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# Value of Amniotic Fluid Index Measurement in Predicting Perinatal Outcome

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**Abstract :** *Objective :* The aim of this study was to evaluate the value of amniotic fluid index (AFI) measurement to predict perinatal outcome in high risk pregnancies. *Method :* High risk patients referred to the Division of Maternal Fetal Medicine at Chulalongkorn Hospital for antepartum fetal assessment had an AFI determined and were divided into two groups. Patients with the AFI  $\leq 5$  cm were placed in the oligohydramnios group. The remaining patients were placed in the normal group (AFI  $> 5$  cm). The outcome of patients with oligohydramnios compared with the normal subjects was evaluated. Perinatal outcome was considered poor when there was perinatal death, intrapartum fetal distress, a five minute Apgar score of less than 7, thick meconium stained amniotic fluid or admission to the neonatal intensive care unit. *Results :* A total of 315 patients were evaluated; 47 in the oligohydramnios group and 268 in the normal group. The oligohydramnios group had a greater incidence of intrauterine growth retardation (55.3% versus 9.3%,  $p < 0.001$ ), poor perinatal outcome (19.1% versus 2.6%,  $p < 0.02$ ) and thick meconium stained amniotic fluid (12.7% versus 1.5%,  $p < 0.05$ ). The sensitivity, specificity, positive predictive value, and negative predictive value of oligohydramnios to predict intrauterine growth retardation were 50.9%, 92.0%, 55.3% and 90.7%, respectively. The sensitivity, specificity, positive predictive value, and negative predictive value of oligohydramnios to predict poor fetal outcome were 56.3%, 87.3%, 19.1%, and 97.3%, respectively. *Conclusion :* The presence of oligohydramnios (AFI  $\leq 5$  cm.) should serve as a warning of possible fetal compromise and as an indication of the need for further detailed fetal assessment analysis. (Thai J Obstet Gynaecol 1995;7:85-93)

**Short title :** Value of amniotic fluid index

**Key words :** amniotic fluid index, perinatal outcome, predicting

The amniotic fluid volume in a normal pregnancy increases gradually to a maximum at 32-36 weeks of gestation and declines thereafter.<sup>(1,2)</sup> Ultrasound assessment of amniotic fluid volume has become an important component of comprehensive fetal assessment. An amniotic fluid volume less than normal for the gestational age has been associated with significant perinatal morbidity including intrauterine growth retardation, Cesarean section for fetal distress, low Apgar scores and is therefore used to assess fetal well-being.<sup>(3,5)</sup>

Several techniques for amniotic fluid volume assessment have been reported, including: subjective assessment, maximum vertical pocket depth measurement, and amniotic fluid index measurement. Of these three techniques, the amniotic fluid index has been recommended as the best technique for amniotic fluid volume assessment because it has been proven to be valid and reproducible.<sup>(1,2,4)</sup> The aim of this prospective study was to evaluate the value of amniotic fluid index measurement to predict perinatal outcome in high risk pregnancies.

## Materials and Methods

High risk patients were referred to the Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, Chulalongkorn University for antepartum fetal assessment between January 1992 and December 1993. All patients had

gestational age greater than 28 weeks and known dating using the confirmed last menstrual period and early antenatal care or 16-24 week dating scan. Exclusion criteria included multiple gestation, known congenital or chromosomal abnormalities, hydrops (defined as an amniotic fluid index  $\geq 24$  cm), evidence of fetal distress, ruptured membranes or no amniotic fluid index measurements performed within 7 days of delivery. Informed written consent was obtained for each patient.

All patients were scanned using a 3.5 MHz convex probe (Aloka 2000, Tokyo, Japan). The amniotic fluid index was assessed using the technique described by Phelan et al,<sup>(1,6)</sup> in which the maternal abdomen is divided into quadrants. The linea nigra was used to divide the abdomen into the right and left halves and the umbilicus was used to separate upper and lower halves. With the transducer held at a position perpendicular to the floor, the largest amniotic fluid pocket in each quadrant was identified. The vertical diameter of the largest pocket in each quadrant was measured (in cm) and a permanent record of the scan was made. The depth for the four quadrants was then added to obtain the amniotic fluid index. Oligohydramnios was defined as an amniotic fluid index  $\leq 5$  cm. The results of the test were revealed to the clinicians. Further obstetric management was based on the clinical situation and other investigatory findings.

Postpartum data collected blindly were presence of intrapartum fetal distress, presence of thick meconium stained amniotic fluid, birth weight, Apgar scores at 1 and 5 min, birth weight centiles (compared to our population data),<sup>(7)</sup> method of delivery and neonatal morbidity. The outcome for patients with oligohydramnios (amniotic fluid index  $\leq 5$  cm) compared with the normal subjects (amniotic fluid index  $> 5$  cm) were evaluated. Perinatal outcome was considered poor when there were perinatal death, intrapartum fetal distress, a five minute Apgar score of less than 7, thick meconium stained amniotic fluid or admission to the neonatal intensive care unit. The diagnosis of fetal distress was made by the obstetrician managing the labour and was based upon fetal heart rate abnormalities (fetal bradycardia, persistent late decelerations, and severe variable decelerations).<sup>(8)</sup> Amniotic fluid was considered to have "thick" meconium only if the fluid was viscous, tenacious, and opaque and contained large amounts of particulate material ("pea soup" meconium). Fluid that appeared to be normal except for greenish or yellowish coloring was deemed "thin" meconium, and thicker, darker fluid was labeled "moderate" meconium.<sup>(9)</sup> Intrauterine growth retardation was defined as birth weight less than the 10th centile for gestational age.<sup>(7)</sup>

Statistical analysis was performed using the chisquare test, two sample student t test, and Fisher exact

test which were appropriate. Significance was set at  $p < 0.05$ . Sensitivity, specificity, positive predictive value and negative predictive value of oligohydramnios to predict poor perinatal outcome or intrauterine growth retardation were evaluated by developing 2 x 2 contingency tables.

## Results

There were 315 patients included in the study. The largest group of subjects were referred for the evaluation of fetal well being because of suspected intrauterine growth retardation (72 patients or 22.8%). A total of 59 patients (18.7%) were assessed because they were postterm, 50 (15.9%) for hypertension, 24 (7.6%) for poor weight gain and 13 (4.2%) for decreased fetal movement (Table 1).

Oligohydramnios was identified in 47 patients (14.9%). Table 2 and 3 show gestational age and mode of delivery in both groups. There was no significant difference between the oligohydramnios and normal groups with respect to gestational age and mode of delivery. Most of the patients were delivered between 37 and 43 weeks gestation. Twelve patients (25.5%) in the oligohydramnios group had normal spontaneous vaginal delivery, 26 (55.3%) had Cesarean section and 9 (19.2%) had operative vaginal delivery. Ninety five (35.4%) of the patients in the normal group had normal spontaneous vaginal

**Table 1** *Indications for ultrasound examination*

Indication	No of patients	Per cent
Suspected IUGR	72	22.8%
Postterm (GA $\geq$ 42 wk)	59	18.7%
Hypertensive disorders	50	15.9%
Poor weight gain	24	7.6%
Decreased fetal movement	13	4.2%
Miscellaneous	97	30.8%
Total	315	100%

IUGR = Intrauterine growth retardation, GA = Gestational age

**Table 2** *Gestational age at delivery*

GA (wk)	Oligohydramnios group (AFI $\leq$ 5 cm)		Normal group (AFI $>$ 5 cm)		Significance
	No	Percent	No	Percent	
28-36	9	19.2%	48	17.9%	NS
37-40	26	55.3%	168	62.7%	NS
$\geq$ 41	12	25.5%	52	19.4%	NS
Total	47	100%	268	100%	

AFI = Amniotic fluid index, GA = Gestational age, NS = Not significant

**Table 3** *Mode of delivery*

Mode	Oligohydramnios group (AFI $\leq$ 5 cm)		Normal group (AFI $>$ 5 cm)		Significance
	No	Percent	No	Percent	
Normal labour	12	25.5%	95	35.4%	NS
Cesarean section	26	55.3%	115	42.9%	NS
Operative vaginal delivery (F/E, V/E, Breech)	9	19.2%	58	21.7%	NS
Total	47	100%	268	100%	

AFI = Amniotic fluid index, F/E = Forcep extraction, V/E = Vacuum extraction  
NS = Not significant

**Table 4** *Results of perinatal outcomes*

Outcome	Oligohydramnios group (AFI $\leq$ 5 cm) (N = 47)		Normal group (AFI > 5 cm) (n = 268)		Significance
	No	Percent	No	Percent	
IUGR	26	55.3%	25	9.3%	p < 0.001
Poor perinatal outcome	9	19.1%	7	2.6%	p < 0.02
Thick meconium	6	12.7%	4	1.5%	p < 0.05

AFI = Amniotic fluid index, IUGR = Intrauterine growth retardation

**Table 5** *Results of amniotic fluid index (AFI) in relation to intrauterine growth retardation (IUGR)*

Result of AFI	No	IUGR	Normal
Oligohydramnios (AFI $\leq$ 5 cm)	47	26	21
Normal (AFI > 5 cm)	268	25	243

Sensitivity = 50.9%

Specificity = 92.0%

Positive predictive value = 55.3%

Negative predictive value = 90.7%

**Table 6** *Results of amniotic fluid index (AFI) in relation to perinatal outcomes*

Result of AFI	Perinatal outcome		
	No	Poor	Good
Oligohydramnios (AFI $\leq$ 5 cm)	47	9	38
Normal (AFI > 5 cm)	268	7	261

Sensitivity = 56.3%

Specificity = 87.3%

Positive predictive value = 19.1%

Negative predictive value = 97.3%



delivery, 115 (42.9%) had Cesarean section and 58 (21.7%) had operative vaginal delivery.

Table 4 presents the outcome of pregnancies with respect to the perinatal data. Twenty six of the 47 subjects in the oligohydramnios group had intrauterine growth retardation, compared with only twenty five of 268 in the normal group (55.3% versus 9.3%,  $p < 0.001$ ). The sensitivity, specificity, positive predictive value and negative predictive value of oligohydramnios (amniotic fluid index  $\leq 5$  cm) to predict intrauterine growth retardation are shown in Table 5.

Sixteen patients were considered poor outcome namely, 3 neonatal deaths, 10 with thick meconium stained amniotic fluid, 2 cases of fetal distress in labour and one case admitted to the neonatal intensive care unit. The causes of death in the 3 neonates were severe intrauterine growth retardation and cardiomegaly (amniotic fluid index = 1 cm), ruptured vasa previa (amniotic fluid index = 12.7 cm) and abruptio placentae (amniotic fluid index = 15 cm). Nine of the 47 patients in the oligohydramnios group had poor perinatal outcome (one neonatal death, 6 with thick meconium stained amniotic fluid, one case of fetal distress, and one case admitted to the neonatal intensive care unit), compared with 7 of 268 in the normal group (19.1% versus 2.6%,  $p < 0.02$ ). The sensitivity, specificity, positive predictive value, and negative predictive value of oligohydramnios (amniotic

fluid index  $\leq 5$  cm) to predict poor fetal outcome are shown in Table 6. Patients with oligohydramnios had high incidence of thick meconium-stained amniotic fluid when compared with patients with a normal amount of amniotic fluid (12.7% versus 1.5%,  $p < 0.05$ ).

## Discussion

Reports in the literature indicate that amniotic fluid index appears to be able to predict various clinical scenarios. Rutherford et al<sup>(5)</sup> demonstrated that, in a mixed high-risk population referred for fetal assessment, an amniotic fluid index of less than 5 cm was associated with a significant increase in the incidence of meconium staining, Cesarean section for fetal distress, 5 min Apgar scores  $< 7$  and intrauterine growth retardation. Shmoys et al<sup>(10)</sup>, using an amniotic fluid index of less than 5 cm to define oligohydramnios, showed an increased risk of decelerations, emergency Cesarean section, meconium and fetal acidosis in a group of patients with oligohydramnios and concluded that the amniotic fluid index is a significant prediction of peripartum morbidity. Phillipson et al<sup>(11)</sup> reported that when oligohydramnios was identified subjectively there was an increased incidence of intrauterine growth retardation but no significant increase in 1 min Apgar or 5 min Apgar scores. Sarno et al<sup>(12)</sup> showed

that when the amniotic fluid index was 5 cm or less, the incidence of meconium staining and variable decelerations increased.

The etiology of oligohydramnios in growth retarded fetuses is speculative. Chronic uteroplacental insufficiency in animals is associated with an increased incidence of intrauterine growth retardation.<sup>(13-17)</sup> Fetal hypoxia is characteristically observed in these fetuses. In the second half of pregnancy, fetal urine and lung liquid are major contributors to the amniotic fluid pool.<sup>(1,4,11)</sup> Experimental hypoxia in chronically instrumented fetal lambs results in reflex redistribution of cardiac output, so that renal blood flow falls dramatically and pulmonary blood flow nearly ceases.<sup>(16)</sup> It has been postulated that one mechanism for oligohydramnios in growth-retarded human fetuses may be a decreased production of fetal urine and lung fluid as a result of hypoxia-induced redistribution of cardiac output.<sup>(15,16)</sup> This hypothesis is supported by reports of decreased production of fetal urine and decreased fetal breathing movements in human fetuses with intrauterine growth retardation.<sup>(17)</sup> In accordance with this hypothesis, quantitative amniotic fluid index determination may be viewed as a functional measure of the effect of intrauterine growth retardation. This concept is important and it implies that screening for intrauterine growth retardation by this method may be largely independent of the gestational

age of the fetus. In addition, the increased incidence of fetal distress and meconium staining in oligohydramnios may be due to umbilical cord compression or chronic fetal hypoxemia.

