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Prevalence of depression and anxiety in women with recurrent pregnancy loss and the associated risk factors

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Abstract

Objective To investigate the prevalence and explore potential risk factors of depression and anxiety in patients with recurrent pregnancy loss (RPL).

Methods 1138 non-pregnant women aged 20–40 years old who attempted to conceive were invited to complete a questionnaire, including basic information, Self-Rating Depression Scale (SDS) and Self-Rating Anxiety Scale (SAS).

Results 782 RPL women, 218 women with one pregnancy loss and 138 women with no history of pregnancy loss were included in this study. We found that both RPL patients and women with one pregnancy loss had significantly higher SDS and SAS scores than the control group ($P = 0.006$, 0.003). Furthermore, in RPL patients, those with lower education level (lower than university), lower household income (< 10,000 yuan) and history of induced abortion had significantly higher levels of depression and anxiety. Women with multiple pregnancy losses (≥ 3) and no live birth had significantly higher SDS scores. Women who had been married for 3 years or more had a significantly higher SAS score. Logistic regression revealed that lower education level (lower than university) was an independent risk factor for depression (adjusted OR = 1.75, 95% CI 1.10–2.77, $P = 0.018$) and anxiety (adjusted OR = 1.80, 95% CI 1.04–3.13, $P = 0.037$), and women with three or more pregnancy losses had increased odds of depression than those with two pregnancy losses (adjusted OR = 1.82, 95% CI 1.15–2.88, $P = 0.012$).

Conclusion RPL patients are more likely to develop depression and anxiety than women with no history of pregnancy loss. Lower education level and multiple pregnancy losses (≥ 3) appear to be two independent risk factors of depression and anxiety in women with RPL. Women with one pregnancy loss also show a significant higher level for depression and anxiety. Appropriate psychological intervention can be considered for such patients.

Keywords Recurrent pregnancy loss · Depression · Anxiety · Risk factors

Introduction

Recurrent pregnancy loss (RPL) is defined as two or more failed pregnancies after a clinical pregnancy documented by ultrasonography or histopathologic examination [1]. While in the guideline for RPL of the European Society of Human Reproduction and Embryology (ESHRE), a diagnosis of RPL could be considered after the loss of two or more pregnancies before 24 weeks' gestation, including pregnancy losses both after spontaneous conception and ART, but ectopic and molar pregnancies and implantation failure are excluded [2]. Despite the difference in definition, RPL affects 1–5% of women worldwide who seek to have children. However, approximately half of patients with RPL have no explanation for their miscarriages [3], which is undoubtedly a traumatic event in women's lives. Women who experienced an unintentional pregnancy loss are more likely to have adverse mental health problems such as depression and anxiety [4]. However, most studies focused on depression and anxiety in RPL were small in sample sizes and varied in scales for evaluation, thereby making the results rather puzzling [5–8]. The prevalence of depression in reported studies varied from < 15 to 33% [6, 8]. The risk factors of depression and anxiety in RPL

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patients remain unknown. Therefore, the present study aims to investigate the prevalence of depression and anxiety in women with RPL and to explore possible factors which may affect their mental health.

Materials and methods

Participants

Non-pregnant women aged 20–40 years old who attempted to conceive in outpatient clinic at Renji Hospital from August 2015 to June 2017 were admitted in present study. Participants were divided into three groups according to number of pregnancy losses: group 1 as RPL; group 2 as a history of a single pregnancy loss; and group 3 with no previous pregnancy loss and not presently in any fertility treatment. In our study RPL was defined as two or more consecutive failed pregnancies before 24 weeks' gestation including biochemical pregnancy loss and confirmed intrauterine pregnancy loss. Subjects with a history of depression, anxiety and other psychological problems or currently using psychotropic drugs were excluded. All participants were given a set of questionnaires on their first clinic visit. The study was approved by the Ethics Review Board of Renji Hospital [Ethical vote No. (2014) N034 on 11 Nov 2014]. All participants were guaranteed anonymity during data processing and written informed consents were obtained.

