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Uncommon Ectopic Pregnancies—Challenges in the Management

Hiralal Konar^{1,7} · Lisley Konar² · Chandrachur Konar³ · Arindam Halder⁴ · Arindam Saha⁵ · J. Khamaru⁶

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Abstract

Background The risk factors for ectopic pregnancy are on the rise. Despite the progress (availability of serum β hCG, USG and MRI), there are diagnostic and therapeutic challenges in the management. Up to 50% of ectopic pregnancies go undetected. Furthermore, cases seen as emergency with hemodynamic instability need urgent intervention with simultaneous arrangement of transport, blood transfusion and at times multidisciplinary team involvement. This is more challenging in a setting where resources are limited.

Objective To evaluate the outcome of women presenting with uncommon ectopic pregnancies as life-threatening emergency. Challenges encountered in diagnosis, pre-operative evaluation, decision for surgery and the procedure are presented.

Patients and Methods This is a series of twelve cases of uncommon ectopic pregnancies belonging to eight different types. These were managed under the first author during the period 2001 to 2019. Subjects were analyzed retrospectively.

Results Diagnostic dilemma was faced in majority of the cases even with the use of ultrasonography. All the conceptions were spontaneous. Emergency surgical interventions were made on the basis of clinical evaluation. Five cases presented with massive hemoperitoneum. Blood transfusion was needed in nine cases. There was no mortality. One woman (case 4), with abdominal pregnancy, went home with a live baby, after the second laparotomy.

Conclusion Uncommon ectopic pregnancies are life-threatening conditions. Clinical acumen and an alert mind are of superior value in diagnosis. Investigations are supportive. Early diagnosis and intervention are lifesaving.

 $\textbf{Keywords} \ \ Uncommon \ ectopic \ pregnancies \cdot Surgical \ emergency \cdot Diagnostic \ dilemma \cdot Management \ options \cdot Maternal \ mortality$

Dr. Hiralal Konar, MBBS, MD, DNB, MNAMS, FACS (US), FRCOG (Lond), Prof and Head, Dept. OB-GYN: Agartala Govt. Medical College and GB Pant Hospital, Agartala, Tripura, India; Dr. Lisley Konar, MBBS, Resident (1st. Yr.M S), Dept OB-GYN, SDU, Academy of Higher Education and Medical Research, Karnataka, India; Dr. Chandrachur Konar, MS, DNB, Assistant Professor, Dept. OB-GYN. SDU Medical College, Karnataka, India; Dr Arindam Halder MBBS, MS, Associate Professor, Dept. OB-GYN, Dinajpur Medical College, West Bengal, India; Dr. Arindam Saha, MD, R.M.O cum Clinical Tutor, Dept. OB-GYN; N.R.S. Medical College, Calcutta, India; Dr. J. Khamaru, MD, Consultant Sonologist, Divine Nursingh Home, Calcutta, India.

- Dept. OB-GYN, Agartala Govt. Medical College and GB Pant Hospital, Agartala, Tripura, India
- Department of OB-GYN, SDU, Academy of Higher Education and Medical Research, Bangaluru, Karnataka, India
- Department of OB-GYN, SDU Medical College, Bangaluru, Karnataka, India

Introduction

Incidence of ectopic pregnancy has been on the rise mainly due to the increase in the number of risk factors and detection of more cases. There are many risk factors for ectopic pregnancy (PID, tubal surgery and ART) though it is not uncommon to see women with ectopic pregnancy without any known risk factor.

- Department of OB-GYN, Dinajpur Medical College, Raianj, West Bengal, India
- Department of OB-GYN, N.R.S. Medical College and Hospital, Calcutta, India
- ⁶ Divine Nursing Home, Calcutta, India
- ⁷ P13, CIT Road, Kolkata, West Bengal 700014, India



Ectopic pregnancy is a medical and surgical emergency. It is a significant cause of maternal mortality and morbidity importantly in the first trimester. Presently the rates of ectopic pregnancy are about 1.5–2% of all pregnancies [1]. Nearly 97% of the cases are tubal ectopic pregnancies. Proportionately there is also rise in non-tubal ectopic pregnancies. Approximately 5–10% are non-tubal ectopic pregnancies [2]. Maternal mortality and morbidity are higher in these cases. Up to 50% of ectopic pregnancies go undetected when seen in the emergency department [1, 3] despite the fact that TVS has a positive predictive value of 94% and negative predictive value of 100% in the diagnosis of ectopic pregnancies [4].

