

# Threatened miscarriage in general practice: diagnostic value of history taking and physical examination

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## SUMMARY

**Background:** Ultrasonography, the gold standard for establishing a diagnosis in first-trimester vaginal bleeding, is not always readily available. Medical history and gynaecological examination are then used instead, to make a provisional diagnosis.

**Aim:** To determine the diagnostic value of history taking and physical examination in first-trimester bleeding, to differentiate between patients requiring immediate further diagnostic examination from those in whom an expectant policy will initially suffice.

**Design of study:** Prospective population-based cohort study.

**Setting:** Seventy-four general practices in Amsterdam.

**Method:** Two hundred and twenty-five patients with first trimester vaginal bleeding were referred for an early pregnancy assessment. The data from 204 patients were analysed. Two diagnostic models were constructed, based on symptoms and the results of gynaecological examination to identify diagnostic sub-groups relevant to clinical practice.

**Results:** Model 1, which separates viable pregnancies from other diagnoses, increased pre-test probability from 47% to a post-test probability of 70%. Model 2, which enabled the identification of complete miscarriages, resulted in a post-test probability of 41% of a complete miscarriage, given a pre-test sample probability of 25%. The tentative diagnosis of a general practitioner, based entirely on clinical judgement, turned out to be a poor predictor for the ultrasonographically confirmed diagnosis (pre-test probability of 47% changed to a post-test probability of 58%).

**Conclusion:** This study shows that, in first trimester bleeding, neither statistical prediction models based on signs and symptoms, nor clinical judgement, are valid replacements for ultrasonographic assessment in establishing a diagnosis.

**Keywords:** threatened abortion; predictive value of tests; physical examination; statistical models; ultrasonography.

## Introduction

First trimester vaginal bleeding is the most common problem in pregnancy and it almost always leads to a consultation in a general or gynaecological practice. The problem occurs in about one-fifth of all pregnancies, with an estimated miscarriage rate of about 50%, while the other 50% of pregnancies continue without serious problems.<sup>1</sup> Ultrasonography, the gold standard tool for establishing a diagnosis in first trimester vaginal bleeding, is not always immediately available. In these circumstances, the patient's medical history and a gynaecological examination are used to make a provisional diagnosis and to decide whether there is a need for referral for any further clinical assessment, i.e. ultrasonographic examination. To date, virtually no information has been available on the discriminative capacity of clinical symptoms and gynaecological examination; for example, in differentiating between viable and non-viable pregnancy, and complete or incomplete miscarriage or ectopic pregnancy.<sup>2</sup>

This paper presents a diagnostic study based on prospectively collected data of a population-based cohort of otherwise unselected women, who presented in general practice with first trimester bleeding and who were referred to one of the participating hospitals for ultrasonographic assessment. Each patient had their history and physical examination analysed to see if they were of any use in predicting the final diagnosis. In addition, there was analysis of the skills of the attending general practitioners (GPs) in making a provisional diagnosis of a viable pregnancy on clinical grounds before referring the patient.

## Method

### Patients

Our study was conducted as part of a randomised trial on the management of miscarriages in two Amsterdam hospitals: the Academic Medical Center and the Onze Lieve Vrouwe Gasthuis, between April 1998 and September 2000. Seventy four GPs who worked in the health district covered by these two hospitals participated in the study. They referred all women with vaginal bleeding, a positive urinary pregnancy test result, and a gestational age of less than 16 weeks, for ultrasonographic assessment. Oral informed consent was obtained from all patients.

The study was approved by the medical ethics committees of both hospitals.

### Data collection

During the first consultation, the participating GPs filled in a

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Submitted: 20 August 2001; Editor's response: 7 November 2001; final acceptance: 8 April 2002.

©British Journal of General Practice, 2002, 52, 825-829.

**HOW THIS FITS IN***What do we know?*

Ultrasonography is the gold standard tool for establishing a diagnosis in the event of first trimester vaginal bleeding.

