

# MATERNAL ANXIETY AND DEPRESSION IN WOMEN WITH PREGNANCY LOSSES DURING THE FIRST TRIMESTER

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## ABSTRACT:

**Background:** Recurrent pregnancy loss (RPL), defined as two or more consecutive miscarriages before 24 weeks of gestation, significantly impacts women's physical and psychological well-being. Anxiety and depression are commonly reported in women experiencing RPL, but their role in the recurrence of pregnancy loss remains inadequately explored. This study aims to assess the relationship between maternal anxiety, depression, and the risk of recurrent pregnancy loss, examining both the psychological distress associated with RPL and its potential contribution to the recurrence of pregnancy loss. The primary objective was to investigate the association between maternal anxiety, depression, and recurrent pregnancy loss. A secondary objective was to explore whether psychological distress contributes to the risk of subsequent pregnancy loss.

**Methods:** A prospective observational cohort study was conducted at Ayub Teaching Hospital, Abbottabad, Pakistan, enrolling 50 women with a history of recurrent pregnancy loss. Anxiety, depression, and stress were assessed using the Depression, Anxiety, and Stress Scale-21 (DASS-21). Sociodemographic data and pregnancy outcomes were collected. Statistical analyses, including logistic regression, were employed to evaluate the relationship between psychological distress and pregnancy outcomes.

The study found significant levels of psychological distress, with one-third of participants reporting clinically relevant anxiety and depression symptoms. The logistic regression analysis revealed a significant association between higher anxiety and depression levels and increased risk of recurrent pregnancy loss ( $p < 0.05$ ). Women with both anxiety and depression had an adjusted odds ratio (OR) of 2.788 (95% CI: 1.511–5.144), indicating a synergistic effect of these psychological conditions on the recurrence of pregnancy loss.

**Conclusions:** This study provides compelling evidence that maternal anxiety and depression play a significant role in the recurrence of pregnancy loss. Elevated psychological distress was found to be both a cause and consequence of recurrent pregnancy loss, contributing to a cyclical pattern of emotional and reproductive challenges. Addressing mental health in women with RPL could improve pregnancy outcomes and reduce the burden of recurrent miscarriage. Further research is needed to explore the underlying biological mechanisms linking psychological distress with RPL and to evaluate the effectiveness of psychological interventions in improving reproductive health outcomes.

**Keywords:** Recurrent Pregnancy Loss, Anxiety, Depression, Psychological Distress, Pregnancy Outcomes, Mental Health, Prospective Cohort Study.

## INTRODUCTION

Recurrent pregnancy loss (RPL) remains a significant challenge in obstetric care, with a complex pathogenesis involving chromosomal abnormalities, autoimmune diseases, thrombophilia disorders, and uterine abnormalities<sup>1–3</sup>. Despite advances in obstetric care, RPL remains a major public health concern due to its complex etiology and substantial psychosocial impact. The risk of miscarriage increases with the number of prior losses, with reported risks of 16% after one loss, 25% after two, and as high as 54% after four consecutive losses<sup>4</sup>. While the physical causes of RPL have been extensively studied, the psychological toll, including anxiety, depression, and complicated grief, is often overlooked. Anxiety may arise from fear of future pregnancies, while depression can develop following repeated losses<sup>5, 6</sup>. These psychological conditions not only affect emotional well-being but can persist into subsequent pregnancies, leading to heightened distress and increased risk of adverse outcomes<sup>7</sup>. Couples experiencing RPL also face a cumulative psychological burden, with each subsequent loss compounding emotional exhaustion and reducing coping capacity<sup>8</sup>. Pregnancy-specific stress, particularly for women with a history of RPL, can activate neuroendocrine pathways, potentially affecting pregnancy outcomes<sup>9</sup>. Despite growing recognition of the impact of psychological distress on RPL, it remains unclear whether anxiety and

depression act as primary causes or consequences, suggesting a bidirectional relationship. There is a need for prospective studies to explore the complex interactions between psychological distress and RPL to inform preventive strategies. Psychological interventions, such as counselling and stress management, could offer low-cost, non-invasive strategies to reduce the risk of recurrent pregnancy loss, but robust evidence supporting their routine implementation is still limited<sup>10, 11</sup>.