Patients and Methods

Twelve cases of uncommon ectopic pregnancies of eight different types, managed under the first author are described. Cases were seen in the Postgraduate Medical Teaching Institutes over a period of 19 years (2001–2019). Details of medical records of these cases during the stated period were analyzed retrospectively Figs. 1,2,3,4.

Methodology

Demographics (age, obstetric profile); relevant obstetric history; clinical presentation; clinical evaluation; provisional diagnosis; USG findings; surgery performed; final diagnosis; intra-operative transfusion; complications and the outcome, were studied (Tables 1, 2, 3).

Follow up: All the cases were followed up, for a varying period of 6–8 weeks of discharge from the hospital and all were well.

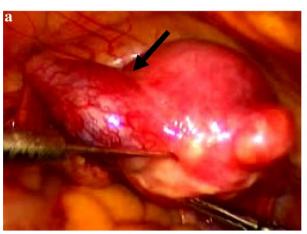
Results

Diagnostic dilemma was faced in majority of the cases. Emergency surgical intervention was made, based on clinical evaluation. The investigations were supportive. The women were in the age group of 25 to 37 years (mean 30). Their parity ranged from 0 to 1(mean 0.67). None had previous ectopic pregnancy. Four had history of (H/O) medical termination of pregnancy. One had H/O IUCD use. All the conceptions were spontaneous. One (case-12) had history of irregular intake of emergency pills. In Table 2; Case no. 7, findings are explained in columns and rows under heading of USG and Surgery. In two cases (case 1, 12) diagnosis was inconclusive; in one (case—12) diagnosis was confirmed on repeat examination at a higher level scan. Five cases (case 2, 7, 8, 10, 11) presented with hemoperitoneum. Blood transfusion was needed in nine cases (case 2, 3, 4, 5, 6, 7, 8, 10, 11); three units (maximum) in one (case-2). There was neither any need for ICU admission nor prolonged hospital (> 5 days) stay. There was no mortality. One woman (case-4), with abdominal pregnancy, went home with a live baby, after the second laparotomy.

Discussion

Diagnostic Dilemma

Despite the use of different diagnostic modalities, majority of our cases with ectopic pregnancy, specially the non-tubal ectopic pregnancies, were diagnosed following