*What does this paper add?*

In primary care, clinical symptoms and physical examination are not discriminative in predicting viability of pregnancy or a complete miscarriage in first trimester bleeding. GPs were unable to discriminate between viable pregnancies and other diagnoses in first trimester bleeding on clinical grounds.



structured form to record data collected on clinical signs and symptoms, obstetric history, and gestational age. Additional findings from the gynaecological examination were recorded. With regard to the gynaecological examination, GPs could fill in a 'not performed' section in the form. A provisional diagnosis was then made, and the GP was asked to estimate the probability of a viable pregnancy being present on a 0% to 100% scale. Information on sociodemographic data was collected by means of a patient questionnaire.

**Ultrasound examination**

A standardised transvaginal sonographic examination was performed by trained physicians using a transvaginal 6.5 MHz sonographic probe (Hitachi Corporation, Tokyo, Japan). Criteria for ultrasonographic diagnoses are mentioned in Table 1.

**Statistical analysis**

This prospective approach implies that all cases were analysed, including relatively rare conditions; for example, ectopic pregnancy and hydatidiform mole, which should be considered in the differential diagnosis of first trimester bleeding.

To control for selection of referral, patients who were referred were compared with those who were not referred in 20 computerised practices participating in this study.

We analysed two diagnostic models, which were based on signs and symptoms of women with first trimester bleeding.

Model 1 predicts the presence of a viable pregnancy, while Model 2 predicts complete miscarriages versus all remaining diagnoses — in practical terms, separating

women who did not require immediate sonographic assessment from those who did.

The relationship between patient characteristics, clinical variables, findings from gynaecological examination, and the diagnosis was analysed, starting with a univariate regression analysis. All variables with a *P*-value of 0.10 were selected and their multicollinearity was checked (conventional Pearson's correlation, threshold = 0.4). In the event of multicollinearity the variable with the highest clinical face validity and/or ease of determination in primary care was selected. A multivariate model was developed, with a cut-off of *P* = 0.05. With multivariate regression analyses, variables were identified as independent predictors and receiver operating characteristic (ROC) curves were constructed, which described the relationship between sensitivity and specificity for each model. The prediction threshold with the lowest sum of false-positives plus false-negatives (highest accuracy) was regarded as optimal, assigning equal weight to both the misclassifications.

In addition, the diagnostic performance of Model 1 was compared with the GPs' estimation of the probability of a viable pregnancy being present.

The Statistical Package of the Social Sciences (SPSS, version 9.0) was used for all analyses.

**Results**

Out of 225 women referred by GPs for an early pregnancy assessment, 217 were eligible for the study; eight women with a negative hCG pregnancy test were excluded. Of these 217 women, 13 were excluded; two of whom were lost to follow-up and 11 owing to missing data. Of the remaining 204 women, 96 (47%) had a viable pregnancy, 51 (25%) a complete miscarriage, 47 (23%) a non-viable pregnancy, two (1%) a hydatidiform mole, and eight (4%) women had an ectopic pregnancy.

No significant differences in patient characteristics were observed between women with viable pregnancies, complete miscarriages, and non-viable pregnancies (Table 2). The number of women with ectopic pregnancies was too small for a meaningful comparison.

With regard to the gynaecological examination, GPs could fill in a 'not performed' section on the data form. Vaginal examination was performed on 57.4% of the patients and speculum examination on 61.3% of the patients (data not shown). Table 3 shows the multivariate models.

In Model 1, independent predictors of a viable pregnancy were stable (odds ratio [OR] = 0.4, 95% confidence interval

Table 1. Criteria for the different diagnoses.

Final diagnosis	Criteria (ultrasound or other)
Viable pregnancy	Fetal heart action
Non-viable pregnancy	Unmeasurable embryonic pole and sac diameter >15 mm, or; embryo without cardiac activity, or; empty gestational sac at a diameter <15 mm not showing any growth after a seven-day interval <sup>3,4</sup>
Incomplete miscarriage	Retained products of conception (RPOC) >15 mm anteroposterior (AP) diameter
Complete miscarriage	RPOC <15 mm (AP diameter) and previous sonographic intrauterine pregnancy or with decreasing serum $\beta$ hCG
Ectopic pregnancy	No intrauterine gestational sac and serum hCG concentration >2.000 IU/l
Hydatidiform mole	Ectopic gestational sac or an ectopic mass and serum hCG concentration >1.500 IU/l <sup>5</sup> Histopathological examination

Table 2. Patient characteristics according to the sonographically confirmed diagnosis.