In our study, amniotic fluid index measurement was useful in differentiating the normal from the growth retarded fetus. Patients with an amniotic fluid index  $> 5$  cm were delivered of a normal infant in 90.7% of instances, whereas, those with an amniotic fluid index  $\leq 5$  cm were delivered of a fetus with intrauterine growth retardation in 55.3% of instances. These differences were highly significant. Our findings also indicated that this method may identify the fetus at risk for poor perinatal outcome and passage of thick meconium, since patients with an amniotic fluid index  $\leq 5$  cm experienced a sevenfold (19.1% versus 2.6%) increase in poor perinatal outcome and an eightfold (12.7% versus 1.5%) increase in thick meconium staining.

The use of amniotic fluid index assessment to predict intrauterine growth retardation had high specificity and a negative predictive value. In order for a screening test to be useful it must provide information that can be used clinically as inexpensively, easily, and as rapidly as possible. In addition, the specificity and negative predictive value of a screening test can be just as important as its sensitivity and positive predictive

value. The time required to perform a four-quadrant amniotic fluid index is less than 5 minutes. Therefore, an ultrasound screen for the amniotic fluid index should be easy, rapid, and inexpensive. Although no one test can predict perinatal morbidity with 100% accuracy, any prediction of perinatal morbidity is clinically useful. In this study, the negative predictive value and specificity of amniotic fluid index to predict fetal outcome were high; the sensitivity was acceptable but the positive predictive value was low. This finding is not surprising, as previously mentioned amniotic fluid volume has been proved as an indirect measure of fetoplacental function. Therefore, it cannot be used solely to predict poor fetal outcome. When oligohydramnios is present, careful fetal surveillance should be obtained especially in the intrapartum period. We have reported that weekly measurement of the amniotic fluid index combined with fetal acoustic stimulation test appears to provide a reliable method of the establishing fetal health in a high risk pregnancy.<sup>(18)</sup>

In conclusion, amniotic fluid index measurement should be one component of a composite of fetal assessment techniques. The presence of oligohydramnios (amniotic fluid index  $\leq 5$  cm) should serve as a warning of a possible growth retarded fetus and possible fetal compromise and as an indicator of the need for further detailed fetal assessment

analysis.

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NINTH INTERNATIONAL  
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# **FETUS AS A PATIENT**

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**THE ROYAL THAI COLLEGE OF OBSTETRICIANS  
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IN COLLABORATION WITH THE INTERNATIONAL SOCIETY  
THE FETUS AS A PATIENT**

# Ectopic Pregnancy : A Prospective Descriptive Study of 376 Cases

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**Abstract:** *This is a prospective study of 376 consecutive cases of ectopic pregnancies at Chiang Mai University Hospital from June 1988 to August 1992. The incidence was 12.5 per 1,000 live births. Common presenting symptoms were abdominal pain (98.4%), amenorrhea (83%) and vaginal bleeding (67.3%). Pelvic examination revealed enlarged uterus in 47.2%, adnexal mass in 42.2% and bulging cul-de-sac in 47.2%. Urine pregnancy and serum  $\beta$ -hCG tests were positive in 66% and 99.2% respectively.*

*The most common site of tubal pregnancy was ampulla, followed by isthmus, fimbria and interstitial. Tubal rupture was found in 52%. More than half had normal pelvis; 31.7% had peritubal or pelvic adhesion. Salpingectomy was performed in 76.6% and salpingo-oophorectomy in 10%. Incidental appendectomy was done in 27.9% without any increase in morbidity. Literature on ectopic pregnancies was briefly reviewed. (Thai J Obstet Gynaecol 1995;7:95-104)*

**Short title:** Prospective study of ectopic pregnancy.

**Key words:** ectopic pregnancy, signs and symptoms, incidental appendectomy.

Ectopic pregnancy is a life-threatening condition, that may cause maternal mortality and compromise future fertility. Its incidence has been increasing during the past decade and may be related to the rising incidence of pelvic inflammatory diseases, liberal use of tuboplasty, or the dramatic

improvement in modern diagnostic measures such as laparoscopy, sensitive  $\beta$ -hCG and ultrasonographic technique.<sup>(1)</sup> Many previous studies on ectopic pregnancy were done by retrospective review of available medical records. Thus the data was, incomplete. In this report, we conducted

a prospective descriptive study of ectopic pregnancy pattern in our university hospital in Northern Thailand.

### Materials and Methods

Three hundred and seventy six consecutive patients who were confirmed surgically and pathologically as having ectopic pregnancies at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand, were interviewed during their postoperative hospitalization from June 1, 1988 to August 31, 1992. Information was obtained on patients' presenting signs and symptoms, contraceptive practices, past obstetrical, gynecological, medical and surgical history. Findings on general physical examination and pelvic examination as well as results from laboratory investigations, ultrasound reports, operative findings, and operative procedures were recorded on a standardized form. Further information, if needed, was obtained by direct contact with surgeons who performed the operations. All information was

obtained as soon as possible in the immediate post operative period (within 24-72 hours after surgery) when both the patients and surgeons still have a fresh memory of the episodes. All patients' records were collected and reviewed by the investigators.

Statistical analyses were performed with two tailed t-test, chi-square and Fisher's exact tests where appropriate. For all analyses statistical significance was assumed at the  $p < 0.05$  level.

### Results

During the four year period from June 1, 1988 to August 31, 1992 we had 30,080 deliveries and altogether 376 cases of ectopic pregnancy, giving an overall incidence of 12.5 ectopic pregnancies per 1,000 deliveries. The yearly incidences were 10.62, 9.39, 15.68 and 13.48 per 1,000 deliveries respectively. The mean age of the patients ( $\pm$  SD) was  $28.2 \pm 5.2$  years (range 16-41 years). Most of them

**Table 1** *Occupation of patients*

Occupation	No.	(%)
Employees	147	(39.1%)
Farmers	75	(20.0%)
Merchants	58	(15.4%)
Housewives	46	(12.2%)
Civil servants	32	(8.5%)
Students	16	(4.3%)
Prostitutes	2	(0.5%)
Total	376	(100)

were employees or farmers (Table 1).

Ninety two per cent were married, 7.4% were single and 0.6% were divorced. Twenty two per cent of patients reported of having multiple sexual partners. Their mean duration of sexual exposure before the occurrence of ectopic pregnancies was  $6.1 \pm 5.2$  years. Nearly half (47.7%) were primigravidas, 33.6% were

second gravidas and 14.1% were having their third pregnancies when the ectopic pregnancy occurred. One hundred and thirty six cases (36.2%) had one or more previous abortion, of which 54 cases were induced abortions. The methods of induced abortions commonly used were dilatation and curettage and menstrual extraction (Table 2)

**Table 2** *Methods of induced abortions*

Methods	No.	(%)
Dilatation and curettage	18	33.3
Menstrual extraction	17	31.5
Forceful uterine massage	6	11.1
Oral medication	4	7.4
Injectable medication	3	5.5
Hypertonic saline	1	1.9
Combination of 2 above methods	2	3.7
Unknown	3	5.6
Total	54	100.0

Sixty one cases (16.2%) had a history of salpingitis, 74 cases (19.7%) had previous pelvic operation and 28 cases (7.4%) had one or more previous ectopic pregnancy. Two cases of ectopic pregnancy in this study resulted from in vitro fertilization and embryo transfer (IVF & ET). The majority of cases (73.3%) were not currently using any contraceptive methods and, in fact, 39.3% of them had been Attempted to conceive for more than one year. Those who practised contraception (26.7%) were using the following methods : combined pills (41 cases), tubal sterilization (16 cases), condom

(12 cases), postcoital pills (11 cases), IUDs (10 cases), DMPA (7 cases) and rhythm method (3 cases).

*Symptoms and signs:* The presenting symptoms and signs are shown in Table 3.

Abdominal pain was experienced in almost all cases. The pain was unilateral in 60.4% of cases, bilateral in 29.5%, localized in the lower midline in 9.8% and epigastric in location in 0.3%. The pain was found to be on the same sides with ectopic pregnancies in 91.6% of patients and on the contralateral sides in 8.4%. The majority of them also



Table 3 *Presenting symptoms and signs\**

	No./Total cases	Percentages
Symptoms		
Abdominal pain	369/375	98.4
Amenorrhea 308/371	83.0	
Vaginal bleeding	253/376	67.3
Symptoms of pregnancy	182/374	48.7
Fainting or syncope	175/375	46.7
Symptoms of shock	106/376	28.2
Shoulder pain	79/371	21.3
Signs		
Fever > 37.5 c	33/376	8.8
Palpable adnexal mass	158/374	42.2
Uterus: Normal size	191/362	52.8
Enlarged	171/362	47.2
Cul-de-sac: Normal	191/362	52.8
Bulging	171/362	47.2

\* Data missing in some cases for the following reasons: one hilltribe patient could not communicate in Thai, some patients were unsure or gave equivocal responses when asked about certain symptoms, some pelvic findings such as uterine size and bulging of cul-de-sac were difficult to assess in some cases.

had amenorrhea, with a mean duration ( $\pm$  SD) of  $59 \pm 21.4$  days. Shoulder pain was reported in only one fifth of patients, of these 51.9% were bilateral.

**Laboratory findings:** Urine pregnancy test using latex agglutination inhibition (Planosec, Organon, sensitivity 2,000 IU/L 1st IRP) was done in 256 out of the 376 patients, with positive results in 169 cases (66%). Serum  $\beta$ -hCG (radioimmunoassay method, sensitivity 5 IU/L, 1st IRP) was performed in 258 cases, with positive results in 256 (99.2%). In the two cases with negative results, pathological reports described exhausted villi. Initial hemoglobin levels were below 10 g/dl in 29.5% of patients ; low hemoglobin levels were seen

more often in patients with ruptured ectopic pregnancy (42.6%) than in the group with unruptured ectopic pregnancy (16.5%). In this study, leukocytosis (defined as white cell count > 10,000/ml.) was noted in 57.6% of patients.

**Culdocentesis :** needle aspiration of blood from cul-de-sac was done in 250 patients, yielding non clotted blood (positive culdocentesis) in 234 (93.6%). Dry tap (no blood or fluid) was obtained in 15 cases (6%). In one case with abdominal pregnancy, clotted blood was obtained, presumably from aspiration of blood from the placental site. Culdocentesis was positive in 134 out of 140 cases with bulging cul-de-sac, which was not

significantly different from 94 out of 103 patients who were recorded as having normal cul-de-sac on initial pelvic examination (status of cul-de-sac was not recorded in 6 cases with positive culdocentesis). The least amount of hemoperitoneum that could give a positive culdocentesis in this study was 30 ml. On the contrary, six out of 91 cases (6.6%), who had culdocentesis performed and were later found to have > 1,000 ml of blood in the peritoneal cavity, were reported to have dry tap.

**Laparoscopy :** Diagnostic laparoscopy was performed in 34 out of 376 cases (9%). Because of its invasive nature, the procedure was done only in selected cases with minimal signs and symptoms. Laparoscopy confirmed the presence of ectopic pregnancy in 29 cases (85.3%). In three patients (8.8%), the diagnosis was missed and in the other two patients (5.9%) laparoscopy was not helpful because visualization of adnexal structures was not possible due to marked pelvic adhesion.

**Ultrasonography :** Pelvic ultrasonography is a non invasive diagnostic tool and was, therefore, liberally performed in 166 out of 376 cases (44.1%) in this study. It confirmed the diagnosis of ectopic pregnancy in 156 cases (94%). Ectopic pregnancy was missed in 10 cases, who were incorrectly diagnosed as follows ovarian cysts (3 cases), tubo-ovarian abscess (3 cases), normal pelvic organ (1 case), intrauterine pregnancy (1

case), incomplete abortion (1 case) and missed abortion (1 case).

Ultrasonography revealed the presence of adnexal masses in 84.5%, pseudosac in uterine cavity in 7.2%, free fluid in cul-de-sac in 76.9%. Uterus was noted to be normal in 69.8%

**Operative findings :** Laparotomy was performed in all patients. The location of ectopic pregnancies was as follows tubal 366 cases, ovarian 1 case, abdominal 3 cases, rudimentary horn 3 cases and unknown in 3 cases (conceptive products were seen intra-abdominally at operation and it was not possible to identify the primary sites, gestational ages of these three cases were 34, 75 and 105 days from the first days of the last menstrual periods respectively). Tubal pregnancy occurred on the right side in 187 patients (51.1%) and on the left side in 179 (48.9%). Tubal pregnancy was located most commonly in the ampulla (64.1%), followed by isthmus (21.3%), fimbria (12.3%) and interstitial (2.3%) respectively. The average dimeter ( $\pm$  S.D.) of tubal gestation was  $3.5 \pm 1.8$  cm. Rupture of tubal pregnancy was seen at the time of operation in 196 cases (53.6%). The percentage of patients with ruptured tubal pregnancy remained relatively constant over the five-year period in this study (55.3%, 60%, 51.9%, 50% and 47% respectively), Corpus luteum was noted to be present in 210 out of 376 cases (55.9%). Their location was on the same side as ectopic gestation

in 69.5% and on the contralateral side in 30.5%

There was no other pelvic pathology in 198 patients (52.7%) with ectopic pregnancy. Peritubal adhesion was seen in 56 cases (14.9%); pelvic adhesion in 63 cases (16.8), ovarian cysts in 23 cases (6.1%), pelvic endometriosis in 5 cases (1.3%) and myoma uteri in 3 cases (0.8%)

**Operative procedures :** The most common operation was unilateral salpingectomy (76.6%), followed by unilateral salpingo-oophorectomy (10.1%), salpingotomy (7.4%), hysterectomy (2.1%) and miscellaneous i.e. removal of abdominal pregnancy, ovarian wedge resection, etc ; in 3.8%). Incidental appendectomy was performed in 105 cases (27.9%). When compared with patients who did not have incidental appendectomy, we found that operative time was significantly longer in the group with incidental appendectomy ( $79.4 \pm 27.9$  minutes vs  $61.8 \pm 20.7$  minutes,  $p < 0.001$ , t-test), but there was no difference in febrile morbidity ( $p = 0.237$ , Chisquare test) or wound infection rates ( $p = 0.4265$ , Fisher's exact test) among the two groups. The overall mean operative time ( $\pm$  S.D) was  $70.2 \pm 26.4$  minutes. There were 191 (50.8%) patients who required blood transfusion for an average volume ( $\pm$  S.D.) of  $977.1 \pm 511.2$  ml.

