Original Article

Muscular and Vascular Fallopian Tube Morphology in Ectopic Tubal Pregnancy

Seema N. Baxi, Mitesh Koyani, Md Hashmi Sabugar, Dhwani Pandya*

Department of Pathology, Pathology, Govt Medical college, Bhavnagar

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***Corresponding Author**:
Dr Dhwani Pandya
tinadhwani@gmail.com

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Abstract

Background

Although literature is full of articles on histopathological changes in fallopian tube in ectopic pregnancy and the predisposing conditions associated with ectopic pregnancy, none have mentioned or reported abnormal muscle and vascular architecture of the tube. The study was undertaken to find the percentage of different sites of ectopic pregnancies coming to the institute for treatment and to calculate the proportion of various morphological risk factors which could have led to the ectopic pregnancy and to discern the various histopathological changes in cases of ectopic tubal pregnancies.

Methods

A retrospective study was conducted on all the cases of ectopic pregnancies in the year of 2021 and 2022. For comparison of morphological changes equal number of tubes received for tubal ligation were assessed as they served age matching purpose. Hematoxylin & eosin-stained slides were retrieved and re-examined for the histological patterns.

Results

92% of the ectopic pregnancies were tubal pregnancies. Amongst predisposing factors of tubal pregnancies detected morphologically, chronic salpingitis was seen in 71.5% of cases while Salpingitis Isthmica Nodosa (SIN) was seen in 26.1% of cases.

Conclusion

Abnormal morphological findings like tubal muscle splaying, arterial wall thickening leading to grotesque shapes, clear changes in different layers of tunica of blood vessel with or without concentric muscle splaying were seen in tubal ectopic pregnancies in significant numbers of cases.

Keywords:

atherosis, chronic salpingitis, ectopic tubal pregnancy, grotesque vessels, salpingitis isthmica nodosa, tubal muscle splaying, vascular muscle splaying

Introduction

The incidence of ectopic pregnancy appears to be increasing probably due to tubal surgeries [1], previous ectopic [2,3], intra uterine devices[4], novel techniques for Assisted Reproductive Technology(ART) and Pelvic inflammatory diseases (PID)[5]. Though many studies have noted histopathological changes in fallopian tube in ectopic pregnancy and have classified associated

predisposing conditions [6,7,8], none have reported abnormal muscle and vascular architecture of the tube which were noted by the authors during this study. The first author of this study had been seeing abnormal vascular and muscular morphologies in tubal ectopic specimens, hence a retrospective 2 year study was conducted to find the percentage of different sites of ectopic pregnancies appearing at the institute, to calculate the proportion of various morphological risk factors which could have led to the ectopic pregnancy and to discern the abnormal histopathological changes in ectopic tubal pregnancy.

Materials and Methods

After ethical committee approval, a retrospective study was conducted on all the cases of ectopic pregnancies in the years of 2021 and 2022. For comparison of morphological changes in the tubes in ectopic cases, an equal number of tubes received for tubal ligation were assessed as the age group of ectopic pregnancies and women undergoing sterilization are the same. Hematoxylin & eosin-stained slides were retrieved and re-examined of histological patterns. Statistics – Proportion of ectopic pregnancies and percentage of various risk factors were calculated using simple mathematical formula. Comparison of morphological abnormalities between normal fallopian tubes and those of ectopic pregnancies was done by chi-square test.

50 cases of ectopic pregnancy were available during the study period. So, 50 cases of tubal ligation tubes were also reviewed for morphology as controls.

Results

Out of 50 cases of ectopic pregnancies 92% (46 cases) were those of ectopic tubal pregnancies. Out of those 46 cases, glass slides of 4 cases were not available. So these 4 cases were excluded from further study for morphological assessment.