Characteristic	Viable pregnancy n = 96 (%)	Complete miscarriage n = 51 (%)	Non-viable pregnancy <sup>a</sup> n = 49 (%)
Age in years (mean)	29.3	30.9	31.4
Parity			
0	56 (58.3)	30 (58.8)	25 (51.0)
1	25 (26.0)	14 (27.5)	14 (28.6)
>1	15 (15.6)	7 (13.7)	10 (20.4)
Prior miscarriage			
0	54 (56.3)	38 (74.5)	33 (67.3)
1	28 (29.2)	7 (13.7)	10 (20.4)
>1	14 (14.6)	6 (11.8)	6 (12.2)
Prior ectopic pregnancy	1 (1.0)	–	–
Gestational age			
<8 weeks	35 (36.5)	21 (41.2)	10 (20.4)
8 to 12 weeks	37 (38.5)	21 (41.2)	23 (46.9)
12 to 16 weeks	12 (12.5)	5 (9.8)	8 (16.3)
Uncertain	12 (12.5)	4 (7.8)	8 (16.3)
Native country			
Western: Europe and USA	48 (50.0)	29 (56.9)	27 (55.1)
African country	11 (11.5)	5 (9.8)	5 (10.2)
Surinam and Antilles	26 (27.1)	11 (21.6)	9 (18.4)
Other and unknown	11 (11.5)	6 (11.8)	8 (16.3)

<sup>a</sup>These figures include two hydatidiform mole pregnancies.

Table 3. Multivariate logistic regression analyses in two models.

	Model 1 <sup>a</sup> OR (95% CI)	Model 2 <sup>b</sup> OR (95% CI)
Bleeding		
Decreasing	1	1
Stable	0.4 (0.2–0.8)	1.5 (0.6–3.8)
Increasing	0.1 (0.0–0.3)	4.9 (1.9–12.7)
History of passing blood clots		
Yes	1	1
No	2.2 (1.0–4.6)	0.4 (0.2–0.8)
Speculum examination		
Not done	1	
Done, no blood present	1.0 (0.4–2.9)	
Done, blood present	0.4 (0.2–0.8)	

<sup>a</sup>Viable pregnancy versus all other diagnoses. The variables used were: age, prior miscarriage, amount of bleeding, history of passing blood clots, and blood at speculum examination. <sup>b</sup>Complete miscarriage versus all other diagnoses. Variables used were: prior miscarriage, amount of bleeding, history of passing blood clots, blood colour, abdominal pain, and blood at speculum examination. Owing to multicollinearity, six of the variables selected with univariate analysis were removed from both models.

[CI] = 0.2 to 0.8) and increasing bleeding (OR = 0.1, 95% CI = 0.0 to 0.3). The presence of blood at speculum examination was negatively associated with a viable pregnancy (OR = 0.4, 95% CI = 0.2 to 0.8). A negative history of passing blood clots was a predictor of a viable pregnancy (OR = 2.2, 95% CI = 1.0 to 4.6).

For Model 2, independent predictors of a complete miscarriage were stable (OR = 1.5, 95% CI = 0.6 to 3.8) or increasing bleeding (OR = 4.9, 95% CI = 1.9 to 12.7) and a negative history of passing blood clots.

In Figure 1, the ROC curves of the two models and the prediction of the GPs are shown.

The defined optimal point in the ROC curve of Model 1 predicted the presence of viable pregnancies with a sensitivity of 68% and a specificity of 74% (Likelihood ratio, LR<sup>+</sup> = 2.6). The pre-test probability of a viable pregnancy changed

from 47% to a post-test value of 70%.

The best threshold in the ROC curve of Model 2, separating complete miscarriages from all other diagnoses, has a sensitivity of 78% and a specificity of 65% (LR<sup>+</sup> = 2.2). The probability of a complete miscarriage increases from 25% pre-test to a post-test value of 41%.

In the ROC curve describing the prediction by GPs of a viable pregnancy being present, the best point, with a sensitivity of 89% and a specificity of 42%, gives an LR<sup>+</sup> of 1.5. This changes the pre-test probability of 47% to a post-test probability of 58%, which is worse than the post-test probability of 70% in Model 1. The weak relation between the prediction by Model 1 and by the GPs' estimates on a viable pregnancy being present, is illustrated by scatter plot in Figure 2.