There were six patients (1.6%) who had wound infection. Urinary tract infection occurred in 1 case. Thrombocytopenia was diagnosed in

1 patient, who had ruptured uterine horn and required 8 units of blood transfusion. There was no maternal mortality in this study.

## Discussion

The incidence of ectopic pregnancy can be calculated in at least three different ways.<sup>(2)</sup> First, one can use reproductive age women (15-44 years old) as the denominator but such calculation will be less helpful in determining risk factors because women are included regardless of their sexual exposures.<sup>(3)</sup> Total pregnancies can also be used as the denominator and, as such, will theoretically reflect the true proportion of pregnancies that are ectopic in location. In practice, however, spontaneous and illegal abortions are usually under reported and will, therefore, result in an over estimation of ectopic pregnancy rate. In this study, we calculated the incidence of ectopic pregnancy by using live-birth as the denominator. This has the advantage in that it allows us to compare our data with that reported from other hospitals.

Our data agreed with other reports<sup>(4-7)</sup> in that ectopic pregnancy can occur in any woman of reproductive age and that it should be suspected in patients with a history of infertility, previous abortion or previous ectopic pregnancy, previous history of pelvic inflammatory disease, tuboplasty or other pelvic operations. It is interesting to note that 26.7% of ectopic pregnancy

in our study occurred in women who were practising contraception. Of these, 59% were using hormonal contraception, 16% were cases of sterilization failure and 10% were IUD failures. It has been hypothesized that progesterone in contraceptive pills can inhibit oviductal propulsion at the ampullary isthmic junction and, therefore, ovum trapping may result.<sup>(8)</sup> According to Tatum and Schmidt,<sup>(9)</sup> the incidence of ectopic pregnancy after elective tubal sterilization is approximately 16%. It may result from the development of tuboperitoneal fistula after failure of sterilization, allowing sperm to pass into the distal segment of the oviduct and fertilize the egg. Ory,<sup>(10)</sup> in a collaborative multicenter case-control study of the incidence of ectopic pregnancy in the United States from 1965 through 1977, showed that IUD did not play a significant role in the increased incidence of ectopic pregnancy. However, pregnancy during IUD wearing was more likely to cause tubal pregnancy because IUD acted preferentially to impair intrauterine implantation.

Like other studies,<sup>(4,11)</sup> the most common presenting symptoms in our patients were pain, amenorrhea and vaginal bleeding. Other significant clues for diagnosis included symptoms of pregnancy, fainting or syncope and palpable adnexal mass. Urine pregnancy (latex hemagglutination inhibition) test is imprecise and gives a positive result in only 66% of patients with ectopic pregnancy. This is so because the

hCG level in ectopic pregnancy is often lower than the sensitivity of conventional urine pregnancy tests. The current availability of a very sensitive and accurate serum pregnancy test has resulted in an increased use of this method in the detection of ectopic pregnancy. In our hands, serum  $\beta$ -hCG a sensitivity of 10 mIU/ml is almost always (99.2%) positive, which agrees with the experience of others.<sup>(8,12)</sup>

Romero et al<sup>(13)</sup> reported positive culdocentesis in 83.5% of patients with ectopic pregnancy. The present study gives a higher positive rate of 94% and confirms that culdocentesis is a valuable diagnostic procedure despite its invasive nature. We feel that a positive culdocentesis in conjunction with a clinical history and physical examination suggestive of ectopic pregnancy warrants an immediate laparotomy.

Pelvic ultrasound is a noninvasive procedure that is helpful in localizing the site of pregnancy. The use of  $\beta$ -hCG combined with endovaginal ultrasound will assist the physician in making an early diagnosis of this condition.<sup>(14,15)</sup> Laparoscopy is useful in suspected cases of unruptured ectopic pregnancy, who have minimal signs and symptoms. It allows precise visualization of the entire female reproductive tract and has limited the need for laparotomy.<sup>(8)</sup> Nevertheless, laparoscopy has limitation in cases where adnexal pathology is obscured by marked pelvic adhesion as were

seen in 5.9% of our patients. In three cases, no lesion was seen during laparoscopy, presumably due to the small size of very early ectopic gestations and the relative inexperience of the involved laparoscopist.

As in other studies,<sup>(1-4,8,11)</sup> tubal pregnancy is the most common type of ectopic pregnancy ; the most common site of which is located in the ampullar part, followed by the isthmic, fimbria and interstitial part respectively. Despite the availability of sensitive  $\beta$ -hCG test and vaginal ultrasound in our institution, the incidence of ruptured tubal pregnancy was still very high. This may be due to the fact that many patients were misdiagnosed and had been treated elsewhere, by local practitioners and traditional healers, without improvement before they were referred to out center.

Insunza et al.<sup>(16)</sup> reported that about one in every four tubal pregnancies, the corpus luteum is on the opposite ovary, which agrees well with our data (30.5%). This finding supports the theory of transperitoneal migration of fertilized ovum.<sup>(17)</sup>

Although many options exist, operative measure is still the milestone of treatment for ectopic pregnancy. In our report, salpingectomy was the treatment of choice for most cases of tubal pregnancy. Salpingotomy was done in selected cases with small, unruptured tubal pregnancy, in whom clinical condition was stable and future fertility was desired. However, some

authorities<sup>(18-19)</sup> would advocate medical treatment with either methotrexate or RU-486 rather than surgery for such patients. Recently, laparoscopic surgery has been introduced for both conservative and radical treatment of ectopic pregnancy with very good results.<sup>(20-21)</sup> Unfortunately, facilities for operative laparoscopy were not available in our hospital at the time of this study.

There is no consensus regarding incidental appendectomy at the time of surgery for ectopic pregnancy. According to a recent ACOG Technical Bulletin,<sup>(22)</sup> incidental appendectomy is not advised and any ancillary surgical procedures should best be limited to simple lysis of adhesion. The primary concern is that bacterial contamination of tubal wound and free blood in the peritoneal cavity can occur during appendectomy. Thompson<sup>(23)</sup> believes that the prognosis for subsequent pregnancy is so dismal after operation for ectopic pregnancy that any additional insult such as elective appendectomy should be avoided. On the contrary, many studies<sup>(23-26)</sup> demonstrate that incidental appendectomy at surgery for ectopic pregnancy does not place the patients at increased operative risk and even spares them from the possible subsequent development of acute appendicitis. Our study also reveals that the added procedure carries no increased risk in morbidity or mortality rates. However, to maintain this low level of risk, incidental appendectomy should only be done when the patient's condition

is satisfactorily near the end of the operation and the appendix is easily located and accessible.

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# Cryosurgical Treatment of Benign Lesions of the Cervix

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**Abstract :** *The cryosurgery was performed in the treatment of benign lesions and neoplasia of the cervix. Group I patients who had glandular erosion or erosio vera were treated by single freezing of 3 minutes. Group II patients who had positive Papanicolaou smear consistent with CIN II-III but negative colposcopic biopsy and endocervical curettage, and group III patients who had colposcopic biopsy or endocervical curettage positive for CIN were treated by double freezing technique. The minimal pelvic pain during freezing was common (41.67%) The watery of serous bloody vaginal discharge occurred in second day after freezing and lasted for 1-2 weeks in all of cases. Group I, II and III patients had failure rate of 3.22%, 13.5% and 17.39%. This procedure was adequate in selected group I and II only. (Thai J Obstet Gynaecol 1995;7:105-108)*

**Short title :** *Cryosurgery of cervical benign lesions*

**Key words :** *cryosurgical treatment, benign cervical lesions*

The glandular erosion, true erosion or erosio vera and cervical intraepithelial neoplasia (CIN) usually manifested as abnormal vaginal discharge and contact bleeding. Local treatment by electric cautery and cervical conization required an adequate anaesthesia and perhaps hospitalization. In contrast, by cryosurgery these

lesion could be treated as an out patient. The aim of this study was to basis our experience in the cryosurgical treatment for these lesions described.

## Materials and Methods

The nitrous oxide cryosurgical apparatus of Spemby company with



the cryoprobe number 6 F diameter 2.0 cms was used in this study. The patients were ended into 3 groups. Group I, glandular erosion and erosio vera, group II, patients with abnormal Papanicolaou smear and normal colposcopic biopsy, group III, patients who had abnormal colposcopic examination either endocervical curettage or colposcopic biopsy showed CIN. The first group were treated by single freezing 3 minutes. Group 2 and 3 had double freezing (3 minutes freezing with 1 minute pause.)

The immediate postcryosurgical pelvic pain and late effects of increasing abnormal vaginal discharge or haemorrhage were recorded. Ampicillin or urfamycin was given as a prophylaxis following the procedure and sexual intercourse was prohibited for 3 months.

Patients were instructed to return to our clinic visit at 1.5, 3.0, 6.0

and 12.0 months. The Papanicolaou smear and colposcopy were indicated for group II and III patients. Abnormal Papanicolaou smear or colposcopy after 3-month visit would be called failure of treatment, as well as a persisting glandular erosion in spite of negative Papanicolaou smear or colposcopy. Cold knife conization, laser conization or loop electrocoagulation excision procedure would be used as a definitive treatment.

## Results

From January 1992-December 1993, 96 patients were included in the study (Table 1). Group I patients (age range of 26-48 years) had glandular erosion, (n = 19) and erosio vera, (n = 12 cases). 20 cases had lesion size less than 2 cms, 8 cases had lesion size 2.0-2.5 cms and 3 cases > 2.5

**Table 1**

Patients characteristics	Number of cases	Initial success	Failure
Group I			
Glandular erosion	19	30/31 (96.77%)	1/31 (3.22%)
Erosio vera	12		
Group II			
Papanicolaou smear positive CIN II-III, Colposcopic biopsy and, endocervical curettage negative	37	32/37 (86.48%)	5/37 (13.5%)
Group III			
Colposcopic biopsy or curettage positive			
CIN-I	5	5/5 (100.0%)	0
CIN-II	12	11/12 (91.66%)	1/12 (8.33%)
CIN-III	11	8/11 (72.72%)	3/11 (27.27%)

cms. Patients returned to visit our colposcopy clinic after 3 months and found to have 1 persistent cervical erosion, ( $1/31 = 3.2\%$ ). This case had lesion size greater than 2.5 cms in diameter.

Thirty seven patients (age range of 18-50 years) had abnormal Papanicolaou smear (Group II) underwent cryosurgery with double freezing method. 5 of 37 cases (13.5%) had persistent abnormal smears and underwent diagnostic conization later. The pathologic results showed CIN II-III. Two of these had neoplastic change in the endocervical canal.

Twenty eight cases were in Group 3 (age range 20-40 years). Five had CIN I, 12 had CIN II and 11 had CIN III. After cryosurgery, 4 patients had persistent cervical neoplasia, CIN II-III diagnosed by cervical conization, ( $4/28 = 14.28\%$ ). The patient who preliminary CIN III had high risk for failure after cryosurgery ( $3/11 = 27\%$ )

Forty cases had immediate pelvic pain during cryosurgical procedure (41%), serous bloody discharge was very common and lasted 1-2 weeks.

## Discussion

The failure of cryosurgical treatment occurred only in one case of group I and had lesion diameter greater than 2.5 cms. This might be explained by inadequate destruction

because the frozen area by cryoprobe number 6F had the lateral spread only 0.6 cms from our observation, and 0.62 cms by other,<sup>(1)</sup> which required repeated freezing after 3.0 months. The failure in this study occurred 3.22%, whereas the other series had 5.0-15.0% failure rate.<sup>(2-4)</sup>

The group II patients had persistent symptoms after cryosurgery. The failure rate was 13.5%, and all had CIN II-III after conization. This outcome reflected our colposcopy inaccuracy.

The patients in group III had failure rate of 8.33% in CIN II, and 27.27% in CIN III respectively. Other series had failure rate for CIN I, II and III of 6.0-11.0%,<sup>(5-6)</sup> 7.0-24.2%,<sup>(6-8)</sup> and 7.0-39.0%<sup>(1,4,6,8-15)</sup> respectively

The cause of failure may be attributed to neoplastic change extending into endocervical canal ( $5/9 = 55.5\%$ ). Obviously, the flat cryoprobe number 6F was incapable of eradicating all CIN in the endocervical glandular clefts. For these reasons we would advocate the use of cryotherapy for CIN I or II after a well performed colposcopic evaluation. Those who had CIN III should undergo the other alternative ablative procedure.

## Conclusion

The cryosurgery was an adequate treatment for benign cervical lesion and CIN I-II. This procedure was convenient, low cost and safely

performed in the office setting.

