Published Online: 6 July 2026 eISSN 2984-8644

https://doi.org/10.70552/pjaai.26.1.15979

ORIGINAL ARTICLE

Philippine Journal of Allergy, Asthma and Immunology

Predictors of Pregnancy Outcomes in Women with Immunologic Causes of Recurrent Pregnancy Loss: A Retrospective Study at the Philippine General Hospital (2018-2022)

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ABSTRACT

Introduction: Recurrent pregnancy loss (RPL) affects 1-5% of couples and has a significant consequence on the couple's relationship and quality of life. Various studies have concluded that the predictors of good pregnancy outcomes include younger age during pregnancy, normal BMI, and no history of any thyroid and autoimmune-related diseases.

Objective: This study aims to identify the predictors of good fetal outcomes in pregnant women with RPL seen at the Philippine General Hospital.

Methodology: This is a retrospective study that reviews the different factors that may have a bearing on the outcome of pregnant patients with a history of recurrent pregnancy loss admitted and referred to the Division of Allergy and Immunology for co-management over a span of five years (2018-2022). A total of 173 patient charts were retrieved and analyzed.

Results: A total of 173 gathered charts of pregnant women were included in this study. The study population comprised mostly 31-40 years old (n = 105), married (56.6%), and unemployed (57.2%) women. In terms of clinical profile, the substantial majority had a normal BMI before pregnancy (91.2%), RPL diagnosis was obtained during a prior pregnancy (59.1%) and 47.1% of patients were gravida 4 or higher. The statistical analysis utilizing Fisher's exact test showed a significant association between maternal age and the birth outcomes – 'stillbirth' and 'term' births. Marital status also showed a significant association with primary outcomes studied at $p = 0.041$. Among the factors examined, pre-pregnancy BMI status ($p = 0.004$) emerged as the sole significant predictor of the primary fetal outcome. On the other hand, maternal age ($p = 0.017$), timing of RPL diagnosis ($p = 0.03$), and gravidity ($p = 0.003$) emerged as significant predictors of the secondary fetal outcome.

Conclusion: The findings in this study underscore the multifactorial nature of the risk factors for the primary outcome occurring among pregnant women diagnosed with RPL. Factors such as maternal age, timing of RPL diagnosis, pre-pregnancy BMI status, and gravidity play crucial roles in predicting the likelihood of primary and secondary outcomes and guiding clinical management strategies. Understanding and addressing these factors can help healthcare providers optimize prenatal care and improve pregnancy outcomes for women affected by RPL

Keywords: miscarriage, predictors, recurrent pregnancy loss

INTRODUCTION

Background of the study

Recurrent pregnancy loss (RPL) affects 1-5% of couples and has a significant consequence on a couple's relationship and quality of life. The World Health Organization (WHO) defines RPL as having three or more consecutive pregnancy losses before the 20th-week gestation, while the American Society for Reproductive Medicine (ASRM) defines RPL as two pregnancy losses with clinical evidence of pregnancy (sonographic or histopathological evidence of pregnancy).[1] A subset of RPLC cases is associated with immunologic causes, including antiphospholipid antibody syndrome (APAS), autoimmune diseases (such as anti-thyroid antibody and anti-nuclear antibody positivity), HLA compatibility issues, and high NK cell counts. These conditions are often overlooked, as patients with RPL are typically only screened for APAS, leaving many immunologic causes undiagnosed.

Early studies, such as those by Gleicher and El-Roeiy, first defined reproductive autoimmune failure syndrome (RAFS), suggesting that autoimmune activity can lead to pregnancy failure, particularly through impaired immune tolerance toward the fetus during pregnancy.[2] Women with abnormal immune responses are at higher risk of miscarriage, and this failure can occur at any stage of pregnancy, depending on the immune triggers involved. This study focuses on women with RPL who have identified immunologic causes, including the conditions mentioned above and aims to identify predictors for good pregnancy outcomes.

Several studies have pointed to key factors affecting pregnancy outcomes in women with RPL. Maternal age, body mass index (BMI), and thyroid autoimmunity are well-established risk factors for miscarriage and adverse pregnancy outcomes.[3,4] Advanced maternal age, particularly over 35 years, is linked with increased risks of miscarriage and stillbirth.[5] Similarly, an elevated BMI (>25) has been identified as a risk factor for pregnancy loss.[3] In the context of immunologic causes, recent studies have highlighted the link between autoimmune conditions with an increased risk of miscarriage.[6] However, a significant knowledge gap remains in understanding how other immunologic conditions, such as high NK cell count or HLA compatibility issues, contribute to pregnancy loss, particularly in low- and middle-income countries where these causes are often underexplored.