To control for selection of referral, referred and non-

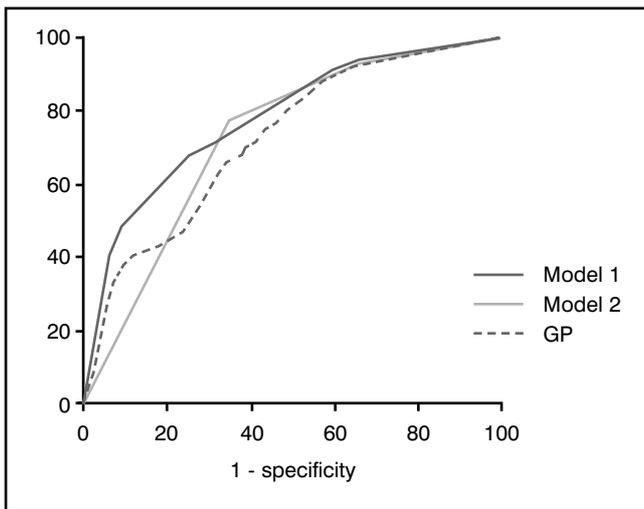


Figure 1. ROC curves of the pre-specified models and of the GP prediction. Model 1 aims to distinguish between viable pregnancies on the one hand and all other diagnoses on the other; Model 2 distinguishes complete miscarriages from all other diagnoses. The GP model shows the prediction of a viable pregnancy by GPs.

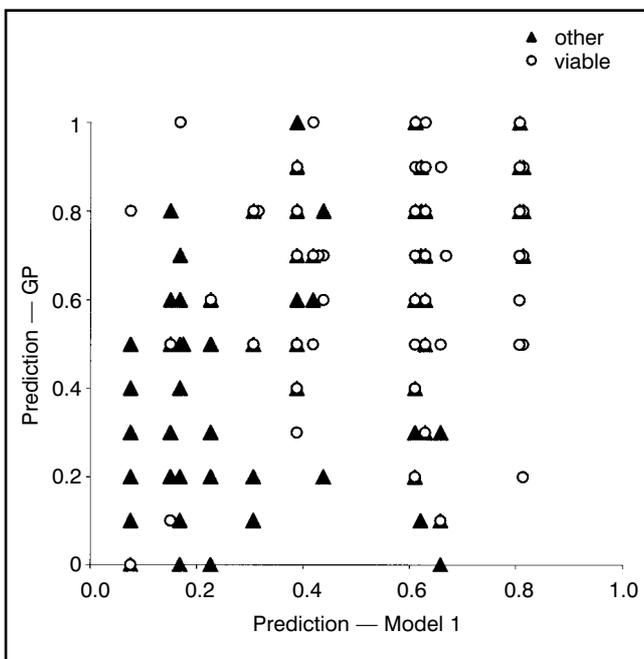


Figure 2. Scatter plot of the prediction of a viable pregnancy by GPs versus prediction of a viable pregnancy by Model 1.

referred patients from 20 computerised practices participating in this study were compared. On average, 30% of the women with first trimester bleeding were not referred for the study. However, signs, symptoms, and ultimate diagnosis were comparable between the two groups. Also, the percentage of viable pregnancies was as expected.

### Discussion

In this prospective study of pregnant women with first trimester bleeding, the patients' histories and physical examinations were looked at to see if they were of any help in enhancing the efficiency of referral for ultrasonographic

assessment. ROC curve analysis showed that the post-test value for the prediction of viable pregnancies was 70%, with incorrect diagnosis in 58% and false-positives and false-negatives taken together.

These results suggest that whenever a diagnosis is required by either doctor or patient, ultrasonographic assessment is inevitable. Consideration of the benefits and drawbacks can be regarded as an opportunity for shared decision making. The decision to stay at home without a certain diagnosis will depend on the perception of both doctor and patient of safety and easy access to primary and secondary care facilities when needed. In a perceived safe environment the balance between application of Model 1 or an ultrasonography for all women with bleeding in the first trimester can be considered. Application of Model 1 will result in 65 (32%) women wrongly considering their pregnancy viable. We assume that a large number of this group of women will eventually undergo a scan. With a specificity of 74%, 53 (26%) women with a viable pregnancy will be referred for ultrasonography. Application of Model 1 will therefore save carrying out half the scans, if all the patients accept the uncertainty of not having a diagnosis. The impression is that most women do experience this uncertainty as a psychological burden and a substantial number of them will prefer ultrasonography. In this prospective study a significant number of women had a strong preference for curettage after being informed about a non-viable pregnancy. Ultrasound facilities that are easily accessible to women in primary care will give women with a miscarriage the opportunity to make a well-considered choice between curettage or expectant management in primary care.