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# Subendometrial Contractions in Subfertile Women : A Preliminary Observation

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**Abstract :** *Fifty endovaginal ultrasonographic examinations were screened for the presence of subendometrial myometrial contractions in subfertile women. The contractions were evaluated during the periovulatory phase of ovulation induction programs. The results showed that the contractions can be divided into 3 types according to directions. (1) Retrograde type, was the direction from endocervix to the fundus. (2) Antegrade type, was the direction from the fundus to endocervix. (3) Turbulent type, contractions moved in alternating directions over a short segment. More than half of the contractions observed are turbulent type. The conclusion is that there are definite patterns of subendometrial contractions in subfertile women but with a significant difference in percentage compared to study in fertile women. (Thai J obstet Gynaecol 1995;7:109-111)*

**Key Words :** endovaginal ultrasonography, subendometrial myometrial contraction, subfertile women.

Anovulation is one of the common factors attributed to infertility. However, pregnancy is still not achieved after an induction of ovulation in the absence of other known causes. Lyons et al demonstrated subendometrial peristaltic activity throughout the entire menstrual cycle in 18 healthy fertile volunteers by transvaginal ultrasound. It was revealed that the subendometrial myometrial contractions increased in frequency, amplitude and percentage toward the fundus throughout

follicular and periovulatory phase. The pattern of subendometrial myometrial contraction, recorded and displayed via videocinematography was divided into 4 types; antegrade, retrograde, quiescent and turbulent type. More than 80 percent of contractile pattern were retrograde type during periovulatory phase. At present time, there is lack of information regarding subendometrial contractile pattern in subfertile women. The purpose of this study was to determine the periovula-

tory contractile patterns in subfertile women compared to that previously reported in fertile women.<sup>(4)</sup>

## Materials and Methods

50 subfertile women were enrolled into our study. Mean age was 32.6 years (25-39). All had ovulation induction and required clomiphene citrate, clomiphene citrate plus human menopausal gonadotropin (HMG) or long protocol superovulation using HMG for ovulation induction. Real-time transvaginal ultrasonography was performed during periovulatory period (Day 7-11, 12-17 and 12-18 for HMG protocol, clomiphene citrate only and clomiphene citrate-HMG protocol respectively) using a 5 MHz/120 degree transvaginal transducer (ALOKA, SSD 1200, Japan). The ultrasonograph of endometrium was identified by a midsagittal scan and recorded on a videotape for 120 seconds. A video

cassette recorder VCR ( model SCV-X37 PS, SONY, Japan) was used. The tapes were reviewed at 5 times regular speed, which enhanced appreciation wave to analyse the pattern and direction of contractions.

## Evaluation of the Contraction Wave.

The propagation of the contraction waves was analysed. The direction of wave propagation was described depending on the pattern observed in the midsagittal plane.

Definition of contraction waves were as follows :

1. **Retrograde** was the direction from the endocervix to the fundus.

2. **Antegrade** was the direction from the fundus to the endocervix.

3. **Turbulent** was the contractions which moved in alternating directions over a short segment.

**Results :** Table 1. and Table 2.

Table 1.

Protocol	Number	Antegrade	%	Retrograde	%	Turbulent	%
HMG	11	2	18	3	27	6	54
Clomiphene citrate	16	3	18	2	12	11	68
Clomiphene citrate HMG	23	2	8	6	26	15	65
Total	50	7	14	11	22	32	64

Table 2.

Protocol	Age range	Mean age	Day of u/s scan
HMG	26 - 39	34.09	7 - 11 of inj.
Clomiphene citrate	25 - 37	31.50	12 - 17 of cycle
Clomiphene citrate HMG	25 - 37	32.69	12 - 18 of cycle

## Discussion

Our findings were significantly different from a previous report<sup>(1-4)</sup> in which there were more than 80% of retrograde pattern. Thirty two out of 50 cases (64%) of our study had turbulent type. This may be explained by the different population of women recruited. Only 22% had retrograde pattern in contrast to a previous study undertaken in fertile women which yielded more than 80% result.

Since estrogen was accepted to have a role in the occurrence of retrograde contraction during peri-ovulatory period. Women who had medical induction of ovulation should have a higher estrogen level compare to spontaneous cycle. However, our result was in opposition and needs more physiological elaboration. Since the hypothesis of retrograde subendometrial contraction remained solid in fertile women it was believed that it may influence transportation of sperms and holding of the embryos

within the uterine cavity after fertilization was established both naturally and via in vitro fertilization embryo transfer. Results from our study in subfertile women may reveal subendometrial contraction as another subfertility contributing factor. Anyway, it is too early to state any conclusion. More clinical data is required.

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# Sperm Movement Characteristic in Prediction of in Vitro Fertilization

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**Abstract :** *To determine the relationship between the in vitro fertilization rates and sperm movement characteristics, inseminated sperm suspensions used for in vitro fertilization in 125 patients were assessed using the Hamilton Thorn Motility Analyzer version 10 (HTMA-IVOS). Several sperm movement characteristics of the inseminated sperm suspensions were found to be weakly significantly correlated with the fertilization rate in vitro, such as, straightness (STR) ( $r = -0.1285$ ;  $P < 0.0001$ ), linearity (LIN) ( $r = -0.1188$ ;  $P < 0.0001$ ), amplitude of lateral head displacement (ALH) ( $r = 0.0938$ ;  $P < 0.005$ ), curvilinear velocity (VCL) ( $r = 0.0607$ ;  $P < 0.05$ ) and percentage of rapid motility ( $r = 0.0601$ ;  $P < 0.05$ ). With stepwise regression analysis of all data, poor prediction of fertilization rates ( $R = 0.217$ ) was obtained using a multiple regression equation incorporating 2 variables, including percentage of sperm motility and STR in inseminated sperm suspension. Comparison of sperm preparations giving poor with good in vitro fertilization rates revealed only a significant difference of STR in the inseminated sperm suspensions between both groups ( $p = 0.0339$ ). The STR in the inseminated sperm suspension was the most significant factor negatively related to fertilization rate in vitro. However, the overall predictivity of sperm movement characteristics for in vitro fertilization was still poor. In conclusion, the objective measurement of the sperm movement characteristics by HTMA has no practical value in predicting fertilization rate in vitro. (Thai J Obstet Gynaecol 1995;7:113-122)*

**Short title :** Sperm movement characteristic and in vitro fertilization

**Key words :** sperm movement characteristic, conventional semen analysis, in vitro fertilization

The sperm motility has long been recognized as an important functional characteristic for evaluating the fertility potential of spermatozoa because it is necessary not only for sperm penetration through cumulus

and zona pellucida but also in sperm-egg interaction. The measurement and analysis of sperm motion are technologically challenging. Sperm cell motions are kinematically complex, and are optically difficult to image with high resolution using the light microscope. Historically, the clinical assessment of sperm motility was based on subjective visual impressions with limited accuracy and precision. The limitations themselves contributed to the paucity of direct evidence of positive relationships between measures of conventional seminal sperm motility and fertilization in vitro.<sup>(1,2)</sup> In recent years, the evolution of computer vision technology has given rise to a new generation of instruments that have overcome these historical limitations and are becoming amenable to practical clinical utilization. Computer-aided sperm analysis (CASA) technology has become commercialized and is now used in several laboratories worldwide. It has been demonstrated clearly that they provide objective assessment of sperm motility and details of movement characteristics not obtainable by subjective assessment of motility. At least six CASA systems are currently available. Hamilton Thorn Motility Analyzer (HTMA) used in this study is one of the most popular CASA systems.

Several sperm motility parameters were evaluated to allow the clinician to predict the relative probability of fertilization in vitro.<sup>(3-5)</sup> Among those parameters, curvilinear

velocity (VCL),<sup>(4)</sup> amplitude of lateral head displacement (ALH),<sup>(3)</sup> linearity (LIN) and straight line velocity (VSL)<sup>(5)</sup> have been reported to be a useful predictor of fertilization rate in vitro. However, very few studies have analyzed the relationship between sperm movement characteristics and fertilization rate in vitro and available data are still controversial.

The aim of this study was to examine the clinical value of the sperm movement characteristics obtained by HTMA together with data from standard semen analysis. In this prospective study, inseminated sperm suspensions were assessed with the Hamilton-Thorn Motility Analyzer (HTMA) to determine which sperm movement characteristics are related to IVF rates and assess whether these sperm movement characteristics have any relevance in predicting fertilization rate in vitro.

## Materials and Methods

### Study population

The study population consisted of a cohort of 125 unselected patients undergoing IVF therapy at the Simpson Maternity Memorial Pavilion, Edinburgh, between February and May 1994, without the use of donor gametes.

### In vitro fertilization

Controlled ovarian hyperstimulation consisted of the following regimen : pituitary down regulation was achieved with a GnRH agonist



(Suprefact,<sup>®</sup> Buserelin, Hoechst, Middlesex, UK) starting on day 1 of menstrual cycle. When ovarian suppression was documented by the absence of ovarian follicles and attenuation of the endometrial lining by ultrasound evaluation, ovulation was initiated with hMG (Pergonal<sup>®</sup> ; Serono Laboratories, Herts, UK or Humegon<sup>®</sup> ; Organon Laboratories, Cambridge, UK). Changes in gonadotrophin dosage were based on follicular development as reflected by changes in follicular diameter and number assessed by serial transvaginal ultrasonography. Human chorionic gonadotrophin (Profasi<sup>®</sup> ; Serono Laboratories), 5,000 IU, was administered when at least three leading follicles reached a mean diameter of at least 16 mm. Oocyte retrieval was performed 34 hours after the hCG injection, using transvaginal ultrasound.

### **Semen samples and semen preparation**

One hour before the scheduled time of oocyte retrieval, a semen sample was collected by the male partner by masturbation into sterile containers. After liquefaction, routine semen analyses according to WHO guidelines<sup>(6)</sup> and sperm movement characteristics assessment as described below were performed. The semen samples were then prepared by two-layer (40% and 80%) discontinuous Percoll<sup>®</sup> (Pharmacia, Uppsala, Sweden) centrifugation, after which the sperm pellet was gently overlaid with Earle's medium (Flow Laboratories, Irvine, UK.) supplemented with 10% human serum

albumin (Human Albumin Solution, 4.5%, Immuno AG, Vienna, Austria.). After one hour of incubation, the upper layer of culture medium containing the motile sperm was used for oocyte insemination. The oocytes were inseminated with 100  $\mu$ l of sperm suspension containing approximately 100,000 motile spermatozoa 1 to 3 hours after oocyte retrieval. Fertilization of the oocytes was assessed after 20 to 22 hours incubation at 37 °C in an atmosphere of 5% CO<sub>2</sub> in air. The remainder of the swim-up sperm suspension was centrifuged (500g for 5 minutes) and resuspended in BWW medium<sup>(7)</sup> at a concentration of 20 x 10<sup>6</sup> sperm/mL for the following sperm movement characteristics assessment.

### *Sperm movement characteristics*

The sperm movement characteristics were assessed using the European (25 Hz) version of the Hamilton Thorn Motility Analyzer (HTMA-IVOS Version 10 : Hamilton Thorn Research, Danvers, MA, USA) at a temperature of 37 °C using the following settings : minimum contrast, 10 ; minimum size, 5 ; low and high head size gates, 0.18 and 2.18, respectively ; low and high head intensity gates, 0.4 and 1.67, respectively ; nonmotile head size, 5 ; nonmotile head intensity, 80 ; magnification factor, 2.53. The measurements were conducted in 200  $\mu$ m deep flat capillary tubes (Camlab, Cambridge, UK) and at least 100 motile cells were assessed for each determination. These deter-

minations were carried out in duplicate and the results were averaged.

The criteria of movement assessed in this study were curvilinear velocity (VCL) straight line velocity (VSL) ; average path velocity (VAP) ; "percentage rapid" (the percentage of cells exhibiting a VAP of  $\geq 25 \mu\text{m/s}$ ) and ALH (the amplitude of lateral sperm head displacement in  $\mu\text{m}$ ). Linearity (LIN) was defined as  $\text{VSL}/\text{VCL} \times 100$ , while straightness (STR) was  $\text{VSL}/\text{VAP} \times 100$ . "Percent progressive motility" equated with an STR of  $>75\%$ . The playback function of the HTMA-IVOS was used to verify the validity of the cell identification process and minor adjustments made to the analyzer set up when necessary.

### Statistical Analysis

All data are presented as means  $\pm$  SEM. The paired  $t$  test was used to assess the statistical significance of differences between the sperm movement characteristics in semen and inseminated sperm suspension. Ten cases were excluded from statistical analysis because the number of oocytes collected were less than four oocytes to avoid misinterpretation of the percentage of fertilization rates and increase statistical significance. The data were weighted with the number of eggs and then analysed by linear and stepwise regression analysis. Stepwise regression analysis identifies the optimum combination of independent variables (conventional semen analysis parameters and sperm

movement characteristics) that can be used to predict the dependent variable (fertilization rate). The unpaired  $t$  test was used to assess the statistical significance of differences between the sperm movement characteristics in samples exhibiting good and poor fertilization. All data were analysed using Statistical Package for the Social Sciences (SPSS for MS Windows Release 6, Microsoft Ltd., Wokingham). Probability values ( $p$ )  $< 0.05$  were considered significant.

### Ethics

This study was approved by the Pediatrics/ Reproductive Medicine Research Ethics Sub-committee of Lothian Health.

### Results

#### Study population

For the 125 couples studied, the indication for IVF was unexplained infertility in 49 (39.2%), bilateral tubal occlusion in 50 (40%), male infertility in 19 (15.2%), and endometriosis in 8 (6.4%).

The semen was assessed according to the World Health Organization guidelines<sup>(6)</sup> with regard to the sperm concentration, motility and morphology. For this cohort of patients, the constituents of the conventional semen profile, expressed as mean  $\pm$  standard error of means (SEM), were : volume,  $3.2 \pm 0.2 \text{ mL}$  ; sperm concentration,  $55.8 \pm 3.1 \times 10^6$  spermatozoa/mL ; normal morphology,  $51.4 \pm 1.1\%$  and

motility,  $49.0 \pm 1.1\%$ .

### Outcome of IVF

For the 125 couples studied, the mean value of the number of oocytes retrieved and inseminated was  $9.6 \pm 0.5$  (1 - 24) while the mean value of fertilization rate was  $69.7 \pm 2.5\%$  (0% - 100%).

### Sperm movement characteristics results

#### *Sperm movement characteristics in semen and inseminated sperm suspension*

Table 1 shows the mean  $\pm$  SEM of all sperm movement characteristics obtained by HTMA-IVOS from 125 patients. Most of the sperm movement characteristics (Percentage of rapid motility, percentage of progressive motility, VAP, VCL, VSL, ALH and BCF) were significantly increased after selection of motile spermatozoa by discontinuous Percoll centrifugation and swim-up techniques.

