

Introduction

Ectopic pregnancy (EP) complicates 1-2% of all pregnancies and Methotrexate (Mtx) is used in the management of ectopic pregnancy since late 1980s. Since then, Mtx based protocols have been accepted as safe, effective and economically cheaper form of treatment to salvage the tube in hemodynamically stable patients. The success rate of Mtx varies between 88-92% with single and multi dose Mtx and the failure rate depends on various factors like ectopic sac >4cm, presence of cardiac activity, initial beta hCG > 5000mu/ml, presence of moderate to severe amount of free fluid in pelvis. The failure of medical management in the form of ruptured ectopic pregnancy is still an important concern in clinical practise even during the falling trend of beta hCG. We had a case of ruptured ectopic pregnancy consequently in two pregnancies in spite of successful fall in beta hCG. This raises the concern whether it could be inherent? and we present the challenges around counselling during and after medical management in addition to recent literature review on factors associated with rupture during medical management.

Case report

30 years, Mrs.G, G3A2, married life of 5 years had one biochemical pregnancy followed by missed miscarriage at 8 weeks which was managed with suction and evacuation.

III pregnancy:

- Presented with history of missed periods by 5 days and faintly positive urine pregnancy test. The serum beta hCG was 246.68mU/ml. Transvaginal USG didn't reveal gestational sac neither inside nor outside the uterus. Endometrial thickness (ET) was 8mm
- Serum beta hCG had raised by 52% in the next 48 hours & she was explained about the possibility of ectopic pregnancy with regular follow-up
- Presented 9 days later with serum beta hCG of 6801 mu/ml with complex adnexal mass of 1.5X1.2cm on USG; no free fluid in pelvis
- She was hemodynamically stable & started on single dose Mtx
- However on next day, she had complained of pain abdomen & was diagnosed as tubal rupture. Emergency laparoscopy was undertaken and left salpingectomy was done as there was left ampullary ruptured ectopic pregnancy
- There was 800ml of hemoperitoneum; other adnexa was normal. Received 2 units of packed cell

IV pregnancy:

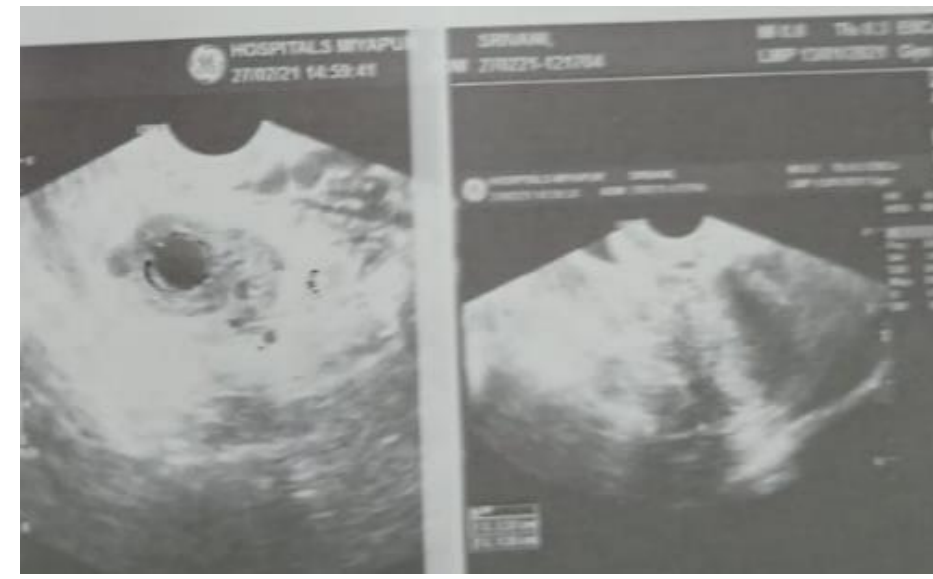
- A year later, she again presented with 35 days of amenorrhoea. Urine pregnancy test was weekly positive. Serum beta hCG was 78mu/ml and after 48 hours it was 187mu/ml
- However the pelvic USG was normal. She returned after 7 days with beta hCG value of 4272mu/ml and there was a gestational sac of 4mm in right adnexa. It was unruptured ectopic pregnancy & she was hemodynamically stable
- Inj.Mtx of 1mg/kg was given (D1) and the serum beta hCG was 8175mu/ml (70%) on D4 and decided for double dose regimen. As the rise in beta hCG was <10% in 48 hours after second dose and was put on regular follow-up
- Subsequent serum beta hCG values had shown significant fall or >25% she was discharged with appropriate advise. Nine days later she returned to emergency with symptoms and signs of acute tubal rupture which warranted emergency laparoscopy
- Hemoperitoneum of 800ml and right salpingectomy was done for ruptured ampullary ectopic pregnancy.