Table 1: Site of ectopic pregnancy

Site	Percentage
Tubal	92%
Scar	04%
Abdominal	02%
Ovarian	02%

Table 2: Pathologies associated with ectopic Tubal pregnancy(n=42)

Probable causal finding	Percentage
Chronic salpingitis	71.5%
Salpingitis isthmica Nodosa (SIN)	26.1%
Foreign body	2.4%
Total	100%

Chronic salpingitis of mild degree was seen in 3/4th of the tubes in ectopic pregnancy, which was seen mainly in the submucosa below the plicae of the tubes. There was also presence of variable thickening of rugae and presence of edema with blunting of plicae. [Fig-1] In cases having SIN morphology, lymphocytes were seen in a perivascular region and diffusely spread deep in the lamina propria or in the muscularis. [Fig-2] In present study, though tubal epithelium was seen in 26% cases in the myosalpinx, smooth muscle hyperplasia around the tubal epithelium was not seen. 2 of the cases had moderate to severe chronic inflammation.

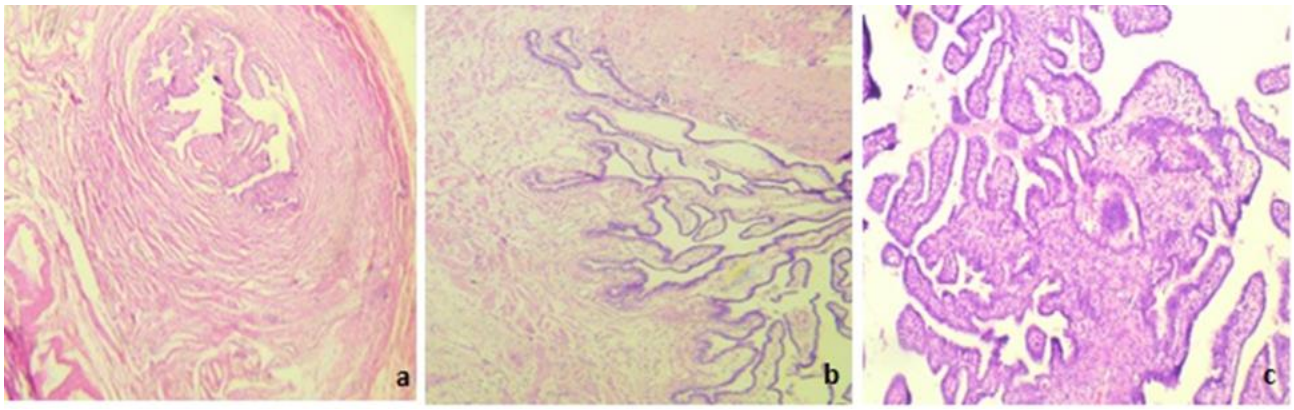

Figure 1: Morphological changes in tubal epithelium suggesting chronic salpingitis. a- Scanner view showing blunting of plica and grotesque vessels in the serosa on the left lower corner (HE, 4x). b- Dilated, blunted and edematous interconnected plica (HE, 10x), c- Blunted and fused plica with inflammatory change (HE, 10x)

