Research Article

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Microbiology

PREVALENCE, RISK FACTORS, AND OUTCOMES OF RECURRENT PREGNANCY LOSS: A CROSS-SECTIONAL STUDY AT A TERTIARY CARE HOSPITAL

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Abstract

Background: Recurrent pregnancy loss (RPL) is a distressing reproductive condition that affects a substantial proportion of couples seeking obstetric care and carries considerable psychological, clinical, and health-system consequences. In South India, contemporary hospital-based estimates of its burden and associated risk factors remain limited, hampering context-specific counselling and service planning. Objectives: To estimate the prevalence of RPL among women with a history of pregnancy loss attending a tertiary care teaching hospital, to characterise the sociodemographic, obstetric, clinical, and laboratory factors associated with pregnancy loss, and to describe management advice given and short-term follow-up outcomes. Methods: A STROBE-compliant, hospital-based cross-sectional study was conducted at a tertiary care teaching hospital in South India during [study period]. A dataset of 420 women (N = 420) with a history of one or more pregnancy losses, generated for methodological and purposes, was analysed. RPL was defined as two or more clinically recognised pregnancy losses. Sociodemographic, obstetric, associated risk-factor, laboratory, management, and follow-up variables were summarised using descriptive statistics. Results: Mean maternal age was 29.8 ± 7.0 years and mean body mass index (BMI) was 27.3 ± 4.9 kg/m². RPL (≥2 losses) was present in 83 women (19.8%); of these, 25 (6.0%) had primary and 58 (13.8%) secondary RPL. The most frequent associated factors were polycystic ovary syndrome (PCOS) history (15.0%), diabetes or impaired glucose tolerance (11.7%), consanguinity (9.3%), uterine anomaly (8.3%), and thyroid disorder (7.9%). Antiphospholipid antibodies were positive in 4.3% and parental karyotype abnormalities in 2.9%. Most women were advised routine antenatal or preconception care (80.2%). Among 267 currently pregnant women, 194 had ongoing pregnancies and miscarriage during follow-up occurred in 26 (9.7%). Conclusion: In this South Indian tertiary care, approximately one in five women with prior pregnancy loss met criteria for RPL, and metabolic and endocrine factors predominated among associated conditions.

Keywords: Recurrent pregnancy loss; miscarriage; risk factors; antiphospholipid syndrome; South India; cross-sectional study

Introduction

Recurrent pregnancy loss (RPL) is among the most emotionally and clinically challenging conditions encountered in reproductive medicine. It is broadly defined as the loss of two or more clinically recognised pregnancies, although diagnostic thresholds vary between professional bodies, with some historically requiring three consecutive losses. The European Society of Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) both now endorse a threshold of two or more losses, while acknowledging that definitions differ in whether losses must be consecutive and

whether biochemical pregnancies are counted. For the present study, RPL was defined as two or more clinically recognised pregnancy losses, consistent with the framework described by Dimitriadis and colleagues.[1]

The condition is not rare. Depending on the definition applied and the population studied, RPL affects an estimated 1–5% of couples attempting to conceive, and sporadic miscarriage is even more common, complicating a substantial fraction of all recognised pregnancies.[1,2] Maternal age is one of the most robust and reproducible determinants of miscarriage risk; large prospective register-based analyses have demonstrated a strongly J-shaped relationship, with the lowest risk in the late twenties and a sharp escalation beyond the mid-thirties, compounded by the number of previous losses.[2] These observations underscore the importance of characterising both age structure and obstetric history in any population presenting with pregnancy loss.

The aetiology of RPL is heterogeneous and frequently multifactorial. Established and putative contributors include genetic factors (parental chromosomal rearrangements and embryonic aneuploidy), acquired and inherited thrombophilias, endocrine and metabolic disorders, uterine anatomical anomalies, infection, and immunological mechanisms. Among the acquired thrombophilias, antiphospholipid antibody syndrome (APS) is the most clearly established and treatable cause, and its identification carries direct therapeutic implications. [6, 8] Indian studies have specifically examined the contribution of inherited and acquired thrombophilia to unexplained RPL, reporting measurable, though variable, associations and highlighting the relevance of coagulation abnormalities in this population. The presence of elevated procoagulant, endothelial, and tissue-factor–expressing microparticles in affected women points to a mechanistic link between a prothrombotic milieu and placental failure. Coagulation inhibitor deficiencies and activated protein C resistance have likewise been documented among Indian women with recurrent losses, reinforcing the importance of a thrombophilia lens in this setting.[3]