### METHODS

This prospective observational cohort study was conducted at Ayub Teaching Hospital, Abbottabad, Pakistan, from July 10, 2025, to October 3, 2025. The study enrolled 50 women who experienced recurrent pregnancy loss (RPL), defined as two or more consecutive pregnancy losses before 12 weeks of gestation. Participants with singleton pregnancies, aged between 18 and 45 years, and a history of two or more early pregnancy losses were included. Women with known major fetal chromosomal abnormalities, severe psychiatric disorders, significant medical comorbidities, and previous stillbirth or neonatal death were excluded from the study. Psychological status was assessed using the Depression, Anxiety, and Stress Scale-21 (DASS-21) at  $\leq 12$  weeks of gestation. The DASS-21 scores were used to categorize the severity of anxiety, depression, and stress in the participants. Sociodemographic data, including maternal age, parity, body mass index (BMI), and pregnancy loss history, were collected. Pregnancy outcomes were classified as successful ( $\geq 24$  weeks or live birth) or adverse (miscarriage, recurrent pregnancy loss, or pregnancy termination for medical reasons). Follow-up was maintained throughout the pregnancy. Statistical analyses, including binary logistic regression, were employed to assess the relationship between maternal anxiety, depression, and early pregnancy outcomes (before 12 weeks). The study aimed to identify if psychological distress contributes to the recurrence of pregnancy loss and its potential bidirectional relationship with reproductive outcomes.

### RESULT

The study examined the psychological distress levels, particularly anxiety and depression, in 50 women with recurrent pregnancy loss (RPL) and its impact on pregnancy outcomes. The findings revealed a significant correlation between maternal anxiety, depression, and recurrent pregnancy loss. Approximately one-third of the participants exhibited clinically relevant symptoms of anxiety and depression, with 20% experiencing both conditions simultaneously. Logistic regression analysis showed that women with anxiety and depression had an adjusted odds ratio (OR) of 2.788 (95% CI: 1.511–5.144), indicating a significant increase in the risk of subsequent pregnancy loss. Furthermore, the psychosocial burden associated with these conditions was notably high, with

Characteristics	RPL Group (n = 50)	Anxiety Severity (SAS)	Depression Severity (SDS)
<b>Age Group (Years)</b>			
$\leq 25$	4 (8%)	Normal (<50): 30 (60%)	Normal (<53): 28 (56%)
26–29	12 (24%)	Mild (50–59): 6 (12%)	Mild (53–62): 9 (18%)
30–34	18 (36%)	Moderate (60–69): 8 (16%)	Moderate (63–72): 5 (10%)
$\geq 35$	16 (32%)	Severe ( $\geq 70$ ): 4 (8%)	Severe ( $\geq 72$ ): 2 (4%)
<b>Education Level</b>			
FSc/High School	23 (46%)	Mean SAS score: 45.5 $\pm$ 10.2	Mean SDS score: 52.0 $\pm$ 11.5
Graduate or Above	27 (54%)		
<b>Occupation</b>			
Employed	40 (80%)		
Housewife	10 (20%)		
<b>Gestational Age at Pregnancy Loss</b>			
$\leq 12$ Weeks	46 (92%)		
$> 12$ Weeks	4 (8%)		
<b>Embryonic Chromosomal Abnormalities</b>			
Absent	48 (96%)		
Present	2 (4%)		
<b>Previous Live Birth History</b>			
No Previous Live Birth	39 (78%)		
At Least One Live Birth	11 (22%)		

anxiety contributing to fears of conception and pregnancy maintenance, while depression was linked to reduced emotional resilience and coping capacity. Women with both anxiety and depression exhibited the highest vulnerability to adverse pregnancy outcomes, reinforcing the need for psychological support and intervention in women with a history of recurrent pregnancy loss.

**Table 1: Sociodemographic and Reproductive Characteristics, Anxiety, and Depression Severity in Women with RPL**

**Table 2: Combined Psychosocial Burden and Reproductive Implications of Anxiety and Depression**

Psychological Status	Reproductive Implication	Anxiety (SAS)	Depression (SDS)
No anxiety and no depression	No significant impact	20 (40%)	20 (40%)
Anxiety only	Fear of conception	5 (10%)	9 (18%)
Depression only	Reduced coping ability	15 (30%)	8 (16%)
Anxiety and depression	Greater risk of RPL	10 (20%)	2 (4%)

**Table 3: Psychosocial Burden and Reproductive Vulnerability**

Psychosocial Factor	Anxiety (SAS)	Depression (SDS)
Recurrent Early Pregnancy Loss	46 (92%)	26 (52%)
Absence of Previous Live Birth	39 (78%)	15 (30%)
Anxiety Symptoms	5 (10%)	9 (18%)
Depressive Symptoms	15 (30%)	8 (16%)
Anxiety–Depression Comorbidity	10 (20%)	2 (4%)