Measures

Background information including age, education level of the participants and their spouses, height and weight (for the calculation of body mass index, BMI), duration of marriage, household income, numbers of abortions (intentional or spontaneous) and numbers of live birth was obtained.

Self-rating Depression Scale (SDS) and Self-rating Anxiety Scale (SAS) were administrated in our study [9, 10]. These are simple and reliable tools for the assessment of depressive and anxious symptoms, and are widely applied in clinical studies. Each of these two scales contains 20 items that describes subjective feelings and manifestation of depression or anxiety. Participants were asked to rate these items using a 1–4 scale where 1 = 'never or rarely', 2 = 'sometimes', 3 = 'often' and 4 = 'most of the time'. A final score of more than 50 was considered to have symptoms of depression or anxiety. The scores of 50–59, 60–69, and 70 or more are classified as mild, moderate, and severe depression or anxiety, respectively [9–11].

Statistical analysis

Chi-square tests were used for the comparison of categorical variables, and unpaired *t* tests for continuous variables. To evaluate the differences among the three groups, analysis of variance (ANOVA) was performed in combination with LSD post-hoc tests. Binary logistic regression analyses were performed to explore possible risk factors for depression and anxiety in RPL patients. Statistical significance was considered at $P < 0.05$. All statistical analyses were performed using Statistical Package for Social Science (SPSS version 22.0, IBM Corp, Armonk, NY, USA).

Results

Basic characteristics of the study participants

Of all the invited participants, 1138 women were included in this study and divided into 3 groups according to their number of pregnancy loss, including 782 RPL women in group 1, 218 women with one pregnancy loss in group 2 and 138 women with no history of pregnancy loss in group 3. 62 participants did not complete the questionnaires (47 cases from Group 1, 11 cases from Group 2 and 4 from Group 3) were excluded from the study. The response rate is 94.1%.

Basic characteristics of the study participants for each group were summarized in Table 1. No significant difference was observed between three groups in age, education level of the participants and their spouses, duration of marriage, monthly household income and history of live birth ($P > 0.05$).

Depression and anxiety

SDS and SAS scores were higher in group 1 and group 2 than group 3, as shown in Table 2. However, no difference was found between group 1 and group 2 regarding their SDS or SAS scores ($P > 0.05$). A total of 56 (7.2%) subjects in groups 1, 19 (8.7%) in groups 2 and 5 (3.6%) in group 3 had mild depression. A total of 21 (2.7%) subjects in group 1, 4 (1.8%) in group 2 and 3 (2.2%) in group 3 had moderate depression. A total of 7 women in group 1 and 1 in group 2 had severe depression, while no subjects in group 3 had severe depression. A total of 39 subjects (5.0%) in group 1, and 11 (5.0%) in group 2 had mild anxiety, while only 2 (1.4%) in group 3 had mild anxiety. A total of 11 subjects (1.4%) in group 1, 4 (1.8%) in group 2 and 2 (1.4%) in group 3 had moderate anxiety. A total of 5

Table 1 Basic characteristics of the study participants

	Group 1 ($n=782$)	Group 2 ($n=218$)	Group 3 ($n=138$)	P
Age (mean ± SD)	31.42 ± 4.63	31.48 ± 4.82	31.91 ± 5.51	0.550
University education (n, %)	427 (54.6%)	125 (57.3%)	70 (50.7%)	0.474
Age of the spouse (mean ± SD)	32.91 ± 5.78	32.62 ± 7.17	33.08 ± 7.46	0.769
University education of the spouse (n, %)	431 (55.1%)	125 (57.3%)	75 (54.3%)	0.811
Duration of marriage (year, mean ± SD)	5.03 ± 3.81	4.48 ± 4.13	5.15 ± 3.70	0.129
Monthly household income ≥ 10 000 yuan[a] (n, %)	334 (42.71%)	94 (43.12%)	60 (43.48%)	0.758
Previous live birth (n, %)	77 (9.9%)	22 (10.1%)	14 (10.1%)	1