#### *Simple linear regression analysis*

Linear regression analysis of fertilization rate weighted by number of eggs against the parameters of the conventional semen profile for this cohort of patients revealed that weakly significant correlations with fertilization rate were observed for the sperm concentration ( $r = 0.0893$ ;  $P < 0.005$ ) and the percentage of sperm motility ( $r = 0.1156$ ;  $P < 0.0001$ ). Several sperm movement characteristics of the inseminated sperm suspensions were

also found to be weakly significantly correlated with the fertilizing potential of the spermatozoa in vitro, such as, STR ( $r = -0.1285$ ;  $P < 0.0001$ ), LIN ( $r = -0.1188$ ;  $P < 0.0001$ ), ALH ( $r = 0.0938$ ;  $P < 0.005$ ), VCL ( $r = 0.0607$ ;  $P < 0.05$ ) and percentage of rapid motility ( $r = 0.0601$ ;  $P < 0.05$ ).

#### *Stepwise regression analysis*

In order to determine whether a combination of variables describing different sperm movement characteristics of the inseminated sperm suspensions and conventional semen analysis could adequately explain the variance in in vitro fertilization rates, a stepwise multiple regression analysis was performed. In this model, independent variables are added to the regression analysis in order of their ability to predict the dependent variable. With this data set a regression equation was generated that gave a multiple regression coefficient of  $R = 0.217$  ( $R^2 = 0.0473$ ) for the relationship between the conventional semen analysis and sperm movement characteristics of the inseminated sperm suspension and in vitro fertilization rate. This analysis was based on 2 variables, comprising, the percentage of sperm motility and STR in inseminated sperm suspension (Table 2). Included in this table are the standardized  $\beta$  coefficients, which give an indication of the relative importance of each of the selected independent variables in predicting the dependent variable, fertilization

rate. Examination of these coefficients reveals that the most important variables were STR in inseminated sperm suspensions.

*(Comparison of samples exhibiting good or poor fertilization)*

The other approach towards assessing the relationship between sperm movement characteristics and in vitro fertilization success was to compare those samples exhibiting an impaired capacity for fertilization with the rest of the study population. For this purpose, a threshold value of less than 60% fertilization was selected ( $n = 29$ ) since it captured those samples in the lowest quartile of the data distribution. Comparison of sperm preparations giving in vitro fertilization rates of less than 60% ( $n = 29$ ) with the remainder of the study population ( $n = 86$ ) revealed only a significant difference of STR in the inseminated sperm suspensions between both groups ( $p = 0.0339$ ) (Table 3).

## Discussion

Recently, it has become possible to assess the fertilization potential directly by observing fertilization in IVF treatment. The advent of in vitro fertilization has contributed in eliminating various male and female factors by bringing human spermatozoa and oocytes into direct physical contact. Therefore, clinical IVF provides a useful approach for evaluation tests of human sperm function<sup>(8)</sup>. In this study, inseminated sperm suspensions were assessed with the Hamilton-Thorn Motility Analyzer (HTMA) to determine which sperm movement characteristics are related to fertilization rate in vitro and assess whether these sperm movement characteristics have any relevance in predicting fertilization rate in vitro. Great care was taken to standardize the fertilizing environment and to use the proper statistics that can evaluate the effect of

**Table 1** *The sperm movement characteristics assessed by HTMA-IVOS in semen and inseminated sperm suspension.*

Sperm movement characteristics	Semen	Inseminated sperm suspension
Percentage of rapid motility (%)	47.7 ± 3.0	76.8 ± 2.8†
Percentage of progressive motility (%)	26.3 ± 1.3	40.9 ± 1.5†
Average path velocity (VAP : µm/s)	40.2 ± 1.3	55.2 ± 1.7†
Straight line velocity (VSL : µm/s)	26.2 ± 0.8	36.0 ± 1.1†
Curvilinear velocity (VCL : µm/s)	56.3 ± 1.9	78.6 ± 2.3†
Straightness (STR : %)	66.7 ± 0.7	66.8 ± 0.8
Amplitude of lateral head displacement (ALH : µm)	3.8 ± 0.1	4.7 ± 0.1†
Linearity (LIN : %)	48.4 ± 0.6	48.0 ± 0.7
Beat cross frequency (BCF : Hz)	9.1 ± 0.2	9.9 ± 0.3*

\*  $p < 0.05$ , †  $p < 0.0001$

sperm movement characteristics on fertilization rate in vitro.

After sperm preparation by discontinuous Percoll centrifugation and swim-up techniques, most of the sperm movement characteristics (Percentage of rapid motility, percentage of progressive motility, VAP, VCL, VSL, ALH and BCF) were significantly increased (Table 1) which confirmed the previous study.<sup>(9)</sup>

Many attempts have been made to correlate standard semen analysis characteristics and fertilization outcome, no single parameter appears to account for enough of the total variation to allow for high predictive value.<sup>(10,11)</sup> In agreement with these studies our study confirmed that conventional semen analysis had limited clinical value for predicting fertilization rate in vitro.

In this study, we used the computer assisted image analyzer to evaluate the movement characteristics of semen and inseminated semen suspension. One advantage of such analysis is that it can provide objective measurements of sperm quality. Our studies demonstrated that several sperm movement characteristics were weakly significantly related to the fertilization rates in vitro, including VCL, ALH, LIN, STR, and the percentage of rapid motility. In previous studies, curvilinear velocity (VCL),<sup>(4)</sup> amplitude of lateral head displacement (ALH),<sup>(3)</sup> linearity (LIN) and straight line velocity (VSL)<sup>(5)</sup> have been reported to be a useful predictor of fertil-

ization rate in vitro. In agreement with these studies, the significant correlation between fertilization rate and some sperm movement characteristics, such as, VCL, ALH, and LIN in inseminated sperm suspension were demonstrated. However, we were unable to confirm these studies, which reported a moderate correlation between these sperm movement characteristics and fertilization rate in vitro. On the basis of our data, it seems that relationship between the sperm movement characteristics and the fertilization rate is very poor. Apart from VCL, ALH and LIN, STR had negatively significant correlation with fertilization rates in vitro.

To determine whether a combination of variables describing different sperm movement characteristics of the inseminated sperm suspensions and conventional semen analysis could adequately explain the variance in in vitro fertilization rates, a stepwise multiple regression analysis was performed. Stepwise regression analysis is the most appropriate method for examining the relationship between the probability to response and multiple explanatory variables. In this study, this approach was used to examine how several sperm movement characteristics and standard semen analysis parameters are related to the fertilization rate in vitro weighted by number of the eggs. With stepwise regression analysis of all data, poor prediction of fertilization rates ( $R = 0.217$ ) was obtained using a multiple regression equation incorporating 2 variables,

**Table 2** *Stepwise regression analysis of the relationship between the combination of conventional semen analysis and sperm movement characteristics of inseminated sperm suspension with subsequent fertilization rates in vitro.*

Variables	Coefficient	Standard coefficient
Intercept	86.1663	
STR in sperm suspension	- 0.4798	- 0.1777
Percentage of sperm motility	0.3084	0.1261

**Table 3** *Comparison of the sperm movement characteristics in samples exhibiting good and poor fertilization.*

Sperm movement characteristics	Good fertilization ( $\geq 60\%$ )	Poor fertilization ( $< 60\%$ )
Percentage of rapid motility (%)	69.9 $\pm$ 3.0	62.5 $\pm$ 5.4
Percentage of progressive motility (%)	40.0 $\pm$ 1.5	42.4 $\pm$ 2.8
Average path velocity (VAP : $\mu\text{m/s}$ )	55.5 $\pm$ 2.6	52.5 $\pm$ 2.6
Straight line velocity (VSL : $\mu\text{m/s}$ )	38.8 $\pm$ 1.4	38.8 $\pm$ 2.5
Curvilinear velocity (VCL : $\mu\text{m/s}$ )	75.5 $\pm$ 2.4	69.6 $\pm$ 3.5
Straightness (STR : %)	69.8 $\pm$ 1.0	74.2 $\pm$ 1.9*
Amplitude of lateral head displacement (ALH : $\mu\text{m}$ )	4.3 $\pm$ 0.2	3.8 $\pm$ 0.3
Linearity (LIN : %)	53.3 $\pm$ 1.3	58.2 $\pm$ 2.7
Beat cross frequency (BCF : Hz)	9.3 $\pm$ 0.3	9.4 $\pm$ 0.4

\*  $p < 0.05$ 

including percentage of sperm motility and straightness (STR) in inseminated sperm suspension (Table 2). Our results illustrate that although sperm movement characteristics have been shown to be correlated with in vitro fertilization, this parameter by itself does not possess a sufficiently high discriminating power to be practical for use in predicting the fertilizing potential of semen samples for IVF.

In this study, the STR in inseminated sperm suspensions seems to be one of the most significant factors related to IVF rates because the STR had negatively significant

correlation with fertilization rates in vitro and it was selected by stepwise regression analysis to incorporate in the multiple regression equation. Furthermore, there was a significant difference of STR in the inseminated sperm suspensions between the good and poor fertilization group. However, the overall predictivity of sperm movement characteristics for in vitro fertilization was still poor.

The predictivity of sperm movement characteristics for in vitro fertilization is not consistent with several previous studies because of many reasons. First, CASA system

reports mean values of each movement characteristics of the whole sperm populations. These values may not reflect the sperm movement characteristics of the spermatozoa with fertilizing potential. Therefore, several sperm movement characteristics are weakly significantly related to the fertilization rates in vitro. The reliance on mean values of sperm movement characteristics in the prediction of fertilization rate in vitro may be inappropriate. This could explain some of the inconsistent results of earlier studies. Identification of the subpopulations of spermatozoa with fertilizing potential, such as, hyperactivated motility is much more logical strategy for finding predictors of fertilization in vitro. Second, in vitro fertilization is influenced by many interactive factors, such as, oocyte quality, culture system, etc.

Although a number of statistically significant correlation were found in this type of study, often none of them are useful in clinical practice for predicting the likelihood of successful IVF. Some of the reasons are the variation of the oocyte quality, the variation of the culture system. However, this study is useful for indicating which measurements are worth further investigation to develop a set of prognostic factors for clinical IVF.

There are some studies about the usefulness of the sperm movement characteristics as a method to predict oocyte fertilization in culture.<sup>(3-5)</sup>

However, the results of the present study could not confirm the above observations. Therefore, we conclude that the sperm movement characteristics have no practical value in predicting fertilization rate in vitro. However, further study is required to identify the appropriate mathematical approach to define the sperm movement characteristics that will be useful clinically. Moreover, further studies on other aspects of human sperm movement characteristics are necessary to identify the other sperm parameters, such as, hyperactivated sperm motility, which is important for the success of IVF and to improve the prediction accuracy.

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# Seroprevalence of Human Immunodeficiency Virus in Patients with Ectopic Pregnancies

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**Abstract :** *Objective :* To determine the prevalence and risk factors of human immuno deficiency virus (HIV) infection in a population of patients with ectopic pregnancies. *Design :* Retrospective anonymous survey of clinical data and anonymous screening of HIV antibody by an indirect enzyme-linked immunoabsorbent assay (ELISA, Abbott®) in stored sera. Positive sera were further tested by another indirect ELISA (Vironostika®) before proceeding to Western blot assay. Statistical analyses were performed using Student's t-test and Chi-square test when appropriate. Prognostic factors were studied in a stepwise logistic regression model. The results were considered significant at a value of  $P < 0.05$ . *Setting :* Department of Obstetrics & Gynecology in a university tertiary care center *Participants :* Based on availability of stored frozen sera. The study population included 210 out of 262 consecutively diagnosed ectopic pregnancies between January 1, 1990 and November 30, 1992. *Results :* Out of the 210 sera tested, 10 were found positive for HIV antibody. Stepwise logistic regression analysis revealed that age, number of sexual partners and history of infertility were significant predicting factors for HIV status. *Conclusion :* The relatively high HIV seroprevalence of 4.3%, with a 90% confidence interval between 2-6.6% suggests that HIV counselling and education should be offered to all such patients. An alternative way is to screen patients with a history of infertility and/or those with  $\geq 2$  sexual partners, which will detect 89% of cases and yet reduce the cost of routine testing by  $>50\%$  (Thai J Obstet Gynaecol 1995;7:123-129)

**Key words :** HIV prevalence, ectopic pregnancies, risk factors.

**Short title :** HIV in ectopic pregnancies.

Acquired immuno deficiency syndrome (AIDS) is a fatal, infectious disease for which there is as yet no cure. Although the disease was first reported among homosexual men and intravenous drug abusers, current evidence suggests that the proportion of patients who have been infected through heterosexual contact are on the increase.<sup>(1,2)</sup> A promiscuous pattern of sexual behavior is well known as a risk factor for many sexually transmitted diseases (STDs) including AIDS.<sup>(2)</sup> Since tubal damage as a result of past pelvic infection is a common cause of ectopic pregnancy, it raises the question whether patients with ectopic pregnancies are also a high risk group for human immunodeficiency virus (HIV) infection. In this study, we conducted a preliminary survey of HIV seroprevalence in patients with ectopic pregnancies.

### Materials and Methods

The study population consisted of 262 consecutive cases with ectopic pregnancies, who were admitted to our University Hospital from January 1, 1990 to November 30, 1992. All patients had blood drawn for routine laboratory investigations and for  $\beta$ -hCG testing. The excess sera from routine laboratory investigations were kept frozen at -70 C until analysed for HIV antibody. Stored sera were not enough or not available in 52 cases, leaving 210 frozen samples for HIV testing. Clinical data of patients were

obtained from information previously collected in another prospective descriptive study of clinical signs, symptoms and findings of ectopic pregnancies in this hospital. To ensure anonymity, a research nurse not involved in this study randomly assigned linked code numbers to patient data and serum samples. Patient identities were then deleted from both sample tubes and records. After this, any connection between patient identifications and code numbers were destroyed. The technician who performed HIV testing knew only the code numbers of sera and reported the results only to one of the investigators who performed statistical analysis of the data. This investigator, who did not take part in patient care or interview, was the only person to gain access to patients' (without patient identifications) and the test results with only linked code numbers.

