Human Reproduction Vol.18, No.9 pp. 1944–1947, 2003 DOI: 10.1093/humrep/deg379

Vaginal bleeding in very early pregnancy

E.W.Harville[1,4], A.J.Wilcox[2], D.D.Baird[2] and C.R.Weinberg[3]

[1]Department of Epidemiology, School of Public Health, University of North Carolina, Chapel Hill, NC, 27599–7435, [2]Epidemiology Branch and [3]Biostatistics Branch, National Institute of Environmental Health Sciences, Durham, NC 27709, USA

[4]To whom correspondence should be addressed. E-mail: ewh@unc.edu

INTRODUCTION: Little is known about the occurrence and patterns of vaginal bleeding during the earliest stages of pregnancy. We explore this in a prospective study of early pregnancy. METHODS: A total of 221 healthy women kept daily diaries and provided daily urine samples while trying to become pregnant. Of these, 151 women became clinically pregnant [i.e. pregnancy that lasted ⩾6 weeks beyond last menstrual period (LMP)] during the study. Diaries provided information on days with vaginal bleeding and sexual intercourse. Urine hormone assays were used to identify ovulation and implantation. Women were interviewed about their medical histories and lifestyle factors. RESULTS: A total of 14 women (9%) recorded at least 1 day of vaginal bleeding during the first 8 weeks of pregnancy. Twelve of these 14 pregnancies continued to a live birth. Bleeding tended to occur around the time when women would expect their periods, although rarely on the day of implantation. Bleeding was not associated with intercourse. CONCLUSIONS: Early bleeding in clinical pregnancies is generally light, and not likely to be mistaken for LMP. Thus, early bleeding is unlikely to contribute to errors in LMP-based gestational age. We found no support for the hypothesis that implantation can produce vaginal bleeding. Similarly, intercourse did not cause bleeding. Nearly all women with bleeding went on to have successful pregnancies.

Key words: bleeding/first trimester/implantation/spontaneous abortion

Introduction

Bleeding is a common complication of pregnancy, with 10–15% of women reporting some bleeding during the first sixteen weeks of pregnancy (Ananth and Savitz, 1994). In general, bleeding is considered to be a risk factor for poor fetal outcomes, including spontaneous abortion, preterm delivery, and low birth weight (Batzofin *et al*., 1984). However, recall bias may explain some of these findings. Also, the timing of bleeding is difficult to determine retrospectively, and studies have sometimes grouped all bleeding during one trimester or half a trimester of pregnancy (Ananth and Savitz, 1994; Everett, 1997).

Because of its timing, bleeding during early pregnancy might be mistaken for menses. Such bleeding has been conjectured to account for errors in gestational age estimation using the last menstrual period (LMP) method (Gjessing *et al*., 1999), especially among pregnancies that end in miscarriage (Iffy *et al*., 1972). Vaginal bleeding has also been thought in some cases to accompany implantation (Speert and Guttmacher, 1954). We carried out an analysis of data from a prospective study of 151 naturally-conceived pregnancies in order to explore these issues in more detail.

Material and methods

Women who planned to become pregnant were recruited by means of newspaper and other advertisements in the local community. The only selection criteria were that women had to be at least 18 years of age, and could have no known fertility problems or serious health problems. We enrolled 221 eligible women at the time they stopped using any method of birth control (Table I). Nearly all women were white, and 92% had some formal education beyond high school. One-third had never been pregnant (Wilcox *et al*., 1988).

Women collected daily urine samples (first morning void) for up to 6 months if they did not become pregnant, or for at least 8 weeks after the last menstrual period if they did become pregnant. At the time of urine collection, women also filled out daily record cards with information on vaginal bleeding (numbers of pads and tampons in the previous 24 h). Some women recorded bleeding that was too light to require pads or tampons; we include these as'spotting'. Women also provided daily records of sexual intercourse. As with the urine samples, these diary records were collected for at least 8 weeks following the last menstrual period.

