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The prevalence of non-viable pregnancy at 10–13 weeks of gestation

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ABSTRACT

In an ultrasound screening study at 10–13 weeks of gestation involving 17 870 women, the prevalence of early pregnancy failure was 2.8% (501 cases), including 313 (62.5%) missed abortions and 188 (37.5%) anembryonic pregnancies. Lower gestation and higher maternal age were associated with a higher prevalence ($\chi^2 = 143.5$; $p < 0.001$ and $\chi^2 = 53.3$; $p < 0.0001$, respectively). The prevalence was higher in women with a history of vaginal bleeding ($\chi^2 = 141.5$; $p < 0.0001$), but there was no significant association with previous pregnancy losses ($\chi^2 = 2.8$), parity ($\chi^2 = 0.6$) or cigarette smoking ($\chi^2 = 0.0$). Recent evidence suggests that the most effective method of screening for chromosomal abnormalities is measurement of fetal nuchal translucency thickness at 10–13 weeks, and therefore ultrasound examination at this gestation is likely to become universally available. As shown in this study, an additional advantage of such a scan is the diagnosis of early pregnancy failure, which will be found in about 3% of patients examined. Elective evacuation of retained products of conception is likely to be more cost effective and potentially safer than emergency surgery in a patient presenting during miscarriage.

INTRODUCTION

The traditional definition of missed abortion is fetal death before 20 weeks of gestation without expulsion of the fetus for at least 8 weeks thereafter[1]. With the introduction of ultrasound, the diagnosis can now be made from as early as 6 weeks of gestation by the demonstration of fetal parts in the absence of a heart beat[2]. When the gestational sac is at least 25 mm in diameter but no fetal part can be seen, the terms 'anembryonic pregnancy' or 'blighted ovum' are used[3]. This condition is presumably the consequence of either breakdown and resorption of the dead embryonic tissues or embryonic death at such an early stage of pregnancy that the size of the embryo is too small to be visualized by ultrasound. In this respect, missed abortion and blighted ovum can be considered to be the two ends of the spectrum of early pregnancy failure.

In this paper, we report the prevalence of early pregnancy failure in a screening study of 17 870 pregnancies undergoing ultrasound examination at 10–13 weeks of gestation.

PATIENTS AND METHODS

This was a cross-sectional ultrasound study at 10–13 weeks of gestation in the Harris Birthright Research Centre for Fetal Medicine. Since September 1992, pregnant women living in London and the surrounding areas were invited to participate in an ultrasound screening study for chromosomal abnormalities by measurement of fetal nuchal translucency thickness[4].

Transabdominal ultrasound examination (Toshiba SSA 250A, Toshiba Medical Systems Limited, Tokyo, Japan or Aloka 650, Aloka Limited, Tokyo, Japan; 5-MHz curvilinear probe) was performed for assessment of fetal viability and to measure both the fetal crown–rump length and the nuchal translucency thickness. If fetal cardiac motion was not seen, then transvaginal sonography (5-MHz or 6.5-MHz transducer) was carried out. Demographic data, medical and obstetric history and ultrasound findings were entered into a computer database at the time of the examination.

A computer search of the database was made according to the following selection criteria: (1) known last menstrual period with a cycle length of 26–30 days; (2) no history of pregnancy or use of oral contraceptives in the 3-month period before conception; and (3) ultrasonographic examination at 70–97 days since the first day of the last menstrual period. The prevalence of early pregnancy failure was examined in relation to maternal age, gestational age, vaginal bleeding (none, spotting, heavy), cigarette smoking

