

## Serum trace elements in gestational diabetes mellitus: A systematic review and dose-response meta-analysis

INPLASY202370039

doi: 10.37766/inplasy2023.7.0039

Received: 11 July 2023

Published: 11 July 2023

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**Review question / Objective** The aim of this review and meta-analysis was to summarize the available evidence on serum Zn, Cu, Fe and Mg concentrations in GDM.

**Condition being studied** Gestational diabetes mellitus (GDM) refers to normal glucose metabolism or underlying impaired glucose tolerance before pregnancy, symptoms disappear with delivery, which is one of the most common complications of pregnancy, recently decades years, the prevalence of GDM has increased 2% in a number of countries. GDM has forming an emerging worldwide epidemic, trace elements are of great significance for maintaining the normal physiological function of the body, and studies in recent years have found that some trace elements can change the signal transduction factors of fat cells and skeletal muscle cells to cause insulin resistance, and can also cause insufficient insulin secretion by increasing oxidative stress to disrupt islet cell function. However, epidemiological results

regarding the association between trace elements and GDM are not consistent. There are few data on serum levels of trace elements in GDM. most of these data were derived from clinical trials assessing outcomes of nutritional supplementation. The aim of this review and meta-analysis was to summarize the available evidence on serum Zn, Cu, Fe and Mg concentrations in GDM.

**METHODS**

**Search strategy** Search subject terms and free text terms was used a combination: “trace elements” OR “zinc” OR “iron” OR “copper” OR “magnesium”) AND (“Diabetes, Gestational” OR “gestational diabetes\*” OR “gestational glucose” OR pregnancy hyperglycemia OR pregnancy diabetes\* OR pregnancy glucose OR maternal hyperglycemia OR maternal diabetes\* OR maternal glucose OR GDM). In addition, the reference lists of the primary studies were evaluated and screened to find other relevant studies.

**Participant or population** Gestational diabetes mellitus.

**Intervention** Assessment of whether trace elements serum levels are associated with GDM.

**Comparator** Non GDM pregnant women.

**Study designs to be included** None restriction.

**Eligibility criteria** Inclusion criteria were included: (1) studies needed to contain specific data relating to the serum concentrations of Zn, Fe, Cu, or Mg. (2) population-based studies. Exclusion criteria were: (1) commentaries, reviews, or conference abstracts, (2) repetitive studies, (3) clinical interventions, (4) animal studies and laboratory studies, (5) lacking a control group.

**Information sources** All searches from the following databases: PubMed, Embase, Web of Science, The Cochran Library, CNKI, CBM, and Wanfang. The search time frame was from database inception to March 20, 2023.

**Main outcome(s)** Serum Zn, Cu, Fe and Mg levels.

**Quality assessment / Risk of bias analysis** The methodological quality of the cross-sectional study was evaluated using the checklist developed by agency for healthcare research and quality (AHRQ) (supplementary table 1), which included 9 items, including: (1) whether the source of the data was identified (survey, literature review); (2) Whether the inclusion criteria of the research objects are clearly defined; (3) Whether to describe the research object and research site in detail; (4) Whether an explanation is provided for the exclusion of some research objects from the analysis; (5) Whether the patient response rate and the integrity of the data collection were summarized, and if the study data was incomplete or there were missing values, how the missing data was processed in the analysis was explained; (6) Whether the confounding factors affecting the research results were identified; (7) Whether measures to evaluate and/or control confounding factors are described; (8) Whether to use effective and credible methods to evaluate outcome indicators; (9) Whether the data analysis method is appropriate. Each entry is answered with "yes", "no", "unclear". Answers "yes" are worth 1 point, answers "no" and "unclear" are worth 0 points. The literature quality evaluation was carried out independently by two researchers, and the decision was made after discussion with the third researcher in case of disagreement.

**Strategy of data synthesis** Serum trace elements levels expressed as mean ( $\pm$ SD) determine the standard mean difference (SMD) and 95% CI. The I<sup>2</sup> tests were used to examine the heterogeneity among studies. In case the I<sup>2</sup> > 50% or the P < 0.05, heterogeneity was considered in the meta-analysis. The SMD was computed by random-effects model with heterogeneity, otherwise, a fixed-effect model was conducted. Potential publication bias of studies was estimated by funnel plots and Egger test. All analyses were conducted using the Stata/SE software version 11.0.

**Subgroup analysis** None planned.

**Sensitivity analysis** Sensitivity analysis was conducted by eliminating individual studies one by one. Egger's tests and Begg's tests were used to assess potential publication bias.

**Country(ies) involved** China.

**Keywords** Gestational diabetes; Zinc; Magnesium; Copper; Iron.

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