Section: Obstetrics and Gynaecology

Original Research Article

PREVALENCE AND ASSOCIATED RISK FACTORS OF RECURRENT PREGNANCY LOSS IN A TERTIARY CARE CENTRE IN ASSAM

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ABSTRACT

Recurrent pregnancy loss (RPL) is a distressing clinical condition affecting a significant percentage of reproductive-aged women. This prospective cross-sectional study at Gauhati Medical College and Hospital aimed to assess the prevalence of RPL and identify associated risk factors in a regional cohort. Of the 798 women studied, 8.27% had RPL.Risk factors such as advanced maternal age, obesity, subclinical hypothyroidism, antiphospholipid antibodies, uterine anomalies, and elevated blood pressure were found to be significantly associated with RPL. These findings underline the importance of early evaluation and multidisciplinary intervention in women with a history of pregnancy loss.

Keywords: Recurrent Pregnancy Loss, Antiphospholipid antibodies, Body Mass Index, Ultrasound, Thyroid Peroxidase Antibodies.

INTRODUCTION

Recurrent pregnancy loss (RPL) is defined by the American Society for Reproductive Medicine (ASRM) and the European Society for Human Reproduction and Embryology (ESHRE) as two or more clinical pregnancy losses confirmed by ultrasonography or histopathology.[1,2] Globally, RPL affects 2–5% of couples.[3,4] Despite advances in reproductive medicine, nearly 50% of RPL cases remain unexplained.[5]

The etiology of RPL is multifactorial, involving chromosomal abnormalities,[6] uterine anomalies,[7] endocrine disorders like thyroid dysfunction and diabetes,[8,9] thrombophilic states such as antiphospholipid syndrome (APS),[10] and environmental and immunologic factors.[11] Additionally, male-related causes such as sperm DNA fragmentation have gained recognition in recent years.[12]

Regional studies are vital for understanding context-specific contributors to RPL. This study aims to determine the prevalence of RPL and its associated risk factors among women attending a tertiary care hospital in Northeast India

MATERIALS AND METHODS

A prospective cross-sectional study was conducted between April 2024 and March 2025 at Gauhati Medical College and Hospital (GMCH), Guwahati. Among 2108 screened women, 798 were included based on a history of at least one spontaneous abortion before 20 weeks gestation. Of these, 66 women met the definition of RPL, defined as two or more consecutive pregnancy losses.

Participants were evaluated using structured interviews, clinical examinations, and biochemical investigations including thyroid-stimulating hormone (TSH), antiphospholipid antibodies (APLA), TORCH serology, and serum prolactin levels. Ultrasonography (USG) was performed to identify structural abnormalities. Data were analyzed using SPSS v16. A p-value <0.05 was considered statistically significant.

Inclusion Criteria

- Females between the ages of 18 and 40 years.
- History of two or more consecutive PLs before 20 weeks of gestation in pregnant and nonpregnant women.
- H/O at least one PL after spontaneous conception and assisted reproductive treatment (ART) are included in this study.
- Females with a known history of chromosomal abnormalities or anatomical abnormalities that can lead to PL are involved.
- Females with known endocrine disorders, such as poorly controlled diabetes or thyroid dysfunction, are included.

Exclusion Criteria

- Postbortal Cases – induced, medical and surgical abortions
- "Ectopic, molar pregnancies, biochemical pregnancy, and implantation failures are excluded from this study.
- Postnatal women, pregnant women with a history of one or more induced or SAs, and pregnant women who are unsure of their date.

RESULTS

Prevalence of Recurrent Pregnancy Loss

Out of the total 798 women included in the study at Gauhati Medical College and Hospital, 66 were diagnosed with Recurrent Pregnancy Loss (RPL), resulting in a prevalence of 8.27%. This finding underscores a considerable burden of RPL in the regional population accessing tertiary care services.

Age Distribution

The **mean age** of the women with RPL was **28.54 ± 6.21 years**. The majority of cases occurred in the **26–30 years** age group, accounting for **34.85% (n = 23)**, followed by the **21–25 years** group at **21.21% (n = 14)**. The remaining distribution was as follows: ≤20 years (12.12%), 31–35 years (13.64%), and >35 years (18.18%). This suggests that while most women with RPL were in their late twenties, a significant proportion also belonged to the older reproductive age group.

