



## NUTRITION

# The association between serum selenium and gestational diabetes mellitus: A systematic review and meta-analysis



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## ABSTRACT

**Background:** Results of the studies about association between serum selenium concentration and gestational hyperglycemia are inconsistent. Some studies have demonstrated that women with gestational diabetes mellitus (GDM) have lower Se concentrations while contrary results are reported in other studies. **Aim:** The aim of this study is to compare the serum Se concentration in women with GDM and normoglycemic pregnant women via a systematic review and meta-analysis.

**Methods:** A computerized literature search on four databases (PubMed, Cochrane register of control trials, Scopus and Google scholar) was performed from inception through August 2013. Necessary data were extracted and random effects model was used to conduct the meta-analysis.

**Results:** Six observational studies (containing 147 women with GDM and 360 normoglycemic pregnant women) were found, which had compared serum Se concentration in women suffering from GDM with normal pregnant ones. Our meta-analysis revealed that serum Se concentration was lower in women with GDM compared to normoglycemic pregnant women (Hedges =  $-1.34$ ; 95% CI:  $-2.33$  to  $-0.36$ ;  $P < 0.01$ ). Stratified meta-analysis demonstrated that concentration of Se in the sera of women with GDM was lower than normal pregnant women both in second and third trimesters, but the result was not significant in second trimester (second trimester: Hedges =  $-0.68$ ; 95% CI:  $-1.60$ – $0.25$ ;  $P = 0.15$ , third trimester: Hedges =  $-2.81$ ; 95% CI:  $-5.21$  to  $-0.42$ ;  $P < 0.05$ ). It was also demonstrated that serum Se status was lower in pregnant women with impaired glucose tolerance (IGT) compared to normoglycemic pregnant women (Hedges =  $-0.85$ ; 95% CI:  $-1.18$  to  $-0.52$ ).

**Conclusion:** The available evidences suggest that serum Se concentration is significantly lower in pregnant women with gestational hyperglycemia compared to normal pregnant women.

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## Introduction

Gestational diabetes mellitus (GDM) as a temporary form of type 2 diabetes mellitus (T2DM) is one of the most prevalent complications in pregnancy [1]. GDM has become more common due to incremental prevalence of obesity and T2DM. Its prevalence varies from 1.7% to 11.7% around the world [2]. During normal pregnancy, insulin resistance increases in parallel with increasing in oxidative stress which leads to reduction in antioxidant levels [3]. These

conditions are more prominent in women with GDM; in whom glucose oxidation, protein glycation, and lipid peroxidation lead to free radicals accumulation [1]. It seems that a positive correlation exists between erythrocyte glutathione peroxidase-1 (GPX1) activity and insulin resistance. This can be explained through the fact that oxidative stress reduces insulin secretion and increases insulin resistance; therefore, it is linked to T2DM [3].

Selenium (Se) as an essential trace element has an important role in the action of antioxidants such as glutathione peroxidases (GPxs) [4]. Also, it is proposed that Se has anti-diabetic functions due to its insulin-like characteristics; hence Se supplementation seems to have beneficial effects in diabetic patients [5,6]. It seems that the relationship between low Se concentration and impaired glucose tolerance is exclusive to pregnancy, because some evidences show that serum Se concentration is higher in patients with