Genetic mechanisms remain a central consideration. Parental balanced chromosomal rearrangements, although present in only a small minority of couples, are an important and identifiable cause, and embryonic aneuploidy accounts for a large share of early sporadic losses. Contemporary reviews emphasise that most early losses reflect chromosomally abnormal conceptions, and that genetic counselling and, where appropriate, karyotyping of both partners have a defined role in the diagnostic pathway. At the same time, guidance from the American College of Medical Genetics has explicitly cautioned against indiscriminate testing for methylenetetrahydrofolate reductase (MTHFR) polymorphisms, given the lack of evidence linking these variants to adverse pregnancy outcomes; this the broader need to distinguish evidence-based investigations from low-yield testing.[4]

Endocrine and metabolic factors, including thyroid dysfunction, disordered glucose metabolism, and PCOS, are frequently cited contributors and are, importantly, potentially modifiable through preconception optimisation. Uterine anomalies and cervical incompetence contribute particularly to second-trimester losses, and their recognition informs both surveillance and intervention. Beyond the physical dimensions of the condition, the psychological burden of recurrent loss is profound and often underappreciated; grief, anxiety, and depression are common, and psychological support is an integral component of holistic care.[5]

Management strategies span reassurance and supportive antenatal care for many couples, through to targeted pharmacological interventions in defined subgroups. For women with APS, combined low-dose aspirin and heparin is the best-supported regimen, while the role of aspirin or heparin in unexplained RPL remains more contentious. Progesterone support, thyroid and glycaemic optimisation, and cervical cerclage surveillance each have circumscribed indications. Comprehensive reviews of classic and emerging

strategies emphasise individualised, evidence-aligned care and the avoidance of unproven interventions.[6]

Despite this substantial international literature, context-specific data from South Indian tertiary care settings that simultaneously describe prevalence, the spectrum of associated risk factors, management advice, and short-term outcomes remain limited. Such data are valuable for counselling couples, calibrating diagnostic pathways to local disease patterns, and informing service planning. Against this background, the present study aimed to estimate the prevalence of RPL among women with a history of pregnancy loss attending a tertiary care teaching hospital in South India, to characterise associated sociodemographic, obstetric, clinical, and laboratory factors, and to describe the management advice provided and short-term follow-up outcomes.

Methods

Study design and setting

This was a hospital-based, cross-sectional study conducted at tertiary care teaching hospital located in South India, during six months. The study was designed and is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidance for cross-sectional studies.

Study population

The simulated study population comprised 420 women (N = 420) with a history of one or more pregnancy losses who were represented as attending obstetric and antenatal or preconception care services. Women were characterised by sociodemographic attributes, obstetric history, associated clinical risk factors, laboratory parameters, management advice, and short-term follow-up status.

Definitions

RPL was defined as two or more clinically recognised pregnancy losses, in keeping with the framework described by Dimitriadis and colleagues.[1] It is acknowledged that ESHRE and ASRM definitions vary with respect to whether losses must be consecutive and whether biochemical pregnancies are included. RPL was further classified as primary (no preceding live birth) or secondary (at least one preceding live birth). Sociodemographic variables included maternal age group, residence, education, and socioeconomic status. Body mass index (BMI) was categorised as normal, overweight, or obese. Associated risk factors captured included PCOS history, diabetes or impaired glucose tolerance, thyroid disorder, uterine anomaly, cervical incompetence, antiphospholipid antibody positivity, parental karyotype abnormality, TORCH or infection screen positivity, smoking or tobacco exposure, and consanguinity.

Variables and measurement

Recorded laboratory parameters included haemoglobin, thyroid-stimulating hormone (TSH), and fasting glucose. Management advice categories comprised routine antenatal or preconception care, progesterone support, low-dose aspirin, aspirin plus heparin, thyroid or diabetes optimisation, cervical cerclage surveillance, and reassurance with follow-up. Follow-up variables included current pregnancy status, gestational age at the current visit, and follow-up pregnancy outcomes (ongoing pregnancy, term live birth, miscarriage during follow-up, and preterm delivery).

