Human chorionic gonadotropin ratio of hemoperitoneum versus venous serum improves early diagnosis of ectopic pregnancy

YuDong Wang, M.D.,[a] *Hong Zhao, Ph.D.,*[b] *YinCheng Teng, M.D.,*[a] *LiHua Lu, B.A.,*[a] *and JianQian Tong, B.A.*[a]

[a] Department of Obstetrics and Gynecology, the Sixth People's Hospital, Shanghai Jiaotong University, Shanghai, People's Republic of China; and [b] Department of Radiology and Pathology, the Methodist Hospital, Weill Medical College, Cornell University, Houston, Texas

Objective: To analyze the value of the hCG ratio of peritoneal serum versus venous serum ($R_{P/V}$) for early diagnosis and prognostic evaluation of ectopic pregnancy (EP).
Design: Retrospective clinical study.
Setting: University hospital.
Patient(s): One hundred three women with hemoperitoneum and positive urine hCG tests underwent laparoscopy or laparotomy.
Intervention(s): Venous serum and peritoneal serum samples were obtained; ultrasound was performed in all the patients; dilatation and curettage was used in 28 patients.
Main Outcome Measure(s): Quantitative hCG and $R_{P/V}$.
Result(s): The $R_{P/V}$ in EP (5.55 ± 4.32) is apparently greater than that in hemoperitoneum with intrauterine pregnancy (hIUP; 0.61 ± 0.18). The median $R_{P/V}$ is 4.07 in the EP group versus 0.60 in the hIUP group, with a suggested threshold value of 1.0 for their differential diagnosis. Moreover, the $R_{P/V}$ of EP shows the dominant difference between the patients with active bleeding (8.03 ± 3.29, $n = 24$) and the patients without active bleeding (4.59 ± 3.88, $n = 16$) when the hCG level of venous serum is more than 1500 U/L.
Conclusion(s): $R_{P/V}$ could instantly diagnose ectopic pregnancy and differentiate it from hIUP. (Fertil Steril® 2010;93:702–5. ©2010 by American Society for Reproductive Medicine.)

Key Words: Peritoneal serum, venous serum, hCG ratio, ectopic pregnancy

Ectopic pregnancy (EP) refers to the implantation of a viable ovum outside the uterine corpus, which is a significant cause of maternal morbidity and mortality as well as fetal loss. In developing countries, the incidence rates vary from one in 44 deliveries to one in 21 deliveries (1). In developed Western countries, the rates are between one in 233 and one in 280 deliveries (2), and the detection rates for unruptured EP range from 88% to 100% (3). However, this is not the case in developing countries. Studies done at the Korle Bu Teaching Hospital in the past three decades show that detection rates for unruptured EP rates are between 1.1% and 8.5% (1). The goal of early diagnosis is the prevention of tubal rupture (4), which is the cause of most EP-related deaths (5) and qualifies as a surgical emergency. Although, the diagnosis of tubal rupture is obvious when patients are hemodynamically unstable, the symptoms in most cases of tubal rupture or tubal abortion are more subtle (6).

The combination of transvaginal ultrasound and serum hCG determination has proven to be reliable for the early diagnosis of EP (7, 8). However, in most of the emergency rooms in developing countries, transvaginal ultrasound is either replaced with transabdominal ultrasound or performed by a nonprofessional gynecologist, which limits the prompt diagnosis of EP. Furthermore, serial β-hCG level measurements are of no use in the case of a concomitant intrauterine pregnancy (IUP), which is associated with the frequent presence of hemorrhagic corpus luteum combined with pregnancy (HCLP), hemorrhagic salpingitis with pregnancy (HSP), heterotopic pregnancy (HP), and ovarian hyperstimulation syndrome after assisted reproductive technology (ART), which impairs the ability to get a definitive diagnosis before surgery. All of these diseases that cause hemoperitoneum with IUP (hIUP) hinder the diagnosis of EP and challenge the practitioners of gynecology (9).

Received July 15, 2008; revised October 7, 2008; accepted October 11, 2008; published online November 30, 2008.
The first two authors contributed equally to this work.
Y.D.W. has nothing to disclose. H.Z. has nothing to disclose. Y.C.T. has nothing to disclose. L.H.L. has nothing to disclose. J.Q.T. has nothing to disclose.
This study was supported by the Foundation of the Sixth People's Hospital, Shanghai Jiaotong University, China, grant no. 0875 (to Y.D.W.).
Reprint requests: YinCheng Teng, Department of Obstetrics and Gynecology, the Sixth People's Hospital, Shanghai Jiaotong University, Shanghai 200233, People's Republic of China (FAX: 0086-021-64701361; E-mail: owangyudong@hotmail.com).

0015-0282/10/$36.00
doi:10.1016/j.fertnstert.2008.10.013

TABLE 1

Descriptive statistics in the hIUP and EP groups.

