

Derivation of a Predictive Model Based on Emergency Ultrasound to Diagnose and Manage Suspected Ectopic Pregnancy

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Abstract

Objective: To determine the validity of clinical predictive model for diagnosis of ectopic pregnancy using bedside ultrasound scan (presence of haemoperitoneum) as a diagnostic aid.

Study Design: Cross sectional study.

Study Duration: From 1st Aug 2010 to 31st Jan 2011.

Methodology: The Study was carried out at the Department of Obstetrics and Gynaecology, CMH Quetta. Women with short period of amenorrhoea i.e. less than 6 weeks, pain abdomen, with or without vaginal bleeding and an empty uterine cavity on USS, were included in the study. Diagnostic model including four parameters, i.e. one step Urine Pregnancy test (UPT), fluid in the pouch of Douglas (POD) at ultrasound scan (USS), tachycardia and pelvic tenderness, were assessed for predictive value in cases of suspected ectopic pregnancy. Sensitivity, Specificity, Positive and Negative predictive values (PPV) & (NPV), for each parameter were calculated using ectopic pregnancy confirmation at surgical intervention, as the 'gold standard'.

Results: The sensitivity and specificity of one step β HCG urine pregnancy test was 100%. The sensitivity of fluid in POD at USS alone for diagnosis of ruptured ectopic pregnancy was 89% and the specificity was 50%. The PPV for the test was 85%, with NPV 60%. The sensitivity of tachycardia was 75% with specificity of 40% while PPV was 83% and the NPV was 28%. The sensitivity of pelvic pain was 70% and specificity was 50% while PPV was 75% and the NPV was 44%.

Conclusion: Predictive model using Fluid in pouch of Douglas at USS with positive one step UPT has a high sensitivity to diagnose leaking ectopic pregnancy. It is a non-invasive diagnostic measure that provides valuable information and can thus expedite patient care in suspected ectopic pregnancies.

Key Words: Ectopic pregnancy, Trans Vaginal Sonography, Emergency Medicine Laparoscopy, Methotrexate.

Introduction

Few areas have seen such rapid recent changes as in the diagnosis and management of early pregnancy problems. The advent of transvaginal scan (TVS) as well as rapid assay of serum Beta HCG (SBHCG) has revolutionized the diagnosis in this area. Advances in these diagnostic techniques have allowed to identify and manage ectopic pregnancy before it causes clinical symptoms.^{1,2} However the situation is not yet the same in developing countries, like ours.

Ground reality is that SBHCG is not readily available in most of our clinics and when available, the results take 48 hours to one week to confirm the diagnosis. As regards TVS either equipment or expertise is not available in most of the hospitals. If available the examination may still remain inconclusive because the classical tubal ring may not always be discernable.³ Furthermore Urinary or serum BHCG can confirm the diagnosis of pregnancy, but it does not confirm the site of pregnancy. It is a high risk situation owing to the fact that by the time investigations conclude ectopic pregnancy, it may have been ruptured giving rise to significant haemoperitoneum.⁴ These limitations have obliged us to re-define our approach towards the diagnosis of ectopic pregnancy using 'indirect methods'.

USS has always been a valuable imaging modality for a physician because of its easy availability, portability, ability to examine more than one system, non-invasive nature and the facility to continuously image structures.⁵ The American Emergency Physicians (EP) have developed a training programme and currently they can perform US examination with a limited number of specific questions. An example of such focused examination includes the detection of an intra-uterine fetus and presence of haemoperitoneum in ectopic pregnancy.⁶ It has also been demonstrated that these EP examina-

tions reduce the time taken to diagnose potentially life threatening conditions and the length of hospital stay of these patients.⁷⁻⁹ It has been suggested that casualty department USS can be an effective triage tool, if based on simple specific parameters.^{10, 11}

Inspired by this strategy we designed a diagnostic model including bedside USS and presence of fluid in the POD for early diagnosis of ectopic pregnancy, in the absence of readily available SBHCG. The model is based on bedside sonographic and clinical parameters for the diagnosis of ectopic pregnancy. The aim of this study was to identify predictive value of these parameters in the diagnosis of ectopic pregnancies so as to design a suitable management protocol for such patients when the presentation is not that of a classical ectopic pregnancy.