Urine samples were assayed for hCG using an extremely sensitive immunoradiometric assay (Canfield *et al*., 1987). The sensitivity of this assay was sufficient to provide an estimate of the day of implantation. Implantation of the blastocyst is not observable directly, and the best indirect marker of implantation is hCG (Hearn *et al*., 1991). We used a highly sensitive radioimmunoassay for hCG in first-morning urine samples to identify the earliest day of pregnancy on which hCG concentration reached 0.15 ng/ml. Initial detection was typically

Human Reproduction 18(9) © European Society of Human Reproduction and Embryology 2003; all rights reserved

Downloaded from https://academic.oup.com/humrep/article/18/9/1944/708284 by guest on 19 August 2023

followed by a steady exponential rise of hCG (Wilcox *et al*., 1999). Radioimmunoassays of daily urine samples were performed for the major metabolic products of estradiol and progesterone. The ratio of these metabolites changes in characteristic ways with the approach and occurrence of ovulation, providing a reliable means to identify day of ovulation (Baird *et al*., 1995). The validity of this measure of ovulation has been confirmed in subsequent studies (Dunson *et al*., 2001; Ecochard *et al*., 2001).

We defined 'clinical pregnancy' as a pregnancy that lasted at least 6 weeks beyond the LMP. There were 151 women who conceived a clinical pregnancy during the study. We defined 'early bleeding' as ⩾1 day of vaginal bleeding between conception and the end of follow-up. In nearly all cases, follow-up was through the week 8 after LMP. One woman who collected data through her week 9 experienced spotting in week 9; those data are included here. We included bleeding only if it was distinct from the bleeding that accompanied the expulsion of an embryo or fetus. No woman contributed more than one clinical pregnancy to the study.

χ^2-tests were used for analyses of categorical variables. When cell counts were small, Pearson tests were used. *t*-tests were used for analyses of continuous variables.

Information on the woman's medical history, medications, smoking and other factors was collected by in-person interview at the time that woman was enrolled. The protocol was approved by the National Institute of Environmental Health Sciences internal review board, and informed consent was obtained.

Table I. Description of early pregnancy study participants

	n	%
Age		
21–25	32	14
26–30	127	57
31–35	51	23
36–42	11	5
Race		
White	212	96
Non-white	9	4
Education		
12	17	8
13–15	46	21
16	84	38
>17	74	33
Gravidity[a]		
0	78	35
1	77	35
2	43	20
3+	22	10
Outcome of most recent pregnancy		
live birth	94	66
induced abortion	25	18
spontaneous abortion	16	11
stillbirth	4	3
molar pregnancy	2	1
ectopic pregnancy	1	1

[a]Data unavailable for one woman

Results

A total of 9% of women with clinical pregnancies (14/151) reported at least 1 day of bleeding during early pregnancy. Data from these pregnancies with bleeding are shown in Figure 1. Bleeding was typically light, requiring only one or two pads or tampons in 24 h. (This pattern is in contrast to the bleeding reported with ordinary menstrual periods, for which women in our study typically used 4–8 pads on the heaviest days of flow.) The heaviest bleeding during early pregnancy was 5 consecutive days, and a maximum of three pads or tampons were used per day (L in Figure 1). This pregnancy ended in a live birth.

We explored the timing of bleeding in relation to implantation, and to the expected onset of menses. No woman reported bleeding between the time of ovulation and implantation. Only one woman (M in Figure 1) had any bleeding on the day of implantation itself. Bleeding was more likely to occur around the time women might expect their next period. For 8 of the 14 pregnancies, bleeding started between cycle days 27 and 31 (the most common cycle lengths in our study). This implies that bleeding may be more common at certain stages of early pregnancy. Curiously, this pattern did not hold when we looked