Group 1 represents subjects with RPL, group 2 subjects with a history of one pregnancy loss, and group 3 subjects with no previous pregnancy loss

[a]10,000 yuan equals approximately 1500 USD or 1270 EUR

Table 2 SDS and SAS scores of the three groups

	Group 1 ($n=782$)	Group 2 ($n=218$)	Group 3 ($n=138$)	F	P	LSD post-hoc
SDS	37.07 ± 9.97	36.51 ± 9.48	34.19 ± 8.60	5.144	0.006	3 < 1, 2
SAS	34.33 ± 9.45	33.77 ± 8.75	31.42 ± 7.24	6.019	0.003	3 < 1, 2

Group 1 represents subjects with RPL, group 2 subjects with a history of one single pregnancy loss, and group 3 subjects with no previous pregnancy loss

RPL recurrent pregnancy loss, *SDS* self-rating depression scale, *SAS* self-rating anxiety scale

subjects in group 1 had severe anxiety, while no subjects in group 2 and 3 scored over 70 points.

Risk factors for depression and anxiety in RPL patients

To explore potential risk factors associated with depression and anxiety in RPL patients, we performed sub-group analysis in SDS and SAS scores in Group 1 (RPL Group). The results were presented in Table 3. Significantly lower SDS scores ($P<0.05$) were found in RPL patients with lower education level (lower than university vs university and higher), lower household income (< 10,000 yuan vs ≥ 10 000 yuan), a history of induced abortion (yes vs no), three or more pregnancy losses (≥ 3 pregnancy losses vs 2 pregnancy losses) and without previous live birth (yes vs no). While significantly lower ($P<0.05$) SAS scores were found in RPL patients with lower education level (lower than university vs university and higher), lower household income (< 10,000 yuan vs ≥ 10 000 yuan), longer duration of marriage (≥ 3 years vs < 3 years) and a history of induced abortion (yes vs no).

Logistic regression controlling for duration of marriage, household income, history of induced abortion and history of previous live birth revealed that low level of education (lower than university) was associated with increased odds of depression (adjusted OR = 1.75, 95% CI 1.10–2.77; $P=0.018$) and anxiety (adjusted OR = 1.80, 95% CI 1.04–3.13; $P=0.037$). History of three or more pregnancy losses was also associated with increased likelihood of depression (adjusted OR = 1.82, 95% CI 1.15–2.88; $P=0.011$) (see Table 4).

Discussion

Pregnancy loss and depression, anxiety

In recent years, the incidence of RPL is rising; however, the etiology of this disorder in nearly half of the patients remains unknown [3]. RPL has not only a great impact on patients' own mental health, but also a negative effect on their families and the society. Most of previous studies on psychological adjustments in RPL patients had relatively small sample sizes and did not analyze risk factors associated with depression or anxiety [6–8, 12–14]. Kolte et al. [5] launched a survey in 301 RPL patients and found that 8.6% of them had moderate/severe depression, while only 2.2% of the women in the comparison group had depression (adjusted OR = 5.53, 95% CI 2.09–14.61). In a study of 81 women with recurrent miscarriage, Craig et al. found that recurrent miscarriage could affect mental health [6].

