

INPLASY202590010  
doi: 10.37766/inplasy2025.9.0010  
Received: 3 September 2025  
Published: 4 September 2025

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**ADMINISTRATIVE INFORMATION**

**Support** - Continuum Oral Health 61 Lincoln Street Framingham, Ma 01702; Advanced Data Corporation 65 Main Street, Framingham, MA 02568.

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

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY202590010

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 4 September 2025 and was last updated on 4 September 2025.

**INTRODUCTION**

**Review question / Objective** Is there an association between variations in oxidant and antioxidant levels in blood and saliva between patients with Behcet disease and healthy individuals?

**Condition being studied** Behcet Disease, a complex aphthosis condition which presents with systemic vasculitis. Formerly designated a triad of oral ulceration, genital ulceration and orbital ulceration. It is now known to exhibit a widespread vasculitis culminating in skin lesions, joint lesions, et al.

**METHODS**

**Search strategy** The keywords related to "oxidative stress", "anti-oxidants" and "Behcet disease" will be used to perform a comprehensive

search on MEDLINE, Embase, Scopus, and Web of Science. Also, a manual snowballing search will be done in the bibliography of related articles, likewise, reference tracking and citation tracking of eligible studies will also be used to retrieve more relevant studies.

**Participant or population** Patients diagnosed with complete and incomplete Behcet disease using established diagnostic criteria such as O'duffy, International Study Group on Behcet, the International Criteria for Behcet Disease, et al. Patients may be in the active or inactive stage.

**Intervention** Hematological or biochemical test evaluating the oxidative - antioxidant status in Behcet disease in blood and salivary samples.

**Comparator** Normal healthy controls who have not been diagnosed with Behcet or other similar complex aphthous lesions.

**Study designs to be included** observational studies, case-control studies, cohort studies, whether retrospective or prospective.

#### Eligibility criteria

- Adulthood
- Patients with diagnosed Behcet's Disease
- Full text manuscripts
- English Language.

#### Information sources

- Electronic databases
- Contact with authors
- Trial registers, or
- Grey literature.

**Main outcome(s)** Concentrations of oxidative stress markers in salivary and blood samples from patients with Behcet Disease. Inclusion criteria comprises studies that provide information to the measurement of biomarkers, oxidants and antioxidants; association between oxidative stress and Behcet's Disease; with oxidative stress as an etiological factor of Behcet Disease.

**Data management** The following relevant information will be retrieved from the selected studies: name of authors; date of publication; type of study, number of participants, age, gender, type of samples (blood or saliva); oxidative parameters, mean (or median) levels of oxidant with standard deviation or interquartile range as indicated, and antioxidant biomarkers in saliva and blood in Behcet Disease and in healthy control groups.

**Quality assessment / Risk of bias analysis** The Newcastle - Ottawa Quality Assessment Scale for Case Control Studies for the risk of bias analysis for selected studies.

**Strategy of data synthesis** The statistical analysis will be carried out using the R statistical package. The mean levels of the serum and salivary markers and / or proportion of markers will be calculated and pooled mean or proportion will be calculated using a fixed-effects model or random-effects model to evaluate the relationship between mean (median) and Behcet Disease . The  $I^2$  statistic will be used to evaluate the between-study heterogeneity analysis in this study. The fixed effects model will be used when there is no significant heterogeneity between the included studies.

**Subgroup analysis** Different groups and subgroups will be established according to the retrieved studies.

**Sensitivity analysis** The leave out sensitivity analysis will be used to show the influence of any individual study while studentized residuals will be utilized for evaluating study outliers.

**Language restriction** English Language.

**Country(ies) involved** Nigeria, Canada, United States.

**Keywords** Behcet Disease; Complex Aphthosis; Oxidative Stress; Anti-oxidant Status.

**Dissemination plans** systematic review and meta-analysis to be published in a peer reviewed journal for dissemination.

#### Contributions of each author

Author 1 - Adetayo Aborisade - Author 1 conceptualized and drafted the manuscript.

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Author 2 - Amina Mohammed - The author drafted part of the protocol and was involved in the conceptualization of the study.

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Author 3 - Olugbenga Akinsanya - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.

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Author 4 - Eniola Ayinde - The author read, provided feedback and approved the final draft proposal.

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