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Relationship between prior pregnancy loss and subsequent adverse pregnancy outcomes in women

Ling Liu[1†], Jian Zhang[1], Ruifang Wang[1,2†], Wei Zhang[1], Kexin Wang[1] and Fang Wang[1*]

Abstract

Pregnancy loss is a prevalent issue among women of childbearing age and can have significant physical and psychological consequences for patients and their families. However, the association between the number of previous pregnancy loss and the risk of adverse pregnancy outcomes (APOs) in subsequent pregnancies remains uncertain. This study aimed to provide clinical data to determine whether the number of previous pregnancy loss increases the risk of APOs in women with a history of pregnancy loss. We conducted a cohort-based, nested case-control study involving 1074 women with a history of pregnancy loss. Detailed demographic and medical history information was collected at baseline, and biological specimens were retained for laboratory testing. APOs were selected as the primary outcome, with cases defined as individuals who experienced any APO events. Cases were matched with event-free control subjects at a 1:2 ratio. Using conditional logistic regression, we examined the relationship between the number of previous pregnancy loss and APO events, using age at first pregnancy as the reference exposure. Among the study participants, we identified 358 cases with APO events and 716 controls. The occurrence of APOs was found to be associated with an increased number of previous pregnancy loss exposures compared to controls without APOs, with an odds ratio (OR) of 1.36 and a 95% confidence interval (CI) of 1.14 to 1.61. This association persisted even after adjusting for patient demographics, the total number of previous pregnancies, and other exposures, with an adjusted odds ratio (aOR) of 1.75 and a 95% CI of 1.28 to 2.4. Furthermore, our study also indicated that age at first pregnancy within a certain range may be a risk factor for APOs. In conclusion, our findings suggest that an increased number of previous pregnancy loss is associated with a higher risk of APOs in subsequent pregnancies among women with a history of pregnancy loss. These results provide valuable clinical data and underscore the importance of considering the number of previous pregnancy loss when assessing the risk of APOs in this population. Additionally, age at first pregnancy may also play a role in APO risk. Further research is warranted to better understand the mechanisms underlying these associations and to develop appropriate interventions to mitigate the risks associated with pregnancy loss.

Keywords Pregnancy loss, Adverse pregnancy outcomes, Previous miscarriages, Risk factors, Cohort study

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Introduction

The global issue of declining birth rates has become increasingly concerning as each year passes [1]. One of the major concerns associated with declining birth rates is the negative impact of adverse pregnancy outcomes (APOs) on fertility [2]. APOs refer to pathological pregnancies and pregnancy complications that deviate from normal live births. These complications affect nearly one in every five live births and have a significant impact on population health and socio-economic development [3]. Studies from a specialized hospital in India have reported a high prevalence of 28.3% of adverse pregnancy outcomes [3]. Pathological pregnancies encompass various conditions such as spontaneous abortion, stillbirth, ectopic pregnancy, preterm birth, low birth weight babies, macrosomia, and birth defects. Pregnancy complications include gestational diabetes, gestational hypertension, intrahepatic cholestasis, and anemia.

Although advancements in maternal and child healthcare systems have led to a significant decrease in maternal stillbirth rates over the past five decades, there is a growing recognition of the occurrence of APOs and their adverse effects on both the mother and the fetus [4]. The incidence rates of each subtype of APO have shown a significant increase from 2014 to 2019 [5]. Adverse pregnancy outcomes not only contribute substantially to maternal mortality but also serve as a key risk factor for cardiovascular events in postpartum individuals and can lead to poor growth and development in offspring [6]. Therefore, it is essential to explore the risk factors associated with APOs and implement early interventions targeting high-risk groups in the fields of perinatal medicine and public health [7].

In this study, 'pregnancy loss' refers to the spontaneous loss of a clinically recognized pregnancy before the fetus reaches viability, encompassing both embryonic and fetal deaths. 'Multiple pregnancy loss' or 'Recurrent Pregnancy Loss (RPL)' is defined as two or more such consecutive or non-consecutive losses, as per the updated criteria from international societies such as the ESHRE. RPL, defined as two or more failed clinically recognized pregnancies, is a distressing reproductive disorder affecting 1–5% of couples trying to conceive. The etiology is multifactorial and often unexplained, posing significant challenges in clinical management [8]. Despite the controversy surrounding the pathogenesis and etiology of RPL, the prognosis for women experiencing RPL is generally favorable, as evidenced by successful repeat pregnancies and fetal deliveries [9]. However, the association between multiple pregnancy loss and adverse pregnancy outcomes remains inconclusive. Therefore, this article aims to examine the relationship between multiple pregnancy loss and the occurrence of adverse pregnancy outcomes, providing valid scientific evidence for the clinical management of couples who have experienced RPL.