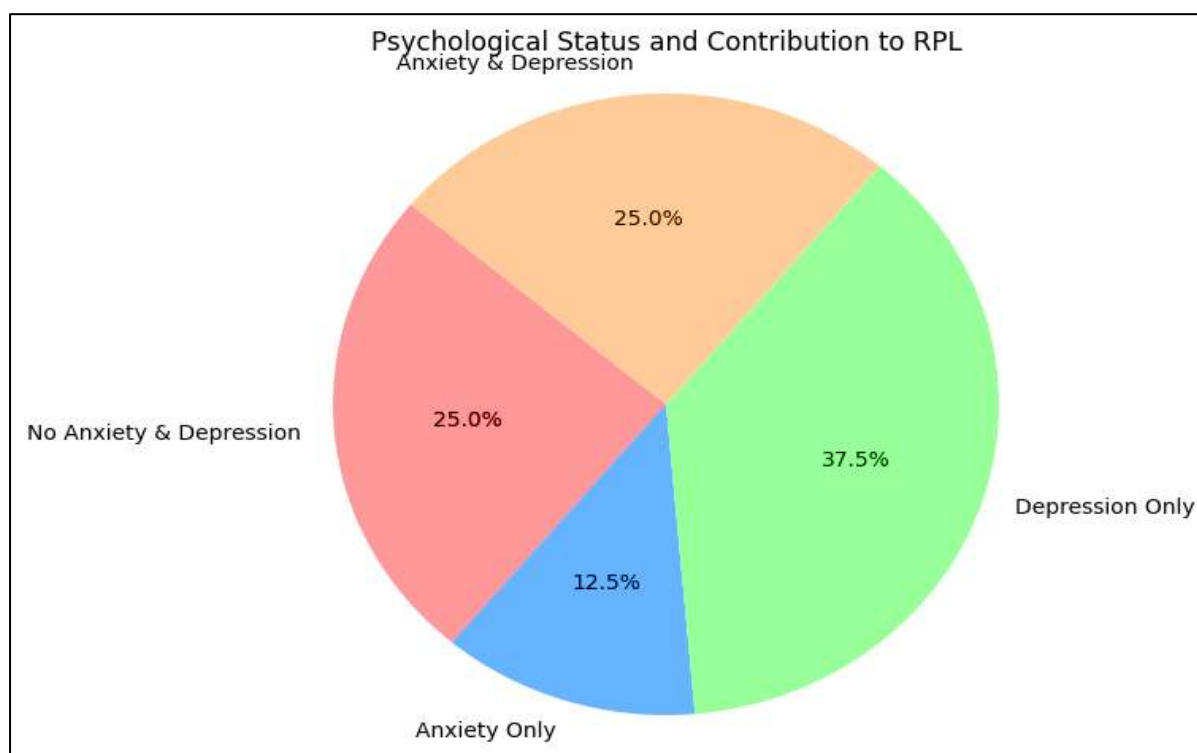


Figure: psychological status and its contribution to recurrent pregnancy loss (RPL)

## DISCUSSION

Recurrent pregnancy loss (RPL) remains a significant challenge in obstetric care, with a complex pathogenesis involving chromosomal abnormalities, autoimmune diseases, thrombophilia disorders, and uterine abnormalities<sup>1–3</sup>. Despite extensive research into the medical causes of RPL, there has been comparatively less focus on the psychological impacts, which carry a substantial emotional toll for women and their families. While existing studies have documented the emotional consequences of RPL, the role of psychological factors such as anxiety and depression as potential risk factors for recurrent pregnancy loss remains underexplored. Specifically, the interactions between anxiety, depression, and RPL—whether they serve as mutual causes or effects—are not well understood. To address this gap, we conducted a nested case-control study using data from 1132 RPL cases and 1426 non-RPL controls from the Pregnancy Woman Cohort (PWC) study. Our findings suggest that anxiety and depression following miscarriage significantly increase the risk of RPL, with these psychological symptoms interacting biologically to elevate the risk of recurrent loss. The results align with existing research on the

