

Original Research Article

A study on histopathological changes in ectopic tubal gestation

Fathima Rasheed*, Lilarani Vijayaraghavan

Department of Pathology, Government Medical College, Thiruvananthapuram, Kerala, India

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***Correspondence:**

Dr. Fathima Rasheed,

E-mail: fathimarasheed2310@yahoo.co.in

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ABSTRACT

Background: Ectopic pregnancy is a serious cause of maternal morbidity and mortality. Fallopian tube is the most common site. Ectopic pregnancy is often the consequence of chronic salpingitis. The aim of the study was to identify the various histopathological changes in the fallopian tube, which are removed following an ectopic tubal gestation. The prevalence of various risk factors in ectopic tubal pregnancy was also investigated.

Methods: This descriptive study included 160 cases of ectopic tubal gestation received in the department during the study period. Slides were studied for various changes like chronic salpingitis, acute salpingitis, salpingitis isthmica nodosa, endometriosis, tuberculosis etc. Patient's clinical details were obtained from the medical records.

Results: The most frequent pathological finding was chronic salpingitis followed by salpingitis isthmica nodosa. It was noted that all cases with a positive history of pelvic inflammatory disease (PID), showed evidence of chronic salpingitis during histopathological examination. Chronic salpingitis was also noted in 45% cases who did not give a history of PID. Among the risk factors, a history of tubal sterilization was the most frequent one.

Conclusions: Even though the mortality has reduced, ectopic pregnancy causes significant morbidity and affects the fertility of women. The rise in incidence could be due to increase in prevalence of sexually transmitted diseases, increase in tubal sterilization practices and frequent use of assisted reproduction technology. It is evident from the study that many cases of PIDs are left unidentified.

Keywords: Ectopic tubal gestation, Chronic salpingitis, Salpingitis isthmica nodosa

INTRODUCTION

Ectopic pregnancy is the term applied to implantation of the foetus in any site other than normal intrauterine location. The most common site (around 97%) is within the fallopian tube.¹

In many parts of the world, it is still a serious cause of maternal morbidity and mortality amounting up to ten percentage of first trimester deaths.² The incidence of ectopic pregnancy has markedly increased in the past decade.

Risk factors for ectopic pregnancy include PID, tubal surgery, previous pelvic surgery, previous ectopic, use of

intra uterine device and progesterone-only pill for contraception.

Ectopic pregnancy is often the consequence of chronic salpingitis leading to inflammatory destruction of lining folds and retention of ovum. Previous studies have shown that there is a high incidence of inflammatory lesions like chronic salpingitis and salpingitis isthmica nodosa in cases of ectopic tubal gestation. But only limited number of studies have been conducted in our population regarding the histopathological changes in fallopian tube in ectopic pregnancy. Hence this study was undertaken to identify the various histopathological changes in the fallopian tube, which are removed following an ectopic tubal gestation. The prevalence of various risk factors in ectopic tubal pregnancy was also investigated.

METHODS

The current study was a descriptive study. The study was conducted in the department of pathology, government medical college, Thiruvananthapuram. The duration of study was one year from February 2013 to January 2014.

Inclusion criteria and exclusion criteria

Inclusion criteria was, all cases with a histopathological diagnosis of ectopic tubal gestation received in the department during the study period. Cases where fallopian tube could not be identified were excluded from the study. A total of the 160 cases were studied during the study period.

Procedure

Salpingectomy specimens of tubal pregnancies received in the department were fixed in 10% formalin. A minimum of 4 cross sections were taken from the proximal, mid and distal portion of the tube and including any hemorrhagic areas. These were processed, paraffin embedded and tissue blocks were made. 5 μ sections were then stained by hematoxylin and eosin (H and E) and examined under light microscopy. Slides were studied for various changes like chronic salpingitis, acute salpingitis, salpingitis isthmica nodosa, endometriosis, tuberculosis etc. Patient’s clinical details were obtained from the medical records.

Data was further entered in excel sheet and appropriate statistics were used in analysis and comparison of histopathological features.

Clearance from the research committee and human ethics committee of medical college Thiruvananthapuram was obtained before starting the study.

RESULTS

During the study period, a total of 160 cases of ectopic tubal gestation were received in the department of pathology, government medical college, Thiruvananthapuram.

Maternal age ranged from 18 years to 41 years in this study. The maximum number of patients in this study belonged to the age group 26-30 years (Table 1).

