CAN THE STATUS OF TUBAL PREGNANCY BE PREDICTED WITH TRANS VAGINAL SONOGRAPHY ? A PROSPECTIVE COMPARISON OF SONOGRAPHY, B-HCG LEVEL AND OPERATIVE FINDINGS

K.K. Das ● Bani kumar mitra

SUMMARY

From April 1991 to April 1995, a total of 35 cases of Ectopic Pregnancy (EP) were diagnosed by combined use of pregnancy test and trans vaginal sonography (TVS). Out of eight subjects diagnosed unruptured, with intact gestational sac (GS), five displayed cardiac flicker. Most common findings were complex adnexal mass found in 21 patients and significant haemoperitoneum was observed in four without any adnexal findings. A thorough understanding of the co-relation between serum β-hCG level and gestational sac by TVS is essential not only to establish an early diagnosis but to offer a prognostic value.

Recently in our diagnostic algorithm, we combined endometrial curettage for evidence of chorionic villi which allowed us to diagnose EP in 4 cases without resorting to laparoscopy. Two cases were treated with local methotrexate injection while other two cases were treated by expectant observation. It appears that spontaneous resolution and resorption of more cases of conceptus occurs than previously thought of.

Dept. of Obstet. & Gynec., Infertility & Endoscopy centre, Bokard Steel City, Bokaro.

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INTRODUCTION

Ectopic pregnancy is like an iceberg - so variable in clinical presentation and so unpredictable in its natural course of

behaviour. At one extreme, the pregnancy progresses to tubal rupture with massive hemorrhage, hypovolemic shock and exsanguination. At the other end of the spectrum, there lies the cases of unruptured yet potentially dangerous forms, some of which may resolve spontaneously without medical or surgical intervention.

A decade ago the gynecologists used to wait and observe for the EP to make itself obvious by a positive culdocentesis. Salpingectomy was the rule rather than an exception. The maternal mortality was considerably high. Although the mortality has gone down, it still remains an important cause. Together with mortality, morbidity, is of great concern particularly for future reproductive potential in a young patient desiring a pregnancy.

Today a dramatic improvement has taken place in the understanding of pathophysiology and management of EP. This is possible because of the introduction of two important noninvasive diagnostic tools, namely, the detection of biomarker β-hCG in the body, and high resolution pelvic scan. Together with this endeavour is being made to develope non surgical modes of conservative medical management.

Another important observation is that the incidence of EP is rising alarmingly almost reaching epidemic proportions (Makinen JI 1987). A 4.5 percent increase is observed in USA alone over seventies (Ory 1991).

How far is this rise in incidence real? Could it be that many such undetected tubal pregnancies which used to resolve spontaneously unnoticed, twenty years ago are being increasingly detected by better diagnostic tools ? Is it a fact that some of them are subjected to surgery without any long term benefits ? Could it be that many of those today treated medically or by conservative surgery, could have been observed and left alone to resolve spontaneously ?

The onus of modern management of tubal pregnancy rests on early detection in order to save the reproductive potential of young women in future. The present study has not only laid emphasis on this but has also tried to prognosticate tubal pregnancies by developing co-relation between β-hCG status, sonographic evaluation and operative findings.

PRESENT STUDY

From April 1991 to April 1995, a total of 35 cases of EP had been diagnosed, 33 in the tube, two in the peritoneal cavity (Table I). Out of 107 clinically suspected EPs, 33 were Ectopic gestation, remaining 40 displayed intra uterine pregnancy (IUP), 21 diagnosed as non pregnant pelvic mass and in 13 no pelvic pathology could be detected. Besides, above 33 cases, another two cases of EP were diagnosed coincidentally being referred to us by other clinician for pelvic scan not suspecting EP.

The technique of TVS and the protocal used in our centre is described in the earlier studies (Das et al 1993). If the patient is clinically unstable we hospitalize her for some invasive procedure like laparoscopy or laparotomy.

We do scan both by trans-abdomen probe (TAS), as well as trans vaginal sonography (TVS) by 5MHz probe (Aloka SSD 630, Japan). We are increasingly avoiding laparoscopy for diagnostic purposes recently, where tubal conservation by

Table I
DISTRIBUTION OF CASES

Study Period - April 91 - April 95		No.	%
Clinical suspected EP			107
ectopic diagnosed		33	30.84
tubal	31		
peritoneal	2		
rest			
intra uterine pregnancy		40	37.38
adnexal pathology		21	19.62
no cause found		13	12.14
EP diagnosed coincidentally	2		
EP total	35		

medical or expectant treatment is indicated.