Recurrent ruptured ectopic pregnancy following successful medical management : Is it inherent? – A Case report

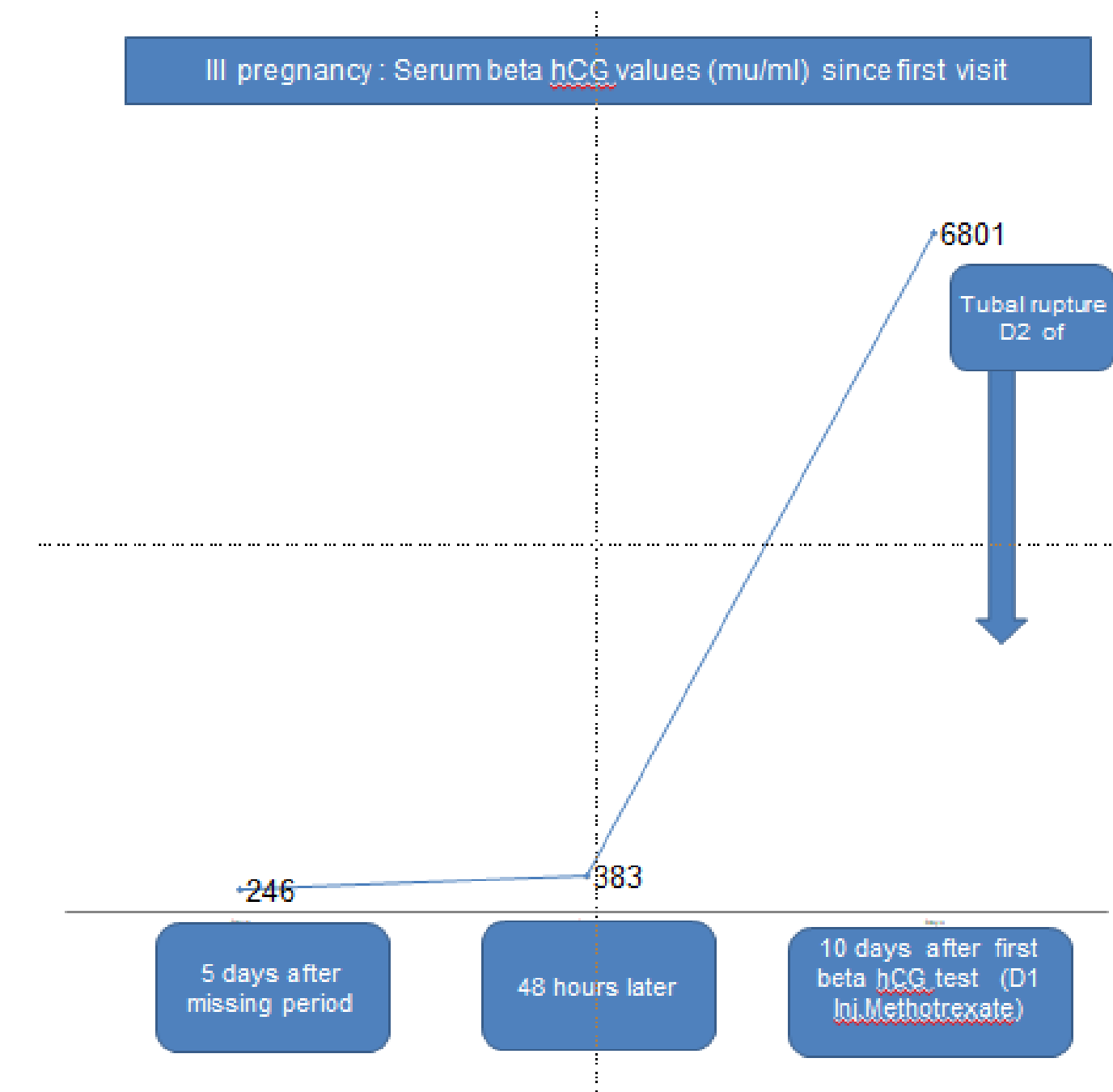
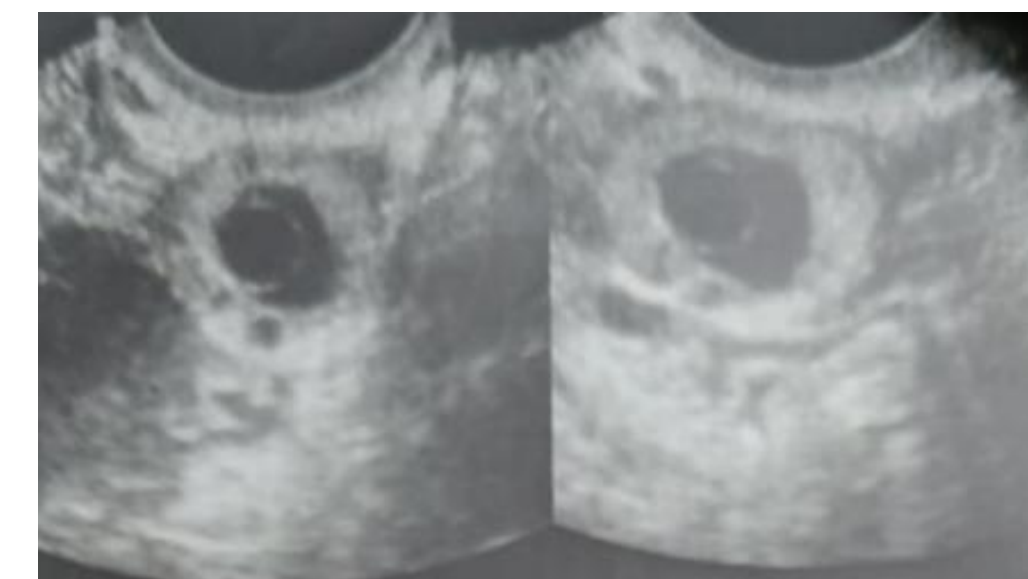
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Ultrasound

