

INPLASY

The relationship between dyslipidemia and recurrent pregnancy loss: systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - No funding.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 April 2026 and was last updated on 17 April 2026.

INTRODUCTION

Review question / Objective Among women of reproductive age, is dyslipidemia associated with recurrent pregnancy loss compared with women without recurrent pregnancy loss?

Rationale Recurrent pregnancy loss (RPL) is a major reproductive health problem, commonly defined as two or more consecutive pregnancy losses before fetal viability. Although several etiologies have been implicated in RPL, including genetic, anatomic, endocrine, thrombophilic, and immunologic causes, a substantial proportion of cases remain unexplained. In recent years, metabolic dysfunction has emerged as a potentially relevant contributor to adverse reproductive outcomes.

Dyslipidemia, characterized by abnormalities in serum lipid fractions such as total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C),

triglycerides, lipoprotein(a), and apolipoproteins, has been associated with endothelial dysfunction, oxidative stress, chronic low-grade inflammation, altered trophoblast invasion, placental vascular impairment, and thrombotic tendency. These pathophysiological mechanisms provide biological plausibility for a relationship between abnormal lipid metabolism and pregnancy loss.

Despite increasing interest in cardiometabolic risk factors in reproductive medicine, the evidence regarding the association between dyslipidemia and RPL remains fragmented and inconsistent. Some studies suggest that women with RPL have a more atherogenic lipid profile than controls, whereas others report no significant differences. A systematic synthesis of the available evidence is needed to clarify whether dyslipidemia is associated with RPL and to identify which lipid abnormalities are most strongly implicated.

Condition being studied The condition of interest is recurrent pregnancy loss, a reproductive disorder associated with significant physical and

emotional burden. This review will focus on the relationship between RPL and dyslipidemia, including abnormalities in total cholesterol, LDL-C, HDL-C, triglycerides, lipoprotein(a), and apolipoproteins. The review will explore whether lipid disturbances may constitute a relevant metabolic risk factor in the pathophysiology of recurrent pregnancy loss.

METHODS

Search strategy A systematic literature search will be conducted in the following electronic databases:

PubMed/MEDLINE
Embase
Web of Science
Scopus

The search strategy will combine controlled vocabulary and free-text terms related to recurrent pregnancy loss and dyslipidemia. Search terms will include combinations of:

“recurrent pregnancy loss”
“recurrent miscarriage”
“habitual abortion”
“recurrent abortion”
“dyslipidemia”
“lipid profile”
“cholesterol”
“triglycerides”
“LDL”
“HDL”
“lipoprotein(a)”
“apolipoprotein”

An example PubMed strategy may include: ("recurrent pregnancy loss" OR "recurrent miscarriage" OR "habitual abortion" OR "recurrent abortion") AND ("dyslipidemia" OR "lipid profile" OR cholesterol OR triglycerides OR LDL OR HDL OR "lipoprotein(a)" OR apolipoprotein).

Participant or population Women of reproductive age diagnosed with recurrent pregnancy loss.

Studies will be eligible if RPL is defined according to the authors' criteria, typically as two or more consecutive or non-consecutive pregnancy losses. The specific definition used in each study will be extracted and considered in interpretation and subgroup analyses where feasible.

Intervention Exposure

Dyslipidemia or abnormal lipid profile parameters, including but not limited to:

Total cholesterol
LDL cholesterol
HDL cholesterol
Triglycerides
Very-low-density lipoprotein (VLDL), if available
Lipoprotein(a)
Apolipoprotein A1
Apolipoprotein B.

Comparator Women without recurrent pregnancy loss, preferably with a history of normal reproductive outcomes or no history of miscarriage.

Study designs to be included The review will include original observational studies, including: Case-control studies; Cohort studies; Cross-sectional studies.

Eligibility criteria Inclusion criteria
Observational studies evaluating lipid profile parameters in women with RPL
Studies including a comparison group without RPL
Studies reporting quantitative data on lipid parameters or measures of association
Peer-reviewed full-text articles

Exclusion criteria
Studies without a control group
Studies not reporting sufficient data for extraction
Reviews, case reports, editorials, commentaries, and conference abstracts
Studies focused exclusively on pregnancy loss related to known chromosomal or major anatomical causes without separate analysis
Animal or laboratory studies.

Information sources

PubMed/MEDLINE
Embase
Web of Science
Scopus.