Methodology

The study was carried out at CMH Quetta. The women, reporting with short period of amenorrhoea i.e. less than 6 weeks, pain abdomen, with or without vaginal bleeding and an empty uterine cavity at USS, were included in the study. The study period was prospectively limited to six months i.e. from 1st August 2010 to 31st January 2011. A pre-designed diagnostic model, including four parameters (clinical/ultrasonographic), was applied for the diagnosis of ectopic pregnancy in One Stop Gynae clinic. The parameters included UPT, tachycardia, pelvic tenderness on examination and ultrasound detection of fluid in POD. Each parameter was assessed independently for sensitivity and specificity and PPV & NPV for the diagnosis of ectopic pregnancy keeping confirmation of ectopic pregnancy at surgical intervention as the 'gold standard'. Ethical approval was obtained from the hospital ethical committee after presenting the detailed proposal.

All patients with above inclusion criteria were included in the study. In addition to which, variables such as age and parity, period of infertility, history of previous ectopic pregnancy, regularity of menstrual cycle and period of amenorrhoea were recorded. All patients with above parameters, but who were in shock already, were excluded from the study.

Clinical evaluation was performed including pelvic examination to rule out pelvic tenderness. Pulse rate and systolic and diastolic blood pressure were recorded. For the purpose of this study tachycardia was defined as a pulse rate of more than 90 beats / minute. The severity of pelvic pain was assessed by the attending registrar using Wong Baker Faces rating scale (Figure 1).¹²



Figure 1. Wong Baker Faces rating scale.



Figure 2. Transvaginal Ultrasound Scan demonstrating Fluid in the Pouch of Douglas.

Urine pregnancy test was performed in the clinic with HCG Rapid Test strip (Sensitivity level -25 IU BHCG) and results were interpreted by the attending doctor using standard methods as described in the kit.

TVS to evaluate for fluid in POD (Figure 2) was performed there and then by the attending registrar/ consultant gynaecologist using Toshiba (Unicam) 7.5 Mega HZ convex vaginal probe.

The views were recorded with the uterus in a strictly midsagittal plane from the cervix to the fundus. The presence of free fluid in POD was defined as liquid behind the uterus in a mid sagittal plane, around the ovary or in the utero-vesical pouch.

Upon surgery, the presence of ectopic pregnancy, its location, state of the tube (intact/rupture or tubal abortion), ovarian and uterine status and a naked eye estimation of blood loss were recorded. The Sensitivity, Specificity and Predictive Value were then calculated, keeping ectopic pregnancy confirmation at laparotomy as the yard stick.

Results

Twenty five patients were evaluated with the above inclusion criteria and in 22 of them UPT was found positive. Among these 22 patients, 3 cases later turned out to be of intra-uterine pregnancies and 19 cases were confirmed to have ectopic pregnancy, at laparotomy.

Fluid in POD was found positive in 21 cases but was actually true positive in only 19 cases, the remaining 3 cases with positive POD fluid, but negative pregnancy test were treated accordingly for perforated appendix, corpus luteum cyst haemorrhage and severe dysmenorrhoea.

Tachycardia was positive in 20 cases but was false negative in 3 cases. Pelvic tenderness was positive in 16 cases and was false negative in 5 cases. There was only one case of negative laparoscopy which later

turned out to be intra-uterine pregnancy.

Based on these results the sensitivity, specificity, PPV and NPV for all four pillar parameters of our study is shown in Table I.

When positive result for fluid in POD was combined with a positive UPT result the sensitivity and specificity for diagnosis of 'ruptured ectopic pregnancy' was 100%. The NPV for absent fluid in POD with positive

Table I. Sensitivity, Specificity and Predictive Value of Sonographic and Clinical Parameters

Parameter	Sensitivity %	Specificity %	PPV %	NPV %
Urinary Beta HCG	100	100	100	100
Fluid in POD	89	50	85	60
Tachycardia	83	40	28	75
Pelvic Tenderness	70	50	75	44

UPT was also 100% for ruptured or leaking ectopic. According to the sensitivity and specificity of each parameter, appropriate scores (specially designed for this study) were allocated as shown in Table II.

Table II. Assigned scoring for each parameter

Parameter	Level	Score
Fluid in POD	present	4
Tachycardia	>90 beats/min	1
	>100 beats/min	2
	>110 beats/min	3
Pelvic tenderness	moderate	1
	severe	2

Based on these results we proposed a diagnostic and management framework for suspected ectopic pregnancy for application in early pregnancy units and emergency departments (Figure 3).

