
Ruptured ectopic products of conception & chorionic villi	02(4.4%)	14 (31.1%)	13 (28.9%)	03 (6.7%)
	Total = 16 (35.6%)		Total = 16 (35.6%)	
Chorionic villi decidual tissue and areas of necrosis	01 (2.2%)	11 (24.4%)	07(15.6%)	5 (11.1%)
	Total =12 (26.7%)		Total =12 (26.7%)	
focal mucosal or intramural patches of necrosis	05 (11.1%)	08 (17.8%)	09 (20.0%)	04 (8.9%)
	Total =13 (28.9%)		Total =13 (28.9%)	
TB granuloma	0 (0.0%)	04 (8.9%)	04 (8.9%)	0 (0.0%)
	Total = 4 (8.9%)		Total = 4 (8.9%)	
Total	8 (17.8%)	37(82.2%)	33 (73.3%)	12(26.7%)
	Total = 45 (100%)		Total = 45 (100%)	
<b>p- Value</b>	<b>0.12</b>		<b>0.32</b>	
<b>x<sup>2</sup>= with df</b>	<b>5.70 with df=3</b>		<b>5.80 with df=3</b>	



Photomicrograph 1 of fallopian tube showing TB Granuloma H&amp;E, 20X



Photomicrograph 2 of fallopian tube showing trophoblastic cells infiltrating wall, muscle and lining epithelium H&amp;E, 20X



Photomicrograph 3 of fallopian tube showing chorionic villi, hemorrhage in lumen of fallopian tube infiltrating wall, H&amp;E, 20X

## DISCUSSION

Ectopic pregnancy can occur at any age from menarche to menopause. In the present study, the most common age group was noted between 21-30 years. This is in concordance with the study by Clement WF et al and Bai et al who noted in the same age group. While another study found the age between 35-40 years with high incidence of EP [20, 21].

Regarding parity this study reveals maximum number of patients were between parity 0 and 2. Most of the cases were seen in women during their second or third pregnancy. The similar was observed by Mehta et al and Rowshon Ara Khatun et al. While study by Wekere et al and Bouzari et al found an increased risk of ectopic pregnancy in nulliparous women compared to multiparous women [22, 23]. The gestational age in this study at presentation was between 6-8 weeks which is similar to the study conducted by Nazia Islam [24].

In the present study 21 patients gave a history of abdominal surgery including 20 cases presents history of caesarian section and 01 case with a history of bilateral tubectomy. Most common risk factor identified in this study is previous caesarian section. Barik S et al also identified previous caesarean section as risk factor in most patients. Similar observations were reported by Rnji.GG et al and Govada et al as well [25, 26, 27].

Among the 45 cases in the present study, 06 patients had a previous history of PID. In contrast to our study Swarnkar GP et al found Past history of pelvic inflammatory disease in 22.4% cases, while study done by Oguejiofor CB et al reported Pelvic inflammatory disease was one of most common associated risk factor. Another study conducted by Panda SR et al showed 50.87 % of patients were associated with pelvic inflammatory disease. Throughout the literature, PID is considered as an important risk factor for an ectopic pregnancy. The relatively lower incidence in the present study could be due to the fact that the infections are often asymptomatic and that it is often difficult to elicit a positive history of PID [28, 29, 30].

In this study the commonest presenting complaints were abdominal pain in 41 cases, amenorrhea 40 cases and abnormal vaginal bleeding 20 cases. Vomiting in 05 cases 17 cases out of 45 showed the triad of ectopic pregnancy including abdominal pain, amenorrhea and vaginal bleeding. Mostly the right fallopian tube was involved than the left one. Kale P in their study found all the cases (100%) had pain abdomen, amenorrhea was present in all cases (100%). Abnormal vaginal bleeding- spotting was present in (85.71%) cases [31].

Ugboma HA et al study showed the commonest presenting complaints in descending order were abdominal pain, amenorrhoea, dizziness, vaginal bleeding, syncope and abdominal distension which are consistent with this study [32].

Histopathological findings of ruptured fallopian tubes were similarly observed by Deonia S et al that showed hemorrhage and edema in all the cases of EP. He reported necrosis as another widely prevalent morphological feature in 64.55% which is twice than our study due to difference in sample size [33]. The invasion of the tubal wall by the chorionic villi/ trophoblasts was transmural, extending up to the serosa in our study was 71% and up to the smooth muscle is 28%, while he reported near similar 35% and 65% respectively [33].