Number of Pregnancy Losses

Among the 66 women with RPL, **42.42% (n = 28)** had experienced **two miscarriages**, making it the most common category. This was followed by **three miscarriages in 37.88% (n = 25)**. Fewer women had higher numbers of losses: **four (13.64%)**, **five (3.03%)**, **six (1.52%)**, and **eight losses (1.52%)** (Figure 1). These data confirm that most RPL patients fall within the early recurrence stage, as defined by the ESHRE/ASRM guidelines.

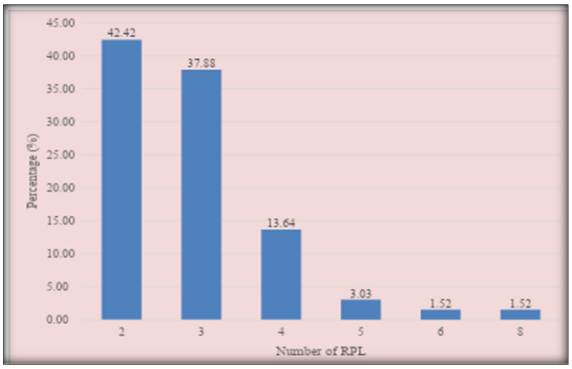

Figure 1: Distribution of the number of RPL

Age and Number of Pregnancy Losses

A comparative analysis showed that women who had experienced **three or more miscarriages** were significantly older than those with fewer than three. Specifically, the **mean age** for ≥3 losses was **30.34 ± 6.21 years**, while for <3 losses it was **26.10 ±6.28 years**. This difference was statistically significant (**p = 0.0082**) (Table 2, Figure 2), indicating that **increasing maternal age is strongly associated with higher miscarriage frequency**.

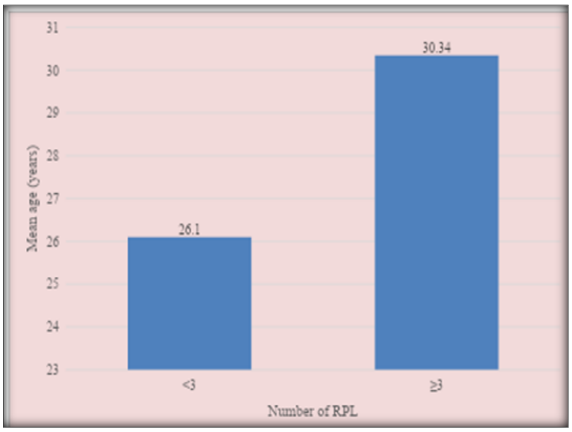

Figure 2: Comparison of age according to number of RPL

Type of RPL

Out of the total RPL cases, **40.91%** had **primary RPL** (no prior viable birth), and **59.10%** had **secondary RPL** (one or more prior live births) (Table 3). The predominance of secondary RPL suggests that prior successful conception does not preclude the possibility of subsequent reproductive failure.

Body Mass Index (BMI)

The **mean BMI** among RPL participants was **24.71 ±2.81 kg/m²**. The distribution of BMI was as follows (Table 4):

- Obese (BMI ≥25): 43.94% (n = 29)
- **Overweight (BMI 23–24.9):** 31.82% (n = 21)
- **Normal (BMI 18.5–22.9):** 24.24% (n = 16)

The data show a **high prevalence of overweight and obesity (75.76%)**, which is a known modifiable risk factor for pregnancy loss due to its association with

hormonal imbalance, chronic inflammation, and insulin resistance.

Thyroid Function (TSH Levels)

Thyroid screening revealed that **31.82% (n = 21)** of women had **TSH > 4 mU/L**, suggestive of **subclinical or overt hypothyroidism**. Another **1.52% (n = 1)** had **TSH < 0.4 mU/L**, indicating possible hyperthyroidism. Only **66.67% (n = 44)** had normal thyroid function. Notably, only **7.58%** of the study participants had a **prior diagnosis of thyroid disorder**, suggesting that **thyroid dysfunction remains underdiagnosed in this population** (Figure 3).

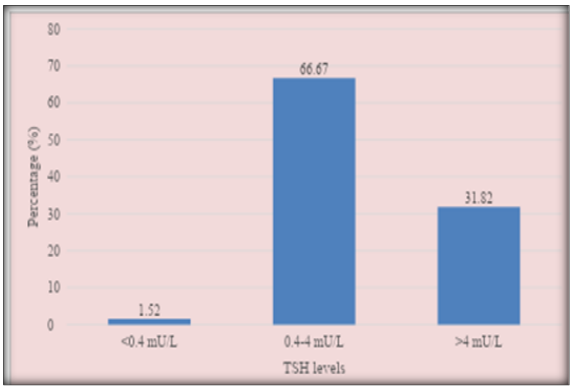

Figure 3. Distribution of TSH levels

Blood Pressure

Evaluation of blood pressure showed that:

- **27.27% (n = 18)** had **prehypertension** (SBP 120–129 mmHg)
- **12.12% (n = 8)** had **hypertension** (SBP ≥130 mmHg)
- **21.21% (n = 14)** had DBP ≥80 mmHg

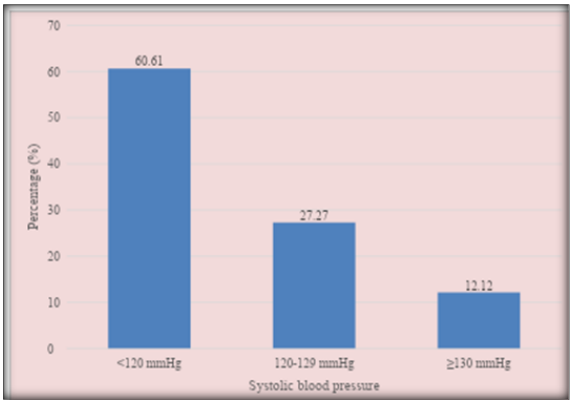

Figure 4. Distribution of SBP

These findings (Figure 4) suggest that a considerable proportion of RPL patients had elevated blood pressure, even if not formally diagnosed with hypertension.

TORCH Serology

Of the 66 women with RPL:

- **10.61% (n = 7)** tested **positive for TORCH IgG antibodies**
- **89.39% (n = 59)** were negative (Table 5, Figure 5)

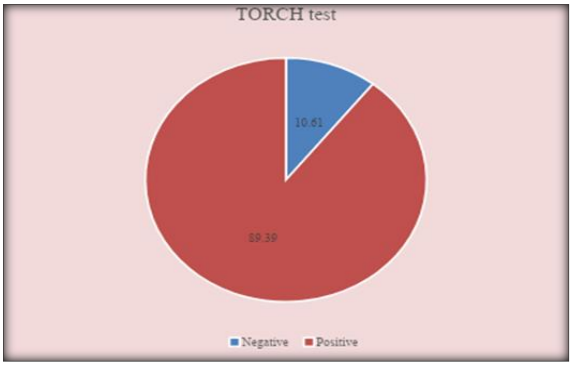

Figure 5: Distribution of TORCH test

Although TORCH IgG positivity does not confirm active infection, its presence suggests **prior exposure to intrauterine infections** (e.g., toxoplasmosis, rubella, cytomegalovirus), which may play a contributory role in fetal loss.

Antiphospholipid Antibody (APLA) Testing

Screening for APLA revealed:

- **12.12% (n = 8)** tested **positive for APLA**
- **87.88% (n = 58)** were negative (Table 6, Figure 6)

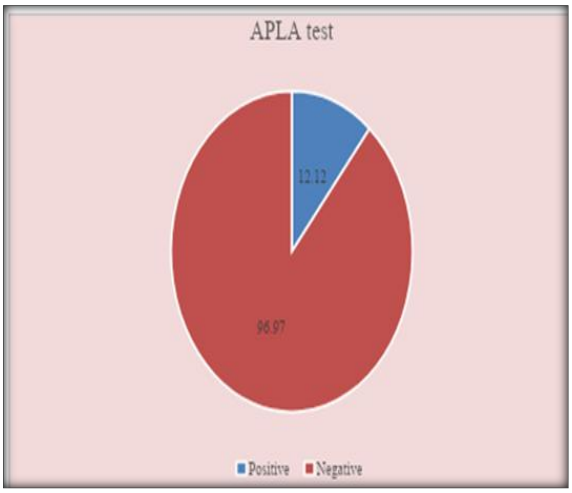

Figure 6: Distribution of APLA test

The detection of APLA antibodies is clinically significant as antiphospholipid syndrome is a well-established cause of RPL due to its impact on placental thrombosis and vascular pathology.

Serum Prolactin

The **mean serum prolactin** level was **14.82 ±9.24 ng/mL**. Only **6.06% (n = 4)** had **elevated prolactin levels (>25 ng/mL)**, while **93.94% (n = 62)** had normal levels (Table 7, Figure 7). Hyperprolactinemia may contribute to luteal phase defects or anovulation, though it appeared to be a **less common finding** in this cohort.