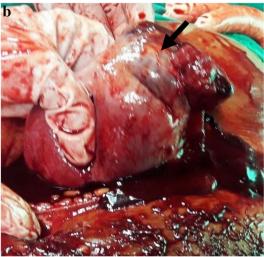


Fig. 1 Interstitial pregnancy: a Laparoscopic surgery, b Laparotomy



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1 3 C C C C C C C C C C C C C C C C C C		Clinical presenta-	Clinical evalu-	Provisional diag-	OSG	Surgery	Final Diagnosis	Intraopn. Trans-	Complications	Outcome
	and relevant Obst. history	tion	ation	nosis (P/D)			(F/D)	fusion (BT)		
(,,	31 yrs. G2, A:1; H/O Sub fertility (2017)	Pain abdomen Delayed cycle by 29 days	UPT + ve	Tubal Ectopic Pregnancy	Inconclusive for extrauterine pregnancy	Laparoscopy Cornuostomy	Lt. sided unruptured interstitial pregnancy (Fig. 1a) Histology confirmed	NIL	NIL	Un- eventful
5	37 yrs G3, P1,L:1,A1 (2016)	Pain abdomen	Massive hemo- peritoneum (paracente- sis+ve)	Traumatic rupture of spleen	ı	Laparotomy TAH+Lt.S-O	Ruptured Interstitial Pregnancy (Lt);Fig. 1b	3 Units PRBC+1U FFP	NIL	Un- eventful
	33 yrs. P1+2(TOP-2) L: I H/O: D & C (2009)	Amenorrhoea: 8 wks Abd. pain Bleeding P/V+	P/V: Conceptus felt through the open os	Cervical miscarriage; D&E under anesthesia: profuse bleeding to shock; Opn. postponed; Resuscitation, further investigations: serum phcG:1700 IU/ml, and USG	USG: Empty Uterine Cavity, Mass adherent to cervical wall: Revised diagnosis Cervical Preg- nancy	Laparotomy ↓ TAH done; Histology – fulfilled Rubin's Criteria:	Cervical pregnancy (Fig. 2)	2 U whole blood	NIL, Serum β hCG returned to normal by 3 weeks	Un- eventful
	31 yrs G2, L: 1 (2018)	Booked case, Apparently normal term pregnancy. Referred to this tertiary care center due to failed attempt of delivery with CS This was due to unusual bleeding & adhesions	Relaparotomy done in this tertiary care center	Relaparotomy: Extensive adhesions with omentum, bowels Unusu- ally dilated omental blood vessels to cause bleeding Dissection con- tinued till the delivery of the baby: Diagnosis: Abdominal pregnancy	USG –done at 20 weeks-normal	LB:Baby boy 1.8 kg; During delivery placental bed separa- tion + Bleed- ing + + + Placenta completely dis- sected out	Abdominal Pregnancy (Fig. 3)	2 Units whole blood 1 Units PRBC 2 Units FFP	NE	Un- eventful





Fig. 2 Cervical pregnancy, hemorrhagic



Fig. 3 The fetus as delivered (arrow-fetal head and the left hand) is seen

laparotomy. Decision was made with a high index of suspicion. Confirmation of diagnosis even with current diagnostic technology is faced with limitations [5]. Unfortunately one has to pay high price for missing the diagnosis. The probable reasons for the missing the diagnosis are:

- (a) As the anatomy in the pelvis is complex, search with imaging study must be made focused with skill and time.
- (b) Obstetrician and radiologist preferably to work closely together in such a situation. Exposure to such a rare clinical entity is rare specially the non-tubal.
- (c) Presentations are variegated, and often there is lack of awareness of the entity.

Management Approach

This study highlights the problems encountered with the diagnosis, preoperative evaluations and surgical interventions. All the patients were seen as an emergency. Majority of the patients (eight) were hemodynamically unstable. Decision for immediate laparotomy was made with the perceived knowledge of impending circulatory collapse. Resuscitation and laparotomy were the management approach.

Value of Preoperative Diagnosis

Preoperative diagnosis for an ectopic pregnancy, specially the non-tubal ectopic, is enormous. Primarily, this is to prevent complications and to reduce the mortality. Prior arrangement of transport, blood transfusion and at times multidisciplinary team involvement is required. This is essential, specially when the resources in the facility are limited. Moreover, treatment can be tailored, depending upon the duration of pregnancy and need for future fertility. Early diagnosis allowed us to do minimally invasive surgery in one case (Case-1, Table -1). Hysterectomy was our last resort to save the life. Maternal mortality associated with non-tubal ectopic pregnancy is higher. Of all the types of ectopic pregnancy, abdominal pregnancy has the highest risk of maternal mortality [6].

Multidisciplinary Team Involvement

We involved the anesthetists and the transfusion department before the surgery. It helped us in a long way.

Medical teachings always stress on the alertness of mind and high index of suspicion. It is said, "be ectopic minded". One should not be ashamed of a negative laparoscopy or laparotomy [7]. Abnormal pregnancy implantations are life threatening. Interpreting physicians' familiarity with this abnormality is critical for early identification and initiation of appropriate therapy [8].

We succeeded in saving lives with the suspicion of ectopic pregnancy but failed to diagnose the site of pregnancy.

Interstitial Pregnancy (Case-1 and 2)

It is a rare type (2-4%) of ectopic pregnancy where implantation occurs in the *interstitial part of fallopian tube*. Clinical presentation of interstitial pregnancy is late (≥ 12 weeks), because of the expansion of the surrounding myometrium allowing pregnancy to progress.