Table 1: Percentage distribution of the sample according to maternal age.

Age (years)	Count	Percentage (%)
≤20	3	1.9
21-25	38	23.8
26-30	75	46.9
31-35	29	18.1
>35	15	9.4
Total	160	100

It was noticed that the maximum number of ectopics occurred among second gravida (Table 2).

Table 2: Percentage distribution of the sample according to parity.

Parity	Count	Percentage (%)
Nulliparous	37	23.1
1	53	33.1
2	64	40.0
3	6	3.8
Total	160	100

In the present study it was noted that in 66 patients, period of gestation was between 7 to 8 weeks (Table 3).

Table 3: Percentage distribution of the sample according to period of gestation in weeks.

Period of gestation (Weeks)	Count	Percentage (%)
3-4	22	13.8
5-6	54	33.8
7-8	66	41.3
>8	18	11.3
Total	160	100

The 38.1% women had 1 risk factor associated with ectopic pregnancy, 21.9% had more than 1 risk factor.

Among the various risk factors studied, 47 patients (29.4%) had undergone tubal surgery as a part of sterilization procedure. 37 women had a history of previous abdominal surgery, which included appendectomy and LSCS. The 15 women gave a history of previous abortion. The 12 patients had a history of use of intrauterine contraceptive device. A positive history of infertility was present in 10 cases (Table 4).

Table 4: Percentage distribution of the sample according to risk factors.

Risk factors	Count	Percentage (%)
Tubal surgery	47	29.4
Previous ectopic	6	3.8
Previous abdominal surgery	37	23.1
PID	9	5.6
Intra uterine contraceptive device	12	7.5
Infertility	10	6.3
Previous abortion	15	9.4

A documented history of PID was noted in 9 cases (5.6%). History of a previous ectopic pregnancy present in 6 cases.

Out of the total 160 cases, 101cases involved the right fallopian tube, whereas 59 cases involved the left fallopian tube.

In the present study, 85.6% of cases were of ampullary pregnancy. There were 13 cases of isthmal pregnancy, 5 cases of pregnancy involving the fimbriae, 4 cases involved the cornua and there was one case involving the isthmo-ampullary region. The 53 patients in this study underwent bilateral salpingectomy. The 42 patients underwent Right partial salpingectomy and 20 patients underwent right salpingectomy. The 35 patients underwent left partial salpingectomy whereas 10 patients underwent left salpingectomy.

Tubal rupture was observed in 94 cases (58.8%) in the present study. In the remaining 66 cases the fallopian tube was intact.

Histopathological findings

Microscopically tube showed effects of developing embryo like the presence of chorionic villi and areas of hemorrhage. Other findings that were observed are given below.

Chronic salpingitis

Chronic salpingitis was suggested by the presence of chronic inflammatory cells like lymphocytes and plasma cells in the lamina propria, thickening of the rugae and blunting of the plicae.

Salpingitis isthmica nodosa

In salpingitis isthmica nodosa, there was presence of tubal epithelium within myosalpinx or beneath the tubal serosa. This was accompanied by smooth muscle hyperplasia.

Endometriosis

In case of tubal endometriosis, endometrial glands and stroma was identified within the wall of the tube.

Acute salpingitis

Microscopic presence of dense inflammatory infiltrate composed predominantly of neutrophils was observed in acute salpingitis. This was also associated with mucosal edema and exudation.

Decidualisation

Decidual change of the tubal wall was noticed in 21 cases.

Walthard nests

These were seen as nests or cysts and they show transitional cell metaplasia.

Of the total 160 cases studied, the most frequent pathological finding was chronic salpingitis which was noted in 77 cases (48.1%). There were 13 cases (8.1%) of

salpingitis isthmica nodosa, all of which was associated with chronic salpingitis. Only one case of tubal endometriosis was noted in this study. No case of tuberculosis of fallopian tube was identified. The tube showed normal histology other than the presence of villi, in 52 cases (Table 5).

Table 5: Percentage distribution of the sample according to histopathological findings.

Histopathological findings	Count	Percentage (%)
Acute salpingitis	30	18.8
Chronic salpingitis	77	48.1
Salpingitis isthmica nodosa	13	8.1
Endometriosis	1	0.6
Normal histology	52	32.5
Tuberculosis	0	0.0
Others	25	15.6

It was noted in the study that all cases with a positive history of PID, showed evidence of chronic salpingitis during histopathological examination. Chronic salpingitis was also noted in 45% cases who did not gave a history of PID.

