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ORIGINAL ARTICLE

Effect of clinical treatments for metabolic syndrome on albuminuria: a systematic review protocol

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KEYWORDS

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ABSTRACT

Introduction: Metabolic syndrome (MetS) predicts cardiovascular disease, and patients with this condition and type 2 diabetes have increased albuminuria, significantly impacting cardiovascular mortality and kidney disease progression. A considerable number of interventions to control MetS exist and are considered efficient, including the use of medication and changes in lifestyle. However, which approaches are effective in controlling albuminuria remains unclear. This systematic review protocol aims to map in the available literature whether lifestyle, medication, and surgical intervention for MetS have an impact on reducing albuminuria in adult patients.
Methods: The Joanna Briggs Institute methodology for systematic reviews will be followed. Cochrane Database of Systematic Reviews, Scopus, Embase, and MEDLINE/PubMed databases will be used. For the Gray Literature, the DART-Europe E-theses Portal. There will be no language restriction. Studies written after 2009 will be included due to the consensus and definition of metabolic syndrome. This review will include studies considering pharmacological and non-pharmacological treatments for controlling albuminuria in patients with MetS. Studies where MetS is described in children and adolescents, animals, pregnant women, and patients with type 1 diabetes will be excluded. First, the selection will be based on reading the title and summary of the texts retrieved in the search strategy, followed by reading the relevant texts in full by two reviewers. After the selection of the studies, the extraction of the data, analysis, and synthesis will be conducted according to the JBI methodology.

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INTRODUCTION

Metabolic syndrome (MetS) is a global epidemic with significant socioeconomic and public health impacts[1]. The prevalence of MetS has been consistently linked with an all-cause mortality[2]. Albuminuria in patients with MetS is a common microvascular complication of the kidney, which is also a significant cause of end-stage kidney disease and is associated with an increased risk of death in general, mainly due to cardiovascular diseases[3]. Increased blood pressure and hyperglycemia are risk factors for chronic kidney disease (CKD) in patients with MetS. In addition, increased waist circumference is significantly correlated with albuminuria and decline in glomerular filtration rate (GFR), suggesting that obesity may be an independent risk factor for CKD[4]. Previous studies have indicated increased urinary albumin excretion correlated with rising glucose levels[5], insulin resistance[6], elevated blood pressure (BP)[7], and MetS[8].

Several old and new drug treatments have been proposed and used to treat MetS and type 2 diabetes mellitus (T2DM)[9,10,11]. In addition, lifestyle modification, including diet and physical exercise, is a fundamental therapeutic approach to improving metabolic parameters in patients with MetS and T2DM[12]. However, the effects and effectiveness of these therapies in decreasing albuminuria remain unclear. Therefore, in this systematic review (SR), we sought to evaluate scientific evidence from the literature on the impact of each treatment available for MetS that can reduce albuminuria.

A preliminary search on PROSPERO, MEDLINE, the Cochrane Database of Systematic Reviews, and the Joanna Briggs Institute (JBI) Database of Systematic Reviews and Implementation Reports was conducted, and no current or ongoing systematic reviews on the topic were identified. In an initial literature search, we identified some primary studies that could lead to conclusions about treatments that support a reduction and control of albuminuria in the context of MetS, justifying the continuation of this systematic review[13-15].

Objectives and research questions

This systematic review aims to synthesize and review studies describing whether there is any available treatment for metabolic syndrome with a reduction in albuminuria in adult patients. The following research question was formulated: What is the impact of the clinical treatments available for patients with MetS in controlling microalbuminuria, albuminuria, and proteinuria?

METHODS

Types of studies

This systematic review will only consider experimental study designs, including randomized and non-randomized controlled trials.

Participant/population

This review will consider studies conducted in adult patients aged 18 years or older with MetS and microalbuminuria, albuminuria, or proteinuria. Furthermore, this study will also consider any context of care for patients with MetS, such as hospitalization or outpatient home care.

Intervention

This review will consider studies that evaluated drug or non-drug treatments and the impact of these different therapies (such as lifestyle, medication, or surgical intervention) for MetS.

Comparator

The comparator factor will be studies that did not perform treatment or use placebo for MetS.

Outcome

This review will consider studies that included the following outcomes: the impact of different therapies for MetS in reducing albuminuria, assessed through the albumin-creatinine ratio in the isolated urine sample, proteinuria, albuminuria, or microalbuminuria in a 24 h period.

Albuminuria will be defined as the persistent increase in urinary albumin excretion above 20 µg/min in overnight samples or above 30 mg/24 h in 24 h urine samples[16]. Alternatively, the albumin/creatinine ratio can be adopted in isolated samples above 30 mg/g or 2.5 mg/mmol[17]. During the evaluation of the results, we will consider changes in blood pressure, blood glucose, and weight loss, which may allow for further sub-analysis.