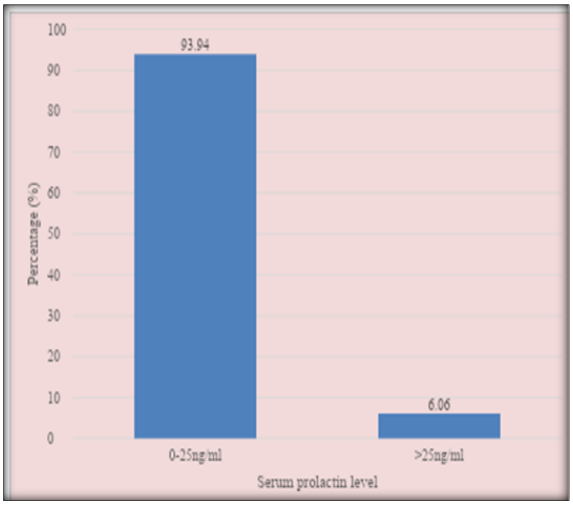

Figure 7. Distribution of serum prolactin levels

- **Fibroids:** 1.52% (n = 1)
- **Adenomyosis:** 1.52% (n = 1)
- **Other uterine anomalies (e.g., bicornuate uterus, endometrial polyp):** 6.06% (n = 4)

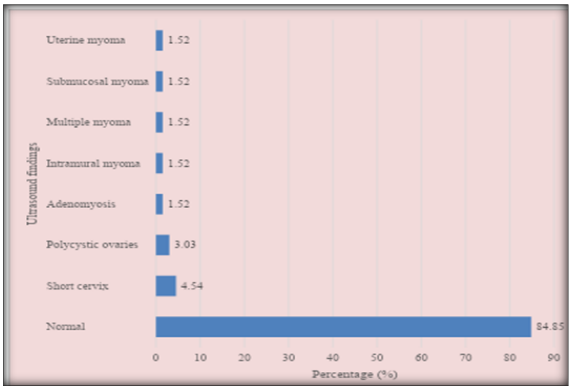

Figure 8: Distribution of US findings

Ultraso und Findings

Ultrasound examination revealed **abnormal findings in 15.15% (n = 10)** of RPL cases, with the following anomalies (Table 8, Figure 8):

- **Short cervix:** 4.54% (n = 3)
- **Polycystic ovarian syndrome (PCOS):** 3.03% (n = 2)

The majority (84.85%) had normal scans, yet the 15.15% with abnormalities suggest that imaging should be a routine part of RPL evaluation, especially in unexplained cases.

Table 1: Distribution of age

Age (years)	Frequency (n)	Percentage (%)
≤20	8	12.12
21-25	14	21.21
26-30	23	34.85
31-35	9	13.64
>35	12	18.18
Total	66	100

Table 2: Comparison of age according to the number of RPL

Number of RPL	Age (years)		P-value
	Mean	SD	
<3	26.10	6.28	0.0082
≥3	30.34	6.21	

Table 3. Distribution of the number of RPL

Number of RPL	Frequency (n)	Percentage (%)
2	28	42.42
3	25	37.88
4	9	13.64
5	2	3.03
6	1	1.52
8	1	1.52
Total	66	100

Table 4: Distribution of BMI

BMI	Frequency (n)	Percentage (%)
Normal weight (18.5-22.9 kg/m2)	16	24.24
Overweight (23-24.9 kg/m2)	21	31.82
Obese (≥25 kg/m2)	29	43.94
Total	66	100

Table 5: Distribution of the TORCH test

TORCH test	Frequency (n)	Percentage (%)
Positive	7	10.61
Negative	59	89.39
Total	66	100

Table 6: Distribution of APLA test

APLA test	Frequency (n)	Percentage (%)
Positive	8	12.12
Negative	58	87.88
Total	66	100

Table 7: Distribution of serum prolactin levels

Serum prolactin level	Frequency (n)	Percentage (%)
0-25ng/ml	62	93.94
>25ng/ml	4	6.06
Total	66	100

Table 8: Distribution of US findings

US findings	Frequency (n)	Percentage (%)
Normal	56	84.85
Short cervix	3	4.54
Polycystic ovaries	2	3.03
Adenomyosis	1	1.52
Intramural myoma	1	1.52
Multiple myoma	1	1.52
Submucosal myoma	1	1.52
Uterine myoma	1	1.52
Total	66	100

DISCUSSION

The RPL prevalence in this study (8.27%) aligns with the upper range of global estimates and is higher than values reported in some Asian cohorts.[3,13] This may be attributable to referral patterns to tertiary centers or regional differences in comorbidities.