In cases of suspected ectopic if all clinical and sonographic features are negative, the patient can be managed as an outpatient awaiting serum beta hCG (score 3). If only fluid in POD is positive in the absence of tachycardia and pelvic pain this may be ovulation haemorrhage or minimal peritoneal fluid and needs only observation (score 4). If moderate tachycardia is present along with moderately severe pelvic pain it is most likely an imminent rupturing ectopic and therefore needs an immediate laparoscopy/laparotomy(score >5). However if along with these features fluid in POD (score 7) is present then it is definitely a leaking ectopic pregnancy and mandates an urgent laparotomy.

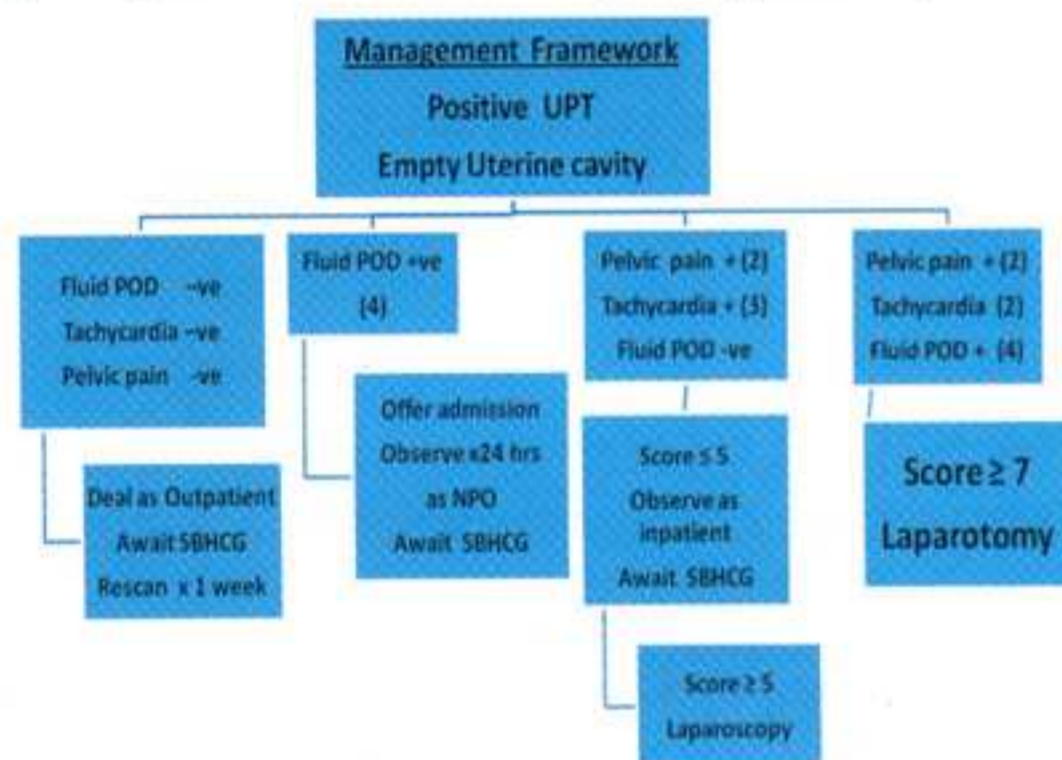


Figure 3. An algorithm of scoring system for management of ectopic pregnancy

Discussion

Reducing time to diagnosis can potentially have a major impact on the treatment of patients with ruptured ectopic pregnancy, who require 'time sensitive' surgical interventions. Although the diagnosis of tubal rupture is obvious when the patients are haemodynamically unstable but the symptoms in most cases of tubal rupture are more subtle. Multiple attempts to formulate diagnostic algorithms for ectopic pregnancy incorporating history, physical examination,¹³ quantitative human chorionic gonadotropin (hCG), serum progesterone,¹⁴ color-flow vaginal Doppler sonography and bedside

ultrasound examination¹⁵ as well as a treatment algorithm combining expectant, medical or surgical management have been proposed.¹⁶

TVS has been widely evaluated to test the sensitivity and specificity of this modality for the purpose of screening the patients of suspected ectopic pregnancy. Mateer and Valley¹⁷ retrospectively compared patients who had no TVS with a prospective group who had TVS and showed that in comparison to 50% missed ectopic pregnancies that later ruptured, only 9% of the discharged patients who had TVS, had ruptured ectopic pregnancies, later. They concluded that an emergency protocol incorporating bedside TVS significantly reduces the incidence of discharged patients with subsequent rupture as compared to controls.