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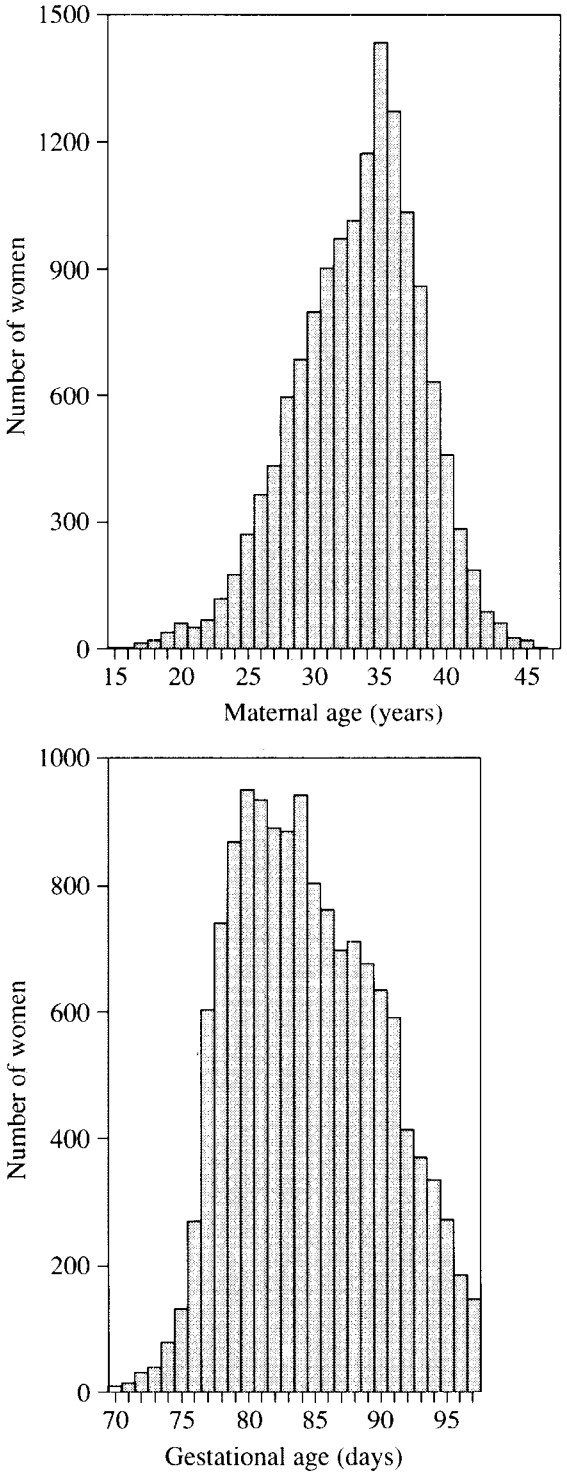

Figure 1 The maternal age and gestational age distribution of the 17 870 women scanned at 10–13 weeks of gestation

(yes, no), previous pregnancies (none, 1–2, ≥ 3) and previous pregnancy losses at less than 24 weeks of gestation (none, 1–2, ≥ 3). Analysis by χ^2 was used to examine the prevalence of pregnancy failure in relation to the above factors. Logistic regression was used to examine the relationship between the presence of viable or non-viable pregnancy and the explanatory variables.

Table 1 The prevalence of pregnancy failure in relation to maternal age, gestational age, vaginal bleeding, cigarette smoking, parity and previous pregnancy losses at less than 24 weeks of gestation. Relative risks were determined from the percentage of live fetuses and the percentage of dead fetuses in each category

	Pregnancy failure		*Relative*		
	n	%	*risk*	χ^2	*p-value*
Maternal age (years)				53.3	< 0.001
< 35	224/9960	2.3	1.00		
35–39	201/6569	3.1	1.35		
≥ 40	76/1341	5.7	2.48		
Gestational age (days)				143.5	< 0.001
70–76	51/688	7.4	1.00		
77–83	295/7454	4.0	0.54		
84–90	116/6809	1.7	0.23		
91–97	39/2919	1.3	0.18		
Vaginal bleeding				141.5	< 0.001
none	325/14 733	2.2	1.00		
spotting	142/2812	5.1	2.32		
heavy	34/325	10.5	4.77		
Previous pregnancies				2.8	NS
none	124/4658	2.7	1.00		
1–2	258/9495	2.7	1.00		
≥ 3	119/3717	3.2	1.19		
Previous pregnancy losses				0.6	NS
none	355/12 848	2.8	1.00		
1–2	130/4538	2.9	1.04		
≥ 3	16/484	3.3	1.18		
Smoking				0.0	NS
no	458/16 348	2.8	1.00		
yes	43/1522	2.8	1.00		