All serum samples were screened for HIV antibody using Abbott® indirect enzyme link immunoabsorbent assay (ELISA) kit. All reactive samples were confirmed with Vironostika® indirect ELISA kit before proceeding to Western blot assays. Statistical analyses were performed using BMDP programs on an IBM PC. Two group student's t-test and Chi-square test were used when appropriate. Potential risk factors were evaluated in a stepwise logistic regression model. The results were considered significant at a value of  $P < 0.05$ .

## Results

Results of HIV tests were available for 210 out of 262 consecutive sera of patients with ectopic pregnancies. Two cases in this report had 2 episodes of ectopic pregnancy, one of whom tested positive for HIV antibody on both occasions. No

seroconversion occurred in the other patient during the period of this study. Ten out of the 210 samples were positive for HIV antibody, giving a seroprevalence rate of 4.76% of samples or 4.3% (9 out of 208) of all patients.

Cases who tested positive for HIV antibody were significantly

**Table 1** *Results of HIV testing in patients with ectopic pregnancies*

	HIV Status		P Value
	Negative	Positive	
Age (mean $\pm$ SD)	27.9 $\pm$ 5.4	23.4 $\pm$ 3.7	0.0147
Occupation			0.5617
Employee	77	4	
Agriculture	34	2	
Civil Service	18	0	
Merchant	33	0	
Housewife	25	3	
Student	9	0	
Prostitute	2	0	
Unemployed	1	0	
Parity			0.2307
0	101	7	
1	68	2	
$\geq 2$	30	0	
Number of Sexual Partners			0.0109
1	159	5	
2	34	2	
$> 2$	6	2	
Duration of sexual exposure in years (mean $\pm$ SD)	7.2 $\pm$ 5.6	4.9 $\pm$ 3.7	0.2038
History of Infertility	65/199	5/9	0.1551
History of Pelvic Inflammatory Disease (PID)	31/199	1/9	0.7164
Contraception			0.2085
None	147	9	
Barrier	7	0	
Nonbarrier	45	0	
Pelvic pathology suggestive of past PID	50/199	3/9	0.5805
Total patients	199	9	208

younger than those who tested negative (Table 1). There was also a statistically significant difference in the number of sexual partners in both groups. Univariate tests revealed that other factors such as occupation, parity, duration of sexual exposure, history of infertility, history of pelvic inflammatory disease (PID) and contraceptive methods were comparable in the two groups. (Table 1).

When multivariate analysis was performed using age (in years), parity (0, 1 and  $\geq 2$ ), number of sexual partners (1,  $\geq 2$ ), duration of sexual exposure (in years), history of infertility (no, yes), contraception (none, barrier and nonbarrier methods) and

pelvic pathology suggestive of past PID (no, yes) as independent variables and HIV status as dependent variable in a stepwise logistic regression model, only age, number of sexual partners and history of infertility emerged as significant predicting factors (Table 2). Younger patients were at increased risks; the odds of having positive HIV serology was 9.1 times in patients with sexual partners  $\geq 2$ , compared with those who had only one sexual partner; similarly, the odds was 6.4 times in those with a history of infertility compared with those without infertility.

The number of patients screened and the number of those who

**Table 2** Summary of stepwise logistic regression analysis

Step No.	Term Entered	DF	Log Likelihood	Improvement Chi-square	P-value
0			- 40.203		
1	Age	1	- 36.627	7.153	0.007
2	No. of sexual partner	2	- 33.188	6.878	0.032
3	History of infertility	1	- 29.948	6.479	0.011

**Table 3** Numbers of patients with risk factor (s) and those who tested positive for HIV antibody

Risk factor (s)	HIV status		Total
	Negative	Positive	
Age $\leq 24$ (F1)	60	5	65
Sexual partner $\geq 2$ (F2)	40	4	44
History of infertility (F3)	65	5	70
F1 and/or F2	96	8	104
F1 and/or F3	113	7	120
F2 and/or F3	90	8	98
F1 and/or F2 and/or F3	136	9	145

tested positive for HIV antibody when the three predicting factors, either alone or in combination, were used as the screening criteria are shown in Table 3.

## Discussion

Studies of HIV seroprevalence in women have been conducted in several settings and populations such as in women attending family planning clinics, prenatal clinics, sexually transmitted disease clinics, drug treatment centers, premarital testing programs, blood donor and infertility clinics.<sup>(2-5)</sup> This report, as far as we know, represents the first study of HIV seroprevalence specifically among patients with ectopic pregnancies. To avoid the possible bias that volunteers have more high risk behavior than non volunteers,<sup>(6)</sup> we tested all available sera left over from routine laboratory investigations. It is unlikely that there was bias in patient recruitment because testing was based solely on availability of sera, which occurred at random and out of the control of patients and investigators. Since the screening covered more than 80% of consecutive cases, it should fairly well reflect the true prevalence of HIV infection in this population.

Our data are in agreement with others who report that multiple sexual partners is a predisposing factor for HIV infection.<sup>(5,7)</sup> The reason why seropositive patients in this study are younger than seronegative cases is not

known. Many possibilities exist ; for example, male partners of these patients may also be younger and more promiscuous than those of the other group or these couples may have other high risk behavior that include intravenous drug use. It is unfortunate that the history of intravenous drug abuse is unknown in our patients to either confirm or refute the above hypothesis. It is also interesting to note that the history of infertility, after adjusting for age and multiple sexual partners, emerges as a significant predicting factor (odds ratio = 6.4). It is possible that other risk factors exist but we may have missed them because this study includes only 9 seropositive cases and does not, therefore, have enough statistical power to show a significant difference in other factors if they indeed exist.

In this preliminary survey, the prevalence of HIV positive sera among patients with ectopic pregnancies is 4.3%, with a 90% confidence interval between 2% to 6.6%. Such a high prevalence of HIV infection raises the issue whether these patients should be considered a high risk group and whether routine HIV testing should be done. Considering the fact that these patients are carrying the virus asymptotically and that they are in the reproductive age group, it is apparent that they have a great potential to spread HIV infection to their sexual partners, prospective children and health care personnel. Although such consideration would favour routine

screening in all cases, there are valid and strong arguments against this approach, such as the cost involved, the possibilities of labeling, stigmatization and loss of employment.<sup>(8)</sup> In addition, knowledge of HIV infection per se may not influence the patients' decision to change their behavior and to avoid pursuing conception.<sup>(9)</sup> Moreover, negative test result does not guarantee an HIV-free status. For these reasons, we believe counselling and education should be made available to all such patients so that they can make their own decision regarding an HIV testing and their future reproductive performance. On the part of health care personnel, we would recommend that universal precaution be strictly observed in the care of all patients with ectopic pregnancies.

One attractive alternative is to screen patients by risk factors. If we use the three predicting factors, either alone or in combination, as screening criteria, we will be able to detect 100% of cases and yet reduce the cost of screening tests by at least 30%. Similarly, history of infertility and/or sexual partners  $\geq 2$  as screening criteria will enable one to detect 89% of cases and cut down the expense of testing by more than half. These risk factors need to be further assessed in a larger study before one can recommend them for general use.

## Conclusion

In this preliminary cross-

sectional survey of HIV seroprevalence among patients with ectopic pregnancies, we found a seropositive rate of 4.3%. However, to really ascertain that the prevalence of HIV in this population is around 5%, with a 90% confidence interval between 4-6%, a larger study involving around 1,300 patients will be needed. Nevertheless, until a more accurate prevalence in this population is known, we believe HIV counselling and education should be offered to all such patients.

## Acknowledgement

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# Objective Structured Clinical Examination (OSCE) the Royal Thai College of Obstetricians and Gynaecologists (RTCOCG) Board Examination

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**Abstract :** *Objective to assess the reliability of OSCE used for assessment of clinical competence for specialists in obstetrics and gynaecology. Design : A descriptive study. Subjects : OSCE used in the Royal Thai College of Obstetricians and Gynaecologists (RTCOCG) board examination, academic year 1992, 1993 and 1994. Methods : Computerized data analyses of scores of OSCE by using SPSS program under window operation. Results : The reliability (Cronbach alpha) of OSCE year 1992, 1993 and 1994 were 0.75, 0.63 and 0.54 respectively. Conclusion : A moderate reliability of OSCE was obtained during the past 3 years of RTCOCG board examination. This is comparable with the reliability of OSCE for medical licensure in North America. (Thai J Obstet Gynaecol 1995;7:131-133)*

**Key words :** OSCE, RTCOCG, board examination

The eligibility for the RTCOCG board examination included one clinical research, six cases report, 150 items of MCQ, 4 items of MEQ, 2 items of Essay, 20 stations of OSCE and oral examination. The RTCOCG has introduced OSCE into the Board Certification Committee since 1990. It was virtually intended to substitute a "long case and short case examination" which was heavily criticized as an unfair and unreliable assessment.

Evidently, after the past five years, OSCE was well accepted by most members of the RTCOCG to be a standard procedure to assess clinical performance and competence for a specialist in Obstetrics and Gynaecology. Nevertheless, psychometric characteristics of those OSCEs have never been described. The purpose of this study was to assess the reliability of OSCE used in the RTCOCG board examination.



## Materials and Methods

Although the RTCOG has already organised OSCEs for five years, the details of data for full analyses was available only three years in 1992, 1993 and 1994. There were 19 stations in 1992 OSCE and 20 stations in 1993 and 1994 OSCEs. There were 85, 88 and 84 candidates for Obstetrics and Gynaecology board certification in 1992, 1993 and 1994 respectively. The stations of each OSCE were classified into six categories to assess history taking skill, physical examination skill communication skill, technical skill, interpretation skill and problem solving skill. The technical skill was emphasized on operative obstetrics (4 stations) and operative gynaecology (2 stations). There were 10 stations of obstetrics, 10 stations of gynaecology and 2 rest stations in most OSCEs. Both obstetric stations and gynaecological stations comprised of 60-70% of process assessment and 30-40% of product assessment. All of these were 5 minute station OSCEs.

Standardized rating scale was used to assess the processes while the product assessment scored by structured answer sets. The scores of each OSCE were fully analysed year by year. The standardized item reliability (Cronbach alpha) was processed by a SPSS program under window operation at the Department of Medical Education, Bhumibol Adulyadej Hospital, Royal Thai Air Force, Bangkok.

## Results

The reliability (Cronbach alpha) was 0.75, 0.63 and 0.54 for OSCE year 1992, 1993 and 1994, respectively. Most candidates criticized the RTCOG-OSCE as a stressful examination. Evidently, 5-8% of the examinees failed. The overall expenses to organize each OSCE was approximately 50,000 bath.

## Discussion

Most medical educators criticized the long case examination as an unobjective and unreliable procedure to assess clinical competence.<sup>(1,2)</sup> Consequently, an OSCE which was firstly published in 1979 by Harden and Gleeson<sup>(3)</sup> has substituted for a long case examination. Although OSCEs have been implemented in medical schools worldwide including Thailand, they are only involved in an undergraduate level.<sup>(4)</sup> Not until recently that the National Board of Medical Examiner (NBME) of U.S.A. and the Medical Council of Canada (MCC) have announced an OSCE as a standard procedure to assess clinical competence of candidates for Medical Licensure.<sup>(5,6)</sup> In Thailand, the RTCOG was the first who considered OSCE as a part of specialist examination. At the beginning, concerns have been expressed about the feasibility, reliability and worth of OSCE. After 5 years of hard work, the Board Certification Committee of the RTCOG

was confident in the success of OSCEs.

Achieving a high reliability of an OSCE was possible but difficult because of the time strain. For example, the reliability (Cronbach alpha) of 0.78 and 0.84 would be obtained if the test length of 6 minutes OSCE were 4.0 and 6.0 hours, respectively.<sup>(7)</sup> But in fact 4-6 hour OSCE was absolutely not practical for both organizers and examiners. The RTCOG usually organized a 22-24 five minutes stations which have shown a moderate reliability of 0.54-0.75. Regretably, the reliability of the OSCE year 1990 and 1991 could not be calculated due to loss of data. However, the obtained reliability was comparable with OSCEs for medical licensure in North America.<sup>(4)</sup>

## Conclusion

The Board Certification Committee of the RTCOG was confident in the success of OSCEs to assess clinical competence of specialists in Obstetrics and Gynaecology. A moderate reliability (Cronbach alpha) or 0.54-0.75 was obtained. This was comparable with the reliability of postgraduate OSCEs in North America.

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# Oxygenation, Ventilation and Hemodynamic Changes during Diagnostic Pelvic Laparoscopy in Siriraj Hospital

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**Abstract :** During laparoscopic procedure, an alteration in hemodynamic and pulmonary mechanic was noted. An appropriate anesthetic technique is still under debate in term of safety and low cost benefit ratio. Thirty five female patients undergoing diagnostic pelvic laparoscopy in Siriraj Hospital for gynaecologic reasons were investigated. Laparoscopy was done under local anaesthetic technique and supplemented with systemic sedation and analgesia. Hemodynamic (MAP, PR, ECG), oxygenation and ventilation ( $SpO_2$ ,  $EtCO_2$ , ABG) changes at baseline control, post sedation, post  $CO_2$  insufflation, post  $CO_2$  exsufflation and postoperative periods were compared. Hemodynamic changes were not significant difference. Pulse oxygen saturation ( $SpO_2$ ) and arterial  $O_2$  tension decreased significantly at post sedation period. Six patients had  $O_2$  saturation less than 95 per cent and three less than 92 per cent. An increase in end tidal  $CO_2$  ( $EtCO_2$ ) was observed at post sedation and postoperative periods. Three patients had  $EtCO_2$  more than 50 mmHg. Although diagnostic pelvic laparoscopy is classified as a minor procedure, oxygenation and ventilation changes could be anticipated due to the effect of posture and pneumoperitoneum with  $CO_2$  gas. Local anaesthetic technique with conscious sedation has an advantage over general anaesthesia because of low cost and simplicity of the technique. Nevertheless on the safe side, simple  $O_2$  supplement, hemodynamic and respiratory monitoring are recommended to avoid a decrease in oxygenation and a prompt response to any abnormalities. (Thai J Obstet Gynaecol 1995;7:135-141)

**Short title :** Hemodynamic changes during laparoscopy

**Key words :** pelvic laparoscopy,  $O_2$  saturation, end tidal  $CO_2$

Pelvic laparoscopy has been commonly performed as a diagnostic procedure for gynaecologic reasons.

