

Psychosocial predictors of successful delivery after unexplained recurrent spontaneous abortions: a cohort study

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Objective: To examine psychosocial predictors of successful pregnancy after recurrent spontaneous abortions (RSA).

Method: We administered two waves of semi-structured interview and self-report questionnaire battery to a consecutive series of 46 couples who had had two RSAs (baseline before third pregnancy, and immediately after third pregnancy was ascertained), and followed them through their third pregnancy.

Results: Of the 46 couples, four miscarried for karyotypal abnormalities and six without any known cause. When the latter six were compared with the remaining 36 women, they reported less social support satisfaction, a more stable attribution for the causes of past abortions, and more depressed mood in the preceding year. Taken altogether, this psychosocial model was able to predict 93% of the pregnancy outcomes correctly.

Conclusion: Psychosocial variables (depression, attribution and social support) are robust predictors of the prospective pregnancy and suggest possible points of intervention in couples with RSA.

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Introduction

Spontaneous abortions are much more frequent than is generally believed and occur in about 10–20% of all pregnancies (1). Chances of carrying the next pregnancy to term decrease as the number of repeated abortions increases and some 2% of women will have recurrent spontaneous abortions (RSA) (2).

Conventional investigation of couples with RSA reveals no putative cause in more than half of cases (3). Aside from anatomical anomalies of the uterus or cervix, endometrial infections, hormonal dysfunctions and chromosomal aberrations, some immunologic factors such as antiphospholipid antibody and natural killer cell activity have recently been implicated in the RSA (4) and the psycho–neuro–immuno–endocrine network has been proposed as a mechanism involved in the maintenance of pregnancy (5).

Immunologic functions are known to be under the influence of various psychosocial factors (6). Studies

to date, however, have only produced conflicting results with regard to psychological and social variables involved in the abortogenic process.

Aims of the study

The present paper reports on the results of a prospective study based on two waves of direct interviews and self-report questionnaires with the women with RSA, and aims to examine the roles of psychosocial factors predictive of the success/failure of the prospective pregnancy after repeated abortions. More specifically, we had hypothesized:

- (i) Poorer housing conditions might lead to repeated abortions.
- (ii) Lack of social support would lead to repeated abortions.
- (iii) Attributional style associated with depression, namely internal (I'm the one responsible), stable (It will happen again) and general (It will affect other things too) attribution of an

uncontrollable (I could not help it) event, would lead to repeated abortions.

- (iv) Psychiatric disorders, especially mood or anxiety disorders, would be abortogenic.

Material and methods

Patients

The recruitment process of the present cohort has been detailed elsewhere (7, 8) and is briefly reviewed here. The study protocol has been approved by the Institutional Review Board of Nagoya City University Medical School.

Subjects were recruited from among couples who presented themselves to the Habitual Abortion Clinic of the Department of Obstetrics and Gynecology of Nagoya City University Hospital between April 1995 and August 1997. The entry criteria were: (i) history of two repeated spontaneous first-trimester miscarriages with the same marital partner, (ii) no prior live birth, (iii) no clearly identifiable causes for recurrent miscarriages, such as uterine anomalies, chromosomal abnormalities in either partner, endocrine abnormalities including luteal-phase defects, polycystic ovary syndrome, autoimmune abnormalities including antiphospholipid antibodies or metabolic disorders, (iv) no other physical comorbidity, and (v) fluency in the Japanese language.

Of a total of 90 couples eligible for this study, 61 gave their written informed consent after full disclosure of the purposes and procedures of the study. The 29 women who chose not to participate in the study were not statistically significantly different from the 61 participating women in terms of age or time since last abortion.

Procedures

A total of 61 couples completed the wave 1 interview and questionnaire, at the time of their recruitment and before their third pregnancy. Wave 1 interview concerned demographics, housing and living conditions, social support, and experiences of the past two abortions. More specifically, the social support section was modeled after the Social Support Questionnaire (9), which measures social support in terms of its objective size and its subjective satisfaction. Each patient was asked to name the persons with whom the subject could feel at home with, who understood her, with whom she could share her innermost feelings, with whom she could share joy, who could provide advice, who could help her when necessary, and who could support her emotionally. She

was also asked how satisfied she was in each of these aspects of social support (10, 11). In the section on the past two abortions, we inquired about the subjective impact of the abortions and the women's attributions about their abortions. The attributional style was measured in terms of its direction (internal vs. external), stability, generality and controllability according to the reformulated learned helplessness theory (12). The questionnaire battery included the Symptom Checklist-90 Revised (13) to measure the women's psychological symptoms for the 1 week preceding the interview.