Methods

Population

Between September 2019 and February 2022, we conducted a rigorous retrospective cohort study with a nested case-control analysis involving women with a history of pregnancy loss who attended the Department of Reproductive Medicine at the Second Hospital of Lanzhou University. The follow-up of pregnancy outcomes was carried out by trained obstetric and gynecological healthcare providers using telephone interviews and access to obstetric delivery history records. The case group consisted of pregnant women who experienced adverse pregnancy outcomes during the follow-up period, while the control group included women who had normal spontaneous deliveries without any adverse events. At the time of enrollment, we collected detailed demographic characteristics, previous pregnancy history, and laboratory test results from all participants. To ensure the study's validity, we excluded women with multiple pregnancies, pre-existing chronic diseases such as diabetes mellitus, hypertension, or heart diseases, those who were lost to follow-up or had incomplete data, and those who were already pregnant at the time of consultation. Out of 1,955 women initially assessed for eligibility, a total of 1,489 women were recruited for this study. Ultimately, 358 cases of adverse pregnancy outcomes were included in the case group, and 716 controls without adverse pregnancy outcomes were randomly selected from the cohort, matching them with the case group based on age within a ± 2-year range. This resulted in a nested case-control study design with a 1:2 frequency matching. Please refer to Fig. 1 for a visual representation of the study selection process.

This study adhered to the principles outlined in the Declaration of Helsinki. Approval was obtained from the Research Ethics Committee of the Second Hospital of Lanzhou University (approval number [NO.2019 A-231]), and written consent was obtained from all participating women.

Outcomes

The primary outcome for this study was a composite of APOs, defined as the occurrence of one or more of the following in the subsequent pregnancy: preeclampsia, gestational hypertension, gestational diabetes mellitus (GDM), preterm delivery (gestational age < 37 weeks), delivery of a neonate with low birth weight (LBW, < 2500 g), placental abruption, or stillbirth.

The association between a history of abortion and subsequent APOs is complex and may not be causal. observed associations could be influenced by shared