Despite advancements in the understanding of reproductive immunology, there remains a limited knowledge regarding immune factors that contribute to RPL and pregnancy outcomes.[6] Currently, RPL patients are only screened for antiphospholipid syndrome; consequently about 50% of RPL cases remain undetected.[1] This study aims to identify the predictors of good pregnancy outcomes in women with RPL who have been evaluated for a variety of immunologic causes, including APAS, autoimmunity, high NK cell count, and HLA compatibility. The patients in this study were comanaged by the Division of Allergy and Immunology at the Philippine General Hospital (PGH), providing a unique opportunity to assess the role of comprehensive immunologic evaluation in improving pregnancy outcomes.

Significance of the study

Immunologic etiologies of RPL remain underrecognized and undertreated, particularly in low-resource settings. At the PGH, referrals for immunologic evaluation are infrequent, potentially delaying appropriate interventions. This study underscores the value of timely diagnosis and co-management with immunology specialists. By delineating predictors of favorable outcomes in patients with immunologic RPL, we aim to advocate for evidence-based, interdisciplinary care pathways that may improve live birth rates and neonatal outcomes in this vulnerable population.

OBJECTIVES

This study aims to identify predictors of favorable pregnancy outcomes among women with immunologic causes of recurrent pregnancy loss seen at the PGH from 2018 to 2022. It seeks to describe the demographic and clinical profiles of these patients, including maternal age, gravidity, and timing of diagnosis. Furthermore, the study aims to determine the associations between these characteristics and pregnancy outcomes such as live birth, gestational age, and birthweight. Additionally, it evaluates the impact of immunologic diagnosis and the timing of immunologic treatment on pregnancy outcomes. Lastly, the study identifies significant predictors of primary outcomes, specifically live birth, as well as secondary outcomes, including term birth and appropriate birth weight.

METHODOLOGY

Study approach and research setting

This retrospective cohort study was conducted at the Philippine General Hospital (PGH), Manila. Medical records from January 2018 to December 2022 were reviewed to evaluate pregnancy outcomes in women with immunologic causes of RPL. The study population included patients co-managed by the hospital's Perinatology Service and Division of Allergy and Immunology.

Study population

The study included pregnant women with a documented history of RPL, defined as two or more pregnancy losses (whether consecutive or not) prior to 20 weeks' gestation, who were evaluated and managed for suspected immunologic etiologies. Immunologic causes included antiphospholipid antibody syndrome (APAS), autoimmune thyroid disease (positive anti-TPO antibodies), antinuclear antibodies (ANA), human leukocyte antigen (HLA) incompatibility, and/or elevated peripheral natural killer (NK) cell counts.

Patients with identifiable non-immunologic causes of RPL, such as fetal aneuploidy, uterine anomalies, thrombophilias unrelated to APAS, cervical insufficiency, or placental causes; or incomplete outcome data were excluded.

Sample size and sample technique

Based on an estimated population of 376 RPL patients evaluated during the study period, a minimum sample size of 174 was calculated using the Slovin formula with a 95% confidence level and a 5% margin of error. Due to incomplete data and exclusion criteria, 159 eligible patients with complete records were consecutively sampled and included in the final analysis. Records were reviewed chronologically per year to ensure temporal representation, but no randomization or self-selection was involved.

Data collection procedure / study instruments

Patient charts with the immunologic cause of RPL from January 2018 to December 2022 were retrieved from PGH's Medical Records Sections. Data extracted included demographics, obstetric history, obstetric history, pre-pregnancy BMI, timing and type of immunologic diagnosis, and treatment of intervention timing.

Gestational age at delivery was primarily determined via first-trimester ultrasound or, if unavailable, by last menstrual period (LMP). To ensure confidentiality, unique numeric identifiers were assigned. Data was entered into a password-protected spreadsheet for analysis.

Outcomes measures

The primary outcome was live birth, defined as the delivery of a neonate beyond 20 weeks of gestation. Secondary outcomes included gestation age at delivery categorized as preterm (<37 weeks), term (37-41 6/7 weeks), or post-term (>42 weeks), and birthweight, classified as small for gestation [SGA] (BW <10th percentile) or appropriate for gestational age [AGA] (BW within the 10th to 90th percentile for gestational age). Stillbirths were defined as intrauterine fetal deaths at <20 weeks' gestation, consistent with WHO criteria.

