

# Histopathological Changes in Early Human Ectopic Pregnancy and Anatomical Considerations for Its Rupture.

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## ABSTRACT

**Background:** Implantation of blastocyst anywhere else, other than uterine cavity is considered as ectopic pregnancy. About 95% of ectopic pregnancies are implanted in the various segments of fallopian tube. Fertilization takes place in the lumen of fallopian tube, from where, aided by the ciliated columnar epithelium of the tube, the fertilized ovum makes its way to the uterine cavity and the implantation occurs. **Methods:** A study was carried out on 50 patients in the department of pathology, GMC Patiala to compare the histopathological and anatomical changes in the lining of the fallopian tube. **Results:** The routine Haematoxylin and Eosin stain was done and the histopathological study was done. **Conclusion:** It was concluded that early diagnosis and treatment before rupture still remains the main option of management.

**Keywords:** Ectopic Pregnancy, Fallopian Tube, Implantation.

## INTRODUCTION

An ectopic pregnancy (EP) refers to the implantation of an embryo outside the uterus. Due to advances in laboratory testing, transvaginal ultrasound, chemotherapy and laparoscopy, the evaluation, diagnosis and management of EP has rapidly evolved. In parallel, maternal mortality due to ectopic pregnancy has declined, from 3.5 of 10,000 pregnancies in 1970 to 2.6 of 10,000 in 1992.<sup>[1]</sup> The most common EP location is in the fallopian tube, predominantly the ampullary region of the fallopian tube. Implantation outside the fallopian tube—in the cervix, ovary, myometrium, abdominal cavity, interstitial (i.e., intramuscular/proximal) portion of the fallopian tube or coincidentally with an intrauterine pregnancy—occurs in less than 10 % of EPs. Heterotopic pregnancy (HP) refers to the coexistence of an intrauterine pregnancy with an EP in any of these locations. ‘Cornual’ pregnancies are those which are implanted in a horn of an anomalous uterus (i.e., unicornuate, bicornuate, didelphys or septate uteri); these do not uniformly require intervention and will not be included in this review.<sup>[2-4]</sup>

The implanted ectopic embryo burrows actively into the tubal lining and its vessels which is responsible for bleeding. The pain perceived is believed to be caused by prostaglandins released at the implantation site and also by the free blood in the peritoneal cavity acting as local irritant. Despite many notable successes in field of diagnosis of the ectopic pregnancy, it remains the source of serious maternal morbidity and mortality.

## MATERIALS AND METHODS

A study was conducted on 50 patients of age ranging between 20 to 37 years and having ectopic pregnancy of 2-3 months of gestation. The excised part of tissue was taken and fixed in 10% formalin solution and processed for light microscopy. Each block was serially sectioned at micron.<sup>[6]</sup> Section was mounted for histological study and stained with haematoxyline and eosin and observed under light microscope. H and E STAINING TECHNIQUE Requirements Xylene,<sup>[5]</sup> Absolute alcohol, Haematoxylin, Alcohols having strengths 50%, 70%, 95% and 1% Eosin Procedure The sections were deparaffinized by using xylene. Series of dips were given to the slides in jars of alcohol having strengths of 95%, 70%, 50% to wash off xylene. 95% alcohol was washed off with distilled water for approximately 5-10 minutes. Slides were put in haematoxylin bath for 20 minutes. Blueing was done by washing the slides in running tap water for 5 minutes. Counterstained with 1% eosin for 1-5 minutes. Then clearing was done by washing the

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slides in xylene. Finally the sections were mounted in DPX.

## RESULTS

The study showed the maximum cases of ectopic were in the age group of 23 to 30 years (56%).

Most commonly women presented in less than 8 weeks of gestation (80%).

There was striking predominance of right sided ectopics (66%).

Ruptured ectopic pregnancy was present in 52% cases that is in 26 cases among 50.

Most common site of involvement in fallopian tube was ampulla (48%) as grossly noted.