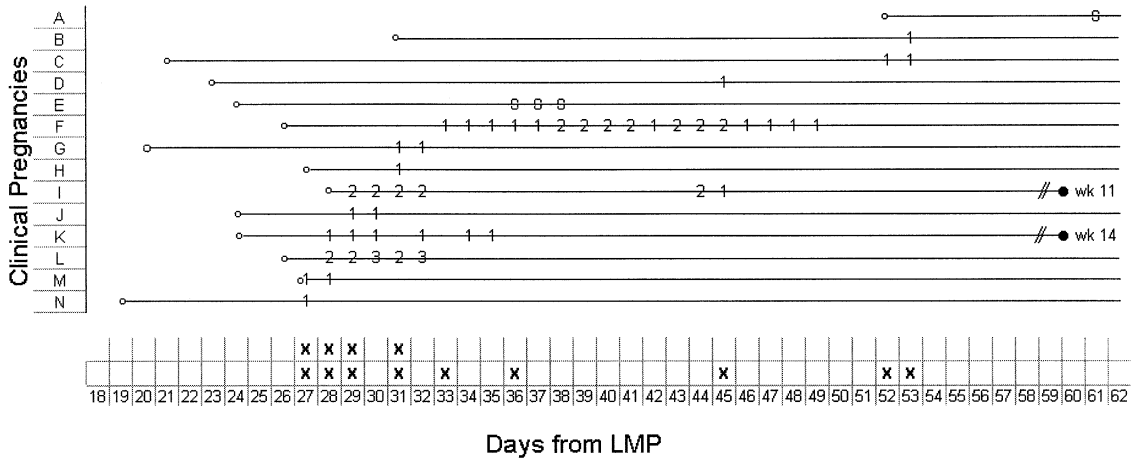

Figure 1. Data from 14 clinical pregnancies with bleeding in early pregnancy. Each line represents a pregnancy. Digits on the line show the number of pads or tampons for vaginal bleeding used on that day; 'S' is for spotting without pads or tampons. The small open circle at the beginning of each line indicates day of implantation. A solid circle at the end of the line marks the pregnancies ending in spontaneous abortion. The 'X's' along the *x*-axis show the frequency distribution of day of bleeding onset.

Downloaded from https://academic.oup.com/humrep/article/18/9/1944/708284 by guest on 19 August 2023

more carefully at bleeding relative to ovulation (the presumed time of conception). In our data, only five of these 14 women had their onset of bleeding 12–16 days after ovulation, when menses most commonly occurs (Baird *et al*., 1995). More generally, in examining pregnancies by time since conception, we found no stage of development at which bleeding appeared

Table II. Potential risk factors for bleeding in early pregnancy among 151 clinical pregnancies

	Overall	No. with bleeding	% with bleeding	*P*-value
Pregnancy outcome				
Live birth	136	12	9	
Miscarriage	15	2	13	0.63
Gestational age				
<37 weeks	6	1	17	
37+ weeks	130	11	8	0.43
Mother's age (years)				
<25	14	1	7	
25–30	76	9	12	
30–35	48	2	4	
35+	13	2	15	0.49
Body mass index (kg/m^2)				
>23	31	3	10	
20–23	67	5	7	
<20	53	6	11	0.83
Previous live births				
0	74	4	5	
1+	77	10	13	0.11
Prior miscarriages (if ever pregnant)				
0	79	10	13	
1+	19	2	11	1.00
Cycle day of ovulation[a]				
<13	22	4	18	
13 to 19	88	8	9	
>19	34	2	6	0.34
Number of bleeding days (in LMP)[b]				
1 to 2	10	2	20	
3 to 5	72	4	6	
6+	50	6	12	0.17
Pads/tampons/day (in LMP)[c]				
1	18	4	22	
2 to 3	41	3	7	
4+	71	5	7	0.15
Irregular menses[d]				
Yes	23	2	9	
No	128	12	9	1.00
Most recent method of birth control				
Diaphragm	65	5	8	
Condom	41	4	10	
Rhythm	19	2	11	
Pill	7	0	0	
Other	19	3	16	0.89
Ever smoker				
No	101	9	9	
Yes	50	5	10	1.00
Pack-years of smoking[e]				
<2	120	9	8	
2+	30	4	13	0.47
Marijuana smoker (current)[d]				
No	131	10	8	
Yes	20	4	20	0.09
Aspirin use (current)[d]				
No	50	4	8	
Yes	101	10	10	0.78
Caffeine use (mg per month)[d]				
<1000	38	5	12	
1000–3500	41	3	7	
3500–6000	30	1	3	
>6000	42	5	11	0.50