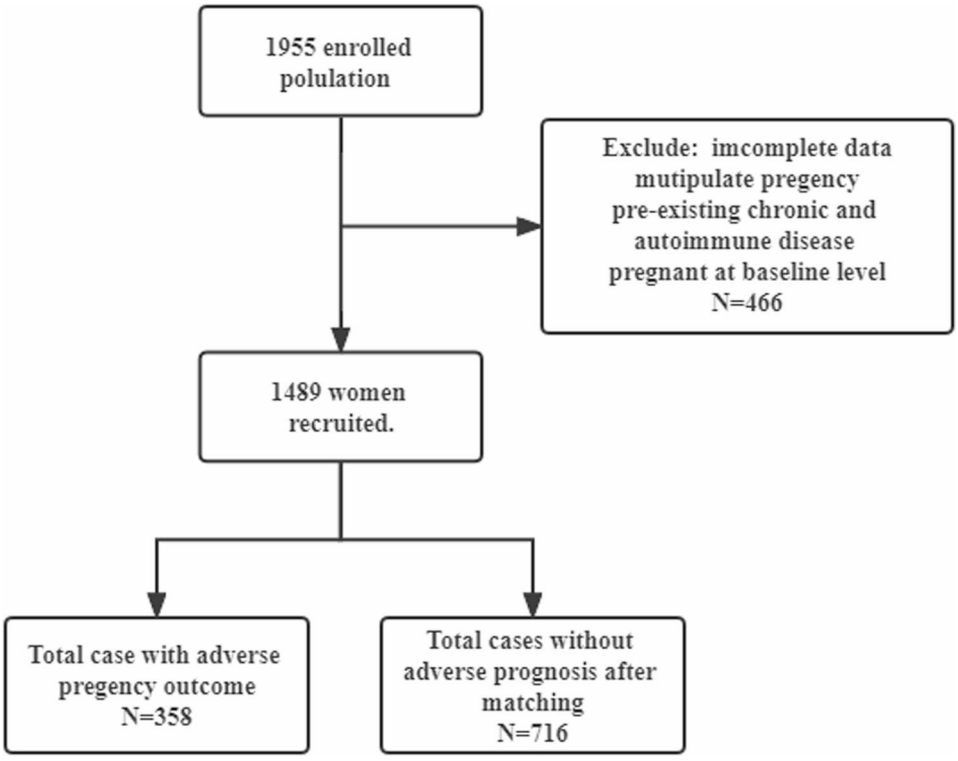

Fig. 1 Study flowchart for identifying case patients

underlying risk factors or confounding variables. However, several physiological mechanisms have been hypothesised in the literature to explain a potential link [10–12]:

- For Induced Abortion: If the exposure is induced abortion, potential mechanisms include iatrogenic injury. For example, surgical procedures could theoretically lead to cervical insufficiency (increasing risk of preterm birth) or uterine adhesions (Asherman's syndrome) (potentially impairing placentation and increasing risk of placental abnormalities or fetal growth restriction).
- For Pregnancy Loss (Miscarriage): If the exposure is spontaneous pregnancy loss, the association may be driven by shared underlying pathologies. For instance, undiagnosed metabolic disorders (e.g., insulin resistance) could predispose women to both miscarriage and later gestational diabetes. Similarly, thrombophilias or autoimmune conditions (e.g., antiphospholipid syndrome) are established causes of pregnancy loss and are also risk factors for placental-mediated complications like preeclampsia, abruption, and fetal growth restriction.

It is critical to note that correlation does not imply causation. A woman's history of abortion may be a marker of her underlying reproductive health status rather than the direct cause of a future adverse outcome. This study aims to quantify the epidemiological association while acknowledging the need for further research to elucidate any causal pathways.

Additionally, the diagnosis of gestational diabetes mellitus (GDM) was conducted using the 75-g oral glucose tolerance test, in accordance with the guidelines set forth by the International Association of Diabetes and Pregnancy Research Groups (IADPSG) [13].

Statistical analysis

We indicated continuous variables as mean (standard deviation) categorical variables are indicated as number with proportion. Differences between groups were assessed using Kruskal–Walli's test for continuous variables, or chi-square test for categorical variables. To examine the correlation between exposure and APO, we use the lowest groups as the reference group for all subjects, conditional logistic regression analysis was performed to assess the ORs and 95% CIs for the risk of adverse maternal and fetal pregnancy outcomes. Baseline variables that were considered clinically relevant or that showed a univariate relationship with outcome were entered into multivariable adjusted model including non-adjusted model (no covariates were adjusted), minimally-adjusted model (only Sociodemographic variables were adjusted) and fully-adjusted model (covariates presented in Table 1 were adjusted). Effect sizes with

Table 1 Comparison of characteristics between no-APO and APO groups

Variables	Total (*n* = 1074)	no-APO (*n* = 716)	APO (*n* = 358)	*p*
Age (years)				0.244
≤ 25	70 (6.5)	53 (7.4)	17 (4.7)	
25 ~ 29	553 (51.5)	367 (51.3)	186 (52)	
≥ 30	451 (42.0)	296 (41.3)	155 (43.3)	
Pre-pregnancy BMI (kg/m2)				0.486
<18.5	89 (8.4)	63 (8.9)	26 (7.4)	
18.5 ~ 22.9	591 (56.0)	399 (56.6)	192 (54.7)	
23 ~ 24.9	200 (18.9)	125 (17.7)	75 (21.4)	
≥ 25	176 (16.7)	118 (16.7)	58 (16.5)	
Education level				0.011
College and above	346 (33.9)	249 (36.6)	97 (28.5)	
High school and under	675 (66.1)	432 (63.4)	243 (71.5)	
Ethnic origin				0.106
Han	952 (89.4)	627 (88.3)	325 (91.5)	
Others	113 (10.6)	83 (11.7)	30 (8.5)	
Menstrual regularity				0.578
Regular	845 (79.4)	562 (78.9)	283 (80.4)	
Irregular	219 (20.6)	150 (21.1)	69 (19.6)	
Age of first menstruation (years)	13.6 ± 1.3	13.6 ± 1.3	13.5 ± 1.2	0.112
Age of first pregnancy(years)	26.1 ± 3.7	25.9 ± 3.7	26.6 ± 3.5	0.002
Age of first pregnancy group				0.007
≤ 25	409 (38.8)	291 (41.7)	118 (33.1)	
≥ 26	645 (61.2)	407 (58.3)	238 (66.9)	
Number of pregnancies				0.115
1	244 (22.7)	174 (24.3)	70 (19.6)	
2	419 (39.0)	266 (37.2)	153 (42.7)	
≥ 3	411 (38.3)	276 (38.5)	135 (37.7)	
Number of pregnancy loss				< 0.001
1	408 (38.0)	300 (41.9)	108 (30.2)	
2	443 (41.2)	280 (39.1)	163 (45.5)	
≥ 3	223 (20.8)	136 (19)	87 (24.3)	
Types of pregnancy loss				0.031
Primary	828 (77.1)	538 (75.1)	290 (81)	
Secondary	246 (22.9)	178 (24.9)	68 (19)	