We first survey the uterus for evidence of intra uterine gestational sac (GS), organized product of conception, pseudogestational sac and endometrial response etc. A simple naked eye examination of endometrial curettage in selected cases by floating in saline and subsequent histopathological examination for evidence of placental tissue proved helpful, to exclude a non viable IUP. Next, the adnexa are inspected carefully for evidence of 'tubal ring', the yolk sac, embryonic structures, cardiac activity, for an empty sonolucent or echogenic gestational sac (GS), and for complex mass. Pelvic cavity is carefully inspected for evidence of fluid in the pouch of Douglas (POD) and around adnexa.

Different bed side urinary β-hCG kits, set at sensitivity ranging from 25 of 500 miu/ml were used. Serum B-hCG assay by RIA was sought for in a few selected subfertile subjects undergoing artificial reproductive procedures and found not suitable for our emergency ward.

OBSERVATION AND DISCUSSION

The diagnosis of EP always poses a challenge to a practicing clinician. The natural history of the disease is not straight forward, but involves several different anatomical, physiological as well as clinical expressions of the disease. There are wide variations, may be viable with live embryo, non viable or missed, ruptured or non ruptured as tubal abortion or as a resolving chronic tubal pregnancy. It is not known why some ectopic trophoblastic tissue remains active, invades the tubal wall, and causes rupture, whereas in others, it remains dormant, inactive and confined and causes tubal abortion or gets resorbed spontaneously. A thorough understanding of the co-relation between serum β-hCG

level and gestational sac therefore, is essential not only for an early diagnosis but to give a prognostic value.

Ectopic pregnancy and β-hCH level

Serum β-hCG levels depend on the number of functionally active trophoblastic cells in the body. As the GS grows in a normal IUP, exponential rise of β-hCG level takes place; becomes double every 48-72 hours, attains the peak by eighth menstrual week, and then declines.

A strong linear co-relation therefore exists between the size of GS, circulatory hCG level and gestational period till the fetal pole appears on postmenstrual day 42-45 (Daya et at 1991).

Chemical pregnancy is established almost immediatley after nidation of the fertilized ova on 22nd-23rd post-menstrual days, and on day 27-28 by rapid bed side kits having sensitivity at 25 miu/ml. A tiny 2-3 mm GS can be discerned in a shining echogenic endometrium by TV probe on day 32-33 of a regular 28 days menstrual cycle (Rajan 1989). Sonographic confirmation of IUP therefore, is established by trans abdominal probe nearly 21 days after the biochemical pregnancy is established, when discriminatory level of β-hCG reaches a zone of 1800-2000 MIU/ml, (Nyberg et al 1987) and by TVS one week earlier at the discriminatory level at 800-1000 miu/ml (2nd IS) (Nyberg et al 1988). TVS therefore, identifies GS much earlier at a much lower hCG titer than TAS.

However, the hCG level of normal and abnormal IUP overlap considerably. Moreover, EP, often like a nonviable IUP, produces a slow rise, or attains low plateau, and slowly declines (Cartwright & Dipletro 1984). Serial β-hCG assay is often, mandatory than a single value and provides four types of pictures offering different prognostic values:

A. If β-hCG level is **above discriminatory zone,** and yet the uterus is empty, the condition strongly suggests EP.

B. Similarly when the B-hCG level is **below discriminatory zone,** TVS has limited role to play since it cannot identify the GS, cannot differentiate intrauterine pregnancy from EP. They are low risk patients at the beginning, but may prove potentially dangerous as the hormone level rises, thus calls for a close observation with further serial scan and quantitative assay and may demand hospitalization.

C. **A subnormal rise** suggests non viable pregnancy, indicating degenerating trophoblastic tissue. EP with low plateau therefore is unlikely to rupture and even can resolve spontaneously. We had two patients treated expectantly with excellent outcome.

D. **A rapidly growing B-hCG level** on the other hand indicates functionally active trophoblastic tissue, likely to grow, display living embryo and may rupture. Such patients should be considered potentially dangerous.

Thus co-relation of hCG level with GS identified by TVS is most useful in non emergent situations. hCG finding alone is not always conclusive to offer prognostic value.