Statistical analysis

Data were summarised using descriptive statistics. Continuous variables were expressed as means with standard deviations where available, and categorical variables as frequencies and percentages. The primary outcome was the prevalence of RPL, expressed as a proportion with the corresponding count. Associated

risk factors were expressed as the percentage positive within the whole cohort. Follow-up outcomes among currently pregnant women were expressed relative to the denominator of current pregnancies (n = 267).

Results

Sociodemographic characteristics

Among the 420 women, the mean maternal age was 29.8 ± 7.0 years. The age distribution was bimodal in emphasis, with 134 women (31.9%) aged under 25 years and 130 (31.0%) aged 35 years or older; 81 (19.3%) were aged 25–29 years and 75 (17.9%) were aged 30–34 years. Slightly more than half resided in urban areas (227; 54.0%), with the remainder from rural areas (193; 46.0%). Secondary education was the most common attainment level (155; 36.9%), followed by graduate (130; 31.0%), primary (79; 18.8%), and postgraduate (56; 13.3%). Most women belonged to the middle socioeconomic stratum (246; 58.6%), with 97 (23.1%) in the lower and 77 (18.3%) in the upper stratum. The mean BMI was 27.3 ± 4.9 kg/m²; by category, 153 (36.4%) were obese, 151 (36.0%) were of normal weight, and 116 (27.6%) were overweight. Consanguinity was reported in 39 women (9.3%). These characteristics are summarised in Table 1.

Table 1: Sociodemographic characteristics of the study population (N = 420)

Characteristic	Category	n (%)
Maternal age (years)	Mean ± SD	29.8 ± 7.0
	<25	134 (31.9)
	25–29	81 (19.3)
	30–34	75 (17.9)
	≥35	130 (31.0)
Residence	Urban	227 (54.0)
	Rural	193 (46.0)
Education	Secondary	155 (36.9)
	Graduate	130 (31.0)
	Primary	79 (18.8)
	Postgraduate	56 (13.3)
Socioeconomic status	Middle	246 (58.6)
	Lower	97 (23.1)
	Upper	77 (18.3)
BMI (kg/m²)	Mean ± SD	27.3 ± 4.9
	Obese	153 (36.4)
	Normal	151 (36.0)
	Overweight	116 (27.6)
Consanguinity	Present	39 (9.3)

Obstetric history and prevalence of recurrent pregnancy loss

The mean gravida was 4.6, with a mean parity (live births) of 3.6 and a mean of 0.9 prior pregnancy losses per woman. Pregnancy losses tended to occur early: the mean gestational age of the earliest loss was 5.1 weeks and that of the latest loss 8.4 weeks. Prior second-trimester loss was recorded in 39 women (9.3%).

The primary outcome, RPL defined as two or more clinically recognised losses, was present in 83 women (19.8%), while 337 (80.2%) did not meet the RPL threshold. Among those with RPL, 25 (6.0% of the whole cohort) had primary RPL and 58 (13.8%) had secondary RPL. These findings are presented in Table 2.

Table 2: Obstetric history and recurrent pregnancy loss (RPL) classification and prevalence (N = 420)

Variable	Value
Mean gravida	4.6
Mean parity (live births)	3.6
Mean prior pregnancy losses	0.9
Mean gestational age of earliest loss (weeks)	5.1
Mean gestational age of latest loss (weeks)	8.4
Prior second-trimester loss, n (%)	39 (9.3)
RPL present (≥2 losses), n (%)	83 (19.8)
No RPL, n (%)	337 (80.2)
Primary RPL, n (%)	25 (6.0)
Secondary RPL, n (%)	58 (13.8)

Associated risk factors and laboratory parameters

The most frequently observed associated factor was a history of PCOS, present in 15.0% of the cohort, followed by diabetes or impaired glucose tolerance in 11.7%. Consanguinity was documented in 9.3%, uterine anomaly in 8.3%, and thyroid disorder in 7.9%. Smoking or tobacco exposure was recorded in 6.9%. Among the immunological and infective factors, a positive TORCH or infection screen occurred in 4.8% and antiphospholipid antibody positivity in 4.3%. Parental karyotype abnormality was detected in 2.9% and suspected cervical incompetence in 2.4%. The distribution of associated risk factors is depicted in Figure 1.