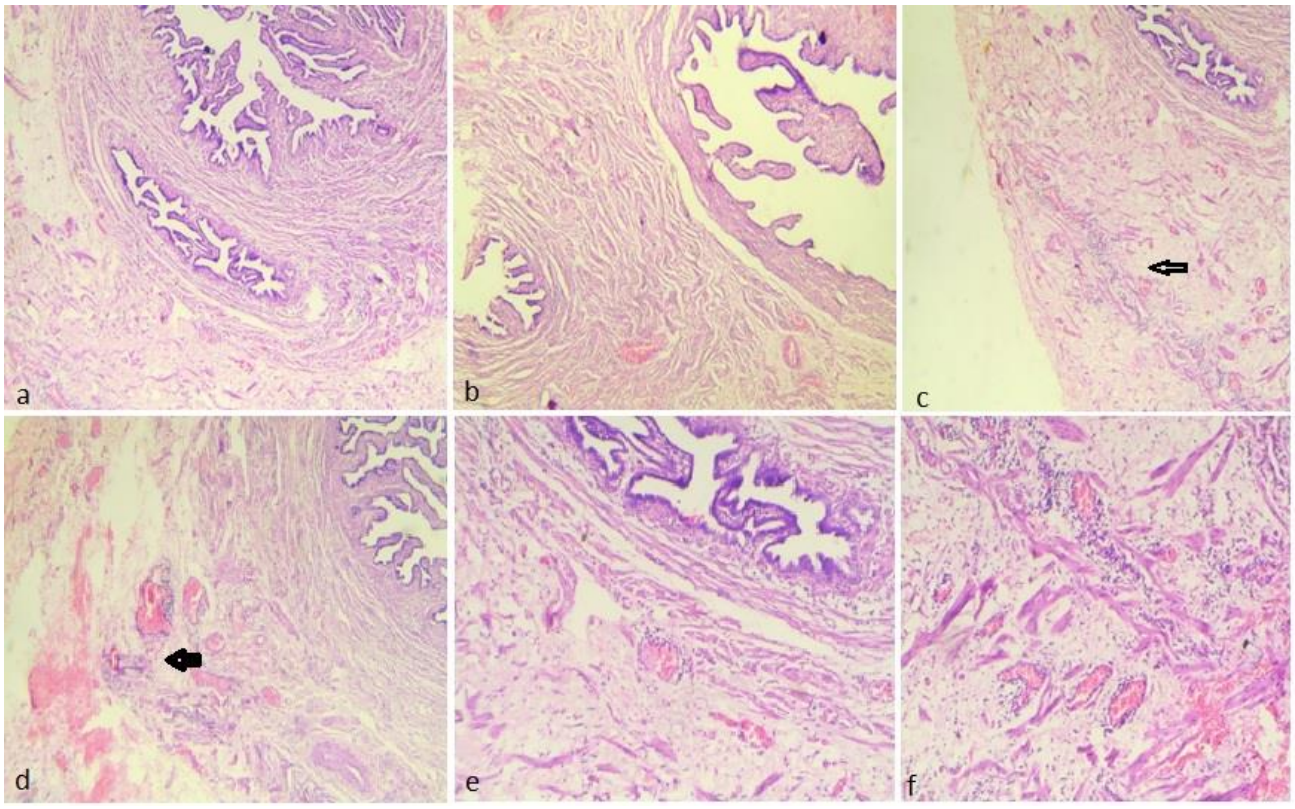

Figure 2: Salpingitis Isthmica Nodosa (SIN) with perivascular and diffuse stromal lymphocytic inflammation. a- A case of SIN showing additional tubal epithelium within the myosalpinx (HE, 4x), b- Another case of SIN showing main lumen with blunted plica on right side with another tubal epithelium on left side with muscle fibres in between separating them (HE, 4x), c- Perivascular inflammation seen at periphery (arrow) (HE, 4x), d- Perivascular inflammation in another case of SIN (arrow) (HE, 4x), e- Perivascular lymphocytic inflammation (HE, 10x), f- Stromal inflammation (HE, 10x)

The sections showing abnormal tubal morphology like tubal muscle splaying, vessel thickening, grotesque vessels, muscle splaying around vessels, vessels with clear muscle cells were all seen at sites away from the areas which showed villi or trophoblastic cells.

Table 3: Abnormal architecture of fallopian tube in cases of tubal ectopic

Microscopic findings in Ectopic	Percentage in controls (N= 50)	Percentage in ectopic (No of cases =42)	P- value
Tubal muscle splaying	0	90.4%	<0.00001
Vessel thickening	0	64.2%	<0.00001
Grotesque vessels	0	45.2%	<0.00001
Vessels with clear muscle cells	0	30.9%	0.000118
Muscle splaying around vessels	0	16.7%	0.012888
Atherosis in vessels	0	7.1%	0.239590

Muscle fibers of the wall of fallopian tube in case of ectopic pregnancies were seen to be separated, at times appearing at 45 degrees or more to their normal circular position in the wall of the fallopian tube. [Fig-3] This is referred to as muscle splaying in this article. The fibers were separated by edema in many cases; however no trophoblastic cells were seen encroaching these areas. In cases of SIN muscle splaying was seen both near to and away from glandular epithelium.