During this procedure, patients should not only be placed in the lithotomy plus Trendelenberg position but also

be insufflated with CO<sub>2</sub> gas into peritoneal cavity to facilitate surgical procedure. Clinical observation found an increase in arterial CO<sub>2</sub> tension either with spontaneous or controlled ventilation<sup>(1-3)</sup> and in cardiac arrhythmia with halothane anesthesia.<sup>(1,4,5)</sup> The anaesthetic technique and agents should be considered based on a safe practice and low cost benefit ratio.

In Siriraj Hospital this procedure is routinely done under local anaesthesia with systemic sedation and analgesia.

Although there was no claim on any serious complications under this technique, no academic on hemodynamic and respiratory changes has been reported. So we would like to evaluate an alteration in oxygenation, ventilation and hemodynamic status during this procedure as well as the appraisal of both surgeons and patients towards this technique.

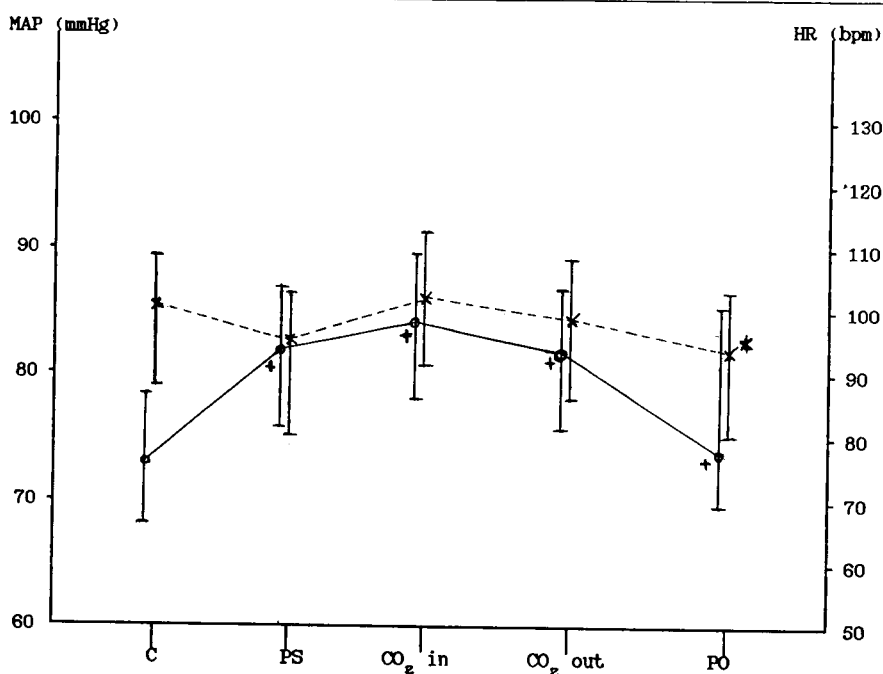
## Materials and Methods

Thirty five female patients (American Society of Anesthesiologists' physical status I, II) undergoing elective diagnostic pelvic laparoscopy in Obstetric and Gynaecology department of Siriraj hospital were studied. Written consent were received after preoperative explanation of anaesthetic technique and surgical procedure. Noninvasive blood pressure (NIBP), oscilloscopic electrocardiography (ECG), pulse oxygen saturation (SpO<sub>2</sub>), end tidal CO<sub>2</sub> (EtCO<sub>2</sub>) and arterial blood

gases (ABG) were monitored at pre-anaesthetic control, 15 min. postsedation, 5 min. post CO<sub>2</sub> insufflation, 5 min. post CO<sub>2</sub> exsufflation and 30 min. post operative periods. Arterial blood gas samples were drawn from an indwelling 22 G radial artery canula inserted at a nondependent site after negative abnormal Allen's test. Dehydrobenzperidol 2.5-5.0 mg, pethidine 50-100 mg and atropine 0.3 mg were given intravenously for sedation and analgesia. Regarding the safety criteria, if SpO<sub>2</sub> dropped down to 90 per cent or less for more than 1 min, O<sub>2</sub> 6 litres per minute (LPM) supplementation via face mask would be given; if EtCO<sub>2</sub> rose up to 50 mmHg or more for more than 1 min., assisted ventilation would be performed. All data were statistically analysed.

## Results

Table 1 showed patients' characteristics, operative time, intra-abdominal pressure and total CO<sub>2</sub> volume. There was no significant change in mean arterial pressure (MAP) compared at different times except a significant decrease at postoperative time. A significant increase in heart rate during postmedication, and procedure was observed due either to an effect of atropine, a response to pain or an increase in EtCO<sub>2</sub>. Nevertheless no cardiac arrhythmia was noted in this study (Fig. 1). Although there was a statistically significant decrease in SpO<sub>2</sub> at post-



**Fig. 1** Hemodynamic parameter ( MAP, HR) at baseline control (C), post sedation (PS) post CO<sub>2</sub> insufflation (CO<sub>2</sub> in), post CO<sub>2</sub> exsufflation (CO<sub>2</sub> out) and postoperation period (PO)

X-----X MAP \* Sig diff  $p < 0.05$   
 O\_\_\_\_\_O HR + Sig diff  $p < 0.05$

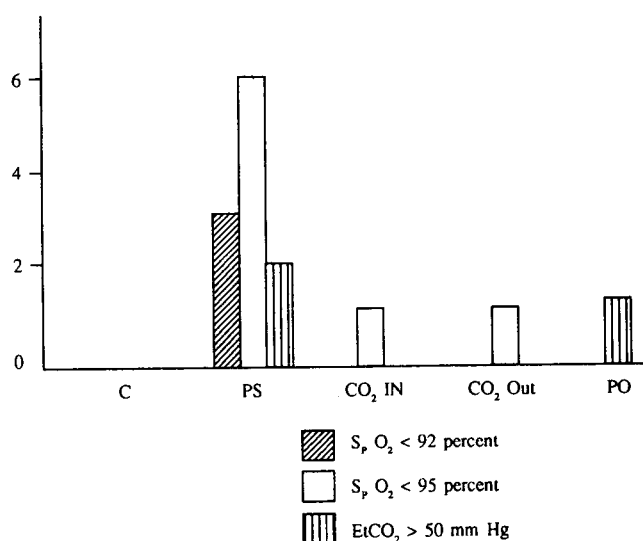
**Table 1** Patients' characteristics, operative time (Op time), intraabdominal pressure (intraabd. pr.) and the total CO<sub>2</sub> volume

	Age (yr)	Wt (kg)	Ht (cm)	Op time (min)	Intraabd. pr. (mm Hg)	Total CO <sub>2</sub> (L)
Mean $\pm$ SD	29.9 $\pm$ 5.78	50.27 $\pm$ 8.41	155.92 $\pm$ 5.14	11 $\pm$ 4.97	17.7 $\pm$ 3.55	1.88 $\pm$ 0.82
Range	18 - 44	31 - 67	148 - 170	7 - 26	12 - 25	1 - 5

**Table 2** Pulse O<sub>2</sub> saturation (SpO<sub>2</sub>) at baseline control (C), post sedation (PS), post CO<sub>2</sub> insufflation (CO<sub>2</sub> in), post CO<sub>2</sub> exsufflation (CO<sub>2</sub> out), and postoperative periods (PO).

	C	PS	CO <sub>2</sub> in	CO <sub>2</sub> out	PO
Mean $\pm$ SD	98.4 $\pm$ 1.16	95.52 $\pm$ 2.35*	97.44 $\pm$ 1.50*	97.17 $\pm$ 1.46*	97.48 $\pm$ 1.46*
Range	96 - 100	89 - 99	94 - 100	93 - 99	94 - 100

\* sig diff  $p < 0.05$



**Fig. 2** Number of patients having O<sub>2</sub> saturation less than 95 and 92 percent and end tidal CO<sub>2</sub> more than 50 mm Hg at different period of times.

sedation, during the procedure and postoperative period. The mean SpO<sub>2</sub> were higher than 95 per cent (Table 2). However a decrease in SpO<sub>2</sub> was markedly observed at postsedation, six and three patients had SpO<sub>2</sub> less than 95 and 92 per cent respectively (Fig. 2). An increase in EtCO<sub>2</sub> was highest at postsedation possibly due to a lack of surgical stimulation. Two patients had EtCO<sub>2</sub> more than 50 mmHg. (Fig. 2). Respiratory rate increased during the procedure (Table 3). The change of arterial blood gases was similar to the change of SpO<sub>2</sub> and EtCO<sub>2</sub> (Table 4).

Before the patients were discharged home, they were asked about their satisfaction and comment on this anesthetic technique. Fifty-seven per cent of the patients were satisfied, 15 per cent requested general anesthesia and 28 per cent had no

comment. Some of those who have had a previous general anesthesia preferred this technique to general anesthesia, some did not. Most of the patients who had no comment would like to leave the choice of anesthetic technique to their doctors. Nevertheless the most common two complaints of this technique were pain and uncomfortable feeling during the procedure.

## Discussion

Nowadays pelvic laparoscopy has been increasing in popularity for diagnostic and therapeutic reasons. The surgical demand of Trendelenburg position and pneumoperitoneum with CO<sub>2</sub> gas create untoward effects to respiratory and cardiovascular homeostasis.<sup>(5)</sup> An increase in MAP, initially after pneumoperitoneum, is usually noted which is caused by a squeeze of

blood from the abdominal cavity. After that MAP tends to maintain or decrease depend on a balance effect among pneumoperitoneum, anesthetic effect and an enhanced sympathetic activity following an increase in arterial CO<sub>2</sub> tension.<sup>(2)</sup> Bradycardia is common due to vagal stimulation.<sup>(2)</sup> Desmond & Gordon<sup>(6)</sup> reported cardiac arrhythmia in spontaneous breathing patients anesthetized with halothane and concluded that this group of patients should be ventilated mechanically. Scott<sup>(7)</sup> reported the incidence of cardiac arrhythmia during laparoscopy using halothane and spontaneous ventilation to be as high as 20 per cent. Halothane anesthesia is not recommended since it may cause severe cardiovascular depression during or after performing the pneumoperitoneum and increase the incidence of cardiac arrhythmia if hypercarbia occurs.<sup>(3)</sup> Although there are some controversies on spontaneous ventilation technique for laparoscopy, some institutes still perform this procedure under spontaneous ventilation.

In this study dehydrobenzperidol and pethidine were given for sedation and analgesic effect. Bradycardia was prevented by atropinization. A slight increase without any decrease in MAP during the procedure was noted which was possibly caused by an effect of atropine, an early response to pneumoperitoneum, a sympathetic stimulation to pain and an increase in EtCO<sub>2</sub>.

Heart rate initially increased postmedication and maintained throughout the procedure. An unopposed sedative effect and the lack of surgical stimulation could be an explanation of a significant decrease in MAP at postoperative period. Although a decrease in heart rate was noted at postoperative period compared to during the procedure, it was higher than the baseline control. This would be an effect of an increase in EtCO<sub>2</sub>. Since this technique used local anesthesia plus sedation and spontaneous breathing, we anticipated a decrease in arterial O<sub>2</sub> tension and an increase in arterial CO<sub>2</sub> tension. Even if there was no clinically significant difference in mean SpO<sub>2</sub> and EtCO<sub>2</sub>, there were 3 and 2 patients who had SpO<sub>2</sub> less than 92 per cent and EtCO<sub>2</sub> more than 50 mmHg respectively. We believed that the short operative time, an experienced surgeon and an ability of the patient to compensate for respiratory insult were the important factors which explained the result above.

Although the most acceptable technique for laparoscopy is general anesthesia, local anaesthesia had advantages over general anesthesia in term of simplicity, low cost, avoidance of untoward effects of general anaesthesia and an ability to be done on a day case basis. Local anaesthesia still has some disadvantages such as a feeling of pain and discomfort, a possible risk of hypoxia and hypercapnia and a lack of prompt treatment

of airway problems.

## Conclusion

We concluded from this study that diagnostic pelvic laparoscopy can be done under local anaesthesia plus systemic sedation. To overcome the feeling of pain and discomfort,

intravenous titration of short acting sedative and analgesic agents during the procedure should be an answer. However the safety of the procedure probably depends more on short operative time, an experience of anesthetist and surgeon and careful hemodynamic and respiratory monitoring than the particular technique used.