In the present study tuberculosis granuloma was observed in 4 cases (8%). Comparable findings were observed by Spandana B et al who observed 4 cases with TB/caseous granuloma and Ruchi Hooda et al noted in 4.2 % cases [34].

While study by Ahmed MI et al and Ravindra S et al found only one case of tuberculous salpingitis [35]

## **Conclusion**

This study found non-significant association with tuberculosis in ruptured tubal ectopic pregnancy. Although cases of both ectopic pregnancy and tuberculosis are rising day by day, results will not be generalized as this study was based on small sample size and in a single center. There is need of further studies as available medical literature reveals few local studies on association of ectopic pregnancy with genital tuberculosis.

## References

1. Tankou CS, Sama CB, Nekame JL. Occurrence of spontaneous bilateral tubal pregnancy in a low-income setting in rural Cameroon: a case report. *BMC research notes*. 2017; 10(1):1-3.
2. Bharti P. A clinical study of incidence, management and outcome of ectopic pregnancy. *Int. J. Heal. Clin. Res.* 2020; 3 (11):239-44.
3. Pati BK. Ectopic pregnancy: one-year retrospective study on clinical, investigational and operative correlation in a tertiary care hospital. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2017;6(12):5519-23.
4. Sultana S, Asif HM, Akhtar N. Incidence rate and prevalence of major risk factors for ectopic pregnancy in the Pakistani population: mini-review. *Asian Pacific Journal of Tropical Disease*. 2015 1;5(3):246-50.
5. Jyothsna P, Devi V. A Study of Incidence, clinical presentation, risk factors and morbidity associated with ectopic pregnancy in CKM-Government maternity hospital Matwada Warangal. *J Contemporary Med Dent*. 2020;8(1):25-30.
6. Ashfaq S, Sultan S, Aziz S, Irfan SM, Hasan M, Siddique A. Ectopic pregnancy with tubal rupture: an analysis of 80 cases. *Journal of Ayub Medical College Abbottabad*. 2017 Apr 8;29(2):254-7.
7. Yahya SA. Evaluation of ectopic pregnancy in Al-Salam hospital in Mosul, Iraq. *Iraq Medical Journal*. 2020 Mar 26;4(1).
8. Chatterjee S, Bagchi B, Chowdhury RG, Dutta A. Latent Genital Tuberculosis—A Causative Factor for Ectopic Pregnancy—A Retrospective Analysis. *AGE*. 2020;21:25.
9. Gyamtsho S, Tenzin K, Choeda T, Lhaden K. Clinical profile of ectopic pregnancies in a national referral hospital in Bhutan: A two-year retrospective study.
10. Jehangir F, Hashmi R, Lateef TK, Zubair M, Tasleem A, Giani A, Ghaffar A, Usman J. Prevalence and outcomes of tuberculosis treatment in a primary care center in Karachi, Pakistan. *Archives of Medicine*. 2020;12(6):0-.
11. Kour KK, Allahabadia G, Singh M. Advances in diagnosis and management of female genital tuberculosis—A comprehensive review. *Acta Sci Microbiol*. 2019;2(6):138-44.
12. Kaur S, Santpur U, Mor S. The incidence detection of tuberculosis in patients with infertility and abnormal uterine bleed: a study in North Indian population. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2019 Aug 1;8(8):3041-7.
13. Mahmood MK. Ectopic Pregnancy; Causes and Management in Kerbala Maternity Hospital. *Karbala Journal of Medicine*. 2019;12(2).
14. Sahib MS, Mughir HA. Risk factors for ectopic pregnancy. *risk.*;7(15):2020.
15. Jadoon S, Qadir M, Khan SM. Ectopic Pregnancy: An Analysis of 54 Cases in A Tertiary Care Hospital of Mardan. *Journal of The Society of Obstetricians and Gynaecologists of Pakistan*. 2018;8(4):238-42.
16. Mahadevan LS, Park BU, Yeh IT. Grossing Issues in Ovarian and Fallopian Tube Pathology. *AJSP: Reviews & Reports*. 2020 Jul 1;25(4):174-80.
17. Rani S, Goswami P, Rajpar F, Awan S, Gul F. Clinical Analysis of Ectopic Pregnancy in a Tertiary Care Hospitals. *J Liaquat Uni Med Health Sci*. 2019; 18 (04):266-71.
18. Sowmya S, Priya R, Meenakshi P, Shwetha B. Study of trophoblasts and histological changes of fallopian tube in tubal pregnancy an anatomical considerations for its early rupture. *Int J Anat Res*. 2014;2(4):609-13.
19. Sharma JB, Roy KK, Pushparaj M, Kumar S, Malhotra N, Mittal S. Laparoscopic findings in female genital tuberculosis. *Archives of gynecology and obstetrics*. 2008 Oct 1;278(4):359-64.
20. Clement WF, Ijeoma NE, Ledee KP. Ectopic pregnancy in Rivers State University Teaching Hospital, Port Harcourt, southern Nigeria: a five-year review. *World Journal of Advanced Research and Reviews*. 2020;6(2):044-53.
21. Bai S, Sujatha R. A study of incidence, clinical presentation and risk factors associated with ectopic pregnancy. *J Evidence Based Med Health Care*. 2015;2(19):2700-8.
22. Mehta D, Kukadiya DS, Guru DM, Pandya DN. Ectopic tales of kachcch: A study of ectopic pregnancies. *Int J Clin Obstet Gynaecol [Internet]*. 2019;3(5):10-6.