Vessels in cases of tubal ectopic were markedly enlarged and thickened in majority (64%) of the cases and the shape of vessels were grotesque in 45 % of cases. [Fig- 4] Clear cells were seen in the thickened vessels, either in the tunica intima, or media or the externa. Many of these vessels showed splayed muscle fiber around the external circumference of vessel. [Fig-5] 3 of the cases showed changes of vacuolation or atherosis as seen in [Fig-6].

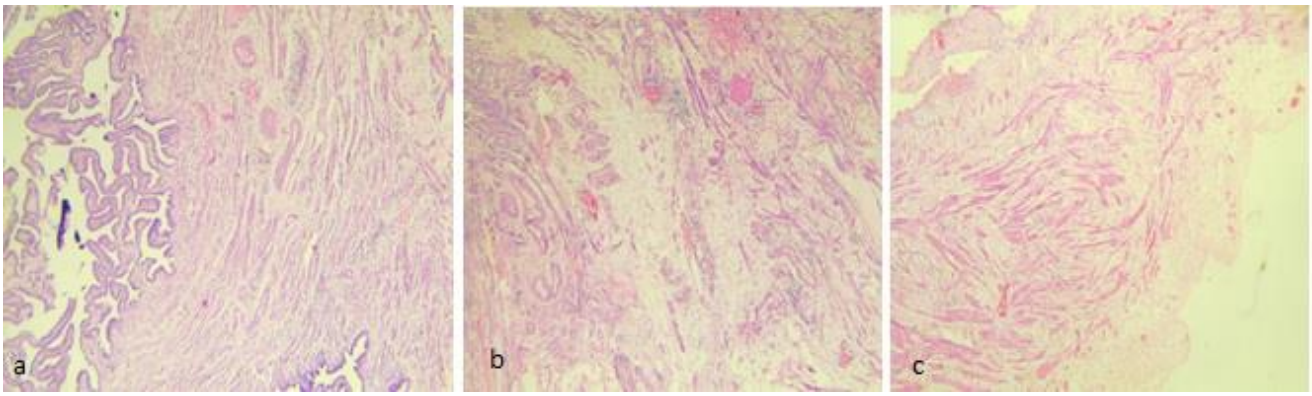

Figure 3: Showing tubal muscle splaying. All pictures are scanner view (HE, 4x). a- SIN is seen on right lower side and mild degree of muscle splaying in right upper corner. The separation is due to oedema. Muscle fibre splaying is minimal being almost parallel to each other, b- Splaying of tubal muscle fibres at 20 to 40 degrees, c- Splaying of tubal muscle fibres is more marked and is at 45 to 70 degrees to each other.