Statistical tools

All analyses were conducted using SPSS version 28. Descriptive statistics, including frequency counts, percentages, means, and standard deviations, were used to summarize demographic and clinical variables. Chi-square test was utilized to analyse categorical variables, while independent t-test was used for continuous variables. Binary logistic regression identifies independent predictors of live birth, term delivery and AGA status.

Ethical consideration

This study was approved by the University of the Philippines Manila Research Ethics Board. Patient data were de-identified to maintain confidentiality in compliance with institutional and national data privacy regulations.

RESULTS

This study analyzed the demographic and clinical characteristics of patients with immunologic recurrent pregnancy loss (RPL) and their association with pregnancy outcomes. Among the variables assessed, maternal age, timing of diagnosis, gravidity, and pre-pregnancy BMI emerged as statistically significant predictors for selected outcomes.

The majority of participants were aged 31–40 years (66.0%), married (56.6%), and unemployed (57.2%), suggesting a population at typical reproductive age with potential socioeconomic vulnerabilities (Table 1).

The clinical characteristics of participants are presented below, with the majority having normal pre-pregnancy BMI (91.2%), underscoring generally good metabolic health prior to conception. The timing of RPL diagnosis was split between pre-pregnancy (40.9%) and during pregnancy (59.1%), which allowed exploration of the effect of early versus late diagnosis on outcomes. Gravida status was nearly evenly divided, with 47.1% having more than

Table 1. Demographic and clinical characteristics of study population (n = 159)

Variable	Classification	Frequency	Percent
Age (years)	18-30	54	34.0
	31-40	105	66.0
Marital status	Single	69	43.4
	Married	90	56.6
Employment	Employed	68	42.8
	Unemployed	91	57.2
Total		159	100.0

Table 2. Clinical profile of study participants (n = 159)

Variable	Classification	Frequency	Percent
BMI Status (Pre-pregnancy)	Normal BMI	145	91.2
	Not Normal	14	8.8
Timing of RPL Diagnosis	Pre-pregnancy period	65	40.9
	Pregnancy period	94	59.1
Gravida status	<4	84	52.9
	>4	75	47.1
Total		159	100.0

Table 3. Associations of demographic and clinical variables with pregnancy outcomes using Fisher's Exact Test (n = 159)

Variables		Primary outcome (Alive vs Stillbirth)	Secondary outcome (Term vs Preterm)	Secondary outcome (SGA vs AGA)
Age (<35 yrs vs >35 yrs)	Test statistic	0.938	6.340	6.900
	p-value	0.367	0.012	0.012
Marital status (married vs not married)	Test statistic	4.522	2.622	2.007
	p-value	0.041	0.123	0.174
Employment (employed vs unemployed)	Test statistic	4.051	3.760	4.517
	p-value	0.076	0.059	0.040
BMI status (Pre-pregnancy)	Test statistic	15.507	0.130	0.093
	p-value	0.002	0.766	0.770
Timing of RPL diagnosis (Pre-pregnancy vs pregnancy)	Test statistic	0.985	8.599	9.353
	p-value	0.383	0.003	0.003
Gravida status (<4 vs >4)	Test statistic	0.000	0.000	0.000
	p-value	0.000	0.000	0.000

four pregnancies, suggesting a significant proportion of multiparous women within the cohort (Table 2).

The associations between demographic and clinical variables with pregnancy outcomes highlight several important findings (Table 3).

Maternal age was not significantly linked to live birth versus stillbirth (p = 0.367), suggesting age alone does not determine fetal viability in immunologic RPL. However, women over 35 years demonstrated significantly increased risks of preterm birth and SGA infants (p = 0.012), consistent with the known obstetric risks of advanced maternal age.[5,7]

Marital status was significantly associated with live birth (p = 0.041), indicating that married women experienced better fetal survival, possibly reflecting psychosocial support advantages. Employment status showed borderline significance for live birth (p = 0.076) and preterm birth (p = 0.059) and was significantly associated with SGA (p = 0.040), suggesting that socioeconomic factors may affect fetal growth and delivery timing.

On the other hand, pre-pregnancy BMI was strongly associated with live birth outcomes (p = 0.002), underscoring the importance of maternal metabolic health as a determinant of fetal viability in this population.[3,8] With this result, overweight women have 7.87 times greater odds of experiencing a stillbirth compared to women with normal BMI (p <0.05). However, 91.2% of women in this study had a normal BMI, and overweight or obese individuals were underrepresented. Therefore, while the statistical association is notable, the limited variability in BMI may exaggerate the predictive strength and should be interpreted with caution.