In this study, we analyzed data of 1138 subjects. We found that RPL subjects had significantly higher SDS and SAS scores, compared to those with no history of pregnancy loss, consistent with previous studies [5–8]. Moreover, women with a single pregnancy loss also experienced a significantly higher level of depression and anxiety, and

Table 3 The SDS and SAS scores in RPL patients

	n	SDS	*P*	SAS	*P*
Age					
≤ 29	278	36.89 ± 9.21	0.541	33.72 ± 8.34	0.406
30–35	371	37.44 ± 10.57		34.69 ± 9.93	
≥ 36	133	36.38 ± 9.78		34.58 ± 10.25	
BMI					
< 18.5	80	37.98 ± 10.44	0.571	35.58 ± 9.66	0.278
18.5–24	534	36.83 ± 9.93		33.98 ± 8.81	
≥ 24	168	37.37 ± 9.88		34.82 ± 11.16	
Education level					
University and higher	427	36.11 ± 9.72	0.003	33.35 ± 8.56	0.002
Lower education level	355	38.22 ± 10.15		35.51 ± 10.31	
Age of the spouse					
≤ 29	188	37.31 ± 10.45	0.728	33.98 ± 9.45	0.842
30–35	402	37.18 ± 10.04		34.46 ± 9.22	
≥ 36	192	36.58 ± 9.34		34.40 ± 9.96	
Education of the spouse					
University and higher	431	36.54 ± 9.33	0.107	33.99 ± 9.17	0.270
Lower education level	351	37.71 ± 10.68		34.74 ± 9.78	
Duration of marriage (years)					
< 3	198	36.24 ± 10.11	0.177	32.79 ± 9.12	0.007
≥ 3	584	37.35 ± 9.91		34.85 ± 9.51	
Household income (monthly, yuan)					
< 10 000	448	37.93 ± 9.37	0.000	34.73 ± 8.91	0.004
≥ 10 000	334	35.31 ± 9.46		33.21 ± 9.15	
Induced abortion					
Yes	202	38.44 ± 10.52	0.023	35.73 ± 10.50	0.023
No	580	36.59 ± 9.74		33.84 ± 9.01	
Pregnancy loss					
2	443	36.08 ± 9.71	0.038	33.72 ± 9.32	0.471
≥ 3	339	38.35 ± 10.17		35.12 ± 9.58	
Pregnancy loss > 12 weeks					
Yes	159	37.05 ± 9.87	0.567	34.23 ± 9.42	0.420
No	623	37.12 ± 10.39		34.35 ± 9.47	
Live birth					
Yes	77	34.95 ± 8.53	0.027	35.34 ± 11.86	0.422
No	705	37.30 ± 10.09		34.22 ± 9.15	

Table 4 Logistic regression analysis of factors in association with depression and anxiety in RPL patients

	Depression (SDS ≥ 50)		Anxiety (SAS ≥ 50)	
	Adjusted OR[a] (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Pregnancy loss				
2	1			
≥ 3	1.82 (1.15–2.88)	0.011		
Education level				
University or higher	1		1	
Lower education level	1.75 (1.10–2.77)	0.018	1.80 (1.04–3.13)	0.037

[a]Adjusted for: duration of marriage, household income, history of induced abortion and history of previous live birth

we found no significant difference in SDS and SAS score between this group and the RPL group. It has been reported that, in comparison with pregnant women with no history of miscarriage, those with a history of miscarriage (whether sporadic or recurrent) had higher levels of pregnancy-related fear and anxiety state during the first trimester [15]. This study also found that the level of anxiety differed between pregnant women who had experienced a single miscarriage and those who had experienced recurrent miscarriages, as anxiety level in women with one prior miscarriage was markedly elevated until the week of gestation of the prior pregnancy loss and diminished after passing this critical window of time, while no decline in anxiety level was found in pregnant women with two or more prior miscarriages. Perhaps their anxiety had a more generalized pattern or was not as easy to overcome due to several prior experiences of miscarriage. In our study, our participants were not pregnant and who attempted to conceive, so their anxiety was more likely to last for a longer time no matter how many pregnancy losses they have experienced. In addition, women with only a single pregnancy loss who visited the outpatient clinic and entered our study may be more aware of their experience of pregnancy loss and the resulting psychological problems, which made them more motivated to participate. Our results above indicated that attention should be paid to women with a history of pregnancy loss, whether sporadic or recurrent.