Of the 61 couples entering the study, there were 46 pregnancies between July 1995 and June 1999. Of these 46, 41 couples cooperated with the wave 2 interview and questionnaires. Wave 2 interview, which was performed within 2 weeks after third pregnancy was ascertained, concerned the women's reaction to the third pregnancy, their past and present mental illness, and their working conditions at home and/or outside home. The section of the semi-structured interview for the psychiatric illnesses was modeled after the Diagnostic Interview Schedule (14): the present status section inquired about a series of psychiatric symptoms for the past 12 months, and the section on the past psychiatric illnesses was limited to seven psychiatric syndromes (generalized anxiety disorder, panic disorder, phobic disorder, obsessive-compulsive disorder, major depressive episode, dysthymic disorder, manic episode, according to DSM-III-R) in the subject's lifetime up to 12 months before. The second wave questionnaire battery contained the SCL-90-R again.

Statistical analyses

We used SPSS for Windows Version 11.0 (15) for the statistical analyses. We compared baseline variables between the abortion group and the birth group, using Fisher exact test for dichotomous variables and Mann-Whitney *U*-test for continuous variable because some of the latter were not normally distributed and the sample size was rather small for the abortion group. Where appropriate, we showed the central tendency of the variable by the median, and its dispersion by the lower quartile and the upper quartile. All the statistical tests were two-tailed and an alpha of 0.05 was considered statistically significant. When statistically significant variables emerged at this conventional level of alpha, we examined the predictive value of these predictors by way of logistic regression analysis where assumption of normality of distribution is not required and where possible moderating effect of any of the variables can be teased out.

	Third pregnancy outcome		P-value
	Miscarriage (n = 6)	Delivery (n = 36)	
Age (years)	29.7 (25.0, 41.1)	29.8 (27.7, 31.2)	0.93
Number of previous miscarriages	2	2	1.00
Number of previous live births	0	0	1.00
Number of previous elective abortions	0	0	1.00
Education (years)	13.0 (9.8, 14.0)	14.0 (12.0, 14.0)	0.47
Occupation (number of housewife)	4 (67%)	15 (42%)	0.24
Interval between second miscarriage and first interview (months)	5.5 (5.0, 41.3)	6.0 (4.0, 10.5)	0.61
Interval between first interview and third pregnancy (months)	5.2 (1.7, 10.3)	5.6 (2.1, 14.1)	0.65
Housing area (m ²)	69.3 (32.2, 136)	66.0 (46.2, 84.2)	0.18
Satisfaction with living condition*	2.5 (2.0, 4.5)	4.0 (2.5, 5.0)	0.43
Social support number	3.9 (2.9, 5.4)	4.5 (3.1, 5.7)	0.56
Social support satisfaction†	2.9 (2.6, 3.2)	3.7 (3.3, 4.0)	0.001

For each dichotomous variable, the absolute number is followed by the percentage in parentheses. For each continuous variable the central tendency is expressed by the median, and the dispersion is expressed by the lower quartile and the upper quartile in parentheses.

* The higher the score, the greater the satisfaction, with 1, very unsatisfied and 5, very satisfied.

† The higher the score, the greater the satisfaction, with 1, very unsatisfied and 4, very satisfied.

Results

Of the 46 couples for whom the third pregnancy was ascertained, it ended in miscarriage in 10 couples (21.7%). However, because four of these miscarrying women had fetuses with karyotype abnormalities, in the following analyses on psychosocial predictors of unexplained spontaneous abortions, we would like to concentrate on the 36 women with successful third pregnancy and the six women who miscarried without known cause.

The mean age of these 42 women were 29.8 years (95% CI: 28.8–30.8). The couples had been married, on average, for 3.1 (2.5–3.8) years. At the time of the first interview, 8.9 (6.2–11.5, range: 2–53) months had passed since their last spontaneous abortion.

Table 1 shows the baseline demographic variables, living conditions and perceived social support for the miscarriage group and successful delivery group. Women whose third pregnancy ended in miscarriage tended to be less satisfied with the available social support.

The attributional style of the women was evaluated with regard to the cause of their first and second spontaneous abortions in terms of direction (internal vs. external), stability (stable vs. unstable), generality (global vs. specific) and controllability (controllable vs. uncontrollable) (Table 2). Women whose third pregnancy ended in miscarriage tended to make a stable attribution as to the cause of their second miscarriage.