On microscopic examination of slides, Chorionic villi were seen lined by cytotrophoblast and syncytiotrophoblast with trophoblastic tissue, invading the tubal wall along with congested blood vessels, areas of hemorrhage with acute and chronic inflammatory infiltrate. Two of the cases showed gestational sac.

Spread of the trophoblast and the hemorrhage could be classified as predominantly intraluminal and predominantly extraluminal.

All of our cases were with predominantly intraluminal trophoblastic proliferation, the pattern of spread of trophoblast and pattern of the hemorrhage in all of the cases was proportionate to each other. In 48% of cases the tube was not ruptured. In some cases the entire tubal epithelial lining was intact. In other cases the tubal epithelium was either eroded by invading trophoblast.

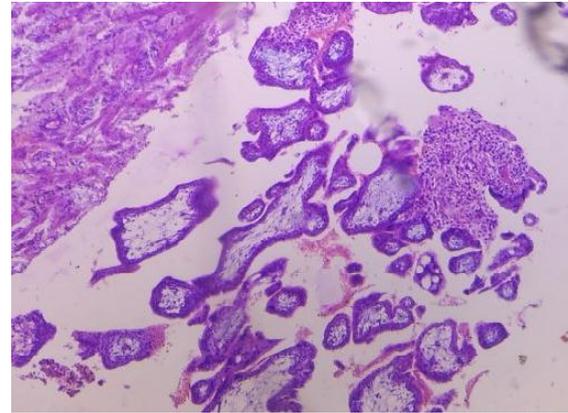
The predominantly extraluminal trophoblastic proliferation was not found in any case in our study.

Histologically, the trophoblastic tissue was proliferated in sheets, between the tissue layers. The accompanying hemorrhage dissected the tissue layers and compressed the tubal lumen. Lymphocytic infiltration of the lamina propria were common near the implantation site.

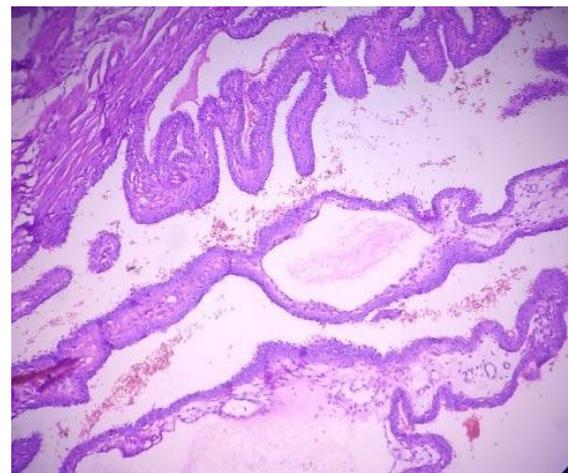
Changes in the myosalpinx appeared to depend upon the stage of pregnancy and whether or not predominant trophoblastic growth proceeded to intraluminal or extraluminal sites. Where luminal distension was less marked, swelling and edema of the myosalpinx were commonly seen as marked circumferential lymphatics distention. When hemorrhages occurred into myosalpinx blood filled spaces were also visible. When luminal distension was marked the myosalpinx became stressed and compressed. Trophoblastic invasion into the myosalpinx ranged from localized penetration by anchoring villi to complete destruction of muscularis. In all of the cases trophoblastic invasion was limited to luminal aspect of the myosalpinx along with inflammatory cell infiltration.

The serosa and subserosa overlying the site of ectopic pregnancy was usually thinned out so much so that it became only single layer of mesothelial cell closely applied to a thin layer of underlying

connective tissue which in turn interfaced with the product of pregnancy. The mesothelial swelling was common along with lymphocyte infiltration of both serosa and subserosa. In cases of rupture the serosa was breached by the invading trophoblast which eroded through the tubal tissue. In many cases, the invading trophoblast invaded subserosal blood vessels.