DISCUSSION

Age

Ectopic pregnancy can occur at any age from menarche to menopause. In the present study, 70.7% cases were noted between 21-30 years. This is in concordance with the study by Bai et al who noted an incidence of 70.7% in the same age group.³

Parity

In the present study maximum number of patients were between parity 0 and 2. Most of the cases were seen in women during their second or third pregnancy. This finding is similar to that observed by Rose et al and Bai et al.^{3,4}

Risk factors

History of tubal surgery

In this study, 47 cases (29.4%) had previous tubal surgery for the purpose of sterilization. But the exact procedure that the patient underwent was not clear from the records available.

Literature search showed that the chances of failure of voluntary sterilization is relatively small, but if pregnancy does occur in these patients, there is a higher chance of being an ectopic. The proportion of pregnancies which are ectopic will also depend upon the type of procedure that

was undertaken. The proportion of ectopic pregnancy was 4.4% following clipping, 19.5% after ligation, 43-51% after laparoscopic diathermy and 60% following application of Falope ring Tatum et al.⁵ This difference in the rates could be due to the difference in efficiency of a particular procedure in effectively preventing an intra uterine pregnancy.

The exact mechanism that results in tubal gestation after a tubal sterilization procedure is uncertain, but the possible factors are recanalization and formation of tubo-peritoneal fistulas, that are sufficiently large to allow the passage of a sperm but not that of an embryo.

In the present study, the number of women who had a history of tubal sterilization was higher (29.4%) than most of the other studies except in the study by Bai et al.³ This could be due to the fact that ours is a referral institute and there is a very high chance of women with a sterilization failure to be referred to us from the various peripheral institutions.

Previous abdominal surgery

In the present study, 37 (23.1%) patients gave a history of abdominal surgery including 5 cases with a history of appendectomy, 31 cases with history of caesarian section and 1 case with a history of myomectomy. In the study by Bai et al it was observed that 1.1% patients had a history of appendectomy.

Previous abortion

History of abortion, either spontaneous or induced, was noted in 15 (9.4%) cases in the present study. Bai et al in their study noticed that 20.8% patients gave a history of previous abortion.³

Intra uterine contraceptive device (IUCD)

In the present study, 12 patients gave a history of use of an IUCD, out of which in one patient the current pregnancy resulted with an IUCD in situ. When a pregnancy results in a woman wearing an IUCD, it is likely to be ectopically placed in 4 -8% of cases Tatum et al and Vessey et al.^{5,6} IUCD s are thought to be more effective in preventing a uterine implantation than they are in inhibiting a tubal implantation, Lehfeltd et al.⁷

Infertility

In the present study, 10 patients (6.3%) gave a history of infertility.

PID

Among the 160 cases in the present study, 9 patients (5.6%) had a previous history of PID. Throughout the literature, PID is considered as an important risk factor for an ectopic pregnancy. PID cause 3.3-to-6-fold increase in

ectopic pregnancy. According to ICMR multicentric case control study, the relative risk was 6.4.⁸ Brunham et al found a strong association between chlamydial infection and tubal pregnancy, by using serological tests for chlamydia. It is now recognized that chlamydia trachomatis is the single most important cause of PID. However, infection by this organism is often asymptomatic. Studies by Chow et al and De Muylder et al and several others showed that in women who are seropositive for Chlamydia, there is a markedly increased risk of ectopic pregnancy.^{9,10}

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.

Previous ectopic

In the present study, 6 patients (3.8%) gave a history of previous ectopic pregnancy. This is in concurrence with studies by Rose et al and Bai et al who quoted an incidence of 3.2% and 2.3% of recurrent ectopic pregnancies respectively.^{3,4}

Site of involvement

In the present study, the most common site of involvement of tubal pregnancy was the ampulla of the tube. 85.6% of cases involved the ampulla. Studies by Devi and Khera showed maximum number of cases involving the ampulla which was 61.53% and 71.7% respectively.^{11,12}

Histopathological findings

Chronic salpingitis

In the present study, the most frequent histopathological lesion in the fallopian tube harbouring the gestation was Chronic Salpingitis which was observed in 77 cases (Figure 1 and 2).