Table 3 compares the past and present psychiatric illnesses between the miscarriage group and the successful delivery group. There was no stati-

Table 1. Demographics and living conditions for the miscarriage and successful delivery groups

stically significant difference in the number of subjects suffering from either current or past generalized anxiety disorder, panic disorder, phobic disorder, obsessive-compulsive disorder, dysthymic disorder or manic episode. The women whose third pregnancy was going to abort reported a greater number of psychiatric symptoms during the past 12 months preceding the second interview, and more often reported depressed mood during the past 12 months than

Table 2. Attributional style for the miscarriage and successful delivery groups

	Third pregnancy outcome		P-value
	Miscarriage (n = 6)	Delivery (n = 33)	
Direction*			
First abortion	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	0.85
Second abortion	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	0.83
Stability†			
First abortion	2.0 (1.8, 4.0)	2.0 (1.0, 2.0)	0.11
Second abortion	3.0 (3.0, 4.0)	2.0 (2.0, 3.0)	0.002
Generality‡			
First abortion	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0
Second abortion	1.5 (1.0, 2.0)	1.0 (1.0, 1.0)	0.25
Controllability§			
First abortion	3.0 (1.0, 4.0)	3.0 (2.0, 4.0)	0.59
Second abortion	4.0 (3.0, 4.0)	4.0 (3.0, 4.0)	0.88

For each variable the central tendency is expressed by the median, and the dispersion is expressed by the lower quartile and the upper quartile in parentheses.

* The higher the score, the more internal the attribution, with 1, totally external and 4, totally internal.

† The higher the score, the more stable the attribution, with 1, for this abortion only and 4, bound to affect the next pregnancy.

‡ The higher the score, the more global the attribution, with 1, for this abortion only and 4, causing many other events.

§ The higher the score, the less controllable the attribution, with 1, controllable by myself and 4, totally beyond control.

Table 3. Psychiatric symptoms and diagnoses for the miscarriage and successful delivery groups

	Third pregnancy outcome		P-value
	Miscarriage (n = 4)	Delivery (n = 33)	
Total number of symptoms for the past year	10.0 (7.3, 21.8)	4.0 (2.0, 9.5)	0.06
Depressed mood during the past 12 months	3 (75%)	5 (15%)	0.03
Major depressive episode during the past 12 months	0	1 (3%)	0.89
Major depressive episode during lifetime	0	8 (24%)	0.46
Depressive disorder NOS during the past 12 months	3 (75%)	4 (12%)	0.02
Depressive disorder NOS during lifetime	2 (67%)*	5 (15%)	0.09

For each dichotomous variable, the absolute number is followed by the percentage in parentheses. For each continuous variable the central tendency is expressed by the median, and the dispersion is expressed by the lower quartile and the upper quartile in parentheses.

NOS: not otherwise specified.

* Data not available for one of the four in the miscarriage group.

those whose next pregnancy was going to deliver. Although they did not report a full syndromatic major depressive episode, they also reported depressive disorder not otherwise specified more often in the past 12 months as well as in their lifetime than their counterparts.

The self-reported emotional distress according to SCL-90-R at the time of the first and second interviews is tabulated in Table 4. In order to correct for multiple comparisons, we performed two supplementary analyses. Firstly, we did multivariate analysis of variance (MANOVA), taking

Table 4. Self-reported psychiatric symptoms for the miscarriage and successful delivery groups

SCL-90-R	Third pregnancy outcome		P-value
	Miscarriage (n = 6)	Delivery (n = 35)	
Wave 1			
Depression	1.08 (0.77, 1.29)	0.31 (0.08, 0.69)	0.003
Somatization	0.67 (0.33, 1.04)	0.25 (0.08, 0.50)	0.09
Anxiety	0.70 (0.18, 1.15)	0.10 (0.00, 0.30)	0.02
Obsessive-compulsive	0.75 (0.60, 0.88)	0.40 (0.10, 0.80)	0.12
Interpersonal sensitivity	0.72 (0.64, 1.03)	0.11 (0.00, 0.78)	0.06
Hostility	0.67 (0.29, 1.29)	0.17 (0.00, 0.33)	0.01
Phobic anxiety	0.21 (0.11, 0.46)	0.00 (0.00, 0.14)	0.10
Paranoid ideation	0.42 (0.13, 1.00)	0.00 (0.00, 0.33)	0.07
Psychoticism	0.50 (0.30, 0.75)	0.00 (0.00, 0.20)	0.01
Global Severity Index	0.76 (0.50, 0.83)	0.18 (0.09, 0.54)	0.01
	Miscarriage (n = 4)	Delivery (n = 32)	
Wave 2			
Depression	0.93	0.35	0.10
Somatization	0.50 (0.35, 0.71)	0.25 (0.17, 0.58)	0.19
Anxiety	0.50 (0.20, 1.70)	0.20 (0.03, 0.48)	0.21
Obsessive-compulsive	0.35 (0.15, 0.55)	0.50 (0.03, 0.80)	0.72
Interpersonal sensitivity	0.56 (0.28, 1.00)	0.28 (0.11, 0.67)	0.19
Hostility	0.59 (0.37, 0.67)	0.17 (0.00, 0.29)	0.01
Phobic anxiety	0.07 (0.00, 0.14)	0.14 (0.00, 0.32)	0.48
Paranoid ideation	0.00 (0.00, 0.38)	0.00 (0.00, 0.13)	0.94
Psychoticism	0.25 (0.03, 0.48)	0.05 (0.00, 0.20)	0.34
Global Severity Index	0.53 (0.27, 0.74)	0.29 (0.16, 0.47)	0.21