Surprisingly, gynaecological examination proved to be of little diagnostic value in our modelling approach. This could be caused by the relatively subjective measures used to describe findings; for example, 'open/closed cervical os'. It appears that physical examination is essential to evaluate the degree of bleeding, to rule out emergency situations, and to find conception products in the vagina and the cervical os. In this pragmatic study, in which GPs were asked to carry on their usual practice, vaginal examination was only performed on 57% of the patients and speculum examination in 61% of them. A survey in Wessex that studied the management of bleeding in early pregnancy showed that 24% of GPs never perform a vaginal examination, while in this study, at a comparable level (38%), a speculum examination was never done.<sup>2</sup>

If gynaecological examination had been performed on all the patients in this study, it cannot be excluded that the multivariate analysis would have given more support for this examination. However, these results are a good reflection of daily practice.

One might remark on these findings that it is possible that the study did not reflect the reality of the decision process in general practice, where patients are not always referred immediately, and an observation period with more time for making a decision may be valuable in reaching a definite diagnosis.

One might also argue that the right variables were not used in the models. With the possible limitations of the models in mind, the ability of GPs to discriminate between viable

and non-viable pregnancies based entirely on their clinical skills was also studied. However, they were correct only 58% of the time. A potential drawback of the study was the delay between the measurements of classifying variables and the ultrasonographic verification, with a median time of two days (25 to 75 percentiles = 1 to 3 days). This is owing to normal clinical practice in The Netherlands. Perhaps a better diagnostic performance could be achieved without delay between GP consultation and sonographic assessment. However, it is not likely that the post-test probabilities will increase in such a way that more clinical relevance will be reached. Also, such a procedure setting may be feasible for research purposes, but has little relevance for practices without direct access to ultrasonographic facilities.

It was not possible to pay specific attention to ectopic pregnancies because of the limited number of patients. Also, earlier studies showed that a physical examination is insufficient for diagnosing an ectopic pregnancy in the majority of patients.<sup>6,7</sup> Those patients in whom there was a high suspicion were usually referred directly to the gynaecology department and thus were not included in the study. Of the eight ectopic pregnancies diagnosed at the unit, only two were referred for suspected ectopic pregnancy. Three patients with ectopic pregnancies were treated surgically (including the two suspected patients), four self-limiting cases with declining serum hCG concentrations were managed expectantly, and one patient with an ectopic pregnancy was treated with a single dose of methotrexate. The question as to whether it is acceptable to withhold an immediate ultrasonographic assessment from patients with first trimester bleeding, thereby postponing the diagnosis of ectopic pregnancy, cannot be answered from the data.

Chung found discrepancy in uterine size to be the most significant predictor of non-viable pregnancies.<sup>8</sup> This item was also included in the case record form in our study, but its prognostic value could not be confirmed. In our study, GPs did not carry out a vaginal examination in 37% of the patients. In the remaining 63% of the patients, GPs reported the uterine size to be according to gestational age in 32%, indeterminate in 23%, while a discrepancy in uterine size was reported in only 8%. This study differs from Chung's in both its setting (primary care versus secondary care) and in its analyses. All cases were analysed, including ectopic and molar pregnancies, to mimic as much as possible the situation in which the physician has to make a decision in daily practice. The variables analysed in the study all derive from the standard management of women with first trimester bleeding and can easily be obtained.

In conclusion, clinical symptoms and physical examination are not useful in a primary care setting in predicting a viable pregnancy or a complete miscarriage in first trimester bleeding. To establish a certain diagnosis, sonographic assessment is required.

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## Acknowledgements

The study was supported by grants from the Dutch Health Research and Development Council (ZON) and the Dutch Ministry of Health, Welfare and Sports.