Timing of RPL diagnosis did not significantly affect live birth (p = 0.383), but earlier diagnosis before pregnancy was associated with reduced risks of preterm birth and SGA (p = 0.003), emphasizing the clinical benefit of early detection and intervention.

In this cohort, higher gravidity was statistically associated with an increased likelihood of term delivery (p <0.05). However, this finding must be carefully interpreted as gravidity does not differentiate between successful and failed pregnancies. Therefore, this variable may reflect greater reproductive experience or increased healthcare engagement, rather than a direct protective effect. Importantly, the number of prior pregnancy losses, which has stronger predictive value in RPL literature, was not specifically analyzed in this study due to inconsistent documentation.[9,10]

Table 4. Binary logistic regression analysis of demographic and clinical predictors of live birth among women with immunologic RPL (n = 159)

Variable	Estimates	Wald statistic	*p*-value	OR exp (β)	95% CI Lower	95% CI Upper
Age	0.588	0.780	0.377	1.801	0.488	6.642
Marital status	-1.102	1.637	0.201	0.332	0.061	1.798
Employment status	-0.706	1.036	0.309	0.493	0.127	1.923
BMI Status (Pre-pregnancy)	2.063	8.079	0.004	7.870	1.897	32.640
Timing of RPL diagnosis	0.724	1.198	0.274	2.062	0.564	7.535
Gravida status	0.182	0.420	0.517	1.199	0.693	2.076
Constant	0.535	0.120	0.729	1.707		

Table 5. Multiple logistic regression analysis of factors associated with secondary outcome (full-term vs. preterm delivery) (n = 159)

Variable	Estimates	Wald statistic	*p*-value	OR exp (β)	95% CI Lower	95% CI Upper
Age	-1.062	5.698	0.017	0.346	0.145	0.827
Marital status	-0.465	0.974	0.324	0.628	0.250	1.581
Employment status	-0.594	1.769	0.184	0.552	0.230	1.325
BMI status (Pre-pregnancy)	0.130	0.038	0.845	1.138	0.311	4.171
Timing of RPL diagnosis	-1.256	8.659	0.003	0.285	0.123	0.657
Gravida status	0.494	8.876	0.003	1.638	1.184	2.267
Constant	0.961	0.971	0.324	2.615		

Table 6. Multiple logistic regression analysis of factors associated with secondary fetal outcome (appropriate gestational age) (n = 159)

Variable	Estimates	Wald statistic	*p*-value	OR exp (β)	95% CI Lower	95% CI Upper
Age	-1.163	6.759	0.009	0.312	0.130	0.751
Marital status	-0.297	0.402	0.526	0.743	0.297	1.861
Employment status	-0.784	3.017	0.082	0.457	0.189	1.106
BMI status (Pre-pregnancy)	0.095	0.020	0.887	1.100	0.295	4.093
Timing of RPL diagnosis	-1.284	9.037	0.003	0.277	0.120	0.640
Gravida status	0.548	10.246	0.001	1.729	1.237	2.419
Constant	0.839	0.730	0.393	2.315		

In evaluating predictors of delivery timing, maternal age was significantly associated with preterm birth, with increasing age linked to decreased likelihood of full-term delivery (OR = 0.346, p = 0.017). This finding reflects established risks of advanced maternal age on preterm labor in high-risk pregnancies.[5,7]

Timing of RPL diagnosis was also a strong predictor; earlier diagnosis significantly increased odds of term delivery (OR = 0.285, p = 0.003), supporting the clinical importance of early immunological screening and intervention.

Interestingly, higher gravidity was associated with increased risk of preterm birth (OR = 1.638, p = 0.003), contrasting its positive association with live birth and indicating complex relationships between reproductive history and pregnancy timing. However, because treatment regimens were not captured in this study, we cannot conclusively determine whether the improved outcomes were due to earlier clinical recognition or subsequent interventions.

Analysis of fetal growth outcomes demonstrated that advanced maternal age was significantly associated with decreased odds of delivering infants at appropriate gestational age (OR = 0.312, p = 0.009), aligning with literature on age-related risks for fetal growth restriction due to vascular and placental insufficiencies.[5,7]

Timing of diagnosis (OR = 0.277, p = 0.003) and higher gravidity (OR = 1.729, p = 0.001) also emerged as significant predictors (Table 6).