Differences between groups were assessed using chi-square test for categorical variables

BMI Body mass index

95% confidence intervals were estimated. The restricted cubic spline method, a commonly used nonparametric approach in statistical modeling, was employed to capture the nonlinear relationship between the continuous independent variable and the dependent variable. This method involves placing multiple knots within the range of the independent variable and fitting cubic polynomials between adjacent knots, allowing for the modeling of nonlinear relationships. In this study, the restricted cubic spline analysis was employed to examine the association between the age at first pregnancy and the risk of adverse pregnancy outcomes.

To test the robustness of our results, we performed a sensitivity analysis. We converted age of first pregnancy into a categorical variable according to the APO, and calculated the P for trend in order to verify the results of age of first pregnancy as the continuous variable, and to examine the possibility of nonlinearity. Data were analyzed using the statistical software packages R (http://www.R-project.org, The R Foundation) and Empower Stats (http://www.empowerstats.com, X&Y Solutions, Inc, Boston, MA). All statistical tests were 2-sided, and a P-value < 0.05 was considered statistically significant.

Results

Participant characteristics

The demographic and clinical characteristics were presented in Table 1. The study included 1074 pregnant women as participants, with an average age at first pregnancy of 26.1 years. Among the participants, 346 cases (33.9%) had less than a high school education, while 675 cases (66.1%) had a college education or higher. Regarding their pregnancy history, 244 cases (22.7%) had one previous pregnancy, 419 cases (39.0%) had two previous pregnancies, and 411 cases (38.3%) had three or more previous pregnancies. It is important to note that all participants had prior experience with pregnancy loss due to the nature of the cohort study. Specifically, 408 cases (38.0%) had experienced one pregnancy loss, 443 cases (41.2%) had experienced two pregnancy loss, and 223 cases (20.8%) had experienced three or more pregnancy loss. Furthermore, 828 cases (77.1%) had a primary pregnancy loss. The majority of the subjects, 952 individuals (89.4%), were Han Chinese women, while the remaining 113 subjects (10.6%) belonged to other ethnic minorities.

Distribution of adverse pregnancy outcomes in women with a history of pregnancy loss

As depicted in Fig. 2, the analysis encompassed a total of 358 participants, among whom 286 cases were classified as single APO, denoting instances where only one APO event occurred. Additionally, there were 72 cases of compound APO, defined as the presence of two or more APO events within the same participant. The cumulative frequency of APO events amounted to 460, with the distribution as follows: 161 cases of pregnancy loss, 51 cases of amniotic fluid problems (including amniotic fluid contamination, excessive amniotic fluid, low amniotic fluid, etc.), 48 cases of preterm delivery, 38 cases of intrauterine fetal distress, 31 cases of gestational diabetes, 27 cases of LBW, 22 cases of anemia, 21 cases of pre-eclampsia (PE) or pregnancy-induced hypertension, 16 cases of macrosomia, 16 cases of placental problems (including placenta previa, placental abruption, etc.), 13 cases of premature