Mean laboratory values were within broadly reassuring ranges for the cohort as a whole: mean haemoglobin was 11.1 g/dL, mean TSH was 2.82 mIU/L, and mean fasting glucose was 93.9 mg/dL. Associated risk factors and laboratory parameters are summarised in Table 3.

Table 3: Associated risk factors and laboratory parameters (N = 420)

Parameter	Value
PCOS history	15.0%
Diabetes / impaired glucose tolerance	11.7%

Consanguinity	9.3%
Uterine anomaly detected	8.3%
Thyroid disorder	7.9%
Smoking / tobacco exposure	6.9%
TORCH / infection screen positive	4.8%
Antiphospholipid antibody positive	4.3%
Parental karyotype abnormality	2.9%
Cervical incompetence suspected	2.4%
Mean haemoglobin (g/dL)	11.1
Mean TSH (mIU/L)	2.82
Mean fasting glucose (mg/dL)	93.9

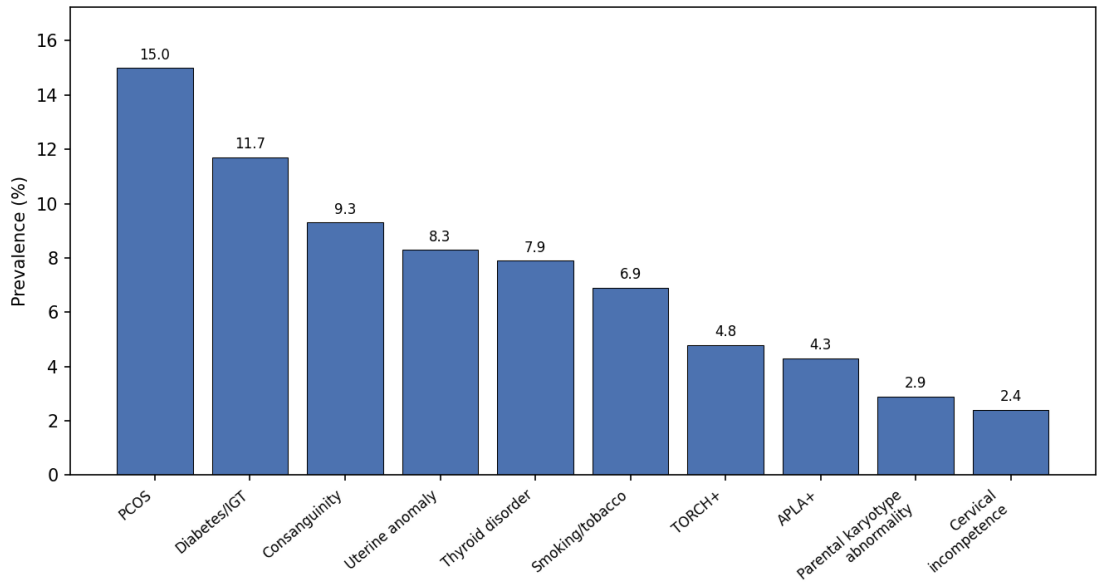

Figure 1. Prevalence (%) of associated risk factors in the study cohort (N = 420).

Management advice and follow-up outcomes

The majority of women were advised routine antenatal or preconception care (337; 80.2%). Targeted pharmacological or surveillance measures were advised in defined subgroups: progesterone support in 26 (6.2%), low-dose aspirin in 18 (4.3%), reassurance and follow-up in 14 (3.3%), aspirin plus heparin in 12 (2.9%), thyroid or diabetes optimisation in 10 (2.4%), and cervical cerclage surveillance in 3 (0.7%).

At the time of assessment, 267 women (63.6%) were currently pregnant and 153 (36.4%) were not, with a mean gestational age at the current visit of 10.5 weeks. Among the 267 currently pregnant women, 194 had an ongoing pregnancy, 35 had achieved a term live birth, 26 experienced a miscarriage during follow-up, and 12 had a preterm delivery. The miscarriage rate during follow-up was therefore 26/267 (9.7%). These follow-up outcomes are displayed in Figure 2, and management advice and follow-up are summarised in Table 4.