For each continuous variable the central tendency is expressed by the median, and the dispersion is expressed by the lower quartile and the upper quartile in parentheses.

all the SCL-90-R subscale scores as dependent variables and the outcome of the third pregnancy as a dichotomous independent variable. The overall model was statistically significant for SCL-90-R at wave 1 ($F = 3.57$, d.f. = 9, $P = 0.004$) as well as for SCL-90-R at wave 2 ($F = 3.57$, d.f. = 9, $P = 0.005$). Secondly, we adopted Bonferroni correction for each subscale scores at wave 1 and wave 2, separately. After Bonferroni correction, at wave 1, only depression subscale remained a statistically significant predictor of the outcome of the third pregnancy; at wave 2, no subscale score was predictive. These self-report findings apparently reflected the depressed mood and other psychological symptoms during the 12 months preceding the third pregnancy as ascertained by direct interviewing at wave 2.

In order to examine if the identified predictors were still significant when controlled for the other variables, we entered social support satisfaction, stability of attribution for the second abortion, and depressed mood during the past year into multiple logistic regression at the same time. All of these three factors remained statistically significant and the model was able to predict 92.6% of the outcomes correctly (Table 5). When we entered, instead of the depressed mood ascertained by direct interview, the SCL-90-R depression score at wave 1, the model was still able to predict 93.3% of the third pregnancy outcomes correctly.

Table 5. Predictive power of the psychosocial variables

	Third pregnancy outcome		Total
	Miscarriage (n = 4)	Delivery (n = 33)	
<i>Prediction by social support, attribution and depressed mood</i>			
Miscarriage	3	1	
Delivery	1	22	
Percentage correct (%)	75.0	95.7	92.6

Discussion

We conducted a systematic, two-wave follow-up study of a consecutive series of 61 couples with RSA by way of direct interviews and questionnaires, and found that satisfaction with perceived social support, stable attribution of the causes of the past abortion, and some psychological symptoms especially depression predicted the outcome of the prospective pregnancy. Taken altogether, this model was able to predict above 90% of the prospective pregnancy outcomes correctly.

Previous studies and their limitations

Earlier reports of non-randomized controlled studies of ‘tender loving care’ or ‘supportive care’ for women with RSA reported a dramatic increase in the success rate of the prospective pregnancy (2, 16, 17). Unfortunately, in these studies the interventions were not randomly allocated and we cannot rule out confounding factors such as depression or low social support, simultaneously preventing the women from attending the antenatal care frequently and contributing to the next miscarriage.

Several recent studies have prospectively examined psychological factors in women undergoing *in vitro* fertilization. Two studies confirmed the association between anxiety/depression and reproductive failure (18, 19) while one study failed to find a significant association (20).

With regard to RSA, a prospective cohort study of 36 women revealed that neither anxiety nor depression nor social support was associated with the success or failure of the next pregnancy (21). However, their sample was heavily represented by women with abnormal physical findings (of the 18 women who miscarried, five did not complete required investigations; of the remaining, 10 had abnormal physical findings and six had a chronic disease). We, therefore, cannot exclude the involvement of psychosocial factors among the majority of women with RSA who have no known organic causes. When limited to couples with RSA without identifiable causes, we have previously demonstrated that baseline depression score on a self-report questionnaire predicted subsequent miscarriage (7). None of these studies, however, have used structured clinical interviews directly with the women and are therefore subject to self-report biases.