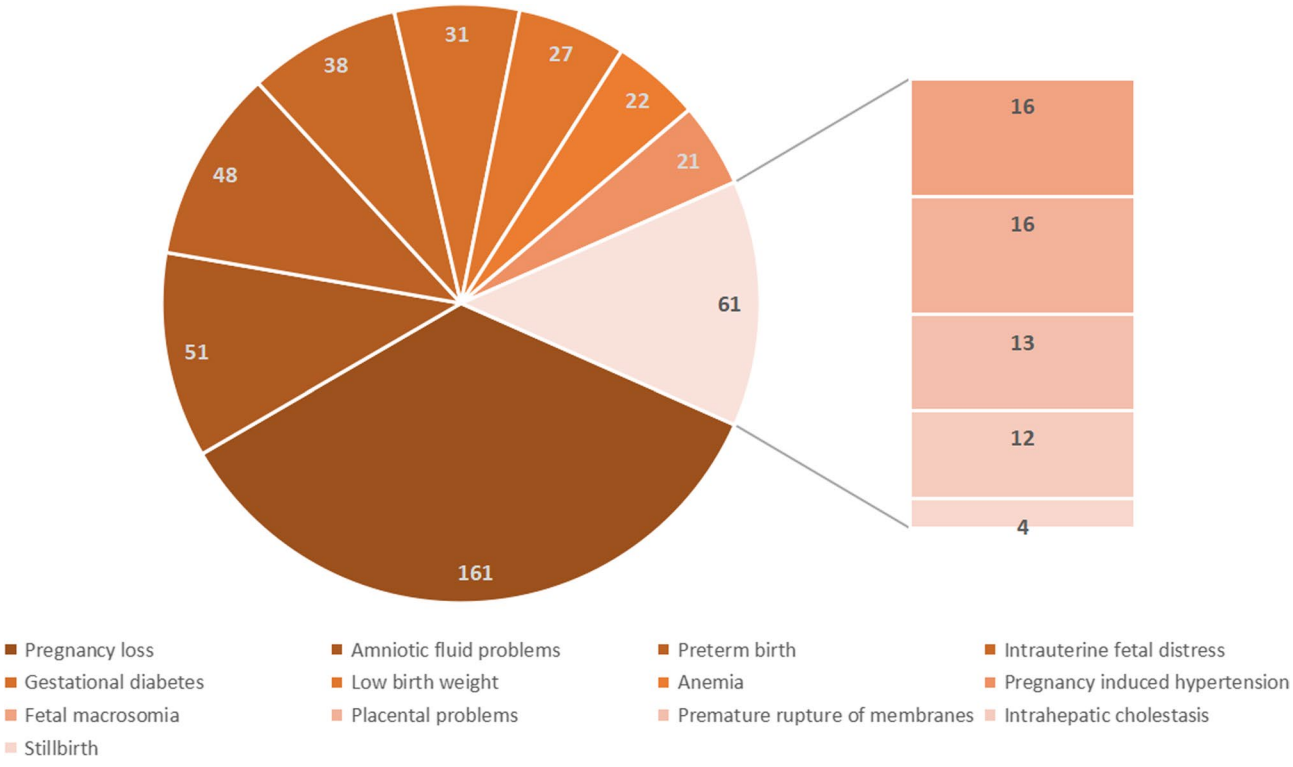

Fig. 2 Distribution of adverse pregnancy outcomes in women with a history of pregnancy loss

Table 2 Association of regency loss and APO

Exposure	Unadjusted OR (95%CI)	*P*	Model1 OR (95%CI)	*P*	Model2 OR (95%CI)	*P*
Number of pregnancy loss						
1	1		1		1	
2	1.62 (1.21 ~ 2.17)	0.001	1.56 (1.15 ~ 2.11)	0.004	1.96 (1.26 ~ 3.05)	0.003
≥ 3	1.78 (1.26 ~ 2.52)	0.001	1.72 (1.23 ~ 2.47)	0.003	3.03 (1.61 ~ 5.71)	0.001
Trend. Test	1.36 (1.14 ~ 1.61)	< 0.001	1.33 (1.12 ~ 1.59)	0.002	1.75 (1.28 ~ 2.46)	< 0.001
Education level						
College and above	1		1		1	
High school and under	1.44 (1.09 ~ 1.92)	0.011	1.41 (1.04 ~ 1.91)	0.025	1.33 (0.97 ~ 1.81)	0.076
Age of first pregnancy(years)	1.06 (1.02 ~ 1.09)	0.002	1.06 (1.01 ~ 1.14)	0.014	1.05 (1.00 ~ 1.15)	0.035
Age of first pregnancy group						
≤ 25	1		1		1	
≥ 26	1.44 (1.17 ~ 1.88)	0.007	1.26 (1.00 ~ 1.72)	0.147	1.27 (1.04 ~ 1.76)	0.049

