INPLASY PROTOCOL

To cite: Zhang et al. Prevalence, Risk Factors, and Outcomes of Rheumatoid Arthritis secondary to Asthma: A Protocol for Systematic Review and Meta-Analysis. Inplasy protocol 202230132. doi: 10.37766/inplasy2022.3.0132

Received: 23 March 2022

Published: 24 March 2022

Corresponding author:
Haiyan Zhou

zhouhaiyan@cdutcm.edu.cn

Author Affiliation:
Acupuncture and Moxibustion College, Chengdu University of Traditional Chinese Medicine.

Support: **NSFC of China(NO.81973959).**

Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
None declared.

Prevalence, Risk Factors, and Outcomes of Rheumatoid Arthritis secondary to Asthma: A Protocol for Systematic Review and Meta-Analysis

Zhang, LL[1]; Lu, WT[2]; Chen, XY[3]; Shang, YN[4]; Zhao, Y[5]; Zhou, HY[6].

Review question / Objective: **Previous studies have focused on the incidence or prevalence of RA and Asthma, but little is known about the causes of patients with RA secondary to asthma and there is no relevant systematic review. The purpose of this study is to conduct a meta-analysis of RA and asthma and to further explore the risk factors for asthma affecting the prevalence of RA, which will contribute to the study of the mechanistic links between these two diseases.**
Condition being studied: **T-helper (Th) 1 and Th2 cells have counter-regulatory relationships. Several studies discussed the relations between asthma and rheumatoid arthritis (RA) but the results were controversial. RA is a Th1 disease of unknow etiology, and analysis of its association with asthma helps to explore its causative factors.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 March 2022 and was last updated on 24 March 2022 (registration number INPLASY202230132).

INTRODUCTION

Review question / Objective: **Previous studies have focused on the incidence or prevalence of RA and Asthma, but little is known about the causes of patients with RA secondary to asthma and there is no relevant systematic review. The purpose of this study is to conduct a meta-analysis of RA and asthma and to further explore the risk factors for asthma affecting the prevalence of RA, which will contribute to the study of the mechanistic links between these two diseases.**

Condition being studied: T-helper (Th) 1 and Th2 cells have counter-regulatory relationships. Several studies discussed the relations between asthma and rheumatoid arthritis (RA) but the results were controversial. RA is a Th1 disease of unknow etiology, and analysis of its association with asthma helps to explore its causative factors.

METHODS

Participant or population: Inclusion: male or female of all ages. (1) RA patients with a history of asthma, we will include both definite and probable asthma because most probable asthmatics become definite over time. Studies of patients were diagnosed as RA by a physician through physical or imaging examination, or defined by the classification criteria of ACR in 1987 or ACR/EULAR in 2010. (2) control group: RA participants without asthma.Exclusion: asthma patients with a history of RA.

Intervention: Inclusion: If an adequate description of risk factors can be provided, the study will be considered. Potential risk factors will involve clinical characteristics, environmental factors, biological and genetic factors. Clinical characteristics will include demographic features (race, sex, age, and BMI), lifestyle (tobacco and alcohol use), history of other diseases, systemic diseases (such as cardiovascular disease, depression, substantial malignancies, etc.), and treatment.

Comparator: Exclusion: inadequate description of potential risk factors; odd ratios (ORs)/ relative risks (RRs)/hazard ratio (HR) are neither provided or calculated.

Study designs to be included: 1. the primary outcome includes the prevalence of RA in patients with asthma compared to RA participants without asthma. Outcome measures may include ORs, RRs, or HR. 2. the secondary outcomes include the risk factors for RA patients secondary to asthma (for example, sex, age, diet, and smoking).3. the third outcomes include cytokines in participants' serum, joint synovial fluid, or sputum (for example, serum tumor necrosis factor, interleukin, C-reactive protein).