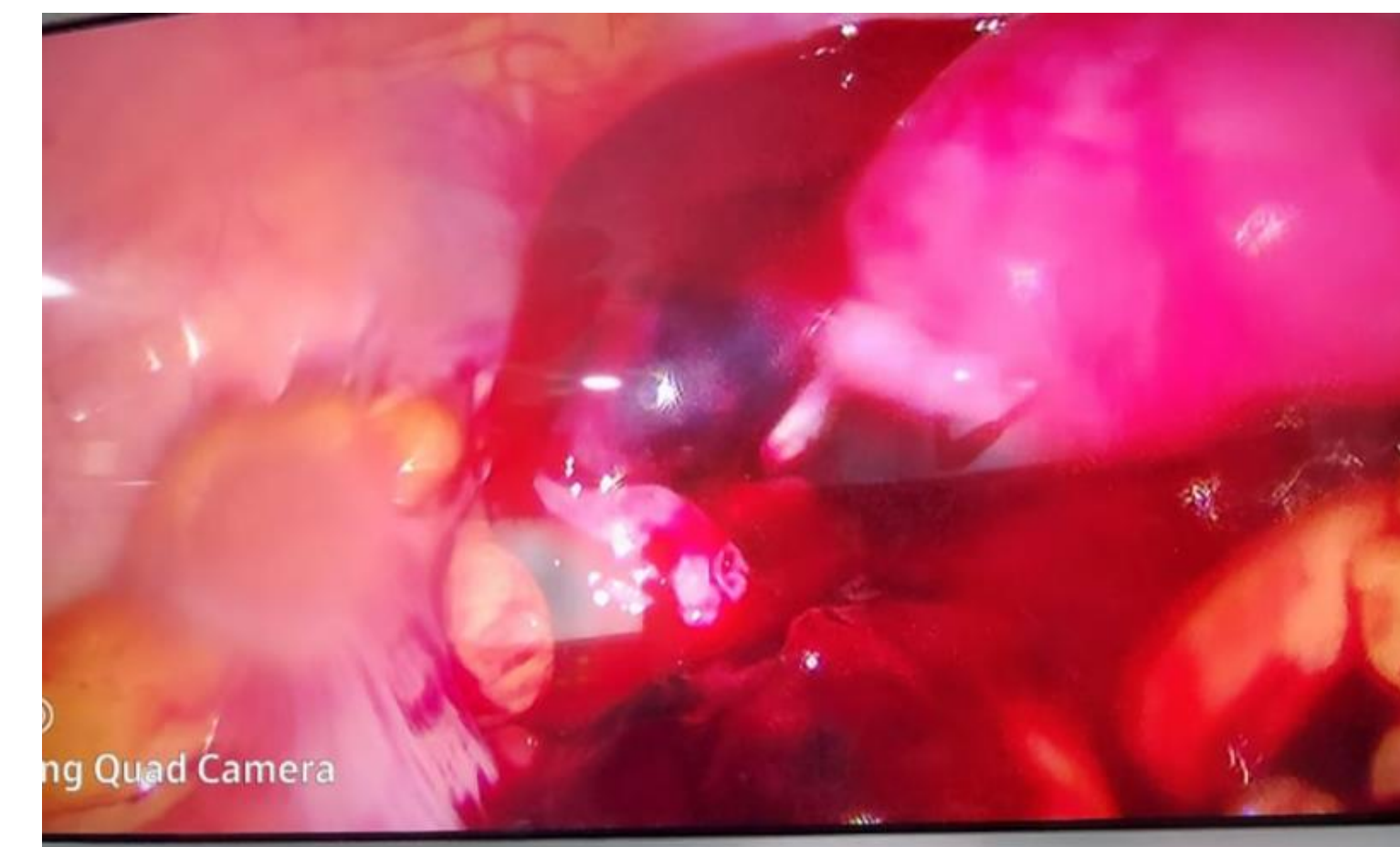


Serum beta hCG (in both the times)

