

Future pregnancy outcome in unexplained recurrent first trimester miscarriage

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The future pregnancy outcome of 201 consecutive women, median age 34 years (range 22–43), with a history of unexplained recurrent first trimester miscarriage (median 3; range 3–13), was studied. All women and their partners had normal peripheral blood karyotypes; none had antiphospholipid antibodies and none hypersecreted luteinizing hormone (LH). No pharmacological treatment was prescribed and early pregnancy supportive care was encouraged. Women aged ≤ 30 years had a subsequent miscarriage rate of 25% (14/57) which rose to 52% (13/25) in women aged ≥ 40 years ($P = 0.02$). After three consecutive miscarriages, the risk of miscarriage of the next pregnancy was 29% (34/119) but increased to 53% (9/17) after six or more previous losses ($P = 0.04$). A past history of a livebirth did not influence the outcome of the next pregnancy. Supportive care in early pregnancy conferred a significant beneficial effect on pregnancy outcome. Of 160 women who attended the early pregnancy clinic, 42 (26%) miscarried in the next pregnancy compared with 21 out of 41 (51%) who did not attend the clinic ($P = 0.002$). After thorough investigation, women with unexplained recurrent first trimester miscarriage have an excellent pregnancy outcome without pharmacological intervention if offered supportive care alone in the setting of a dedicated miscarriage clinic.

Key words: early pregnancy clinic/habitual abortion/pregnancy outcome/recurrent miscarriage/supportive care

Introduction

Recurrent miscarriage, the loss of three or more consecutive pregnancies, affects ~1% of women. Although investigation is now able to identify aetiological factors in up to 50% of cases (Clifford *et al.*, 1994), unexplained recurrent miscarriage remains a frustrating problem for the clinician and a distressing condition for the affected couple. In the past many anecdotal treatments have been prescribed in an attempt to improve the outcome of pregnancy, leading to a wide variety of pharmacological and other therapies. It is important, however, to establish the outcome of the next pregnancy without treatment. This provides information that can be used to counsel affected couples about their chance of success in the future and also prevents unwarranted intervention.

Materials and methods

All women attending the St Mary's Hospital Recurrent Miscarriage Clinic with a history of three or more consecutive first trimester miscarriages were investigated according to our protocol (Clifford *et al.*, 1994). The following investigations were performed: peripheral blood karyotyping of both partners; pelvic ultrasound scanning to determine uterine anatomy and ovarian morphology; screening for antiphospholipid antibodies, both anticardiolipin antibodies and lupus anticoagulant on at least two occasions (Haemostasis and Thrombosis Task Force, 1991; Khamashta and Hughes, 1993); mid-follicular phase serum gonadotrophin measurements [luteinizing hormone (LH) and follicle stimulating hormone (FSH)] and a complete menstrual cycle of urinary LH measurements (Watson *et al.*, 1993). Women in whom no abnormality was detected and who subsequently became pregnant formed the study population.

In the next pregnancy all women were encouraged to attend a dedicated early pregnancy clinic until 12 weeks gestation. At this clinic, staffed by a team of three clinicians, women were seen weekly for ultrasound confirmation of fetal viability and measurement of fetal growth. No pharmacological treatment was prescribed before or during pregnancy. The outcome of the next pregnancy was recorded. Women who did not attend the clinic were contacted by telephone or letter to document information about the outcome of their pregnancy.

Statistical analysis was performed using the χ^2 and Mann–Whitney *U*-tests.

Results

The pregnancy outcome of 201 consecutive women [182 (91%) Caucasian; 9 (4%) Afro-Caribbean; 10 (5%) Asian] was studied. The median age was 34 years (range 22–43) and the median number of previous first trimester losses was three (range 3–13). Overall, 63 women (31%) miscarried in the next pregnancy. All the miscarriages occurred before 12 completed weeks of pregnancy with no late miscarriages or stillbirths in this series. There were three ectopic pregnancies and two pregnancies were terminated for fetal aneuploidy (one Down's syndrome and one Turner's syndrome).

Increasing maternal age and number of previous miscarriages exerted a negative effect on pregnancy outcome (Tables I and II). A previous livebirth in the past obstetric history conferred no advantage to the outcome of the next pregnancy. Of women who had never achieved a livebirth, 35/114 (31%) miscarried in the next pregnancy compared to 28/87 (32%) of women who had achieved a livebirth in the past.