Another recent study compared the volume and echogenicity of fluid in POD to diagnose ectopic pregnancy and found that patients with isolated cul-de-sac fluid are at moderate risk of ectopic pregnancy and that the risk of ectopic pregnancy increases if the fluid is echogenic or the volume is large. They concluded that the fluid in mid sagittal plane has shown excellent correlation with intra-operative findings.¹⁸

We are in strong agreement with the finding of fluid in POD as a strong predictor of leaking/ruptured ectopic in suspected ectopic pregnancies as it showed a PPV as high as 85% in our study.

Ankum and Vanderdan¹⁹ challenged laparoscopy as a dispensable tool using an algorithm combining serum β hCG with TVS. They calculated a sensitivity of 97% and a specificity of 95% for this algorithm and a likelihood ratio for a positive test of 19.4, and a likelihood ratio for a negative test of 0.03. They considered this diagnostic strategy to be extremely reliable in the safe management of patients at risk of ectopic pregnancy, and rendered laparoscopy obsolete.

McRane, Murray and Edmonds performed a systematic review on role of Emergency Department Targeted Ultrasonography (EDTU) in evaluation of pain and bleeding in first trimester and concluded that specificity of EDTU to detect intra-uterine pregnancy and thus rule out ectopic pregnancy in most studies exceeds 98% and sensitivity exceeds 90%.²⁰ Published evidence indicates that EDTU reduces frequency of missed ectopic pregnancy, reduces time before surgery, shortens the length of hospital stay, for patients with normal pregnancy and may be more cost effective than diagnostic strategies requiring formal ultrasound scan. The high specificity and sensitivity of EDTU justifies its adoption as a routine emergency care.²¹

Bedside USS can be useful in even more complex situations as ectopic pregnancies at unusual locations. These are less frequent but more morbid. An astute clinician should have a significant threshold for suspicion of ectopic pregnancy in the cervix, abdomen or ovary.²² It was interesting to note that among 25 study cases, we encountered 4 interesting and unusual cases of ectopic pregnancy. A case of right intraligamentary ectopic pregnancy harbouring a huge haematoma distending the right paracolic gutter and extending into the hepato-renal pouch was found at laparotomy. Another case of heterotopic pregnancy was encountered in a patient who had a spontaneous conception after 11 years of infertility and had a confirmed intra-uterine pregnancy on USS alone. The couple was convinced with extreme difficulty for surgical exploration on the basis of predictive scoring (positive fluid in POD and moderate pelvic tenderness). A case of ectopic pregnancy in caesarean section scar at 11 weeks and another secondary abdominal pregnancy at 15 weeks of gestation respectively were diagnosed on the basis of this predictive model. Treatment of these pregnancies may not be as common place as treatment of tubal ec-

topic pregnancy but with early diagnosis and careful planning the treatment can be equally effective.²³

Single dose Methotrexate therapy has been shown to be as effective as multi-dose regime.²⁴ But the disadvantage of single dose Methotrexate includes prolonged time for resorption of ectopic pregnancy lasting may be up to 70-120 days. Therefore the patients must be observed carefully for secondary rupture.^{25,26} Applying the same predictive scoring we timely diagnosed and managed 2 cases of haemoperitoneum following secondary rupture after Methotrexate therapy.

We found this predictive model highly reliable to rule out or confirm pre-operatively the existence of a significant haemoperitoneum, which thus facilitated the decision making in choosing an appropriate surgical route. It establishes an early and speedy diagnosis for leaking/ruptured ectopic pregnancy and thus allows timely intervention. It also indirectly reduces the risk of maternal compromise, blood transfusion and hospital stay with involvement of minimal expertise.

Absent fluid in POD reliably rules out haemoperitoneum. The high NPV of fluid in POD (60%) does not rule out intact ectopic pregnancy, but it does allow a confident monitoring while the clinician is awaiting the serum β hCG results. Large scale prospective studies from different centres evaluating the predictive accuracy of this diagnostic model will validate it further.

Conclusion

Predictive model using Fluid in pouch of Douglas on USS with positive one step UPT has a high sensitivity to diagnose leaking/ ectopic pregnancy. It is a non-invasive diagnostic measure that provides valuable information and can thus expedite patient care in suspected ectopic pregnancies.

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