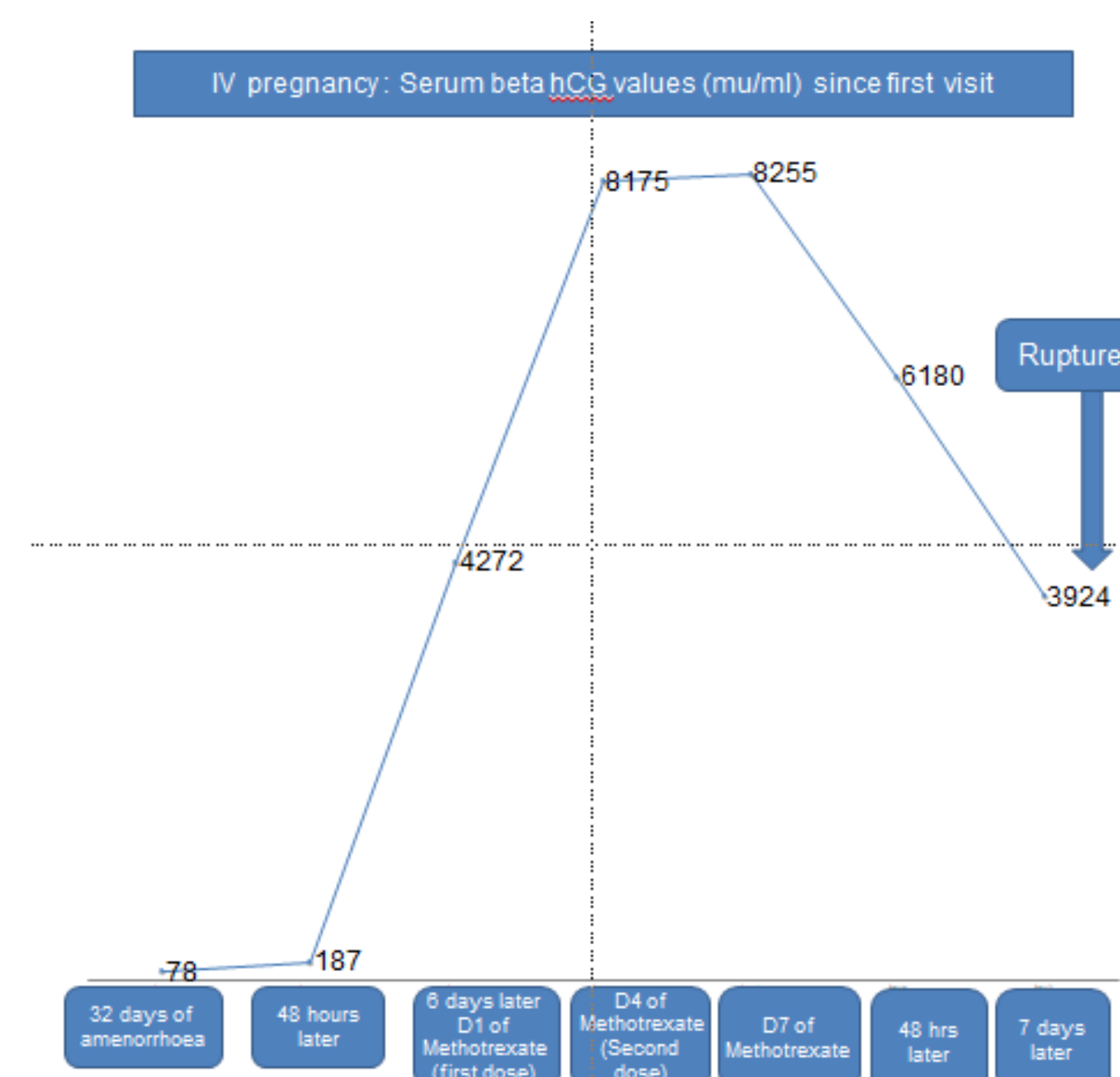


Intraoperative images

III pregnancy



IV pregnancy



Discussion

- Ruptured EP despite Mtx treatment is still a concern and the rupture can occur many days after Mtx treatment despite a >15% fall in serum beta hCG levels
- The study on trend in the beta hCG values predicting failure has shown a 5% rise of beta hCG between D1/D4 [68% (95%CI 49-83%), specificity 69% (95%CI 56-78%) and AUC 0.77 (95%CI 0.68-0.86), $p<0.001$] and fall of <17% between [sensitivity 83% (95%CI 64-94%), specificity 82% (95%CI 71-90%), and AUC 0.90 (95%CI 0.84-0.96)] predicted failure rate with good sensitivity and specificity. Goh A et al had concluded that the trend in beta hCG values between Day1 and day 4 could be used to decide about additional dose of Mtx and to counsel women with high risk factors
- A meta-analysis on single versus two dose regimen has shown that two dose regimen was found to be successful in patients with high beta hCG values (OR, 3.23; 95% CI, 1.53 - 6.84) and large gestational sac (OR, 2.93; 95% CI, 1.23, 6.9). Though the odds of surgery for tubal rupture was less in two dose regimen, the difference was not statistically significant
- Hutchinson et al looked at the factors associated with risk of ruptured EP despite medical management with Mtx. The risk of ruptured ectopic pregnancy was more when they presented with vaginal spotting and had less reduction in serum beta hCG between day of Mtx and Day 4 or Day 7
- Though she presented to us for evaluation of infertility, she ended up undergoing B/L salpingectomy for recurrent ruptured EP despite Mtx during the covid pandemic. In her third pregnancy, EP ruptured next day after single dose Mtx and in her fourth pregnancy it happened after double dose Mtx.

Conclusion

- Despite medical management, the risk of ruptured EP exist for many days after Mtx
- Recurrent EP despite Mtx in a nulliparous woman is always challenging and compounds the issues like counselling
- Alternative factors other than serum beta hCG D4 & D7 are to be explored to find out the risk of rupture at the earliest
- Whether the risk of rupture is inherent in a woman could be altogether a new area of interesting!
- However, careful monitoring/follow-up and through counselling are important to identify the failure of medical management at the earliest to salvage the fallopian tube

References

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