Together, these findings reveal a nuanced interplay of demographic, clinical, and socioeconomic factors influencing pregnancy outcomes in women with immunologic RPL. While maternal metabolic health, as reflected by pre-pregnancy BMI, stands out as the strongest independent predictor of live birth, early diagnosis of RPL significantly benefits secondary outcomes such as preterm birth and fetal growth.

The associations between gravida and improved fetal growth and survival suggest that physiological or immune adaptations across pregnancies may enhance outcomes, emphasizing the value of personalized monitoring based on reproductive history.

These results advocate comprehensive preconception care that prioritizes metabolic health optimization and timely immunologic assessment. Given the burden of immunologic RPL in settings like the Philippine General Hospital, integrating these approaches could improve fetal survival and reduce adverse perinatal outcomes in this vulnerable population.

DISCUSSION

Understanding the epidemiology and outcome predictors of recurrent pregnancy loss (RPL) is critical to improving care and prognosis for affected women. This study examined maternal demographic and clinical factors among women diagnosed with immunologic RPL, focusing on their association with pregnancy outcomes such as term delivery, preterm birth, and stillbirth.

The age distribution of the study population closely mirrors trends observed in previous research. The majority of participants were between 31–40 years, a demographic associated with elevated risk for RPL and adverse pregnancy outcomes. This finding is consistent with a meta-analysis by Eleje et al., where most patients were aged 26–35 years.[11]

Maternal age is among the most recognized risk factors for pregnancy loss. Women under 35 have the lowest miscarriage risk, which rises substantially beyond age 30 and increases nearly linearly thereafter.[5,9] In this study, older maternal age was significantly associated with preterm birth and stillbirth, consistent with literature implicating age-related immunologic shifts, such as altered maternal immune tolerance, in the pathogenesis of RPL.[7,12,13]

Studies across multiple populations, including Lamont et al., have reinforced the relationship between maternal age and recurrence of stillbirth.[14] While many prior studies confirm age as a risk factor, few specify the age distribution in immunologic RPL cohorts. This study helps address that gap, highlighting that even within immunologic subtypes, maternal age remains a potent and independent predictor of gestational outcomes.

Marital status also showed a statistically significant association with fetal survival. Married women had better outcomes, potentially reflecting the role of psychosocial support, shared decision-making, and stable care environments. While causality cannot be inferred, this finding supports prior research suggesting that emotional well-being and family/social support systems can positively influence pregnancy resilience, particularly in high-risk groups.[15]

Pre-pregnancy BMI was significantly associated with the primary outcome, specifically, overweight women had a markedly higher risk of stillbirth. This aligns with earlier studies linking higher BMI to impaired placentation, thrombotic tendencies, and adverse pregnancy complications, including recurrent pregnancy loss.[3,8]

However, this interpretation must be tempered by context. In this study, 91.2% of participants had normal BMI, suggesting a limited spread in BMI categories. The small proportion of overweight patients may inflate odds ratios and does not allow us to fully examine the spectrum of weight-related risk. Moreover, continued pregnancy losses in normal-weight women underscore that BMI, while modifiable, is not the sole or even primary driver of outcomes in immunologic RPL.

Another limitation is the lack of stratification by immunologic subtype. APS, elevated NK cell activity, and alloimmune causes may each interact differently with BMI. Furthermore, treatment regimens were not recorded, yet therapies such as low molecular weight heparin, corticosteroids, or IVIG could have confounded observed associations. Without adjusting for treatment, we cannot determine whether BMI acted independently or as a surrogate for another factor.

Therefore, while pre-pregnancy BMI achieved statistical significance, its clinical utility in this population is limited. Future research should include a more balanced BMI distribution, longitudinal data, and detailed treatment variables.

Women diagnosed before pregnancy had a significantly greater likelihood of achieving a live birth and term delivery. This finding supports the hypothesis that early recognition of immunologic RPL enables timely intervention, whether through medical treatment or close monitoring. However, this remains speculative given that treatment details were not collected, and early diagnosis may correlate with other favorable factors such as health literacy or access to care.

Several studies, including those by Wojcieszek et al., and Musters et al., have shown mixed or inconclusive benefits of immunologic interventions before conception, partly due to small sample sizes and population heterogeneity.[16,17] Nonetheless, some literature, such as Tomkiewicz and Darmochwal-Kolarz, suggests that early diagnosis and supportive care alone may improve outcomes even in the absence of medication.[18]

Thus, while causality cannot be definitively established, our findings underscore the potential value of pre-pregnancy diagnosis and proactive care, especially in immunologic RPL, where time-sensitive immunomodulation may influence implantation and placentation.