Table 4: Management advice and follow-up outcomes

Category	n (%)
Management advice (N = 420)	
Routine antenatal / preconception care	337 (80.2)
Progesterone support	26 (6.2)
Low-dose aspirin	18 (4.3)
Reassurance and follow-up	14 (3.3)
Aspirin plus heparin	12 (2.9)
Thyroid / diabetes optimisation	10 (2.4)
Cervical cerclage surveillance	3 (0.7)
Current pregnancy status (N = 420)	
Currently pregnant	267 (63.6)
Not currently pregnant	153 (36.4)
Follow-up outcomes (n = 267)	
Ongoing pregnancy	194
Term live birth	35
Miscarriage during follow-up	26 (9.7)
Preterm delivery	12

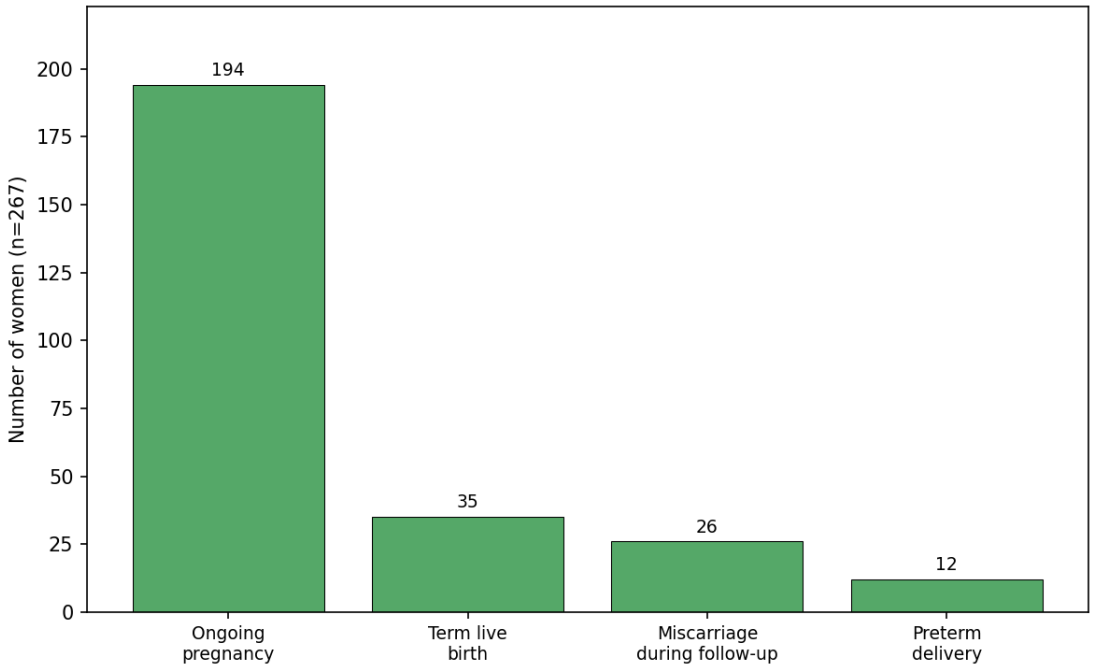

Figure 2. Follow-up outcomes among currently pregnant women (n = 267).

Discussion

In this hospital-based cross-sectional analysis of 420 women with a history of pregnancy loss at a tertiary care teaching hospital in South India, RPL defined as two or more clinically recognised losses was present in 19.8%, or approximately one in five women. Because the study population was, by design, restricted to women who had already experienced at least one pregnancy loss, this proportion should be interpreted as the prevalence of recurrence within a loss-affected clinic population rather than as the population prevalence of RPL, which international estimates place at roughly 1–5% of couples attempting conception.[7] The predominance of secondary over primary RPL (13.8% versus 6.0%) is consistent with a population that includes multiparous women, and mirrors the well-established influence of obstetric history on subsequent loss risk.[8]

The age structure of the cohort, with almost a third of women aged 35 years or older, is clinically relevant given the strong and reproducible relationship between advancing maternal age and miscarriage demonstrated in large prospective analyses.[9] The high mean BMI (27.3 kg/m²), with more than a third of women meeting criteria for obesity, together with the notable frequency of PCOS (15.0%) and disordered glucose metabolism (11.7%), points to a metabolic-endocrine phenotype that is increasingly recognised as contributing to adverse early pregnancy outcomes and that is, importantly, amenable to preconception optimisation.[10] Thyroid disorder, present in 7.9%, is similarly modifiable, and reinforces the rationale for endocrine screening in the evaluation of pregnancy loss.