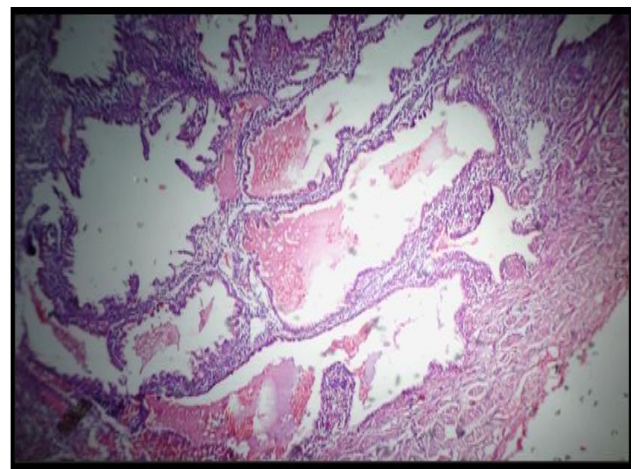


Figure 1: Chronic salpingitis-distorted plicae H and E (40X).

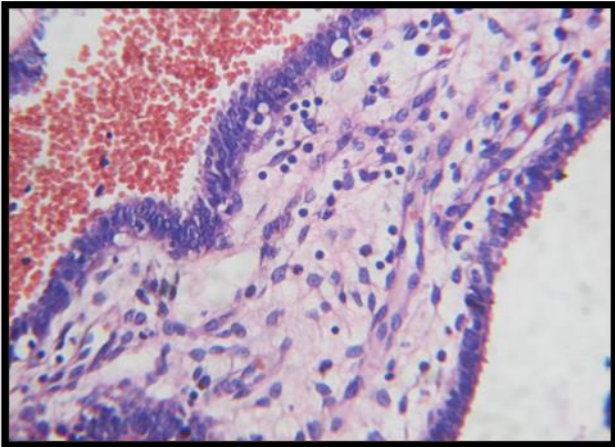


Figure 2: Chronic salpingitis-lamina propria showing lymphoplasmacytic infiltration H and E (400X).

Among the various causes of ectopic pregnancy, the most widely accepted one is the delay or blockage of transport of the ovum by a tubal lesion. The most important cause for this condition is scarring of the tube as a result of infection or inflammation. In literature, the reported range of chronic salpingitis varies from 29-89%. The results obtained in the present study was similar to that obtained by Kutluay et al.¹³

Salpingitis isthmica nodosa

This lesion was observed in 8.1% of cases in the present study. In all cases it was associated with chronic salpingitis.

Salpingitis isthmica nodosa is a lesion of unknown etiology, which is defined by the microscopic presence of tubal epithelium, in the myosalpinx or beneath the serosa of the tube (Figure 3-5). This lesion may be visible grossly as a nodularity, but according to Honore, 80% cases are grossly undetectable.

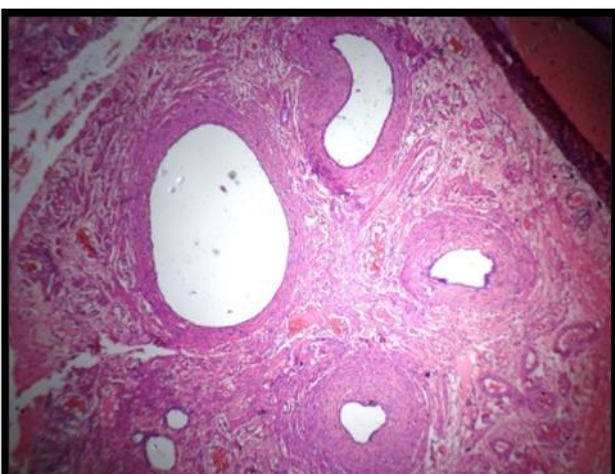


Figure 3: Salpingitis isthmica nodosa-glands infiltrating the wall of the fallopian tube H and E (40X).

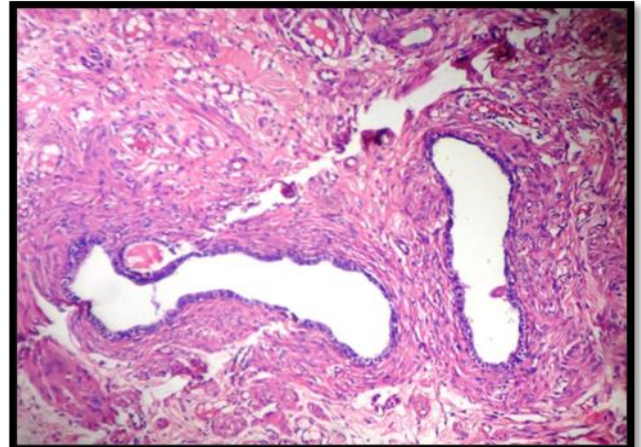


Figure 4: Salpingitis isthmica nodosa-glands surrounded by smooth muscle hyperplasia H and E (100X).