[a]Data unavailable for 7 women
[b]Data unavailable for 19 women
[c]Data unavailable for 21 women
[d]Self-report at intake
[e]Data unavailable for one woman

Downloaded from https://academic.oup.com/humrep/article/18/9/1944/708284 by guest on 19 August 2023

to cluster.

Of pregnancies with bleeding, 14% miscarried (2/14), compared with 9% of those without bleeding (13/137). The relative risk of miscarriage after bleeding was 1.5, with broad confidence limits (0.4–6.0). While these numbers are too small for formal analysis, it is notable that both miscarriages among the bleeders had bleeding within 30 days after LMP (I and K in Figure 1). These were also the only two pregnancies for which bleeding stopped and then resumed. None of the pregnancies with a single uninterrupted bleeding episode miscarried. Conversely, the great majority of pregnancies that eventually miscarried (13/15) had no bleeding in early pregnancy.

We could identify no particular characteristics that predisposed women to bleeding during early pregnancy (Table II). Some characteristics were more common among women with bleeding, but we cannot be sure that these associations were not due to chance. Multiple comparisons were made on a small amount of data, and none of the associations reached statistical significance at $\alpha = 0.05$. Women whose usual periods were heavy were not at increased risk of bleeding in pregnancy; if anything, their risk was lower. Similarly, a history of irregular periods did not predict bleeding in pregnancy. Nulliparous women had a lower risk of bleeding in early pregnancy than parous women (5 versus 13%, $P = 0.11$); there is no obvious explanation for such a pattern. None of the women with bleeding smoked at the time of the interview. There appeared to be a slight association between Marijuana smoking and bleeding (20% of current marijuana smokers reporting bleeding versus 8% of non-smokers; $P = 0.09$). However, there was no association with previous tobacco use, and no clear physiologic explanation for a higher risk among marijuana users.

Intercourse has been suspected to trigger bleeding in early pregnancy. We did not see this pattern. Intercourse was no more common on the day before bleeding than on other days in this time period.

Conclusions

These data on bleeding are unique in that they were collected prospectively by women throughout the earliest stages of pregnancy, even before pregnancy was apparent. The study includes detailed information on the events of ovulation and implantation, which provides unusually precise benchmarks for the embryonic stages at which bleeding was observed. Prospective data collection on bleeding has the further advantage of eliminating biases that can distort recollections collected later in pregnancy.

A total of 9% of women with clinical pregnancies reported bleeding during the first 8 weeks of pregnancy. These data suggest that a few days of bleeding in early pregnancy is not a rare event, and furthermore that such bleeding has little relevance to the ultimate success of the pregnancy. Bleeding that stops and then resumes may be more ominous—both such episodes in our study ended in miscarriage several weeks later.

Some authors have speculated that bleeding in early pregnancy might be mistaken for menses, leading to errors in the 'LMP' as a basis for gestational age estimation (Iffy *et al*., 1972; Gjessing *et al*., 1999). This is not supported by our data. Only one of the 136 successful pregnancies in our study had a bleeding episode of a length and intensity that was similar to usual menses. Certainly the majority of women with spontaneous abortions did not have an 'apparent menstrual period' after conception, as has been inferred from other data (Iffy *et al*., 1972). Only two of the fifteen miscarriages in our study had bleeding in the earliest stages of pregnancy, and even these bleeding events were too light to be mistaken for menses. We found no data to suggest that early bleeding contributes substantially to errors in LMP-based gestational age.