In our present series, out of 107 clinically suspected cases, 75 had positive β-hCG including 40 IUPs. Out of a total of 35 EP cases, β-hCG was positive in all except in one old chronic case. Another clinically suspected subject, displayed normal pelvic scan but offered inconsistent β-hCG

report (false positive). The increasing pelvic pain raised an alarm of EP which was ruled out by negative laparoscopy.

Ultrasonography and Ectopic pregnancy

The accuracy of TVS in the early diagnosis of EP has been well documented in recent years (Nyberg et al 1987, Timor et al 1989, Das et al 1993). TVS proved to be sensitive in suspected EPs in 93% on admission, and 100% on repeat scan and was associated with high specificity of 99% (Ylostalo & Cacciatore 1995). Therefore today vast majority of EPs are diagnosed unruptured in early stages. As a result our approach regarding the treatment has dramatically changed from a much invasive to conservative surgery and to medical management and lastly to an expectant observation only.

TVS offers two types of findings.

1. findings specific of EP like GS, cardiac flicker, yolk sac, other embryonic structures etc. in the tube displaying its outline.

2. indirect findings are like empty uterus, nonspecific complex adnexal mass and fluid in POD. Such findings however, are often not available in the early stages of unruptured EP. A high resolution TV probe with its close proximity to the target organ, can offer an amazingly sharp clear picture, not only characterize the indirect findings better, but display the tubal outline and identify the direct findings in about 87% cases (Rottem et al 1991).

The GS with living embryo outside uterus clinches the diagnosis irrevocably, withut the aid of B-hCG assay. On the other hand in a chronic old EP, when the pregnancy test is negative displaying adnexal mass may be confusing, calls for laparoscopy or laparotomy for confirmation. We had one young subject desiring pregnancy, reported to us as chronic pelvic inflammatory disease after being treated by different physicians nearly 3-4 months after her initial attack of pelvic pain. Exploratory laparoscopy offered us an impression of "chronic endometriosis". Final histopathological report only clinched the diagnosis of old EP. A serum B-hCG radio immune assay could have been helpful since an hCG threshold at 3 miu/ml (IRP) identified 100% of EP in one study (Olson et al 1983). A case of interstitial pregnancy carrying 14 weeks could not be discerned by TVS, since the GS was high up above the pelvic brim beyond the short focal zone. The diagnosis was made by trans-abdominal sonography (TAS), only to be confirmed by laparotomy. TVS therefore, cannot identify all cases of EP; TAS and TVS are complimentary to each other.

We diagnosed one case as cervical pregnancy displaying irregular but intact GS in the cervical canal, which was proved to be inevitable abortion and was excluded from this series. TVS in our series proved to have a specificity of 97.0%. Rottem et al (1991), using 6.0-7.5 MHz TV probes observed two cases of false positive in 191 cases. TVS thus had 99.5% specificity in there series. In a series of 200 EPs they further observed 8 subjects of small unruptured GS undetected by TVS associated with low B-hCG level confirmed during surgery based on clinical feature. We did not observe similar cases in our series.

A complex tubal mass is the most common finding (63.63%) in our study. Its genesis is due to local haematoma, tissue oedema,

and not merely due to trophoblastic tissue which may be active or even degenerating in the tubal wall and thus logically, associated with unpredictable β-hCG level.

Once a diagnosis of EP is confirmed, the prognostic status of the disease should be offered so that an appropriate treatment can be planned. Based on the different type of presentations, patients age and parity the treatment options are also different. Rottem et al 1991 classified EPs diagnosed by TVS into three different categories (Table II).

In our study, comprising of 33 cases of tubal gestation, tubal ring with cardiac flicker was detected in five and tubal ring without cardiac pulsation in three subjects (Table III).

Less specific complex adnexal mass was observed in 21 subjects (63.63%), 18 displaying peritoneal fluid, and in seven moderate to serve haemoperitoneum (more than 500 cc). We had four patients in type III, displaying significant amount of blood but no adnexal mass. Out of 11 having significant peritoneal fluid six desplayed echogenic particulate fluid suggesting blood clot which was confirmed during surgery. Particulate echogenic fluid thus suggested high risk patients.