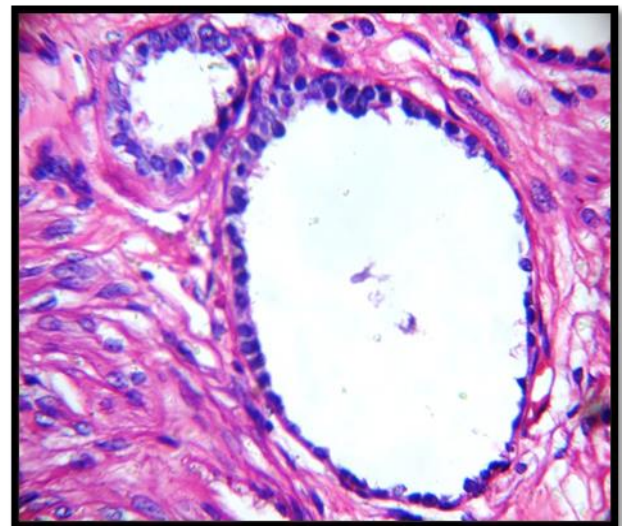


Figure 5: Salpingitis isthmica nodosa-glands lined by single layer of bland tubal epithelium H and E (400X).

Salpingitis isthmica nodosa is said to hinder the tubal motility by undergoing spasm of the hypertrophied muscle. It is also possible that the ovum gets entrapped with in these glandular spaces which has connection with the lumen of the tube.

The incidence of salpingitis isthmica nodosa in literature is widely variable. Majmudar et al in their study quoted an incidence of 57% in a black population.¹⁴ Gonzalez et al reported an incidence of 9.9%.¹⁵ The present study shows an incidence in concordance with that obtained by Dahiya et al.¹⁶

Tubal endometriosis

In the present study out of the total 160 cases, only one case of endometriosis of fallopian tube was noted which accounted for 0.6% (Figure 6 and 7).

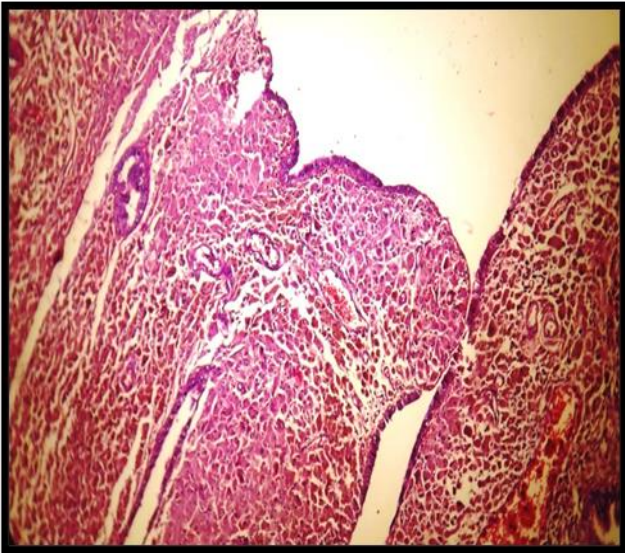


Figure 6: Tubal endometriosis-showing entrapped glands H and E (100X).

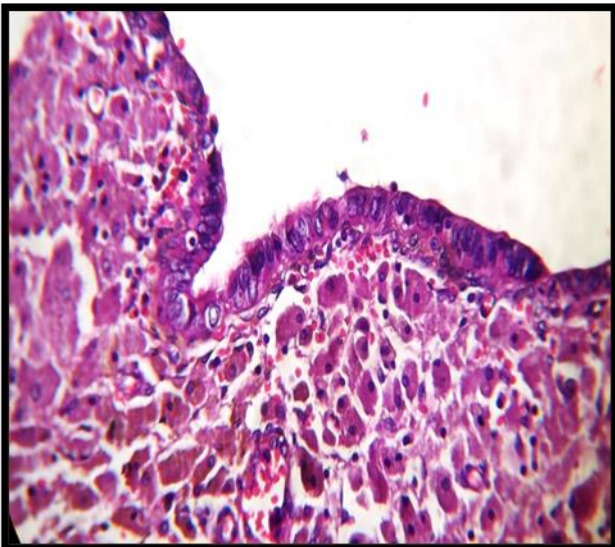


Figure 7: Tubal endometriosis showing sheets of hemosiderin laden macrophages H and E (400X).