NS, not significant

RESULTS

During the study period (September 1992 to May 1995), 17 870 women had an ultrasound examination at 10–13 weeks of gestation and fulfilled the selection criteria. The maternal age and gestational age distributions of the population are shown in Figure 1. The prevalence of early pregnancy failures was 2.8% (501 cases), including 313 (62.5%) missed abortions and 188 (37.5%) anembryonic pregnancies.

In the pregnancy failure group, compared to those with a live fetus, the median maternal age was higher (34 compared to 33 years), the median gestational age was lower (82 compared to 85 days) and vaginal bleeding was more common (35% compared to 17%); there was a tendency for an increase in the prevalence with parity and previous early pregnancy losses and no association with cigarette smoking (Table 1). Logistic regression analysis demonstrated a significant independent effect of maternal age ($W = 34.1$, $p < 0.0001$), gestational age ($W = 113.5$, $p < 0.0001$) and vaginal bleeding ($W = 122.9$, $p < 0.0001$) on the prevalence of early pregnancy failure (Table 2). In women who had had at least two live births and previous early pregnancy failure, the prevalence of early pregnancy loss was relatively high (4.7%, Table 3). However, this was

secondary to a relatively high incidence of bleeding (22%); if women who had had bleeding prior to examination were excluded, the incidence was 2.2%, irrespective of presence or absence of previous pregnancy failure.

DISCUSSION

In this ultrasound study of 17 870 pregnancies at 10–13 weeks of gestation, the prevalence of missed abortion or anembryonic pregnancy was 2.8%. Furthermore, the prevalence of fetal loss decreased with gestation, increased with maternal age and was higher in women with episodes of vaginal bleeding before examination, but there was no significant association with previous pregnancy history or cigarette smoking.

Previous ultrasound studies have reported the prevalence of early pregnancy failure to range from 3 to 53% (Table 4)[2,5–12]. This variation may be a consequence of the relatively small number of cases examined in each study (from about 200 to 2000), the wide range of gestations of the study populations (5–16 weeks), differences in the maternal age distribution of the population and differences in the indications for the ultrasound scans (routine examination with a prevalence of pregnancy failure of 3–12%, or examination because of vaginal bleeding with a prevalence of 25–52%).

Vaginal bleeding is a manifestation of miscarriage and inevitably both the incidence and severity of bleeding are associated with the prevalence of early pregnancy failure. The most likely explanation for the relationship with maternal age and gestation is that a high proportion of pregnancies that result in early miscarriage are chromosomally abnormal. There is a well recognized association between chromosomal abnormalities and maternal age. Additionally, the rate of intrauterine lethality of chromosomally abnormal pregnancies is higher than in normals and this is more marked in early pregnancy; consequently, the maternal age-specific risk for aneuploidies decreases with gestational age[13]. Cytogenetic investigations of miscarriages at 8–15 weeks of gestation have demonstrated that in 45–70% of cases there were associated chromosomal

Table 2 The prevalence of pregnancy failure in relation to a combination of maternal age, gestational age and vaginal bleeding

Gestational age (weeks)	*Maternal age* (years) < 35		35–39		≥ 40	
	n	%	*n*	%	*n*	%
10 weeks						
No bleeding	15/285	5.3	10/226	4.4	7/58	12.1
Spotting	6/52	11.5	4/38	10.5	5/12	41.7
Heavy bleeding	1/7	14.3	2/8	25.0	1/2	50.0
11 weeks						
No bleeding	85/3314	2.6	83/2355	3.5	29/469	6.2
Spotting	32/610	5.3	33/460	7.2	15/124	12.1
Heavy bleeding	7/58	12.1	8/51	15.7	3/13	23.1
12 weeks						
No bleeding	36/3235	1.1	29/2017	1.4	7/355	2.0
Spotting	18/590	3.1	13/400	3.3	4/85	4.7
Heavy bleeding	3/67	4.5	5/50	10.0	1/10	10.0
13 weeks						
No bleeding	14/1463	1.0	10/783	1.3	0/173	0.0
Spotting	6/247	2.4	3/159	1.9	3/35	8.6
Heavy bleeding	1/32	3.1	1/22	4.6	1/5	20.0

