

**Preconception Th1/Th2/Th17/ Treg-associated cytokine imbalance in patients with unexplained recurrent abortion: a meta-analysis**

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University Of Guangzhou.**ADMINISTRATIVE INFORMATION****Support** - Project of Guangdong Administration of Traditional Chinese Medicine: 20241308.**Review Stage at time of this submission** - Data analysis.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202450038**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 May 2024 and was last updated on 08 May 2024.**INTRODUCTION**

**Review question / Objective** The purpose of this study was to investigate the difference of relevant cytokines in Th1/Th2/Th17/Treg balance between patients with unexplained recurrent abortion before pregnancy and the normal population.

**Condition being studied** Recurrent spontaneous abortion (RSA) is a common complication of early pregnancy, and in recent years has gradually become one of the difficult challenges for doctors and infertility patients, with an incidence of 1% to 3%. At present, the international definition of RSA has not been unified, and there are still disputes about the number of abortions, pregnancy weeks and whether biochemical pregnancy is included. The Royal College of Obstetricians and Gynaecologists (RCOG) defines RSA as three or more consecutive fetal losses before 24 weeks of gestation with the same spouse, and the European Society of Human Reproduction and Embryology

(ESHRE) defines RSA as two or more pregnancy failures before 24 weeks of gestation. These include biochemical pregnancies, and the American Society for Reproductive Medicine (ASRM) defines RSA as two or more consecutive pregnancy failures and explicitly excludes biochemical pregnancies. At present, it is recommended to define spontaneous abortion before 28 weeks of gestation with the same spouse for two or more consecutive times as RSA, and it is recommended to include biochemical pregnancy management. Maternal age, parental chromosomal abnormalities, uterine anatomic factors, antiphospholipid syndrome, hereditary thrombotic disorders, endocrine disorders, thyroid diseases, and even environmental factors are known to be associated with RSA, yet the cause of RSA remains unknown in nearly 50% of cases. Such cases are often referred to as unexplained recurrent spontaneous abortion (URSA) or idiopathic recurrent abortion and have a significant psychological impact on the affected couple. Most studies support that immunological factors are the

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prerequisite for successful pregnancy, and a clear understanding of the influence of isoimmune factors on URSA will provide new clues to explain and elucidate the pathological mechanism.

## METHODS

**Participant or population** Patient: Patients with recurrent abortion. Population: normal people.

**Intervention** No intervention.

**Comparator** No Comparator.

**Study designs to be included** Case-control study.

**Eligibility criteria** Inclusion criteria: Patients with unexplained recurrent abortion were not pregnant at the time of blood collection.

**Information sources** Electronic databases: PubMed, Web of science, Embase, GeenMedical, CNKI, WanFang, VIP.

**Main outcome(s)** Th1/Th2 peripheral related cytokines (IFN- $\gamma$ , TNF- $\alpha$ , IL-2, IL-6, IL-4, IL-10) levels, Th17/Treg peripheral related cytokines (IL-17, TGF- $\beta$ ) levels.

**Quality assessment / Risk of bias analysis** NOS scale.

**Strategy of data synthesis** In this study, Revman5.4 software was used for statistical processing. Due to different measurement units included in the study, measurement data were expressed as standard mean difference (SMD) and 95%CI, and presented as forest maps.  $P > 0.10$  and  $I^2 \leq 50\%$ , there was no or little heterogeneity among the studies, and the fixed-effect model was used for analysis. When  $P \leq 0.10$  and  $I^2 > 50\%$ , the heterogeneity between the studies was large, and the random effects model was used for analysis.

**Subgroup analysis** Subgroup analysis was performed according to the number of miscarriages (2 and 3).

**Sensitivity analysis** Revman software performs a sensitivity analysis to reflect the sensitivity of an article by how the effect size changes after the deletion of one of the articles.

**Country(ies) involved** China.

**Keywords** Unexplained recurrent abortion; Th1; Th2; Th17; Treg; Cytokines.

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