APO indicates adverse pregnancy outcome

logistic regression analysis was performed to assess the ORs and 95% CIs for the risk of adverse maternal and fetal pregnancy outcomes

Model 1: adjustment was made for age, BMI, education, ethnics

Model 2: adjustment was made for age, BMI, education, ethnics, menstrual regularity, Number of pregnancy, Types of pregnancy loss

OR Odds ratio, *CI* Confidence interval

*Indicates that the average annual percent change is significantly different from 0 at the α = 0.05 level

rupture of membranes, 12 cases of intrahepatic cholestasis during pregnancy, and 4 cases of stillbirth.

Association of pregnancy loss and adverse pregnancy outcomes

In the initial analysis, there was a clear association between the risk of APO and the number of previous pregnancy loss. Specifically, women with two previous pregnancy loss had an increased risk of APO (odds ratio [OR], 1.62; 95% confidence interval [CI], 1.21–2.17), while women with three or more previous pregnancy loss had an even higher risk of APO (OR, 1.78; 95% CI, 1.14–1.61). Importantly, this increased risk remained significant even after adjusting for demographic factors, menstrual regularity, and pregnancy history (Table 2). Furthermore, the association between the number of

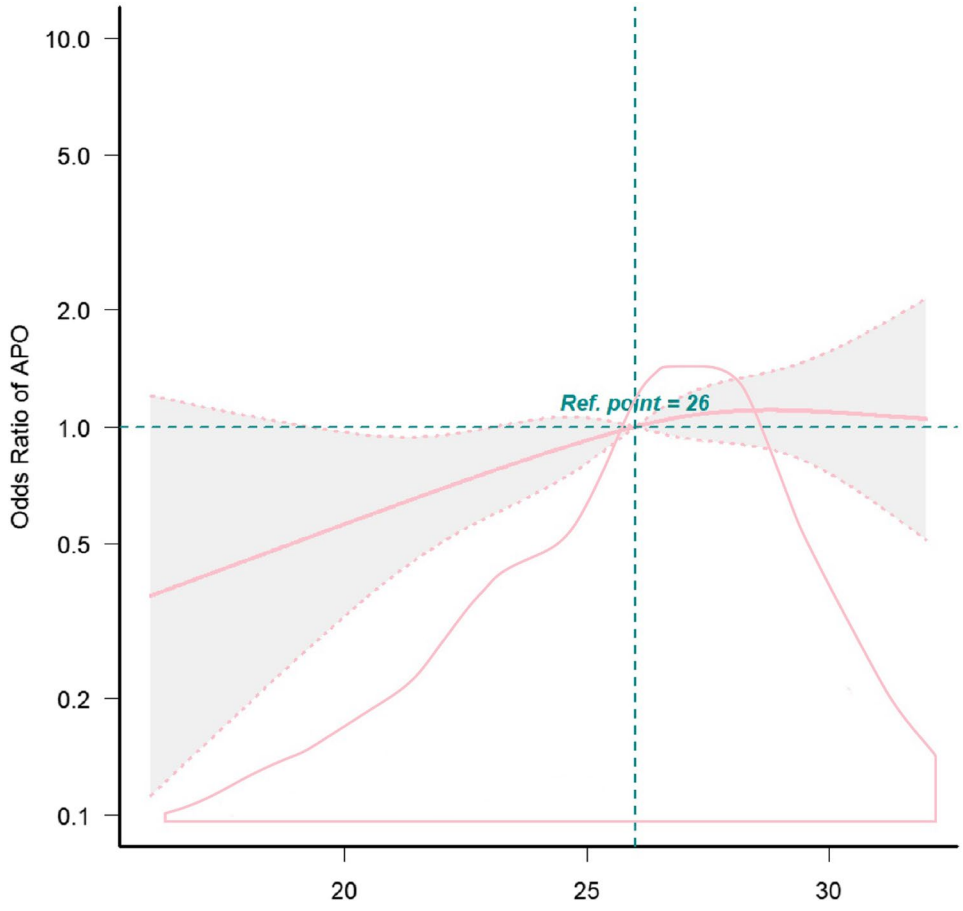

Fig. 3 Association of the first pregnancy age and OR of adverse pregnancy outcomes (adjustment was made for age, BMI, education, ethnics)

previous pregnancies and the risk of APO remained consistent across all three models (model 1 and model 2), indicating a stable relationship. Additionally, these associations exhibited a statistically significant trend ($P < 0.001$).