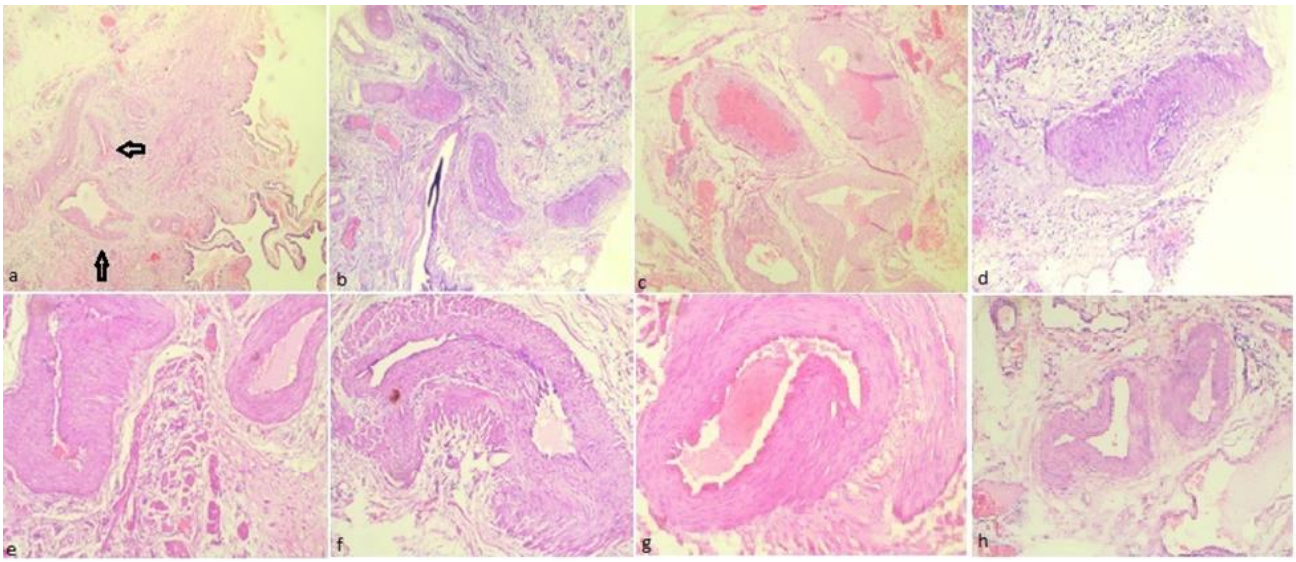

Figure 4: Grotesque vessels in different cases of ectopic pregnancy. a- Many abnormally thickened, tortuous and grotesque arteries visible even on scanner view (arrows) (HE, 4x), b- Abnormally thickened arteries seen even on scanner (HE, 4x), c- Thickened and Grotesque vessel with fibrin clot (HE, 10x), d- Abnormal thickened grotesque artery near serosa (HE, 10x), e- Markedly thickened and enlarged vessel walls with muscle splaying in between (HE, 10x), f- A tortuous markedly thickened and enlarged vessel, with splaying of tunica externa (HE, 10x), g- Another case showing markedly thickened tortuous artery (HE, 10x), h- Abnormal grotesque arteries with tortuous dilated vein and lymphatics in lower right corner (HE, 10x)

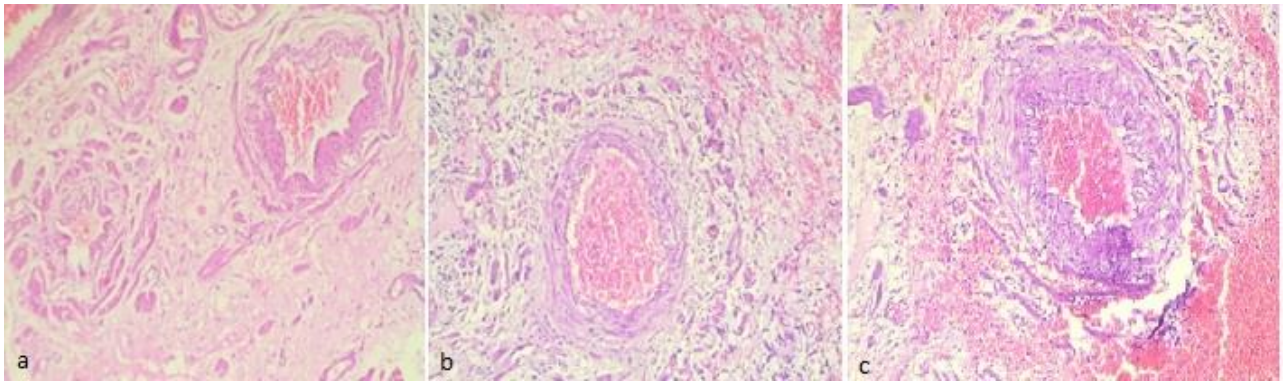

Figure 5: Vascular muscle splaying in fallopian tubes of different cases of tubal ectopic pregnancies. No trophoblastic cells are seen within the vessels or in the vicinity. All photos are H&E, 10X. a- Markedly thickened arteries. Right upper one is showing separation of tunica externa and all the muscle layers are splayed in the artery seen in the left lower side. b- Marked splaying of Tunica media and externa by oedema. There is inflammation and interstitial hemorrhage at the periphery. c- Marked vascular thickening with splaying of externa. Oedema, inflammation and interstitial hemorrhage are seen in the section.