Symptoms are similar to tubal ectopic pregnancy. The terminologies: interstitial pregnancy, cornual pregnancy and angular pregnancy are used interchangeably, though different. For diagnosis "*Interstitial line sign*" on USG, is a very reliable observation [9]. However, this needs more time and



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 Table 2
 Summary of the 12 cases of uncommon ectopic pregnancies with specific areas of highlights

SL. No	Demography and relevant Obst.	SL. No Demography and Clinical presenta- relevant Obst. tion history	Clinical evaluation	Provisional diagnosis (P/D)	USG	Surgery	(F /D)	(BT)	Complications Outcome	Outcome
v ₀	27 yrs G-3, P-1, L-1, TOP-1 (2002)	Preg- nancy:36 weeks Pain abdomen, Uterus contracted Bleeding P/V+ ↓ Fetal movements FHS: not localized CX: tubular closed	Abruptio pla- centa	Abruptio pla- centa	Not done	Laparotomy: Abdominal Pregnancy S/B, Baby girl- 2.5 kg Multiple malformations (non development of eyes, ears) Placenta delivered com- pletely	Abdominal pregnancy	2 Units whole blood	NIL	Un- eventful
9	25 yrs G3, P-0 A-2 (2001)	Preg- nancy-32 weeks, Admitted following successive referrals: With Pain abdomen, ↓Fetal	O/E Abd-distended, Ut. Size: not made out, FHS-not heard Repeated failed induction of labor VIE: Cx-firm	IUFD	IUFD. Oblique lie	Laparotomy: Abdominal pregnancy: Dense adhesions, with bowels and omentum Fetal tissues, skeleton and skull bones recovered, Pla- centa removed	Abdominal pregnancy	2 U whole blood NIL	Ę	Un- eventful
	26 yrs G3, P-1,L-1, A-1, TOP-1 with IUCD insertion (2014)	C/O Pelvic Pain Bleeding P/V O/E: Pallor + + Tachycardia, hypotension, UPT + ve; P/D: Ruptured tubal ectopic preg- nancy	USG: No intrauterine pregnancy Lt. adnexal mass, free fluid in the peritoneal cavity	Ruptured tubal ectopic pregnancy	Not done	Emergent laparotomy done Massive hemoperitoneum Lt sided ovarian mass with bleeding gest. sac embedded. Other adnexa normal. Lt.S- O done. Histology ovarian pregnancy, (Spigelberg criteria ful- filled)	Ovarian pregnancy Fig. 4)	2U PRBC 1U FFP	NIL	Un- eventful



	Outcome	Un- eventful
	Complications Outcome	
	(BT)	2 U whole blood NIL.
	(F/D)	Ruptured cornual pregnancy (Pregnancy-in rudimentary horn of a bicornuate Uterus)
	Surgery	Ruptured horn of a bicornu- ate uterus. Excision of the ruptured horn done Ipsilateral salpingectomy done
	NSG	Not done
	Provisional diag- USG nosis (P/D)	Resuscitation → Emergent Laparotomy: massive hemoperitoneum, two fetuses retrieved from the peritoneal cavity
	Clinical evaluation	O/E Tachycardia (P-140 bpm) Hypotension (BP: 80/60 mm Hg) Abdomen- hemop- eritoneum (Paracentesis- blood+ve)
	SL. No Demography and Clinical presenta- Clinical evalurelevant Obst. tion ation history	Pregnancy -29 wks O/E Pain abdomen Tack vaginal bleeding (P- (B- Hyp (B- Hyp Abd Abd he eri (P- Pain abd (P-
Table 2 (continued)	Demography and relevant Obst. history	28 yrs G2, P0, A1 (2007)
Table 2	SL. No	∞



Fig. 4 Ovarian pregnancy (black arrow: Ovarian pregnancy; white arrow: tubal fimbria, red arrow: uterus)

a skilled radiologist. In the present study, USG: in six cases, could not be organized; diagnosis in five was incorrect; it was inconclusive in two cases and in one case (case—12), it was confirmed on repeat examination at a higher level scan.