Association of the first pregnancy age and adverse pregnancy outcomes

To assess the nonlinear association between age at first pregnancy and adverse pregnancy outcomes, we employed a restricted cubic spline analysis to plot the odds ratios (ORs) and 95% confidence intervals (CIs) for the entire sample. The results demonstrated a significant correlation between age at first pregnancy and adverse pregnancy outcomes. The spline curve exhibited a zenith at the age of 26.3 years, with a long tail on the right side, indicating a non-linear relationship (Fig. 3). This finding aligns with the results of the univariate analysis, which identified an increased age at first pregnancy as a risk factor for adverse pregnancy outcomes (OR 1.06, 95% CI 1.02–1.09). Furthermore, when stratified by age at first pregnancy, women aged 26 years or older at the time of their first pregnancy exhibited a higher risk of adverse pregnancy outcomes compared to those who were younger at the time of their first birth (OR, 1.44; 95% CI, 1.1–1.88).

Discussion

Global data indicates that approximately 42 million miscarriages occur each year [14]. In China, there are an estimated 13 million cases of pregnancy loss annually, with a high repeat miscarriage rate of 55.9% and a trend towards younger age groups [15]. Research has shown that over 80% of women who have experienced a miscarriage will become pregnant again [16]. However, previous miscarriages may result in cervical functional changes, leading to ineffective cervical closure and increased risks of preterm birth and miscarriage [17]. Studies have also suggested that previous miscarriages can induce abnormal immune system reactions, leading to fetal rejection responses and increased risks of pregnancy complications [18]. Additionally, literature reports have highlighted psychological issues such as anxiety and depression in women who have experienced previous miscarriages, which may impact pregnancy outcomes [19]. Nested case-control studies are commonly used to

investigate the relationship between specific exposure factors and particular diseases. They contribute to a better understanding of the mechanisms and influencing factors involved in disease occurrence, thus guiding the development of prevention, diagnosis, and treatment strategies. This study aims to explore the causal relationship between previous miscarriages and adverse pregnancy outcomes by conducting a nested case-control study on factors influencing adverse pregnancy outcomes in women with previous miscarriages. The findings will assist healthcare teams in clinically assessing the risks of women with previous miscarriages and implementing targeted intervention measures to reduce the occurrence of adverse pregnancy outcomes.

In this study, we aimed to provide a comprehensive overview of the composition and incidence of adverse pregnancy outcomes in northwest China. Among the observed adverse pregnancy outcomes, the most prevalent ones were amniotic fluid abnormalities, preterm delivery, intrauterine distress, and pregnancy loss. These findings are in Line with previous studies on pregnancy outcomes, such as the 2019 birth data [20].Previous studies have focused more on the impact of poor lifestyle habits during pregnancy on pregnancy outcomes, such as Excessive gestational weight gain (GWG) [21], early pregnancy BMI [22], blood lipid, dietary balance, sleep quality, activity tolerance, etc [23, 24]. However, the impact of a previous adverse maternal history on subsequent re-pregnancy is also of concern, and early reminders of a prepared pregnancy in patients with a history of pregnancy loss can reduce many of these risks [25]. While the majority of women who experience a pregnancy loss proceeds to have a successful full-term pregnancy, it is noteworthy that a history of previous pregnancy loss is linked to an increased risk of adverse outcomes in subsequent pregnancies. These outcomes encompass preterm birth, fetal growth restriction, and various other obstetric complications [26]. It is important to note that the number and outcomes of pregnancies experienced by a woman significantly influence her overall health status. However, there is no published research comparing the patterns of subsequent pregnancy outcomes following a live birth, natural fetal loss, or pregnancy loss. Women experiencing repeated pregnancies and subsequent pregnancy loss are subjected to an increased exposure to hemorrhage and infection, the major causes of maternal mortality, and other adverse consequences resulting from multiple separation events [27].We hypothesize that this may be the main reason for the altered disease spectrum of adverse pregnancy outcomes. In addition, we found that the total number of previous pregnancies did not increase the risk of adverse pregnancy outcomes, however, the number of previous pregnancy loss (multiple pregnancy loss) was a risk factor for adverse pregnancy outcomes. A recent study noted that number, gestational age, and recency of pregnancy loss at first parity were associated with adverse pregnancy outcomes in U.S. women [28]. A recent meta-analysis of risk factors for adverse pregnancy outcomes in Chinese women showed that the number of pregnancies, education, gestational diabetes mellitus, and age were significantly associated with adverse pregnancy outcomes in Chinese women [29], which is also in good agreement with our findings. In China, with the popularization of the two- and three-child policy, the maternal age has increased significantly [30, 31]. Poor maternal history in advanced maternal age has also become an important concern in maternal and child health care, and the number of previous pregnancy loss appears to be the only prognostic factor significantly associated with time to live birth in subsequent pregnancies [32]. and our study may provide a scientific suggestion for their concerns. At the same time, it may provide some reference for individualized clinical guidance and care protocols for the recurrent pregnancy loss population to help them achieve reasonable fetal preservation throughout pregnancy until live birth. This not only helps to increase the live birth rate of the fetus, but also reduces maternal mortality and improves the effectiveness of maternal and child health care [33].