Table II
TVS & TUBAL PREGNANCY CLASSIFICATION
(ROTTEM ET AL 1991)

Type 1A	-	Well defined tubal ring displaying fetal heart
Type 1B	-	Well defined tubal ring displaying no foetal heart.
Type 2	-	Ill defined tubal mass.
Type 3	-	Free pelvic fluid, empty uterus displaying no adnexal mass.

Table III
OUR SERIES

	No.	%	
Type I A	5	15.15	(HP 2)
Type I B	3	9.09	(HP 0)
Type II	21	63.63	(HP 18) (NO HP 3)
Type III	4	12.12	(HP 4)

HP = Haemoperitoneum

peritoneal pregnancy - 2

Four out of eight cases in group 1A & 1B were picked up from our infertile subjects having regular close follow up. All the remaining patients were either referred to us late or a coincidental EP was diagnosed. This made the diagnosis worst. In subjects displaying adnexal mass and fluid in FOD, laparoscopy/laparotomy was undertaken because either the patients were haemodynamically unstable, or based on clinical consideration or because of undiagnosed mass in sonography.

One case of repeat EP in group 1A, revealed significant amount of blood during surgery; she was carrying GS with max. dia of 4cm displaying a living embryo of seven weeks plus in the same ampullary region that was conservatively repaired three years back by the first author. None in the three cases in type 1B presented with haemoperitoneum. From the above observation it appears that haemoperitoneum can occur at any stages of EP.

Recently in our diagnostic algorithm alongwith the sensitive pregnancy test, and pelvic sonography, we combined endometrial curettage in doubtful cases. This algorithm allowed us to diagnose EP in four cases confidently without restoring to laproscopy. All these four cases were selected for conservative therapy, including two for expectant observation only.

Two subjects in group II showing adnexal mass displaying very little blood in the POD were selected for echo-guided local methotrexate injection under vaginal sonography. one resolved in time but the other one showing adnexal mass of more than 3.5 cm dia displaying B-hCG level of more than 2000 miu/ml ruptured 24 hours later and a laparotomy had to be undertaken. She had highly proliferative trophoblastic tissue indicated by high rising hormone level, better should have been left for surgical approach. The first case who responded successfully to local methotrexate injection had initial B-hCG level of less than 1000 miu/ml and an adnexal mass of 2.5 cm only. She recovered successfully displaying tubal patency after three menstrual cycles.

Two cases were treated expectantly by close surveillance only, till the adnexal mas resolved spontaneously. One had EP following tubal recanalization. Clinically she was stable, her initial B-hCG level was below 1000 miu/ml, a complex adnexal mass measuring less than 2.5 cm. displaying no bleeding in the pelvis. A close surveillance by pelvic scan and B-hCG assay was made keeping crossed matched blood available. The patient experienced moderate degree of abdominal cramps with abdominal tenderness, possible indicating tubal spasm. The pain and tenderness gradually subsided displaying a declining B-hCG level with spontaneous regression and resorption of the adnexal mass. HSG after three spontaneous menstrual cycle displayed patent tube. The second case was of a young nulliparous subject, displaying small GS of 1.5 cm. with a low plateau (<800 miu/ml) and declining hCG titer.

The sonographic intra uterine picture showed thick endometrium, the endometrium curettage revealed fleshy endometrium which sank in saline. Histopathological report offered "endometrial gland shows Ariastella reaction compatible with EP". The final tubal status are yet to be confirmed. With increasing number of early diagnosis of EPs having intact GS, it appears that

spontaneous regression of more cases of conceptus occurs than previously thought of.

CONCLUSION

A high frequency trans vaginal probe proves to be one of the most invaluable diagnostic tool in the hand of a modern gynecologist, offering wealth of information, which were not possible by any other noninvasive modalities before. More and more cases of EPs are detected unruptured at an early stage. β-hCG assay can detect the presence of pregnancy, be it intra uterine, normal, abnormal or extrauterine. TVS, can identify the site of the pregnancy together with the detection of other ancillary pelvic findings. β-hCG level reflects the status of functionally active trophoblastic tissue. A combined β-hCG and TVS can be used to detect early EP and then to prognosticate the pregnancy. A living embryo indicates increasing hormone level, whereas, a nonspecific sonographic findings like complex adnexal mass, POD fluid, endometrial thickness or pseudo gestational sac can occur at any hCG level. A low plateau of hormone or decline in titer can be managed with expectant observation with excellent outcome.

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