Treatment options for interstitial pregnancy depend on the gestational age, need for future fertility and the patient's health. *Case no 1:* was managed by laparoscopic (MIS) surgery. MIS has superiority over open surgery for preservation of fertility. Local infiltration of vasopressin, under laparoscopic view, has many benefits before doing cornuostomy (Fig. 1a). For *case no-2;* decision had to be made on the OT table. Massive hemorrhage occured due to the rupture of combined utero-ovarian circulation. She was treated with emergency subtotal hysterectomy (Fig. 1b). Overall reported mortality is 2.0–2.5% [10]. *Other treatment options are:* cornual evacuation/resection. The risk of uterine rupture in subsequent pregnancy after conservative treatment has been reported [11].

Cervical Pregnancy (Case-3; Fig. 2)

Incidence is 1 in 9000 to 1 in 10,000 [12] ectopic pregnancy. Implantation occurs in the cervical canal below the internal os. It often presents with 1st trimester painless vaginal bleeding. At times bleeding may be heavy and life threatening, as in present case.

In case no. 3 (Table 1), diagnosis was incidental. Massive bleeding was encountered during uterine evacuation. The morbid specimen met the diagnostic criteria made by Rubin (1983). Sliding sign is absent in cervical pregnancy.



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Table 3 Summary of the 12 cases of uncommon ectopic pregnancies with specific areas of highlights

	Outcome	Un- eventful	Un- eventful	Un- eventful
	Complications Outcome			JL V
	(BT)	NE CONTRACTOR OF THE CONTRACTO	2U PRBC	2U PRBC
	(F/D)	Cornual pregnancy (Pregnancy in the rudimentary horn of a bicornuate uterus)	Molar change of an ectopic pregnancy	Cesarean Scar Pregnancy (Fig. 5)
	Surgery	Laparoscopy: bicornuate Uterus with a gravid horn; the other non- gravid horn Laparotomy: hysterotomy— to deliver the fetus, excision of the gravid horn done	Resuscitation and Emergent Laparotomy Rt.Salpingectomy done Histology: Partial mole with ectopic pregnancy. Serum ßhCG became negative by next 3 wks	TAH done Histology CSP
a meameans	USG	USG: Fetus of 14 wks inside the uterus, fetal car- diac motion absent, Liquor reduced P/D (Revised) Missed miscarriage TOP (medi- cal method) attempted → failed on 3 occasions	USG-Not done: Clinical- Ruptured tubal ectopic pregnancy Massive hemoperi- toneum Histology: Focal proliferation of trophoblastic cells; Irregular scalloped vesicular villi. Nucleated RBCs, Fetal tissues noted	USG: Not done
with specific areas	Provisional diagnosis (P/D)	Adnexal mass	P/D: Ruptured tubal ectopic preg-nancy → Surgery	Resuscitation and emergent -laparotomy Hemoperitoneum Ruptured Cesar- ean Scar Preg- nancy (CSP) with extruded products of con- ception (Fig. 7) Bladder not involved
near a community of the releases of ancommon ecopic preferences with specific areas of infernity and in the relationship of th	Clinical evaluation	P/V Uterine size not made out Mass felt through Rt. fornix,	O/E: Hemo dynamically unstable,	Pallor + + Hemodynami- cally unstable Abdomen distended- soft, tender, BI P/V +
cases of anecommo	Clinical presentation	H/O Sub fertility Amenorrhoea Pelvic Pain	Amenorrhoea followed by pain abdomen Vaginal bleeding+ UPT+ve	Pain abdomen Bleeding P/V + UPT + ve
Summary or and 12	Demography and relevant Obst.	27 yrs Married for 4yrs.G-1 (2005)	35 yrs G3,P-1 L-1, A-1 (2019)	30 yrs G4, P1, L1 A-1 TOP-1 H/O prior delivery ery by C.S (2017)
2	SL. No.	5	01	=