Women attending for supportive care were of similar age and ethnic background and had experienced a similar number of previous miscarriages compared to those women who did not attend the early pregnancy clinic (Table III). Attendance for supportive care conferred a significant beneficial effect on the outcome of pregnancy (Table IV). This was independent of

Table I. Rate of miscarriage in the next pregnancy with respect to maternal age

Age (years)	Miscarriage rate (%)
≤30	14/57 (25) ^a
31–35	20/71 (28) ^b
36–39	16/48 (33) ^c
40	13/25 (52) ^d

^a versus ^d: $P = 0.02$; ^b versus ^d: $P = 0.03$; ^c versus ^d: $P = 0.1$ (NS).

Table II. Rate of miscarriage in the next pregnancy with respect to the number of previous miscarriages

No. of previous miscarriages	Miscarriage rate (%)
3	34/119 (29) ^a
4	13/49 (27) ^b
5	7/16 (44) ^c
≥6	9/17 (53) ^d

^a versus ^d: $P = 0.04$; ^b versus ^d: $P = 0.05$; ^c versus ^d: $P = 0.1$ (NS).

both the maternal age and the number of previous miscarriages. Overall the median gestational age at the time of the miscarriage was 8.6 weeks. There was no difference in the gestational age at the time of the miscarriage between those women who attended the early pregnancy clinic and those who did not (8.7 weeks and 7.9 weeks respectively; $P = 0.1$).

We were able to identify a group of women who had the most favourable prognostic features. In all, 129 women (64% of the study population) were aged <40 years with fewer than six miscarriages in the past and who attended for early pregnancy support. The rate of miscarriage of the next pregnancy in this group of women was only 21% (27/129).

Discussion

This large study demonstrates the excellent outcome of pregnancy after unexplained recurrent first trimester miscarriage that can be achieved in a dedicated clinic with supportive care alone. Overall the population fared well with nearly 70% of women achieving a livebirth in the next pregnancy. This figure rose to nearly 80% in women with the most favourable prognostic features. The rate of miscarriage in the next pregnancy rose sharply in women aged ≥40 years and this is similar to the effect of maternal age on the rate of spontaneous abortion (Stein *et al.*, 1980; Alberman, 1987). This is due not only to the loss of aneuploid fetuses but also to an increase in the loss of pregnancies with a normal karyotype (Stein *et al.*, 1980). The negative effect of an increasing number of previous miscarriages on future pregnancy outcome has been previously documented (Naylor and Warburton, 1979; Parazzini *et al.*, 1988; Regan *et al.*, 1989; Cauchi *et al.*, 1991). However in this study even after six or more previous losses >45% of women achieved a livebirth without treatment.

Supportive care in early pregnancy conferred a significant beneficial effect on the outcome of pregnancy. Although attendance at the early pregnancy clinic was not randomly allocated we have not been able to find any demographic

Table III. Characteristics of women attending for supportive care versus those that did not attend (EPC = early pregnancy clinic)

	Attended EPC ($n = 160$)	Did not attend EPC ($n = 41$)	
Ethnic group	91% Caucasian	92% Caucasian	
Median age (range)	33 (22–43)	35 (25–42)	$P = 0.5$
No. of previous miscarriages	3 (3–13)	3 (3–6)	$P = 0.7$

Table IV. Rate of miscarriage with respect to care received in early pregnancy

Care in early pregnancy	Miscarriage rate (%)
Early pregnancy clinic	42/160 (26) ^a
None	21/41 (51) ^b

^a versus ^b: $P = 0.002$.

differences between women attending the clinic and those who did not. The beneficial effect of supportive care has been previously reported by our own group (Clifford *et al.*, 1996) and by others (Stray-Pederson and Stray-Pederson, 1984; Liddell *et al.*, 1991). The accumulation of data on this subject suggests that this is a genuine phenomenon although the mechanism is unclear. Early pregnancy support may be time-consuming and costly in terms of staff and equipment but our data justify the use of such an intensive management.

This study emphasizes the importance of separating women with a history of recurrent miscarriage into two groups: those with identifiable pathology and those in whom thorough investigation reveals no abnormality. Women in the latter group can be counselled on the basis of our data that the outcome for the next pregnancy with supportive care alone is excellent. Drug treatment or other intervention is often requested even in the absence of any aetiological factor in an attempt to improve the outcome of future pregnancies. The data presented here should provide reassurance that such management is unnecessary and should therefore be resisted. Furthermore the excellent background livebirth rate should be remembered when assessing new treatments for women with unexplained recurrent miscarriage.

Acknowledgements

K.C. was funded by the Medical Research Council; R.R. was funded by the Arthritis and Rheumatism Council. The authors thank Toni Rae for her scanning expertise in the early pregnancy clinic.

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Received on August 27, 1996; accepted on November 18, 1996