**Table 3** Respiratory parameters (Et CO<sub>2</sub>, RR) at different periods of time

	C	PS	CO <sub>2</sub> in	CO <sub>2</sub> out	PO
EtCO <sub>2</sub> (mmHg)		*	*	*	*
Mean ± SD	37.51 ± 3.39	45.17 ± 4.39	39.8 ± 5.07	42.97 ± 4.58	42.97 ± 4.41
Range	29 - 44	36 - 53	25 - 47	31 - 50	32 - 51
RR (bpm)		*	*	*	*
Mean ± SD	18.17 ± 3.22	14.76 ± 5.57	22.14 ± 5.91	19.65 ± 4.0	15.51 ± 4.01
Range	12 - 25	6 - 37	12 - 37	10 - 28	8 - 26

\* sig diff p < 0.05

**Table 4** Arterial blood gases at different periods of time

	C	PS	CO <sub>2</sub> in	PO
pH.				
Mean ± SD	7.36 ± 0.04	7.32 ± 0.04*	7.31 ± 0.03*	7.32 ± 0.01*
Range	7.32 - 7.47	7.27 - 7.42	7.24 - 7.37	7.30 - 7.35
PaO <sub>2</sub> (torr)				
Mean ± SD	106.29 ± 8.68	97.27 ± 8.11	108.24 ± 8.74	115.38 ± 21.9
Range	92 - 123	83 - 105	91 - 116	90 - 152
PaCO <sub>2</sub> (torr)				
Mean ± SD	40.78 ± 3.77	47.28 ± 3.35*	43.33 ± 4.25*	42.96 ± 2.74*
Range	36 - 49	41 - 51	35 - 51	37 - 46

\* sig diff p < 0.05



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## **Xlth Annual Scientific Meeting**

The Royal Thai College of Obstetricians  
and Gynaecologists

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### **THEME :**

Modern Technology for  
the Betterment of Maternal Health Care  
Beyond  
the Year 2000

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October 16 - 18, 1996  
The Dusit Resort Pattaya,  
Pattaya City, THAILAND

## **HIV Infection in Pregnant Women in Thailand 1994**

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### **Epidemiology**

In Thailand, it has been reported that women of reproductive age (15-44 years) with AIDS have increased in number from 1 case (6.67%) in the years (1984-1988) to 483 cases (8.67%) in the years (1989-1994).<sup>(1)</sup> It was estimated that the HIV seropositivity in women of reproductive age and pregnant women would increase in prevalence also.

Siriwasin W. et al reported that the HIV seroprevalence among pregnant women at Rajavithi Hospital, Bangkok, has increased 4 fold over 2 years from 0.4% to 1.4% among pregnant women in the Antenatal clinic.<sup>(2)</sup> HIV Sentinel Serosurveillance June 1993, Thailand reported that the Seropositivity rate of pregnant women in the Antenatal clinic in a provincial hospital and district hospital was 0-7.6% (mean 1.4%) and 0.4-5% respectively.<sup>(3)</sup> The majority of studies of the prevalence of HIV seropositivity in pregnant women have been

based on anonymous cord blood or newborn heel stick surveys.<sup>(4-7)</sup>

In Thailand, HIV Sentinel Serosurveillance in the pregnant women group using unlinked anonymous blood screening reported an increasing rate from 0 in Dec. 1990 to 1.4% in June 1994.<sup>(3)</sup> Using routine voluntary HIV screening in pregnant women (regardless of risk status) was 4.5-5.9%<sup>(8,9)</sup> in 1988.

In Thailand, HIV seropositivity in pregnant women in Rajavithi and Siriraj Hospitals in 1992 was 1.4%<sup>(2)</sup> and 1.7%<sup>(10)</sup> respectively. In Lerdsin Hospital, HIV seroprevalence in pregnant women was 5.9/1,000 of total deliveries in 1989-1993.<sup>(11)</sup> In Chiangrai Prachanukrao Hospital in 1991, HIV seroprevalence in pregnant women and in parturient was 5.90% and 3.35% respectively.<sup>(12)</sup> Lindsay reported that there was significantly more unregistered parturients with HIV infection compared with registered parturients (1.4% vs 0.4%).<sup>(13)</sup> In Rajavithi Hospital delivering women

not attending the Antenatal clinic have a three fold higher seroprevalence than pregnant women attending the Antenatal clinic.<sup>(2)</sup>

### **Prenatal HIV counselling and Testing**

Prenatal HIV counselling and testing is an important process that provides patients acceptability for follow up in the Antenatal clinic and delivery. Kovavisarach, reported 25%<sup>(11)</sup> of pregnant women attending the Antenatal clinic at Lerdsin Hospital Bangkok from 1989 to 1993, were lost to follow up after the first diagnosis of HIV infection possibly because of limitation of timing and staff for proper pretest and post test HIV counselling. The improper attitudes of some staff members to the HIV seropositive pregnant women is the other reason for the large group lost to follow up.

From 1992 to 1994 at Rajavithi and Siriraj Hospitals the follow up rate of HIV seropositive pregnant women until delivery was 87 and 88%. One of the reasons for the good follow up rate may be good pretest and posttest counselling<sup>(14)</sup>

### **Diagnosis**

The symptoms and signs of HIV infection vary with a wide range from asymptomatic to full blown AIDS. At the time of initial infection, the individual may be asymptomatic

or may develop an acute mononucleosis like syndrome that may be accompanied by aseptic meningitis. Antibodies can be detected in most individuals 6-12 weeks after exposure but in rare circumstances the latent period can be longer<sup>(15,16)</sup> After seroconversion has occurred, a symptomatic period of variable length usually follows. Very few infected person (less than 5%) develop AIDS within 3 years.<sup>(17)</sup>

In Thailand, AIDS patients are classified into 3 classes and one for symptomatic HIV patients.<sup>(18)</sup> All the patients must be confirmed with laboratory evidence of HIV infection

### **Management of HIV infected pregnant women**

General principles of management of HIV infected patients<sup>(19)</sup> are

*Psychological support.* Psychological support is the first important management because of the social impact. This management is consisted of counselling and social welfare

*Treatment of opportunistic diseases.* Occasionally some opportunistic diseases are infectious diseases that can be treated by antibiotics. Other malignant diseases may be treated by chemotherapy or radiotherapy. The most common opportunistic disease is pneumocystis carinii pneumonia that can be treated by Co-trimoxazol<sup>(20)</sup>

*Antiviral therapy.*

Zidovudine (AZT) has not

been frequently used in pregnancy. Among nonpregnant HIV infected women with CD4+ cell counts below 500/mm<sup>3</sup>. Zidovudine has been shown to substantially slow the rate of progression to AIDS.<sup>(21)</sup> Currently AZT is recommended for HIV infected women with CD4T cell count below 500 mm.<sup>3</sup> Pregnant women with counts between 200-500/mm.<sup>3</sup> should be offered AZT therapy, after the first trimester if possible.<sup>(22)</sup> Some institutes suggest that if counts fall below 200/mm.<sup>3</sup> prophylaxis against *P. carinii* pneumonia should be instituted and antiviral therapy should be advised, beginning after the first trimester.<sup>(23)</sup> The maternal and fetal effects of AZT in pregnancy have not been well characterized.<sup>(24-26)</sup> In one study, there were two instances of maternal toxicity : gastrointestinal and hematologic. There were no teratogenic abnormalities but only intrauterine growth retardation.<sup>(26)</sup> The study of ACTG (AIDS Clinical trial group) 076 resulted in decrease of perinatal transmission in AZT therapy group from 25% to 8% in the control group<sup>(27)</sup>

#### *Immunity reconstruction therapy*

This method of therapy is still in the research process. Interleukin 2, interferon gamma, Imuthiol, isoprinosine,<sup>(28)</sup> Bone marrow transplantation, lymphocyte transfusion, transfer factor, granulocyte macrophage colony stimulating factor<sup>(29-32)</sup>

These four principles of man-

agement are used in each period of pregnancy antepartum, intrapartum and postpartum period

Antepartum period : Psychological support and counselling are important and CD4+ cell count follow up each trimester and AZT therapy and prophylaxis against *P. Carinii* pneumonia if CD4 cell count fall below 200/mm.<sup>3</sup> <sup>(23)</sup> Also usual prenatal care should be done

Intrapartum period : Normal standard of obstetric intrapartum care should be done and prevention of nosocomial spread of HIV infection and prevention of direct skin contact to potentially infected secretions.<sup>(33)</sup> The mode of delivery can not alter the perinatal transmission rates. Cesarean section didn't reduce the rate of perinatal transmission<sup>(34)</sup>

Postpartum period : Although the risk of HIV transmission during breast feeding is unknown, recent evidence has confirmed its occurrence.<sup>(35,36)</sup> The current recommendations include prescription of breast feeding by HIV-infected mothers if safe alternatives are available.<sup>(37,38)</sup> A recent analysis estimated that where the mother was infected prenatally, the additional risk of transmission through breast feeding, over and above transmission in utero or during delivery was 14% (95% CI, 7-22)<sup>(39)</sup>

The most popular contraceptive method in HIV-infected women is surgical sterilization.<sup>(22)</sup> Vasectomy is also another choice for male contraception. The second choice of

contraception is implantable hormonal contraception and the third choice is injectable and oral hormonal contraception. But with all of these methods, barrier contraception should be used for prevention of transmission of virus between the couples. In Lerdsin Hospital, tubal sterilization and oral hormonal contraception are used in HIV-infected women at the same rate (15.69%). It is interesting that 56.86% were lost to follow up after pregnancy termination at Lerdsin Hospital and the reason would be the same as the previous lost to follow up rate 25% after acknowledging their first diagnosis of HIV infection<sup>(11)</sup>

### HIV perinatal transmission

The rate of perinatal transmission varies from 15%<sup>(40-45)</sup> in Europe, to 15-30%<sup>(44,45)</sup> in the US, 25%<sup>(44,45)</sup> in Haiti, 30-35%<sup>(44,45)</sup> in Africa and 25-42% in Thailand<sup>(46)</sup>

The wide range of transmission reported is thought to be secondary to methodological differences or distribution of risk factors in the population being studied<sup>(40)</sup>

The exact timing of perinatal transmission is unknown but may occur antepartum, intrapartum or postpartum.<sup>(47)</sup> Many studies reported perinatal HIV transmission occurred in the last trimester of pregnancy or during delivery<sup>(40,44,48,49)</sup>

*The possible seven risk factors for perinatal transmission were :*

1. Fetal genetic factor of

susceptibility to HIV infection.<sup>(50)</sup>

2. The maternal clinical and immunological status during pregnancy and the duration of infection are likely to influence viral load and infectivity.<sup>(51)</sup>

3. Sexually transmitted diseases could enhance the HIV viral load in the genital tract and increase the risk of intrapartum infection to the baby.

4. Primary infection during pregnancy should be associated with high HIV viral load and low level of HIV antibody that may increase the risk to the fetus.<sup>(52)</sup>

5. Premature delivery has been associated with an increased risk of perinatal infection because of inadequate levels of maternal antibodies which occurs late in pregnancy.<sup>(40,53)</sup>

6. Mode of delivery did not alter the perinatal transmission rate.<sup>(34)</sup>

7. Recent evidence about breast feeding has confirmed that breast feeding increases the risk of perinatal transmission.<sup>(35,36)</sup>

### Prognosis

Women fared less well than men. One woman in six died during the illness that led to diagnosis, compared with one man in nine. Calculated median survival was 263 days for women and 357 days for men<sup>(54)</sup>

*Effect of pregnancy on HIV disease progression*

Several investigators found

no evidence that pregnancy has an impact on the progression of HIV disease.<sup>(55-57)</sup> As most pregnant women with HIV present early in the course of clinical infection, years of follow up are required to determine the time of AIDS or death in these women compared with appropriate controls<sup>(22)</sup>

#### *Effect of HIV disease on pregnancy outcome*

The HIV perinatal transmission has been discussed previously

There are different rates of adverse pregnancy outcomes between developing and developed countries. Studies in Africa show an increased rate with low birth weight, premature labor and neonatal death of babies born to HIV positive mothers compared with infants born to HIV negative controls.<sup>(58)</sup> In contrast, studies from Western countries showed no increased risk of premature labor, IUGR, asphyxia, neonatal and maternal morbidity<sup>(56,59)</sup>

#### **Perspective view of HIV perinatal transmission in Thailand**

In Thailand, since June 1989 we have done sentinel serosurveillance for the prediction in trend of HIV spread every 6 months in 6 groups.<sup>(3)</sup> :

1. Intravenous drug users (IDU) in 39 provinces.

2. Female direct commercial sex workers in every province and female indirect commercial sex workers in 60 provinces.

3. Male commercial sex workers in 5 provinces.

4. STD male patients at STD clinics in every province.

5. Pregnant women at Antenatal clinics in every province.

6. Every unit of donor blood in every province.

The trend of HIV spread from sentinel serosurveillance June 1993 is shown in 4 graphs. The trend of HIV infected rate in IDU was stable with the rate of 30%. The reason may be better health education about safer use of needles. The trend of HIV infected rate in donor blood increased slowly to the rate 0.74%. The reason may be the use of self high risk screening for inhibition of blood donation. The trend of HIV infection rate of female direct commercial sex workers and male commercial sex workers was increasing slowly. The trend of STD male patients, female direct commercial sex workers and pregnant women at Antenatal clinics was increasing quickly at the seroprevalent rate of 5.7%, 28.5% and 1.4%.

From these trends, we may predict in the short term, the sero prevalence in STD male patients, female direct commercial sex workers and pregnant women at Antenatal clinics have been increasing so HIV infected pregnant women and HIV vertical transmitted babies will present a large group of HIV/AIDS patients in the future because of the high rate of heterosexual transmission and the high prevalence of HIV/AIDS in

reproductive women compared to the other age group in our country

The government national policy about HIV disease control is divided into 4 major plans :

1. Public relations concerning HIV infection by every mass communication to all age groups.

2. Treatment and rehabilitation.

3. Research and evaluation.

4. Protection of human rights about HIV testing and social welfare.<sup>(60)</sup>

## Conclusion

HIV infection in pregnant women is now increasing in Thailand because of the rising number of HIV infected women of reproductive age. Routine voluntary screening of pregnant women after proper pre test counselling and informed consent is suggested because some infected pregnant women have no identifying risk factors. Diagnosis of HIV infection based on laboratory HIV infection and indicative diseases. The management of HIV infected pregnant women follows 4 principles. Psychological support, treatment of opportunistic diseases, antiviral therapy and immunomodulators treatment used during the antepartum, intrapartum and postpartum periods. The pregnancy may have little effect on HIV disease progression. Complications were seen more frequently in HIV infected mothers and children than in controls in developing countries, but in

developed countries there were no difference. HIV perinatal transmission rate in Thailand ranges from 25 to 42%. We verdict that HIV infected pregnant women and HIV vertical transmitted babies will be a large group of HIV/AIDS patients in Thailand.

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