Identification of studies

The proposed systematic review will follow the JBI methodology for systematic reviews[18]. An initial search aimed to identify the presence of specific literature that met the inclusion and exclusion criteria described above. The second step defined the keywords of the literature search. The following words and their possible variations were defined as search words: metabolic syndrome, albuminuria, proteinuria, microalbuminuria, and treatment. Only studies conducted in humans and those published in the last 10 years will be included (because they refer to the recent definition of metabolic syndrome currently accepted in the scientific community[19]). The titles and abstracts of the retrieved articles will be arranged in Excel and read by two independent reviewers (MGFL and BLP). In case of divergence between the reviewers, the assistance of a third reviewer (KBS) will be requested to define the article maintenance.

Search strategy

The search strategy aims to locate both published and unpublished studies. An initial limited search of MEDLINE, Cochrane Database of Systematic Reviews, and JBI Database was conducted to identify articles on the topic. The words contained in the titles and abstracts of relevant articles and the index terms used to describe

the articles were used to develop a complete search strategy for reporting the name of the relevant database, as described in the Supplement.

The search strategy, including all identified keywords and index terms, was adapted for each information source. The reference list of all studies selected for critical appraisal will be screened for additional studies. The databases used were MEDLINE through PubMed (U.S. National Library of Medicine), Embase, Cochrane, and Scopus. Sources of unpublished studies and gray literature to be reviewed include the DART- Europe E-theses Portal. Studies published from 2009 onwards will be selected without language restriction in anything databases. The potentially relevant articles are reviewed in full. Two independent reviewers will thoroughly evaluate the full text of the selected citations against the inclusion criteria. Reasons for the exclusion of full-text articles that do not meet the inclusion criteria will be recorded and reported in the systematic review. The search strategy was performed between August and September 2021.

Types of outcome measures

Assess the impact of pharmacological and non-pharmacological treatments (such as lifestyle, medication, or surgical intervention) in reducing microalbuminuria, albuminuria, and proteinuria.

Study selection

Following the search, all identified citations will be uploaded into the Mendeley management platform, and duplicates will be removed. Two independent reviewers will then screen titles and abstracts to assess the inclusion criteria for the review. Potentially relevant studies will be retrieved in full, and their citation details will be imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI, Adelaide, Australia)[20].

Any disagreements that arise between the reviewers at each stage of the study selection process will be resolved through discussion or by a third reviewer (MFCL). The search results will be fully reported in the systematic review and presented in a PRISMA flow diagram[21].

Data collection and data extraction

Two independent reviewers will collect and extract the data using an Excel table. They should contain the following information: study title, place of study, year of publication, authors, periodical, the age range of study population, type of study, abstract, relevant points, sample size (n), diagnostic criteria for MetS (independent of the organizations) and albuminuria, limitations and clinical management strategy used, calculation of creatinine clearance, follow-up, criteria for inclusion, and limitations of the study. The studies' authors will be contacted when there is no clear data or some information needs clarification.

Analysis plan

The data will be organized and tabulated to answer the questions of this review, and a narrative description of the data was developed such that the available evidence on the subject could be synthesized.

Risk of Bias

The methodological quality of the selected studies will be evaluated by two independent reviewers, applying the JBI checklist[22]. The checklist-based tool structure consists of 13 questions to evaluate the following domains: selection and allocation; administration of intervention/exposure; assessment, detection, and measurement of the outcome and participant retention. Studies may be classified as "low risk of bias", "unclear/moderate risk of bias" and "high risk of bias". Studies with low methodological quality will be excluded.

Quality of Evidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system will be used to determine the level of evidence for recommendations.

Metanalysis

The studies evaluating comparable treatment strategies and showing homogeneity in their methodological design will be combined to perform the meta-analysis. To combine the continuous results of the studies, the Mantel–Haenszel random effects model and differences between standardized means will be used to measure the effect. Additionally, the I^2 statistical test results will be interpreted considering the magnitude and direction of the effect. The meta-analysis procedures will be performed using Cochrane Review Manager software (RevMan, version 5.4.1).

DISCUSSION

Several previous studies have examined the role of MetS and its components in the risk of proteinuria/albuminuria, and the evidence is consistent[23]. Albuminuria is recognized as an isolated cardiovascular risk factor and a critical progression factor for chronic kidney disease[24,25].

Several studies have been published, and substantial research has been conducted to determine the best approach to control MetS and its components[26], but little is known about its impact on albuminuria. To our knowledge, the present review will be the first to comprehensively analyze the association between MetS treatment and reduced albuminuria.

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Writing of the manuscript: BLP, KBS, MGFL, MFCL, CTS
Critical revision of the article: CTS
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