INPLASY

Correlation of Serum Irisin Levels with Diabetic Nephropathy: An Exhaustive Systematic Appraisal and Meta-Analytical Investigation

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ADMINISTRATIVE INFORMATION

Support - No.

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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 13 March 2025 and was last updated on 13 March 2025.

INTRODUCTION

Review question / Objective Diabetic nephropathy (DN) is a major complication of diabetes, contributing significantly to end - stage renal disease. Irisin, an exercise - induced myokine, has been linked to metabolic disorders, but its relationship with DN remains unclear. This study aims to comprehensively and accurately explore the association between serum irisin levels and DN through a systematic review and meta - analysis.

Condition being studied The research was conducted following the Meta - analysis of Observational Studies in Epidemiology (MOOSE) guidelines. Multiple electronic databases, including Cochrane Library, Embase, Web of Science, PubMed, China National Knowledge Infrastructure (CNKI), China Biology Medicine disc (CBM), and Wanfang Database, were systematically searched using relevant keywords related to irisin and DN. Studies were included if they were randomized controlled trials (RCTs) or observational studies that stratified Type 2 diabetes mellitus (T2DM) patients based on the presence or absence of DN, measured serum irisin levels in both groups, and provided data in a suitable format. Two independent reviewers performed literature screening, data extraction, and quality assessment. The Jadad scale was used for RCTs, and the Newcastle - Ottawa Scale (NOS) was applied for cohort and case - control studies. Statistical analysis was carried out using RevMan 5.3 software, with heterogeneity evaluated by Q and I^2 tests, and appropriate models (fixed - effects or random - effects) selected accordingly.

METHODS

Participant or population Patient with Type 2 diabetes mellitus.

Intervention (b) stratifying Type 2 diabetes mellitus (T2DM) patients into case and control groups based on the presence or absence of diabetic nephropathy (DN).

Comparator (b) stratifying Type 2 diabetes mellitus (T2DM) patients into case and control groups based on the presence or absence of diabetic nephropathy (DN).

Study designs to be included (a) published randomized controlled trials (RCTs) or observational studies.

Eligibility criteria (1) Case reports: Case reports typically describe individual cases and lack the sample size and statistical power necessary for a meta - analysis. Since our study aims to pool data from multiple studies to draw a comprehensive conclusion about the relationship between serum irisin levels and diabetic nephropathy, case reports were excluded. They do not provide sufficient information to contribute to the overall statistical analysis and may introduce bias due to their limited representativeness.
(2) Inability to extract relevant outcome indicators such as incidence rates: In order to conduct a valid meta - analysis, it is crucial to have consistent and extractable data on relevant outcome measures. Studies that did not report data in a format that allowed for the extraction of key indicators, such as serum irisin levels in a comparable manner or the incidence of different stages of diabetic nephropathy, were excluded. Without these data, it would be impossible to accurately assess the relationship between the variables of interest and would compromise the integrity of the meta - analysis.
(3) Inclusion of patients with concomitant diseases: Patients with concomitant diseases may have different physiological states and confounding factors that can affect serum irisin levels and the development of diabetic nephropathy. For example, patients with other serious metabolic disorders or autoimmune diseases may have altered irisin production or metabolism, which could confound the relationship we are trying to establish. To isolate the impact of diabetic nephropathy on serum irisin levels, studies that included patients with significant concomitant diseases were excluded. This helps to ensure that the results of the meta - analysis are more accurately reflecting the relationship between the two main variables of interest.

Information sources Multiple electronic databases, including Cochrane Library, Embase, Web of Science, PubMed, China National Knowledge Infrastructure (CNKI), China Biology Medicine disc (CBM), and Wanfang Database, were systematically searched using relevant keywords related to irisin and DN.

Main outcome(s) After a rigorous selection process, 7 studies were included in the meta - analysis. The results indicated that irisin could potentially serve as a biomarker for predicting different albuminuria states and estimated glomerular filtration rate (eGFR) in DN patients. For normoalbuminuria vs. microalbuminuria, the relative risk (RR) was 30.84 (95% CI: 7.81, 53.87); for normoalbuminuria vs. macroalbuminuria, RR = 30.84 (95% CI: 7.81, 53.87); for microalbuminuria vs. macroalbuminuria, RR = 12.53 (95% CI: 3.46, 21.59); and for eGFR, RR = 3.43 (95% CI: - 2.90, 9.75). High heterogeneity was observed among the studies, leading to the use of random - effects models. The assessment of publication bias suggested a relatively low likelihood of bias.

Quality assessment / Risk of bias analysis Two independent reviewers conducted literature screening, data extraction, and quality assessment, with any discrepancies resolved by a third reviewer. The extracted data included study design, study population, inclusion and exclusion criteria, interventions, treatment methods of the control group, and outcomes. Mean and standard deviation (SD) were extracted for quantitative data. For randomized controlled trials, the Jadad scale was used to assess study quality, while the Newcastle-Ottawa Scale (NOS) was applied for cohort and case-control studies.

Strategy of data synthesis RevMan 5.3 software was used for statistical analysis. For dichotomous variables, odds ratios (OR) and 95% confidence intervals (CI) were calculated. Heterogeneity was assessed using Q and I2 tests. In instances of low heterogeneity, a fixed-effects model was adopted. A random-effects model (RE) was used for high heterogeneity, and sources of heterogeneity were re-evaluated. Subgroup analysis was employed when significant heterogeneity with statistical differences was observed. Descriptive analysis was carried out when the origin of heterogeneity could not be elucidated. The statistical significance level was set at 0.05.

Subgroup analysis Within the timeframe of 2014 to August 2023, a comprehensive exploration yielded a total of 265 relevant articles. After eliminating duplicate literature, 192 articles remained, comprising 134 in English and 58 in Chinese. Preliminary screening based on titles and abstracts led to the exclusion of 176 articles, including 43 that were unrelated to the research topic, 125 consisting of case reports, reviews, and other irrelevant content, as well as 8 single-group studies. Subsequently, 16 articles were initially included after a thorough assessment, which was

further reduced to 7 articles after reading the full texts[[] Liu JJ, Liu S, Wong MD et al. Relationship between circulating irisin, renal function and body composition in type 2 diabetes. J Diabetes Complicat 2014; 28: 208–213]-[] Shelbaya S, Abu Shady MM, Nasr MS et al. Study of irisin hormone level in type 2 diabetic patients and patients with diabetic nephropathy. Curr Diabetes Rev 2018; 14: 481–486]]. A total of 453 participants from DN cohorts and 346 patients from non-DN groups were compiled. Furthermore, the assessment of publication bias offered a comprehensive perspective on the heterogeneity of constituents. The flowchart depicting the process of literature selection is illustrated in Figure 1. Basic information regarding the included studies is presented in Table 2.

Sensitivity analysis Among the 7 studies included in this paper, 2 were randomized controlled trials, and 5 were retrospective case-control studies. The quality of RCTs was evaluated using the Jadad Scale, with appropriate random sequence generation (2 points), unclear allocation concealment (1 point), lack of blinding (0 points), and insufficient description of withdrawals or dropouts (0 points), resulting in a Jadad score of 3 points, indicating low-quality literature. (Table 3 and Figure 2).

Country(ies) involved China.

Keywords Type 2 diabetes mellitus; Irisin; Diabetic Nephropathy; Systematic review; Meta - analysis.

Contributions of each author
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