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Demography and relevant Obst. history	SL. No. Demography and Clinical presenta- Clinical evalurelevant Obst. tion ation history	Clinical evalu- ation	Provisional diag- USG nosis (P/D)	USG	Surgery	(F/D)	(BT)	Complications Outcome	Outcome
30 yrs 32, L-1, CB 11yrs, LSCS, H/O Irregular use of emergency pills (POPs); (2019)	Amenorrhoea Serum βhCG: 6wks,UPT+ve 11,600 IU/L Seeks TOP (med- Initial USG – ical method) inconclusive	Serum βhCG: 11,600 IU/L Initial USG – inconclusive	TVS at tertiary care level: two GS on the Rt. tube. Uterine cavity empty. Doppler study: Cardiac motion seen (Fig. 6a + b)	Soon following USG, she developed pain abdomen and bleeding P/V Emergent Laparoscopic surgery done: blood in POD, Rt. Tube: unruptured ectopic pregnancy. Rt.Salpingectomy done. Lt. tubenormal	Rt. Salpingectomy done Histology confirmed twin tubal ectopic pregnancy Serum β-hCG returned to normal by next 4 weeks	Twin tubal ectopic pregnancy (Fig. 6a + 6b)	NIL	NIL	Un- eventful

This case was treated by total hysterectomy as a life saving measure. Other treatment options are: tamponade therapy, uterine artery embolisation or systemic methotrexate. Bilateral ligation of descending cervical arteries or making a cervical cerclage suture as close to the level of internal os is effective.

Abdominal Pregnancy (Case No: 4, 5 and 6)

Diagnosis of the three presented cases was confirmed on laparotomy (Tables 1, 2).

Management of the Placenta (Case No: 4; Fig.-3; Table-1)

Conservative management is commonly done. This *case* had history of prior attempt of laparotomy to deliver the baby, in the previous hospital. This resulted in separation of placenta. Brisk hemorrhage was faced during the second surgery. Complications of leaving behind the placenta (hemorrhage, shock, DIC, sepsis and intestinal obstruction) are not uncommon [13]. Placenta could be removed completely and perfect hemostasis was achieved. Placental delivery in late cases (case no. 5 and 6), usually does not pose a problem. This is due to thrombosis of major placental sinuses. Fetal skeleton was recovered as the fetal tissues had autolyzed (case No. 6) Implantation of placenta over the vital structures is a major threat. Exclusive omental insertion has also been reported [14]. However, diagnosis in early pregnancy and use of minimally invasive surgery has been reported [15]. Increased fetal malformations are associated as in case no-5. Case no 4, is of most uncommon variety. She went home with a live and healthy baby.

Ovarian Pregnancy (Case No. 7; Table-2; Fig 4)

Overall incidence is 0.5–3% of all ectopic pregnancies [16]. The patient was provisionally diagnosed as ruptured tubal ectopic pregnancy for which laparotomy was considered on priority. Most ovarian pregnancies are diagnosed during surgery [17]. The present case met the diagnostic criteria of ovarian pregnancy, as defined by Spiegelberg [18].

This patient was treated with ipsilateral salpingo-oophorectomy. Ovarian wedge resection is an alternative treatment modality.



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Fig. 5 Cesarean scar pregnancy

Cornual Pregnancy (Case No: 8 & 9; Table-2&3)

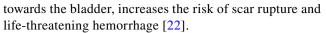
Incidence of cornual pregnancy is 1 in 76,000 pregnancies. USG is less sensitive (29%) in diagnosis of this condition. Majority of the cases of rudimentary horn pregnancy are diagnosed during surgery [19]. Both the cases were treated with excision of the gravid rudimentary horn. Excessive stretching of the uterus due to the twins may be the cause for rupture (case No: 8). Rupture of gravid rudimentary horn with twin fetuses has not been observed in the literature.

Molar Ectopic Pregnancy (Case No: 10; Table-3)

Incidence of molar pregnancy is 1 in 400 in Asian countries. However, the combination of molar changes in an ectopic pregnancy is extremely rare [20] and more difficult to diagnose. Follow-up of these patients with serum βhCG is essential. Mediastinal metastasis of choriocarcinoma following molar ectopic pregnancy has been reported [21].

Cesarean Scar Pregnancy (CSP): (Case No. 11; Fig. no.5; Table no. 3).