Multiple pregnancy loss is above all a difficult area in reproductive medicine because its causes are often unknown and diagnostic and therapeutic strategies are based on scarce evidence [34, 35]. Chinese Government will allow up to three children per couple will do little to boost startlingly low fertility rates [36] In addition to encouraging couples of childbearing age to increase the number of hospitals where they have children, we hope to focus on more potential risk factors that may jeopardize the fertility of women of childbearing age, and to call attention to the importance of fertility preservation for couples of childbearing age and to alleviate the stresses that they may face in the process of childbearing. We will continue to focus on patients with recurrent pregnancy loss in future studies and complete more large-sample, multicenter clinical studies.

This study has several limitations that should be acknowledged. First, despite our efforts to adjust for known confounders, the possibility of residual confounding cannot be entirely ruled out due to the observational nature of our study. For instance, we were unable to account for certain potentially important variables such as detailed lifestyle factors (e.g., smoking, alcohol consumption, stress levels), environmental exposures, or undiagnosed thrombophilic or immunological markers, which might influence both the risk of RPL and subsequent APOs. Second, the sample size, although substantial, was relatively limited and predominantly drawn from a single region in Northwest China, which may affect the

generalizability of our findings to other ethnic or geographic populations. Future research with larger, multicenter, and more diverse cohorts is warranted to enhance the statistical power and external validity of the results. Furthermore, the definition and classification of pregnancy loss relied on medical records and patient recall, which might be subject to misclassification bias. Finally, while we identified a significant association between the number of prior losses and APO risk, our study design cannot definitively establish causality, and the underlying biological mechanisms require further elucidation through more targeted mechanistic studies.

Conclusion

In conclusion, this retrospective cohort study with a nested case-control analysis demonstrates that among women with a history of pregnancy loss, the number of prior spontaneous pregnancy losses is significantly associated with an increased risk of adverse outcomes in a subsequent pregnancy. Specifically, a higher number of previous losses was correlated with greater odds of experiencing an APO, suggesting a potential dose-response relationship. Additionally, a lower education level and an older age at first pregnancy were identified as significant risk factors in this population. These findings underscore the importance of a detailed obstetric history, including the number of prior pregnancy losses, for the risk stratification and clinical management of women seeking pregnancy after RPL. Enhanced prenatal monitoring and tailored interventions should be considered for these high-risk individuals. Future large-scale, prospective studies are needed to validate these associations, explore the underlying causal pathways, and develop effective strategies for improving pregnancy outcomes in this vulnerable group.

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Authors' contributions
Ling Liu and Fang Wang planned and designed the study. Ling Liu and Jian Zhang collected the data. Ruifang Wang and Wei Zhang performed the analysis. Ling Liu and Kexin Wang interpreted the results. Ling Liu and Fang Wang contributed to writing the manuscript. All the authors reviewed and approved the final manuscript.

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Data availability
The data that support the findings of this study are openly available in Fig share at https://doi.org/10.6084/m9.figshare.23625243, reference number 23625243.

Declarations

Ethics approval and consent to participate
Ethics approval and Consent to participate" section- "This study adhered to the principles outlined in the Declaration of Helsinki. Approval was obtained from the Research Ethics Committee of the Second Hospital of Lanzhou University (approval number [NO.2019 A-231]), and written consent was obtained from all participating women.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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