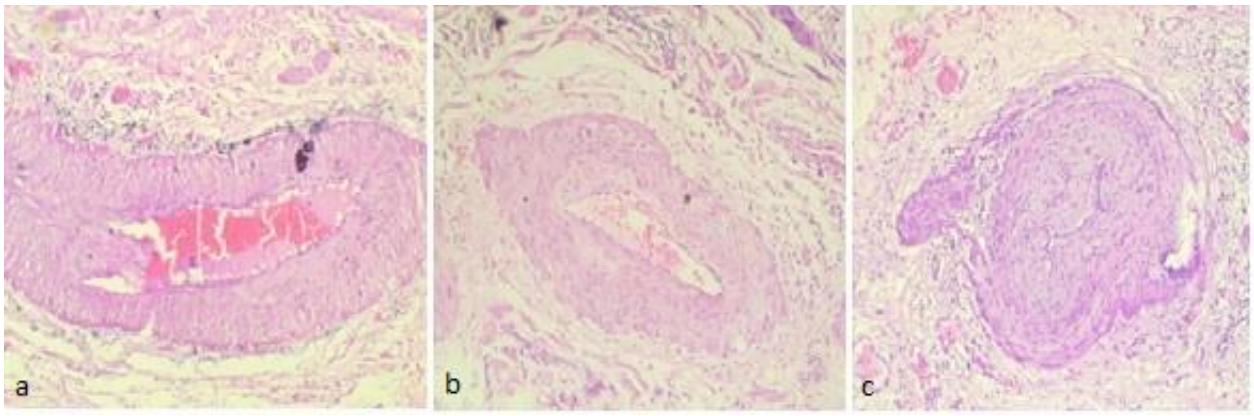

Figure 6: Vacuolation and changes of atherosis in thickened tubal arteries. All pictures are HE, 10x. a- Vacuolation in tunica externa. b- Thickened artery with patchy changes of atherosis seen in tunica intima. c- Marked thickening of all the muscular layers of the artery occluding the lumen along with paleness of the tunica intima and media. There is perivascular infiltration with lymphocytes.