23. Khatun RA, Hossain MM, Rahman M. Risk Factor of Ectopic Pregnancy in Rural Women Bangladesh.
24. Bouzari Z, Alizadeh M, Ghanbarpour A, Bijani A, Lakaei-andy F. The Risk Factors for Ectopic Pregnancy. *Journal of Babol University of Medical Sciences*. 2019;21(1):166-73.
25. Islam A, Fawad A, Shah AA, Jadoon H, Sarwar I. Analysis of two years cases of ectopic pregnancy. *Journal of Ayub Medical College Abbottabad*. 2017 Jan 25;29(1):65-7.
26. Barik S, Malakar A, Laha S. Trends in Ectopic Pregnancy: A Prospective Observational Study from a Tertiary Care Center in Eastern India. *Journal of South Asian Federation of Obstetrics and Gynaecology*. 2021 Feb 10;12(3):172-7.
27. Ranji GG, Usha Rani G, Varshini S. Ectopic pregnancy: risk factors, clinical presentation and management. *The Journal of Obstetrics and Gynecology of India*. 2018 Dec;68:487-92.
28. Govada N, KoNKay K, Pola N, devi ChaGaNti P. Clinical and Histopathological Findings of Ectopic Pregnancy Cases-A Retrospective Study from a Tertiary Care Hospital, Andhra Pradesh, India. *National Journal of Laboratory Medicine*. 2022 Jul, Vol-11(3): PO31-PO35
29. Swarnkar GP, Mishra M, Charles S, Sharma A, Sony A, Gaur K. Clinico-epidemiology and outcome of ectopic pregnancy: An experience of 7 years in St. Stephen's hospital, Delhi.
30. Oguejiofor CB, Ezugwu CJ, Eleje GU, Emeka EA. Ruptured Ectopic Pregnancy in a Nigerian Tertiary Hospital: What has Changed?. *International Journal*. 2020;8:15.
31. Panda SR, Rani A, Meena M. Clinicosociodemographic profile of ruptured ectopic pregnancies at a tertiary care centre. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2017 May 1;6(5):1885-90.
32. Kale P, Jangale K. Tubal Ectopic Pregnancy–A Clinical Study. *British Journal of Medical & Health Sciences (BJMHS)*. 2020 Mar;2(3).
33. Ugboma HA, Oputa OA, Orazulike NC, Allagoa DO. Ectopic pregnancy: recent experience in a tertiary hospital, South-Southern Nigeria. *parity*. 2017; 149:100.
34. Ahmed MI, Begum Z. A Study on Histopathological Findings in Ectopic Tubal Pregnancies and Evaluation of Associated Risk Factors. *Indian Journal of Pathology: Research and Practice*. 2018;7(8):928.
35. Ravindra S, Prasad S, Suguna BV. Histomorphology of fallopian tubes in ectopic pregnancy. *Archives of Medicine and Health Sciences*. 2016 Jul 1;4(2):201.