Incidence is 1 in 1800 pregnancies [22]. Presence of severe pain and significant bleeding was due to rupture of the scar. The deeper implantation of the blastocyst,



Total hysterectomy (Fig. 5), was done to save her life. Other management options are: Inj.methotrexate (IM) or uterine artery embolisation [23]. Absence of fetal cardiac activity often results in an uncomplicated miscarriage. Recurrence of CSP and subsequent successful intrauterine pregnancy have all been reported. Placenta accreta is a possibility [24].

Tubal Twin Pregnancy (Case No: 12; Fig. no: 6A and 6B; Table 3)

Occurrence of two gestation sacs (twins) in one fallopian tube has been observed in 1 in 20,000 pregnancies [25].

To the best of our knowledge, this is the first reported case of tubal twin ectopic pregnancy diagnosed early and operated laparoscopically (Fig. 6a). Medical management with methotrexate either systemic (IM) or local under ultrasound guidance, has been done in unruptured cases (Fig. 6a, b). It is observed that 95% of the twin ectopic pregnancies are monozygotic, however, dizygotic twins have also been reported [26].

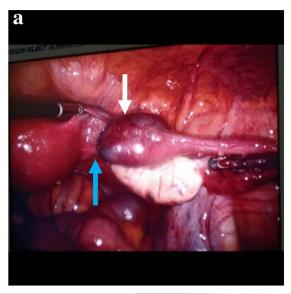
Management Outcome

We did not face any mortality or unusual morbidity. There was no need for ICU admission. All the women were discharged on 5th post-operative day. Majority of our patients were admitted as an emergency with hemodynamic instability. Ultimately it was clinical judgment and planned approach that saved the lives of the women.

Conclusion

Ectopic pregnancy including the uncommon ones pose a diagnostic dilemma and is life threatening. Careful clinical assessment has no alternative. Investigations are supportive. Clinical acumen, presence of hemodynamic instability and/or presence of hemoperitoneum should lead to surgical intervention (laparoscopy/laparotomy), even though the imaging studies are negative. Prior arrangement of a multidisciplinary team and involvement of a senior surgeon, is desirable. Early diagnosis and intervention are lifesaving.





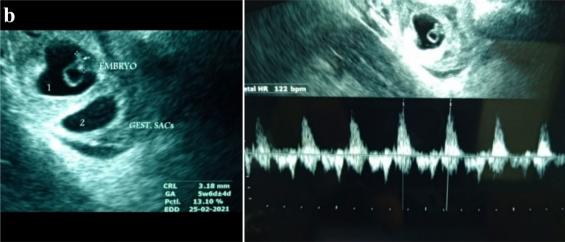


Fig. 6 a Laparoscopic Findings: Ectopic pregnancy (arrow: scar rupture) within the right tube showing (two gestation sacs) b: TVS showing two gestation sacs within right fallopian tube; Doppler Study (TVS) showing cardiac motion of the first fetus

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Declarations

Conflict of interest The authors declare they have no conflict of interest.

Ethical approval Ethical approval was taken from institutional ethics committee.

Ethical Standards All procedures followed were in accordance with the ethical standards of the responsible committee on the human participants (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Informed Consent Informed and written consent was obtained from all the eligible women. Additional informed consent was obtained from all individual participants.

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About the Author



Hiralal Konar an educationist, a teacher per excellence, distinguished academician and a clinician of acclaim. He is currently the Professor and Head of the Department of Obstetrics and Gynecology, Member Oncology Committee of AOFOG (2020-2023) and FOGSI representative AOFOG. Examiner: National-38 Indian universities (MBBS, MS and Ph.D); International: MRCOG and MRCPI. He served FOGSI in the capacity of the chairman of the Indian College of Obstetricians and

Gynecologists (ICOG), Vice president of Federation of Obstetric and Gynecological Societies of India (FOGSI) and as the president of the Bengal Obstetric and Gynecological Society. He represented the committee in India for the Royal College of Obstetricians and Gynecologists (AICC-RCOG), London. His brilliant academic activities and contributions in this field has been documented in the form of nine textbooks, thirty book chapters and 111 research publications in national and international journals. He is the recipient of "Pride of FOGSI" award -2019.