The studies by Dahiya et al and Kutluay et al did not show any case of tubal endometriosis.^{13,16} Gonzalez et al found endometriosis in 1.2% of gravid tubes.¹⁵

Acute salpingitis

There were 30 cases which showed Acute Salpingitis in the present study. This finding was consistent with the results obtained by Dahiya et al.¹⁶ But this is thought to be due to the direct effect of implantation of the ovum.

Normal histology

Even on careful examination, 32.5% of tubes did not show any pathology in the present study, other than effects of

tubal implantation. In the study by Dahiya et al, normal histology was noticed in 14% of cases.¹⁶

Tuberculosis

No case of tuberculosis of the fallopian tube was noticed in the present study. The studies by Dahiya et al and Kutluay also did not reveal any case of tuberculosis.^{13,16}

Other findings

Other histological findings observed were decidualisation and Walthard cell nests (Figure 8).

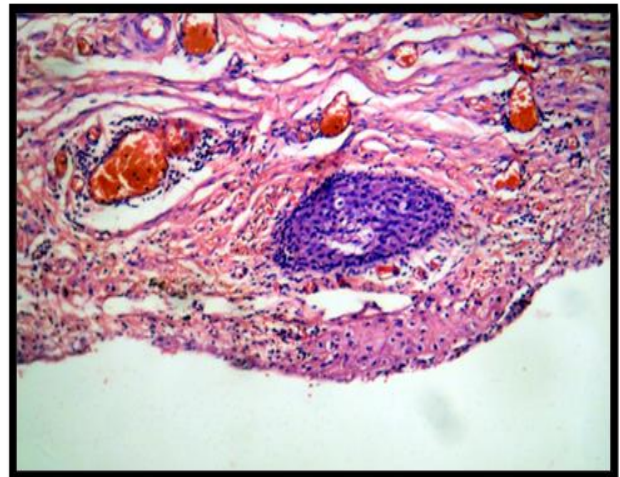


Figure 8: Walthard nests H and E (100X).

Association of chronic salpingitis with PID

In the current study, it was observed that all women who gave a history of PID was found to have chronic salpingitis on histopathological examination. This association was found to be statistically significant ($p=0.001$).

Weinstein et al in their study quoted that 44% of women with a history of PID showed histological evidence of salpingitis.¹⁷

In a five-year study by Powers, it was demonstrated that among 204 cases of ectopic pregnancy, chronic salpingitis was noticed in 44.6%.¹⁸ But among this a positive history of PID was obtained only in 13.2% of patients.

In the large Swedish cohort study by Westrom et al, it was shown that PID causes tubal factor infertility and it was associated with the number and severity of PID episodes.¹⁹

Limitation

The main limitation of the study was that, the technique of sterilization was not taken into consideration during the study. Knowing this data would help us understand the association of tubal pregnancy with a particular tubal sterilization procedure.

CONCLUSION

The incidence of ectopic pregnancy has increased in the last two decades, but the mortality has declined. Nevertheless, this condition is associated with high morbidity and affects the fertility of the woman. The rise in incidence could be because of higher prevalence of sexually transmitted diseases, increase in the tubal sterilization practices and the more frequent use of assisted reproduction technologies. The present study was undertaken in order to provide a better understanding of the histopathological changes in ectopic tubal pregnancy and to identify the various risk factors prevalent in our population. It is evident from this study that many cases of PID are unidentified, and hence better protocols for identification of these cases may be laid. Even though there are diagnostic tools to detect an ectopic early in the pregnancy, most of the time the patient presents with a ruptured ectopic and has to be managed as an emergency. Clinicians should be on alert and consider this possibility whenever dealing with a woman of reproductive age group presenting with abdominal pain, irrespective of whether there is a history of amenorrhoea or not, or even when she had undergone sterilization procedure. Further studies need to be done in order to determine if any particular technique of tubal sterilization is associated with increase in ectopic risk.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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