Eligibility criteria: Types of study design: Inclusion: experimental studies (randomized controlled trials) and all types of observational studies (cohort, case-control, and cross-sectional); Exclusion: case reports, literature reviews, editorials, and commentaries.Types of participant: Inclusion: male or female of all ages. I. RA patients with a history of asthma, we will include both definite and probable asthma because most probable asthmatics become definite over time. Studies of patients were diagnosed as RA by a physician through physical or imaging examination, or defined by the classification criteria of ACR in 1987 or ACR/EULAR in 2010. II. control group: RA participants without asthma; Exclusion: asthma patients with a history of RA.Types of exposures: Inclusion: If an adequate description of risk factors can be provided, the study will be considered. Potential risk factors will involve clinical characteristics, environmental factors, biological and genetic factors. Clinical characteristics will include demographic features (race, sex, age, and BMI), lifestyle (tobacco and alcohol use), history of other diseases, systemic diseases (such as cardiovascular disease, depression, substantial malignancies, etc.), and treatment; Exclusion: inadequate description of potential risk factors; odd ratios (ORs)/ relative risks (RRs)/hazard ratio (HR) are neither provided or calculated.

Information sources: We will search the electronic databases EMBASE, MEDLINE, and the Cochrane library for studies.

Main outcome(s): The primary outcome includes the prevalence of RA in patients with asthma compared to RA participants without asthma. Outcome measures may include ORs, RRs, or HR.

Additional outcome(s): The secondary outcomes include the risk factors for RA patients secondary to asthma (for example, sex, age, diet, and smoking). The third

outcomes include cytokines in participants' serum, joint synovial fluid, or sputum (for example, serum tumor necrosis factor, interleukin, C-reactive protein).

Quality assessment / Risk of bias analysis: One reviewer will independently assess the quality of studies based on items in the Newcastle Ottawa Scale checklist (NOS). any concern on quality scoring will be decided in consultation with another reviewer. The quality score is based on a "star" system (rated on a 0-6 scale for studies without a comparator group and 0-9 for studies with a comparator group); within this, studies with scores 5 or 6 and 8 or 9 will be considered high quality, and all other studies will be considered low quality. With a higher score representing better methodological quality.

Strategy of data synthesis: The RevMan 5.3 software of the Cochrane Collaboration will be used for meta-analysis, and OR or RR will be used for qualitative data. Quantitative data will be obtained by mean difference (MD) or standardized mean difference (SMD). All effects will be expressed as a 95 % confidence interval (CI). If the heterogeneity is low ($P > 0.1$, $I2 \leq 50$ %), a fixed-effect model will be used for meta-analysis. If the heterogeneity is high ($P \leq 0.1$, $I2 > 50$ %), the cause of heterogeneity will be analyzed to determine whether the random-effect model can be used for meta-analysis. However, to estimate the prevalence of RA and risk factors more conservatively, the data will be aggregated using the random-effects model described by DerSimonian and Laird. Risk factors will be identified through a meta-analysis of risk factors by summarizing the maximally adjusted ORs and unadjusted univariate analysis reported in each study (using 2×2 tables, when the required data are available from the individual studies).

Subgroup analysis: If meta-analysis is feasible, subgroup analyses will be conducted based on the characteristics of participants, such as demographic features, smoking or drinking history, intervention characteristics.

Sensitivity analysis: If there is obvious heterogeneity, no synthesis will be carried out and only descriptive qualitative analysis will be carried out. A sensitivity analysis will be carried out. In this study, references with a "high risk of bias" will be eliminated one by one, the remaining studies will be meta-analyzed, and the new synthesis effect will be compared with the results before elimination.

Country(ies) involved: Chengdu, Sichuan, China.

Keywords: Rheumatoid arthritis; asthma; comorbidities; epidemiology; risk factors; systematic review; meta-analysis.

Contributions of each author:

Author 1 - Linlin Zhang.
Email: zhanglinlin015@163.com
Author 2 - Wenting Lu.
Email: apesister@163.com
Author 3 - Xingyu Chen.
Author 4 - Yanan Shang.
Author 5 - Yu Zhao.
Author 6 - Haiyan Zhou.