In an epidemiological study by Patki and Chauhan (2016), 32% of 2,398 individuals reported at least one spontaneous miscarriage. After applying eligibility criteria, 753 participants were enrolled, and 7.46% of them had a history of recurrent pregnancy loss (RPL), aligning with previous research findings.

Consistent with previous findings,[6,9] maternal age was significantly correlated with increased pregnancy loss. Women with three or more losses were on average four years older than those with fewer. Chromosomal aneuploidy, which increases with age, may partially explain this trend.[6]

This result is consistent with the study by Hongmei Sun (2023) on 387 women with recurrent spontaneous abortion (RSA) found that those aged 35 and older had a significantly higher prevalence of intrauterine adhesions and ovarian dysfunction compared to younger women, indicating that age and prior intrauterine surgeries may contribute to reproductive complications in older RSA patients.

Obesity was found in nearly 44% of the cohort—similar to findings from Ticconi et al., where endocrine disorders including high BMI were linked to RPL. Obesity is associated with insulin resistance, hyperandrogenism, and impaired endometrial receptivity, which together increase the risk of miscarriage.

Similarly Metwally M et al. (2010) found that BMI influences the risk of miscarriage in women with recurrent miscarriage (RM). Obese women had a 71% higher risk, underweight women had nearly four times the risk, while overweight women showed no significant increase compared to those with normal BMI.

The proportion of subclinical hypothyroidism (31.82%) was substantial and aligns with reports highlighting thyroid autoimmunity as a key factor in unexplained RPL.[8,16] TSH elevation, even in euthyroid women, has been linked to increased miscarriage rates due to disruption in hormone-mediated endometrial development.[17]

In the study of Verma, P and Roy D (2020) on Relation between Hypothyroidism and early PL, found that 21% of women with early pregnancy loss had elevated TSH levels, with 15% diagnosed with overt and 6% with subclinical hypothyroidism. The study highlights the potential underdiagnosis of thyroid dysfunction and supports routine thyroid screening in women with pregnancy loss, as altered hormone levels may affect implantation and fetal development.

APLA positivity was seen in 12.12% of women, consistent with prior studies where antiphospholipid syndrome accounted for up to 15% of RPL cases.[10,14] These antibodies interfere with trophoblastic invasion and placental development, leading to early fetal demise.

In the study of Sheela HS (2017) of APLA in RPL, positive APLA test was reported
in 21.21% of RPL patients. A “total of 56 patients of RM with two or more prior
PLs were considered. Out of the 56 patients, 23 patients were excluded as per the
exclusion criteria, and 33 patients were included in the present study. Among the 33
patients, 11 patients were APLA positive and showed a significant association with RPL.

These findings recommend that APLA is a significant risk factor associated with RPL.

APLA remains a vital modifiable risk factor in RPL, and all patients with recurrent loss

should be screened as per standard clinical guidelines.

Structural uterine abnormalities were observed in 15.15%, confirming earlier data that congenital anomalies (e.g., septate uterus) or acquired lesions (e.g., fibroids) may impair implantation and pregnancy maintenance.[7,18]

In a similar study of Medarametla, V (2016) on "Ultrasonography: A Key Diagnostic Tool for Uterine Causes of Recurrent Pregnancy Loss, found that 51% of women with recurrent pregnancy loss had abnormal uterine morphology, including cervical incompetence, malformations, fibroids, and adhesions. The study highlights ultrasonography and related imaging techniques as essential tools for diagnosing uterine causes of RPL.

TORCH seropositivity was noted in 10.61% of participants. Although not always indicative of active infection, TORCH antibodies (particularly CMV or Rubella IgM) can adversely impact fetal viability if acquired during early gestation.[11,19]

Kamel HM (2024) found no significant association between CMV or toxoplasmosis infections and recurrent pregnancy loss (RPL). The study, involving 80 women, compared those with and without a history of miscarriage using ELISA testing, suggesting TORCH infections like CMV and toxoplasmosis may not play a major role in RPL.

While elevated serum prolactin was found in only a small subset, its role in anovulation and luteal phase deficiency justifies continued evaluation in selected patients.[9]

CONCLUSION

Recurrent pregnancy loss affects a significant proportion of women in Northeast India. This study identifies advanced maternal age, obesity, subclinical hypothyroidism, APLA positivity, elevated blood pressure, and uterine anomalies as prominent risk factors.

These findings highlight the need for:

- Routine screening for TSH and APLA in women with two or more pregnancy losses
- Preconception BMI management and weight reduction strategies
- Targeted ultrasound and imaging in suspected anatomical causes
- Multidisciplinary evaluation and counseling for affected couples

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