Main outcome(s) The main outcome will be the difference in lipid profile parameters between women with recurrent pregnancy loss and controls. The primary lipid outcomes will include:

Total cholesterol
LDL-C
HDL-C
Triglycerides
Lipoprotein(a)
Apolipoprotein A1
Apolipoprotein B

For continuous outcomes, means and standard deviations will be extracted. If studies report medians and interquartile ranges, conversion methods may be applied when appropriate.

Additional outcome(s) Additional outcomes may include:

Association between dyslipidemia and number of pregnancy losses
 Association between lipid abnormalities and known confounders such as body mass index, polycystic ovary syndrome, insulin resistance, thrombophilia, or autoimmune disease
 Adjusted effect measures reported by individual studies
 Markers of atherogenic lipid ratios, if available.

Data management Search results will be exported to reference management software, and duplicates will be removed. Titles and abstracts will be screened independently by two reviewers. Full texts of potentially eligible studies will then be assessed independently for inclusion. Disagreements will be resolved by consensus or by consultation with a third reviewer.

A standardized data extraction form will be developed and piloted. Extracted information will include:

Author and year
 Country
 Study design
 Sample size
 Definition of RPL
 Participant characteristics
 Lipid parameters measured
 Laboratory methods
 Timing of lipid assessment
 Main findings
 Adjusted and unadjusted effect estimates.

Quality assessment / Risk of bias analysis Risk of bias in included studies will be assessed independently by two reviewers using the Newcastle-Ottawa Scale (NOS) for observational studies. Any disagreement will be resolved by discussion and, if needed, by a third reviewer.

The quality assessment will consider selection of participants, comparability of study groups, and ascertainment of exposure/outcomes.

Strategy of data synthesis A qualitative synthesis will first summarize the characteristics and findings of all included studies.

Where at least two sufficiently homogeneous studies report the same lipid parameter, a meta-analysis will be performed. For continuous variables, pooled effect estimates will be calculated using either mean difference (MD) or standardized mean difference (SMD), with 95% confidence intervals. For dichotomous outcomes, pooled odds ratios (ORs) with 95% confidence intervals will be used.

Statistical heterogeneity will be assessed using Cochran's Q test and quantified using the I^2 statistic. A random-effects model will be used when heterogeneity is substantial or when between-study clinical variability is expected; otherwise, a fixed-effect model may be considered.

Forest plots will be generated for each pooled analysis. Publication bias will be explored by funnel plot inspection and Egger's test when at least 10 studies are available for a given outcome.

Subgroup analysis If sufficient data are available, subgroup analyses will be conducted according to:

Definition of recurrent pregnancy loss
 Number of pregnancy losses
 Type of lipid abnormality
 Presence of obesity or elevated body mass index
 Presence of polycystic ovary syndrome
 Study design
 Geographic region
 Adjustment for confounding factors.

Sensitivity analysis Sensitivity analyses will be performed, where feasible, by:

Excluding studies at high risk of bias
 Excluding studies with non-standard definitions of RPL
 Excluding studies with extreme values or outliers
 Comparing fixed-effect and random-effects models.

Language restriction No language restriction will be applied at the search stage. Studies published in languages accessible to the review team or translatable by reliable means will be considered.

Country(ies) involved Brazil.

Keywords Dyslipidemia; recurrent pregnancy loss; recurrent miscarriage; lipid profile; cholesterol; triglycerides; infertility.

Dissemination plans The results of this systematic review and meta-analysis will be

submitted for publication in a peer-reviewed journal and may also be presented at scientific meetings in reproductive medicine, obstetrics, and gynecology. The review is expected to contribute to the understanding of metabolic risk factors in recurrent pregnancy loss and may support future clinical and translational research.

Contributions of each author

Author 1 - Marcelo Cavalcante - Author 1 (Principal Investigator – Marcelo Borges Cavalcante):

Conceptualized and designed the study, including formulation of the research question, definition of the PICOS framework, and development of the protocol. Led the methodological strategy, including search design, eligibility criteria, and statistical approach for the meta-analysis. Supervised all stages of the review.

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Author 2 - Daniel Sobral - Contributed to the development of the search strategy and conducted systematic literature searches across all databases. Independently screened titles, abstracts, and full texts according to predefined eligibility criteria.

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Author 3 - Lara Alves - Contributed to the development of the search strategy and conducted systematic literature searches across all databases. Independently screened titles, abstracts, and full texts according to predefined eligibility criteria.

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