Variables	n	$R_{P/V}$	*P*
hIUP group	34	0.61 ± 0.18	
EP group	69	5.55 ± 4.32	<.001[a]
Days of abdominal pain of EP:			
1∼5	41	5.88 ± 4.47	
6∼9	28	5.06 ± 4.13	NS
Tubal state of EP:			
Tubal abortion	47	5.73 ± 4.46	NS
Tubal rupture	22	5.17 ± 4.10	
Hemoperitoneum of EP:			
<500	49	5.66 ± 4.39	
≥500	20	5.27 ± 4.27	NS
Active bleeding of EP	36	6.29 ± 4.59	
hCGv ≥1500U/L	24	8.03 ± 3.29	<0.05[b]
hCGv <1500U/L	12	5.42 ± 3.43	
No active bleeding of EP	33	4.74 ± 3.94	
hCGv ≥1500U/L	16	4.59 ± 3.88	
hCGv <1500U/L	17	5.89 ± 4.10	

Note: Values are means ± SD. NS = not significant.

[a] hIUP guoup vs. EP group.

[b] Active bleeding of EP (hCGv ≥1500U/L) group vs. no active bleeding of EP (hCGv ≥1500U/L) group.

Wang. hCG ratio improves early diagnosis of EP. Fertil Steril 2010.

The aim of this study is to determine whether the hCG ratio of peritoneal serum versus venous serum ($R_{P/V}$) could provide an early diagnosis, which would improve the prognosis of EP. In other words, $R_{P/V}$ may be helpful for instantly discriminating early EP from hIUP without any unnecessary surgical intervention if culdocentesis is positive.

MATERIALS AND METHODS

From March 2005 to April 2008, 103 patients with hemoperitoneum and a positive urine hCG test suspicious for EP were evaluated at the outpatient department or emergency center of the Sixth People's Hospital, Shanghai, China. Presenting symptoms were either abdominal pain or bleeding. Transvaginal (n = 60, at the outpatient department) or transabdominal ultrasound (n = 43, at the emergency room) was performed to determine the presence of hemoperitoneum and adnexal mass. The hCG levels of venous serum and peritoneal serum (72 cases had a culdocentesis and the other 31 cases obtained the peritoneal fluid during the surgical operation) were quantified by radioimmunoassay at the same time with the same set and reagent. After the diagnostic evaluation, either laparotomy (n = 22) or laparoscopy (n = 81) was performed. Thirty-five patients underwent salpingostomy, while a salpingectomy was performed in the remaining patients according to their requests and the status of their fallopian tubes. Histological diagnosis via dilatation and curettage was acquired in 28 patients who presented with a mass of vaginal bleeding and no desire for pregnancy. Viable pregnancy with intrauterine fetal heartbeat was confirmed in six cases by serial transvaginal ultrasound examinations.

The following parameters were collected from the medical records: age, gravidity, parity, gestational age, the existence of vaginal bleeding, venous and peritoneal serum hCG concentration (U/L), ectopic position of sac, and type of fallopian pregnancy, with or without active bleeding. A quantitative estimate of the hemoperitoneum was carried out during surgery by recording the volume of aspirated and irrigated fluid.

The study was performed in accordance with the 1975 Helsinki Declaration on Human Experimentation and approved by Institutional Review Board. Both culdocentesis and the quantitative hCG used in the retrospective study were carried out simply and safely for the diagnosis of EP by the gynecologists and biochemists as a part of the current medical treatments, and a patient consent form for the operation and collection of private medical information was obtained.

Statistical Analysis

Analyses were carried out using the Statistical Package for the Social Sciences (SPSS, ver. 11.0, Chicago). The independent-sample *t*-test, Wilcoxon test, or Newman-Keuls test was used to compare the differences between the groups. Unless otherwise stated, values are expressed as means ± SD or are presented as median and range (minimum, maximum).

The diagnostic performance of $R_{P/V}$ in EP was expressed using a scatter diagram and further evaluated using a receiver operator characteristic (ROC) curve analysis. $P<.05$ was considered statistically significant for all tests.

RESULTS

The subjects between the two groups had no difference with respect to mean age, gravidity, parity, and mean duration of amenorrheia. However, Table 1 shows a statistically significant difference in the $R_{P/V}$ between the EP group (5.55 ± 4.32) and the hIUP group (0.61 ± 0.18; $P<.01$). The median $R_{P/V}$ is 4.07 in the EP group (minimum = 1.06, maximum = 18.2) versus 0.60 (minimum = 0.22, maximum = 0.99) in the hIUP group.

Clinical characteristics of the EP group are analyzed in Table 1. There was no significant difference between the volume of hemoperitoneum, days of abdominal pain, tubal abortion, or tubal rupture between the two groups. However, there was a statistically significant difference between the $R_{P/V}$ of the patients with or without active bleeding when the venous hCG (hCGv) of EP was ≥1500 U/L ($P<.05$).

HSP was diagnosed according to acute salpingitis (five cases by surgical exploration finding congestive oviducts