Current findings

In this study focusing on the results from prospectively conducted direct interviews, depressed mood

emerged as a robust predictor of the prospective pregnancy outcome in women with two consecutive spontaneous abortions without known etiology. Our previous findings with self-report questionnaires (7) were replicated. Although the group difference did not reach statistical significance at time 2, likely due to the decreased statistical power, the observation was in line with that at time 1. We are, therefore, led to conclude that depressed mood, while not severe enough to satisfy the diagnostic criteria for major depression, still dramatically increased the likelihood of abortion for the next pregnancy.

The women overall tended to make internal attribution with regard to the causes of their first and second abortions. Although the generality or controllability in their attributional style did not influence the outcome of the third pregnancy, stable attribution, especially with regard to the second abortion, predicted miscarriage. Because the correlations between attributional style and depressed mood were not statistically significant (not shown), the effect of the attributional style on the next pregnancy does not appear to mediate via depressed cognition. We are aware of only one study which examined attributional style of women with repeated abortions; Klock et al. (22) reported that women who had had RSA tended to have external rather than internal locus of control. However, theirs was a cross-sectional study without any control subjects and we cannot know whether such an attributional style was a cause or effect of RSA. We need a more detailed study in order to elucidate the cognitive components in the psycho-neuro-immuno-endocrine network in the maintenance of pregnancy.

On the other hand, our positive finding with regard to perceived social support is in accord with several previous studies, especially several prospective intervention studies (2, 16, 17) and one retrospective case-control study (23). In the latter study, the miscarriage group were more likely to have experienced a severe life event in the 3 months preceding miscarriage and reported poorer relationship with partners and fewer social contacts than the control group of women matched for known predictors of miscarriage. The study by Bergant et al. (21) appears to be the only prospective study which found non-significant contribution of social support for the next pregnancy but, as pointed out above, this study was over-represented by women with physical abnormalities. Because the social support satisfaction and depressed mood, as measured either by the questionnaire or ascertained by the interview, showed significant correlations (Kendall's $\tau = -0.25$,

$P = 0.05$ with SCL-90-R depression subscale and -0.28 , $P = 0.06$ with depressed mood from the structured interview), it may be acting as an important buffer in the stressful situation of repeated abortions for the afflicted women.

What biological or pathophysiological links may explain the associations we found remains largely a matter of speculation. There is some evidence to suggest that unexplained miscarriage may be due to Th1/Th2 cytokine imbalance at the feto-maternal interface (24) and Th2-type immunity and transforming growth factor b secreted by Th3 cells may play protective roles during pregnancy (25). On the other hand, it is well known that immunological functions are under the influence of various psychosocial factors (6, 26). Abnormal psychological conditions including depression and dissatisfaction with social support might thus influence pregnancy outcome via a shift in the balance of the Th1/Th2/Th3 cytokines.

Implications

Several caveats are in order before we conclude. Firstly, our study design cannot exclude contribution of common antecedent factors, such as negative life events (27), personality traits or genetic vulnerabilities (28, 29), leading both to depression, stable attribution, social support dissatisfaction on one hand and to repeated spontaneous abortions on the other. Secondly, the sample size was very small, especially for the miscarriage group. We are currently replicating this study with a new consecutive series of patients with RSA by administering self-report questionnaires for depression and social support. However, we must remember that, while the small sample size may have contributed to false negative findings, what positive findings we did obtain would stand despite the sample size. There are, moreover, several strengths of the current study which would compensate for these weaknesses. Firstly, the prospective nature of the current study design strongly argues for the cause-effect relationships between the baseline variables at waves 1 and 2, and the outcome of the third pregnancy which only became apparent after the two interviews. Furthermore, in contrast to some unchangeable factors such as life events and personality, the three factors that emerged in our analyses offer possible points of intervention. Thirdly, the concordance between interviewer-ascertained factors and self-report results greatly enhances our confidence in the validity of the obtained results. Lastly, the obtained three-variable psychosocial model correctly predicted over 90% of the prospective pregnancy outcomes. This

amazing predictive power may partly derive from overfitting of the data but certainly merits a replication study.

Systematic studies have consistently pointed out three- to fivefold increase in the rate of depression following miscarriage (30–32). And if, as we found in this study, depression contributes to the failure in the next pregnancy, it is evident that we must seek ways to intervene in this vicious cycle. Our results are suggestive in this regard too: social support is apparently one variable that we could work on through ‘tender loving care’ or ‘supportive care’; cognitive restructuring focusing on the attributional style of the women may well be another.

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