Risk factors for depression and anxiety in RPL women

Findings from previous studies regarding risk factors for depression and anxiety in women with RPL are inconsistent, partly due to different sample sizes and the various scales utilized. Craig et al. found that age, cigarette consumption, alcohol intake, previous live birth, number of miscarriages, lateness of miscarriage and length of time since last miscarriage had no effect on the degree of psychiatric morbidity [6]. Other researchers argued that the number of miscarriages contributed to mental health in a negative way. Toffol et al. demonstrated that a high number of miscarriages was associated with worse current state of mood and a higher frequency of a psychiatric diagnosis [14]. Our result revealed that women with three or more pregnancy losses were significantly more depressed than women who experienced two pregnancy losses, and logistic regression analysis suggested that history of three or more pregnancy losses was an independent risk factor for depression in RPL patients. Our studies also demonstrated that history of induced abortion may lead to a higher level of depression and anxiety, while previous studies had different findings [16–19]. No history of live birth is also significantly associated with depression, consistent with the results of former studies [12, 20, 21] which found that women who were involuntarily childless were more likely to be psychologically distressed with complicated grief and poor perceived social support.

Furthermore, we found a significant association between lower education level and higher risk of both depression and anxiety, consistent with findings from a research group from China [22], while another study failed to reach similar conclusions [12]. RPL patients with a lower level of education may not be aware of their disease and have difficulties to follow doctors' orders, especially when some examinations and treatments have to be strict in a certain period of menstrual cycle. Our results also revealed that women with low income had higher SDS and SAS scores. Stressful economic events may be associated with adverse pregnancy outcomes by activating mechanisms such as inflammation, endocrinal system (e.g., corticotrophin-releasing hormone), alcohol consumption and smoking [23].

We also tried to link depression and anxiety level to marital status. Former studies showed that poor quality of marital relationship was significantly associated with impaired psychological adjustment among women [12]. Toedter et al. reported that a strong marital relationship was negatively associated with a woman's grief after pregnancy loss [24]. Our result indicated that women who had been married for 3 years or more had a significantly higher level of anxiety. Otherwise, the anxiety associated with RPL may also have a negative impact on the marital relationship, creating a vicious spiral. We did not find a significant association of depression and anxiety with spouse's age and education. Meanwhile, previous research found that if a husband had a higher educational level, his wife would be less depressive and anxious [22]. This may be because a well-educated husband often can better console and support his wife, and reduce the marital conflict after a pregnancy loss. In regard to depression and anxiety in male partner of RPL women, several studies found that men seemed to be less affected psychologically by RPL than their partners [12, 25], which may lead to a mutual worsening of negative psychological adjustment and marital relationships. It would be an interesting target for future studies on psychological impact in men whose wife experience RPL and how gender difference may affect the quality of marital relationship.

Limitations and strengths

This study was limited by being a single-facility study, and the interval from last pregnancy loss was not included in our questionnaires, which have been reported that it may affect level of depression [26]. Despite these limitations, one of the main strength of this study is its relatively large sample size. The depression and anxiety situation in women with one single pregnancy loss was also analyzed in our study, which was often neglected in previous studies.

Conclusion

RPL patients had a significant higher level of anxiety and depression than women with no history of pregnancy loss. Low educational level (lower than university) can be a risk factor for both anxiety and depression in RPL women, and women with three or more pregnancy losses is an independent risk factor of depression. Low household income, duration of marriage ≥ 3 years, history of induced abortion and no live birth may be potential factors affecting depression and anxiety in patients with RPL. Women with a history of a single pregnancy loss also have a higher tendency of depression and anxiety. Our findings suggested that extra attention and psychological support should be given to patients with pregnancy loss by not only medical professionals, but also their husband, family and society.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest.

Ethical approval This study was approved by the Ethics Review Board of Renji Hospital, School of Medicine, Shanghai Jiaotong University (Ethical vote No. [2014] N034 on 11 Nov 2014).

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