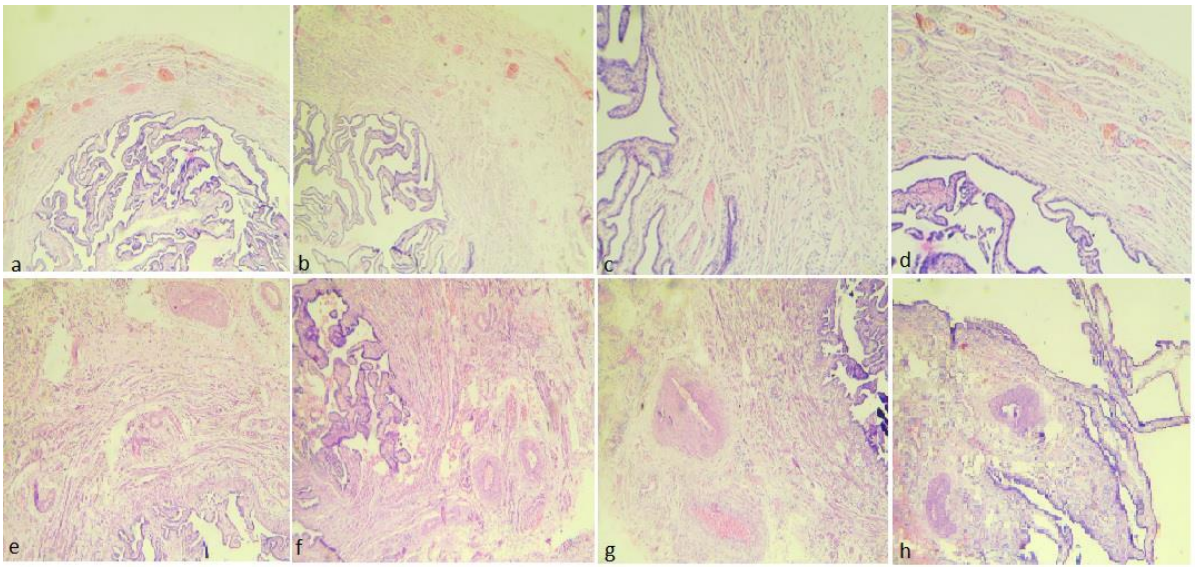

Figure 7: Comparison of fallopian tube morphology in normal and in ectopic tubal pregnancy. a,b 2 normal fallopian tubes showing no tubal muscular splaying and well-arranged and normal sized but congested veins. Arteries are not prominent (HE, 4x). c,d 2 normal fallopian tubes showing no tubal muscular splaying and well-arranged and normal sized but congested veins. Arteries are not prominent (HE, 10x). e,f,g,h 4 cases of ectopic FT showing tubular muscle splaying, arterial thickening, and distortion of morphology of tube in areas not showing villus or trophoblastic cell invasion. (HE, 4x)

Discussion

The site wise occurrence of ectopic pregnancy in this study was 92% tubal, 4% scar, 2% abdominal and 2% ovarian pregnancies which is similar to that seen in studies of Sharma S et al [9] who found 89% of ectopic pregnancies in tube, 4% in ovary, 7% in adnexal structures and 2% in scar or rudimentary structures.

Ectopic pregnancies are on the rise and the suggested reasons are tubal surgeries, previous ectopic, intra uterine devices and novel techniques for ART. [10] PID is another known risk factor for ectopic pregnancy. Acute and chronic including tuberculous infections, chlamydial, neisserial and fungal infections are the reasons of PID.

Chronic salpingitis in the past has been reported in various literature from 5-90% [10]. Dubuisson [11]and Green [12] have reported a high incidence of chronic salpingitis of 89% and 88% in ectopic pregnancies, respectively. Persaud [13] also showed a significantly higher incidence of tubal chronic lesions in the tubal pregnancy group than the control group which is approximately similar to the present study where 71% cases were showing chronic salpingitis. Chlamydia trachomatis is one of the causes for acute as well as chronic salpingitis, where initial transmural and mucosal infiltration of lymphoplasmacytic response of various degree can be observed. Hoenderboom et al [14] observed 0.9% of the females with chlamydia infection and they had one or more ectopic pregnancies. Acute salpingitis can occur with neisserial infection and shows slight swelling and hyperplasia of the mucosa with inflammatory cells and focal necrosis [15]. None of the cases in the present study showed these findings. Comparing the findings associated with ectopic pregnancies with 2 recent Indian studies of Sharma et al and Rasheed et al, the percentage of this study matched with that of Sharma et al. Rasheed et al had almost 30% cases with no associated findings. It is heartening to note that none of these studies including our own showed evidence of tuberculosis in fallopian tube.