An important but complex finding was the positive association between higher gravidity and the likelihood of term delivery. Gravidity reflects the number of times a woman has been pregnant but does not account for pregnancy outcomes. While this association might suggest increased reproductive resilience in multigravidas, it is likely confounded by missing data on the number of prior pregnancy losses.

The literature strongly supports that the number of prior losses, not gravidity alone, predicts subsequent miscarriage risk. For example, Wilcox et al., found miscarriage risk rose sharply after three or more losses. In contrast, gravidity may reflect reproductive opportunity rather than biological advantage.[9,10]

In our analysis, we could not distinguish between women with multiple successful pregnancies and those with multiple losses. Therefore, the observed association between gravidity and term birth must be interpreted cautiously. It may not reflect true biological resilience, but rather an artifact of uncontrolled confounding.

Future studies should capture and stratify patients by number, timing, and etiology of prior losses, not just gravidity. This distinction is crucial for identifying true prognostic factors in RPL.

These findings contribute to a growing understanding of how maternal characteristics intersect with immunologic RPL. However, the retrospective design, absence of treatment data, and lack of immunologic subtype stratification limit generalizability. Future prospective studies should control for treatment, immunologic etiology, and number of previous losses to more precisely identify modifiable and non-modifiable predictors of successful pregnancy.

CONCLUSION

This study analyzed the predictors of good pregnancy outcomes among patients with immunologic causes of recurrent pregnancy loss. The findings underscore the multifactorial nature of pregnancy outcomes among women diagnosed with RPL, highlighting the complex interplay of demographic, clinical, and socioeconomic factors. It showed that pre-pregnancy BMI status (overweight) emerged as the sole significant predictor of the primary fetal outcome with 7.87 times more likely to experience stillbirth. Among other variables, maternal age, timing of RPL diagnosis, and gravida status emerged as significant predictors of the secondary fetal outcome of women diagnosed with RPL. Understanding and addressing these factors in prenatal care and risk assessment can help healthcare providers optimize prenatal care and improve pregnancy outcomes for women affected by RPL. Importantly, the association findings in this study hold particular significance in the context of recurrent pregnancy loss (RPL) with immunologic causes. It emphasizes the need for comprehensive assessments of maternal health, including immunologic status, in the management of RPL cases. Specific interventions addressing both maternal age-related risks and immunologic factors are crucial in mitigating the recurrence of pregnancy loss and promoting successful full-term pregnancies. Further research exploring the specific immunologic mechanisms underlying RPL among older mothers is warranted to inform targeted therapeutic strategies and improve pregnancy outcomes in this vulnerable population.

Limitations of the study

This study has several limitations. First, although all participants were diagnosed with immunologic causes of recurrent pregnancy loss, the specific immunologic diagnoses (e.g., antiphospholipid syndrome, elevated NK cells, HLA mismatches) were not recorded. This lack of diagnostic granularity limits our ability to analyze subgroups and determine which immunologic conditions may be more strongly associated with adverse outcomes.

Second, the study did not assess whether or which treatment interventions were received, such as low molecular weight heparin, corticosteroids, IVIG, or intralipid therapy. These treatments could independently influence pregnancy outcomes and potentially confound the association between demographic factors like BMI and live birth.

Third, although BMI was identified as an independent predictor of live birth, the finding must be interpreted in light of the overwhelming predominance of normal BMI values (91.2%) in the study population. This skewed distribution may limit the generalizability of the result and suggests that BMI alone may not be a sufficient explanatory factor for pregnancy outcomes in women with immunologic RPL.

Another limitation is the use of gravidity rather than the actual number of previous pregnancy losses in the analysis. Gravidity reflects the total number of pregnancies but does not differentiate between pregnancies carried to term, miscarried, or lost. This limits our ability to evaluate the well-established correlation between the number of prior losses and risk of future loss, potentially introducing confounding into the observed association between gravidity and term delivery.

In addition, the retrospective design relies on the completeness and accuracy of clinical documentation, which introduces potential for information bias. Some critical clinical details, such as rationale for omitted tests or varied diagnostic approaches, were not consistently recorded. While antiphospholipid testing was frequently performed, other immunologic tests were missing without documented justification.

Finally, as a single-center study without randomization or control groups, selection bias and limited external validity remain concerns. The findings may not be generalizable to other populations or practice settings where diagnostic workups and treatment protocols differ.

Statement of Authorship
All authors fulfilled ICMJE authorship criteria.

Author Disclosure
The authors declared no conflict of interest.

Funding Source
None.

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