**Figure 1: Photomicrograph showing chorionic villi with inner cytotrophoblast and outer syncytiotrophoblast. H&E, 40 X**



**Figure 2: Photomicrograph showing fallopian tube epithelium and chorionic villi. H&E, 40 X**

## DISCUSSION

Ectopic pregnancy can occur at different sites such as fallopian tubes, ovary, and abdominal cavity. The most common site is the fallopian tube (90–95%).<sup>[6]</sup> A study from North India showed a higher prevalence in adults than in adolescents.<sup>[7]</sup> Other studies from India have also noted that ectopics occur more often in the third decade.<sup>[8]</sup> Ectopic pregnancy has a slightly higher occurrence in the right fallopian tube (52–57%).<sup>[6,9,10]</sup> Findings in the present study were in concordance with the same (66%). The age range in the present study was 20–37 years; most of them were in the third decade. Ectopic pregnancy is usually diagnosed in the first trimester of pregnancy. The most common gestational age at diagnosis is 6 to 10 weeks, but

fetal viability can be discovered until the time of delivery.<sup>[11,12]</sup> Ectopic pregnancy has about the same frequency across a wide range of maternal ages and ethnic origins.

The physical findings depend on whether tubal rupture has occurred. Women with intraperitoneal hemorrhage present with significant abdominal pain and tenderness, along with various degrees of hemodynamic instability. However, women without rupture may also present with pelvic pain or vaginal bleeding, or both.<sup>[13-16]</sup>

Ampulla was the commonest site involved in the fallopian tube where ectopic pregnancy was present, similar to the observation of Shetty et al.<sup>[17]</sup>

Ruptured ectopic pregnancy was present in 52% cases that is in 26 cases among 50, similar to results of Shetty et al (61.3% respectively).<sup>[17]</sup>

All of our cases have predominantly intraluminal involvement as in the study done by M Tariq Zaidi where majority of the cases were predominantly intraluminal and minority were extraluminal.<sup>[18]</sup>

Microscopy of standard slides showed that the muscles of the fallopian tube are vascular and edematous, the tube is lined with decidua and decidual tissue lies free within the lumen. Adherent to the latter area is sheet of cytotrophoblast and a chorionic villus with its pale staining core of myxoid tissue covered with a thin layer of syncytiotrophoblast and cytotrophoblast. No fetal elements were found among the contents of the tube as in the present study.<sup>[19]</sup>

The serosa and subserosa overlying the site of ectopic pregnancy was usually thinned out and became only single layer of mesothelial. In cases of rupture the serosa was breached by the invading trophoblast which eroded through the tubal tissue.<sup>[18]</sup>

In our study similar findings were observed describing the histopathological cause of rupture.

It was observed that majority of the cases had to undergo a laparotomy, because of unstable condition at presentation. Salpingectomy by open method was the most common modality of treatment. Laparotomy with salpingectomy was the most common modality of treatment in other studies too (Shetty et al 90.3%, Maji et al 81.9%).<sup>[17,20]</sup> medical therapy can be given cases who fulfilled the criteria for medical management. Similar number of medically managed cases were reported by Maji et al.<sup>[20]</sup>

Tubal pregnancy has been thought to implant and grow within the tubal lumen. But from the present study it appears that in the tubal implantation the embryo penetrates into the lamina propria and muscularis to become extraluminal.<sup>[21]</sup> The trophoblastic infiltration is predominantly intraluminal. But extra luminal and mixed pattern of trophoblastic infiltration was also found in some cases.

Intratubal hemorrhage usually parallel to trophoblastic spread often leads to marked tubal

destruction. The prognosis of fertility following ectopic pregnancy mainly depends upon prior history of infertility.<sup>[22]</sup> Rate of fertility may be better following salpingostomy than salpingectomy.<sup>[23]</sup>

## CONCLUSION

It was concluded that early diagnosis and treatment before rupture still remains the main option of management.

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