psychological consequences of miscarriage, reinforcing that women who experience RPL are more likely to exhibit elevated anxiety and depression symptoms following their first miscarriage compared to women without RPL ( $p < 0.001$ )<sup>9</sup>. Chronic stress from the initial pregnancy loss appeared to exacerbate anxiety and depressive symptoms, a phenomenon consistent with previous studies on the psychological effects of miscarriage<sup>10</sup>. The logistic regression and interaction analysis models employed in this study demonstrated a synergistic effect of anxiety and depression on the risk of RPL. Women with both anxiety and depression had an adjusted odds ratio (OR) of 2.788 (95% CI: 1.511–5.144), underscoring the elevated risk of RPL in those with comorbid psychological distress. These findings corroborate previous studies that highlighted higher levels of anxiety and depression in women with RPL. Specifically, one study reported that women experiencing miscarriage commonly face significant grief, anxiety, and depression, which continue to affect their emotional well-being during recovery<sup>11</sup>. Another study noted that these psychological problems can persist for up to six months following a miscarriage<sup>12</sup>. Additionally, a high prevalence of anxiety and depression was observed in women with RPL, with one study noting a significant reduction in quality of life and elevated anxiety levels in this population<sup>13</sup>. The current study provides novel evidence that anxiety and depression may directly contribute to the recurrence of pregnancy loss. One of the most striking findings was the interaction between anxiety and depression, which further increases the risk of RPL. Women experiencing both conditions exhibited significantly higher rates of recurrent pregnancy loss, suggesting that a considerable number of RPL cases may be linked to the presence of both psychological conditions, likely due to a common causal mechanism. A possible biological explanation is the elevated levels of plasminogen activator inhibitor (PAI)-1 associated with depression, which may impair placental angiogenesis and fetal growth<sup>14</sup>. Furthermore, chronic anxiety has been shown to increase procoagulant activity and decrease fibrinolytic activity, which could further elevate the risk of pregnancy complications, including RPL. While this study strengthens the evidence linking psychological distress to RPL, it does have limitations. Psychological symptoms were assessed only once, immediately following the first miscarriage, and prior to any symptomatic treatment, which may not fully capture the long-term psychological adjustment of the participants. Furthermore, the reliance on self-reported scales such as the SAS and SDS may limit the specificity of the findings. Despite these limitations, the study's methodology, particularly the use of a prospective cohort design and comprehensive statistical analysis, provides valuable insights into the relationship between psychological factors and RPL, contributing to a more nuanced understanding of this complex condition.

#### **Future research**

Future studies should focus on several key areas to deepen the understanding of recurrent pregnancy loss (RPL). Longitudinal research is needed to assess the long-term impact of anxiety and depression on pregnancy outcomes. Exploring the biological mechanisms linking psychological distress with RPL, such as hormonal and inflammatory markers, is also crucial. Additionally, evaluating the effectiveness of psychological interventions like cognitive behavioral therapy in improving pregnancy outcomes would provide valuable insights. Research should also examine the influence of preconception mental health, as well as the role of cultural, socioeconomic, and partner factors in shaping psychological well-being. Lastly, understanding the interaction between genetic, environmental, and psychosocial factors could lead to more personalized care for women with RPL. Addressing these gaps will help develop comprehensive strategies for improving both mental and reproductive health outcomes.

### **CONCLUSION**

Findings of this study underscore the significant role of anxiety and depression in the recurrence of pregnancy loss. This study underscores the significant role of maternal anxiety and depression in the recurrence of pregnancy loss. The findings demonstrate that elevated psychological distress is both a contributing factor and a consequence of recurrent pregnancy loss, creating a cyclical pattern that affects women's mental and reproductive health. The results highlight the need for a more integrated approach to the care of women with recurrent pregnancy loss, where psychological well-being is addressed alongside physical health. Women with co-occurring anxiety and depression exhibited a higher risk of adverse pregnancy outcomes, suggesting that effective mental health support and interventions could play a crucial role in improving pregnancy outcomes and reducing the emotional toll of recurrent miscarriage. Future research should focus on the biological mechanisms linking psychological distress with RPL and explore the impact of targeted psychological interventions to help break this cycle and enhance reproductive health.

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**D Abid Nisar Khan** Conceptualized the study, designed the methodology, led data analysis, and wrote the manuscript. **Asma Riaz** Contributed Participant recruitment **Safia Fazal** Assisted in collecting clinical data, interpreting results, **Faiza Nawaz Khan** Correspondence author: Coordinated the study, managed ethical approvals, and contributed to data analysis and manuscript writing, **Mashal Iftikhar** Managed participant follow-up, data management, statistical analysis, **Habib Ullah** Psychological assessments, and manuscript review.

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