Table 3 Prevalence of early pregnancy failure in relation to the number of previous live births and previous early pregnancy failure

Previous live births	*Total*		*Previous early pregnancy failure* None		1		2		≥ 3	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
None	193/7163	2.7	154/5666	2.7	33/1150	2.9	5/265	1.9	1/82	1.2
1	168/6442	2.6	116/4541	2.6	38/1350	2.8	9/368	2.5	5/183	2.7
2	93/2959	3.1	60/2234	2.7	20/368	5.4	8/231	3.5	5/126	4.0
≥ 3	47/1306	3.6	25/867	2.9	11/228	4.8	6/118	5.1	5/93	5.4
Total	501/17 870	2.8	355/13 308	2.7	102/3096	3.3	28/982	2.9	16/484	3.3

Table 4 Prevalence of early pregnancy failure in previous ultrasound studies, which were either performed routinely or for vaginal bleeding. In some of the routine studies, patients with vaginal bleeding were excluded (*)

Authors	*Indication*	*Number*	*Gestational age* (weeks)	*Pregnancy failure*	
				n	%
Robinson (1975)[2]	bleeding	425	6–14	138	32.5
Jorgensen *et al.* (1980)[5]	bleeding	191	9–16	101	52.9
Gilmore and McNay (1985)[6]	routine	2139	< 11	179	8.4
Mantoni (1985)[7]	bleeding	214	5–14	76	35.5
Lind and McFayden (1986)[8]	routine*	961	7–12	32	3.3
Stabile *et al.* (1987)[9]	bleeding	406	5–16	101	24.9
Regan *et al.* (1989)[10]	routine	383	8–12	24	6.3
Barret and Brinson (1991)[11]	routine	737	6–13	56	7.6
Goldstein (1994)[12]	routine*	232	5–10	27	11.5

abnormalities and the most common were autosomal trisomies[14–16].

In addition to chromosomal abnormalities, many other factors have been suggested as possible causes of early pregnancy failure. However, some of these conditions, such as maternal illness, infection, teratogens or uterine abnormalities, can account for only a small proportion of cases, whereas the role of others, such as hormonal or immunological factors, remain controversial[17,18]. Nevertheless, there is an association between early pregnancy failure and maternal age, even in chromosomally normal pregnancies[19].

In our study, there was no significant association between the prevalence of early pregnancy failure and a history of previous pregnancy losses. In contrast, a study of 407 pregnancies reported that this was the most relevant predictive factor[10]. It is likely that the results from the latter study reflect selection bias; 69% of the 309 multiparae had a history of miscarriage compared to 38% of multiparae in our population.

Recent evidence suggests that the most effective method of screening for chromosomal abnormalities is measurement of fetal nuchal translucency thickness at 10–13 weeks of gestation[20,21] and therefore ultrasound examination at this gestation is likely to become universally available. Additional advantages of the first-trimester scan are accurate dating of pregnancy, since more than 30% of women attending an antenatal clinic have uncertain or unreliable menstrual dates[22,23], early diagnosis of major fetal abnormalities[24] and, as shown in this study, diagnosis of fetal death. Elective evacuation of retained products of conception is likely to be more cost effective and potentially safer than emergency surgery in a patient presenting during miscarriage. It is important that the diagnosis of fetal death should be clearly established before proceeding to evacuation of the uterus and we propose the recommendations of the public inquiry[25] published in this Journal to avoid the inadvertent termination of a viable pregnancy.

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