The mechanisms of bleeding in early pregnancy remain unclear. Implantation has been discussed as one mechanism (Speert and Guttmacher, 1954). However, we found no evidence to support this. Only one episode of bleeding occurred at implantation; most bleeding began at least 5 days after implantation (Figure 1). Similarly, there was no evidence that intercourse in early pregnancy increased the likelihood of vaginal bleeding.

In conclusion, bleeding during the first 8 weeks of naturally-conceived pregnancies seems to occur without clear physiologic cause. Most pregnancies with very early bleeding proceeded to a normal delivery and a healthy live birth.

Acknowledgement

Emily Harville is a Howard Hughes Predoctoral Fellow.

References

Ananth, C.V. and Savitz, D.A. (1994) Vaginal bleeding and adverse reproductive outcomes: a meta-analysis. *Paediatr. Perinat. Epidemiol.*, **8**, 62–78.

Baird, D.D., McConnaughey, D.R., Weinberg, C.R., Musey, P.I., Collins, D.C., Kesner, J.S., Knecht, E.A. and Wilcox, A.J. (1995) Application of a method for estimating day of ovulation using urinary estrogen and progesterone metabolites. *Epidemiology*, **6**, 547–550.

Batzofin, J.H., Fielding, W.L. and Friedman, E.A. (1984) Effect of vaginal bleeding in early pregnancy on outcome. *Obstet. Gynecol.*, **63**, 515–518.

Canfield, R.E., O'Connor, J.F., Birken, S., Krichevsky, A. and Wilcox, A.J. (1987) Development of an assay for a biomarker of pregnancy and early fetal loss. *Envir. Health. Perspect.*, **74**, 57–66.

Dunson, D.B., Weinberg, C.R., Baird, D.D., Kesner, J.S. and Wilcox, A.J. (2001) Assessing human fertility using several markers of ovulation. *Stat. Med.*, **20**, 965–978.

Ecochard, R., Boehringer, H., Rabilloud, M. and Marret, H. (2001) Chronological aspects of ultrasonic, hormonal, and other indirect indices of ovulation. *Br. J. Gynaecol.*, **108**, 822–829.

Everett, C. (1997) Incidence and outcome of bleeding before the 20th week of pregnancy: prospective study from general practice. *Br. Med. J.*, **315**, 32–34.

Gjessing, H.K., Skjaerven, R. and Wilcox, A.J. (1999) Errors in gestational age: evidence of bleeding early in pregnancy. *Am. J. Public Health*, **89**, 213–218.

Hearn, J.P., Webley, G.E. and Gidley-Baird, A.A. (1991) Chorionic gonadotrophin and embryo-maternal recognition during the peri-implantation period in primates. *J. Reprod. Fertil.*, **92**, 497–509.

Iffy, L., Wingate, M.B. and Jakobovits, A. (1972) Postconception ''Menstrual'' Bleeding. *Int. J. Gynaecol. Obstet.*, **10**, 41–47.

Speert, H. and Guttmacher, A. (1954) Frequency and significance of bleeding in early pregnancy. *JAMA*, **155**, 712–715.

Wilcox, A., Baird, D. and Weinberg, C. (1999) Time of implantation of the conceptus and loss of pregnancy. *N. Engl. J. Med.,* **340**, 1796–1799.

Wilcox, A., Weinberg, C., O'Connor, J., Baird, D., Schlatterer, J., Canfield, R., Armstrong, E. and Nisula, B. (1988) Incidence of early loss of pregnancy. *N. Engl. J. Med.,* **319**, 189–194.

Submitted on February 7, 2003; accepted on May 29, 2003

Downloaded from https://academic.oup.com/humrep/article/18/9/1944/708284 by guest on 19 August 2023