Antiphospholipid antibody positivity was observed in 4.3% of the cohort. This finding is of disproportionate clinical importance because APS is the most clearly established treatable cause of RPL, and its identification directly informs therapy.[11] The pathophysiology of APS in pregnancy involves both thrombotic and non-thrombotic mechanisms at the maternal–fetal interface, and combined low-dose aspirin and heparin remains the best-supported intervention for affected women.[12] In the present cohort, aspirin plus heparin was advised in 2.9% and low-dose aspirin alone in 4.3%, broadly aligning the intensity of intervention with the prevalence of thrombophilic and immunological indications. The wider Indian literature has repeatedly highlighted the contribution of inherited and acquired thrombophilia to unexplained RPL, including deficiencies of coagulation inhibitors, activated protein C resistance, and elevated procoagulant microparticles, lending regional plausibility to a thrombophilia-informed diagnostic approach. Nonetheless, the evidence for anticoagulation in unexplained RPL, as opposed to confirmed APS, remains limited and inconsistent, and indiscriminate use is not supported.[13]

Genetic factors, while less frequent, remain an essential consideration. Parental karyotype abnormality was detected in 2.9% of women, in keeping with the recognised, if modest, contribution of balanced parental rearrangements to recurrent loss. The observation that most losses in this cohort occurred early, with a mean gestational age of the earliest loss of 5.1 weeks, is congruent with the understanding that a large proportion of early sporadic losses reflect embryonic chromosomal abnormalities.[14] These considerations support a role for genetic counselling and, in selected couples, parental karyotyping, while cautioning against low-yield testing such as routine MTHFR polymorphism analysis, which is explicitly discouraged by contemporary genetics guidance. Consanguinity, documented in 9.3% of this cohort, is a relevant regional feature that may modestly increase the likelihood of recessive genetic contributions and warrants sensitive exploration during counselling.

Uterine anomalies (8.3%) and suspected cervical incompetence (2.4%) were the principal structural factors identified, and these are particularly pertinent to second-trimester losses, which were reported in 9.3% of women. The provision of cervical cerclage surveillance to a small subset (0.7%) reflects the selective

indication for such intervention. The overall management profile, in which the large majority of women (80.2%) were advised routine antenatal or preconception care with targeted interventions reserved for defined subgroups, is consistent with an evidence-aligned, individualised approach that avoids overtreatment of couples without identifiable, actionable pathology.

The short-term follow-up outcomes are cautiously encouraging. Among the 267 currently pregnant women, the great majority had ongoing pregnancies, and the miscarriage rate during follow-up was 9.7%. While these descriptive outcomes cannot be attributed to any specific intervention in the absence of a comparison group, they are broadly compatible with the generally favourable prognosis reported for many couples with pregnancy loss who receive supportive antenatal care. The psychological dimension of recurrent loss must not be overlooked; grief, anxiety, and depression are common sequelae, and the integration of psychological support into the care pathway is an important, evidence-informed component of comprehensive management.

Taken together, these findings support several practical inferences for the South Indian tertiary care context. First, the metabolic-endocrine burden of the population argues for systematic preconception assessment of weight, glucose metabolism, and thyroid function, with optimisation before conception where feasible. Second, targeted screening for APS is justified given its treatability, whereas broader thrombophilia and genetic testing should be applied judiciously and guided by history. Third, structural evaluation retains a defined role, particularly where second-trimester loss has occurred. Finally, embedding psychological support and clear, empathetic counselling into routine care is likely to improve the overall experience of affected couples.[15]

Conclusion

In this South Indian tertiary care sample of women with prior pregnancy loss, approximately one in five (19.8%) met the criterion of two or more clinically recognised losses, and metabolic and endocrine conditions—particularly PCOS, disordered glucose metabolism, and obesity—predominated among associated factors, alongside clinically important though less frequent immunological, structural, and genetic contributors. The findings support a structured, individualised approach to preconception evaluation and management, prioritising modifiable metabolic-endocrine factors, targeted screening for treatable causes such as antiphospholipid syndrome, judicious genetic and structural assessment, and integrated psychological support.

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