The percentage of Salpingitis isthmica nodosa (SIN) has been reported to be around 1-57%. It is highest in black population. In India, it is reported in 8-10 % in different studies. [16,17] SIN is a pseudo infiltrative lesion consisting of diverticula of tubal epithelium in the isthmus. It occurs in women between the ages of 25 and 60 years. The aetiology is unknown, but post-inflammatory distortion and an adenomyosis-like process are possibilities. An important complication of SIN is infertility, and there is a strong association with ectopic tubal pregnancy. SIN is considered when there is a direct invasion of the tubal epithelium in the myosalpinx. It may reach up to the tubal serosa in the isthmic portion of fallopian tube [18]. There may or may not be accompanying smooth muscle hyperplasia.[19] In present study, though tubal epithelium was seen in 26% cases in the myosalpinx, smooth muscle hyperplasia around the tubal epithelium was not seen in any of the cases. If both glands and stroma are present in the diverticula, it may be difficult to distinguish SIN from tubal endometriosis in some cases. Lymphocytes were seen in a perivascular region in SIN cases of this study that spread diffusely deep in the lamina propria or in the muscularis.

If any of the above causal findings leading to ectopic pregnancies are found, they should be mentioned in the report as it can help to draw the clinicians' attention to treat latent infections, and do request radiological assessment for SIN. If SIN is noted in radiological examination, the gynaecologist can brief the patient of symptoms of ectopic pregnancy and watch for recurrence of ectopic pregnancy in future in contralateral side and prevent rupture thereby decreasing the morbidity and mortality of young female patients.

Discussing the unusual morphologies, in 90% of cases of tubal ectopic pregnancies of this study, the myosalpinx was seen at 10o to 90o of their normal circular position in different cases such that they appeared to be separated (tubal muscle splaying). The fibers were separated by edema, but were not invaded by trophoblastic cells. Such changes can be expected when trophoblastic cells invade into the muscularis and subserosa. They even involve tubal blood vessels with replacement of the vessel wall by fibrinoid material. In late ectopic pregnancies, chorionic villi may transmurally extend into the serosa.[20] However, none of the cases where muscle splaying was seen in this study showed trophoblasts or villi.

In uterine pregnancy vessels near implantation site show invasion by intermediate trophoblasts, proliferation and accumulation of foam cells in the vascular intima.[19] However, in the tubes, in addition to these findings marked thickening and grotesque

appearance of vessels was seen at sites away from the area showing trophoblasts. Vessel wall thickening was seen in 64% cases and grotesque vessels were seen in 45% cases. This vascular proliferation was far more in thickness than is seen in an uterine pregnancy. Tubal arteries were so markedly enlarged with circumferential thickening and were tortuous in majority of the cases that they appeared grotesque in shape and were strikingly evident even at scanner view in majority of the cases.

Clear cells were seen in 31% cases of the thickened vessels, either in the tunica intima, or media or the externa. In majority of these cases the clear areas were uniformly circumferential. 7 % of them showed atherosis which is equivalent to the changes of acute atherosis seen in uterus of women with pregnancy induced hypertension. [21] Atherosis in fallopian tube has not been reported in any literature.

17% of the cases in this study also showed splayed vascular muscle fibers. This was predominant in externa of the vessels and was circumferential. This finding is also not mentioned in any literature.

All the abnormal findings such as muscle splaying, vessel thickening and grotesque vessels were statistically significant and not found in normal control tubes.[Fig-7] These findings have not been reported in any of literature. Even in a recent article of Kaur M et al who have studied histopathological changes in early human ectopic pregnancy and anatomical consideration for its rupture, such findings have not been mentioned.[22] Whether these findings are related to hormone induced changes due to pregnancy or due to some other underlying etiology remains to be evaluated.

The limitations of the study are that being retrospective, specimens were no longer available for more detailed gross examination and also missing previous clinical history could not be availed. A further prospective study with correlation of past history, part of tube involved and a more detailed morphological work up should be conducted to throw light on the exact mechanism for these abnormal and intriguing muscular and vascular changes.

Conclusion

The significance of abnormal but intriguing tube morphology as mentioned here in ectopic tubal pregnancies needs to be investigated further. Morphological findings like acute or chronic salpingitis and SIN suggesting likely cause of the present ectopic pregnancy if found at histopathology, should be mentioned in the report as it can help the clinicians to treat latent infections, and do radiological assessment for SIN to prevent recurrence of ectopic in contralateral side thereby decreasing the morbidity and mortality in young female patients.

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