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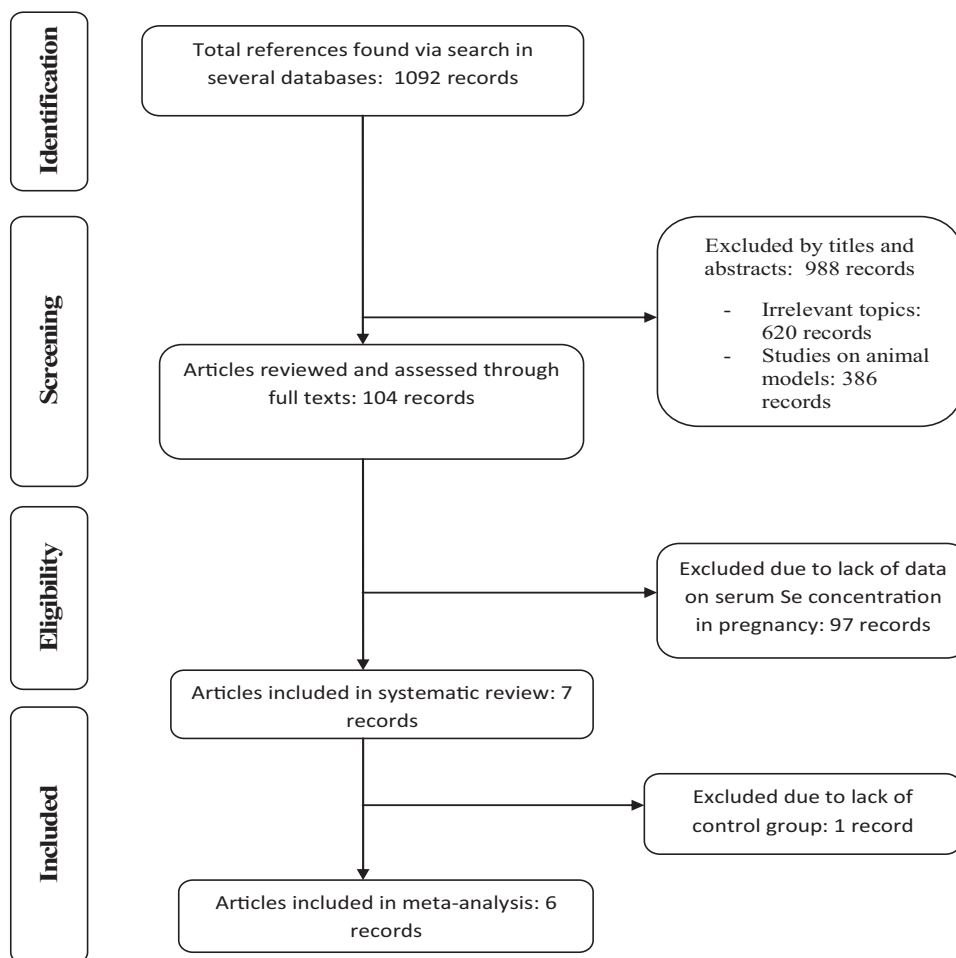


Fig. 1. PRISMA flow diagram of study identification, inclusion and exclusion.

T2DM [7,8]. Stranges et al. also suggested that Se supplementation may increase the risk of T2DM [9]. In a recently published meta-analysis evaluating the effects of Se supplementation on risk of T2DM and cardiovascular disease, the authors concluded that Se supplementation cannot significantly increase the risk of T2DM [10].

The results of the studies about association between selenium status and GDM or gestational hyperglycemia are inconsistent. Some studies have shown that women with GDM have lower concentrations of serum Se compared to healthy pregnant women [11–14]; however, a study performed by Molnar et al. [15] showed that serum Se concentration is significantly higher in GDM patients; while Al-Saleh et al. [16] did not find a significant association between serum Se concentration and GDM.

Referring to the scientific literature, no review article has been published on the association between selenium status and GDM. In the present study, we conducted a meta-analysis on the subject to quantify the association between maternal selenium status and GDM.

## Materials and methods

The study protocol was registered in PROSPERO, an international database of prospectively registered systematic reviews in health and social care, with the registration number: CRD42013005038. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria to conduct and report the results of the present study.

## Search strategy

A computerized literature search on four databases, i.e., PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>), Cochrane register of control trials (<http://onlinelibrary.wiley.com/cochranelibrary/search>), Scopus (<http://www.scopus.com/home.url>) and Google scholar (<http://scholar.google.com>) was performed from inception through August 2013. We used keywords selected from Medical Subject Headings (MeSH; <http://www.ncbi.nlm.nih.gov/mesh>) or other keywords including “Selenium”[Mesh], “Selenium Compounds”, “Selenium-Binding Proteins”, “selenium\*” and “selenate” in combination with “Diabetes, Gestational”, “gestational diabetes mellitus”, “pregnancy”, and “gestation”. Two authors evaluated the studies separately through the review of the titles, abstracts, and if necessary, full texts (TJ and AAF). References of related papers were more extensively read by authors to avoid missing articles. Any disagreements in selecting related papers were resolved by debate with a third author (ASA).

## Inclusion criteria

Observational studies performed in adult women to assess serum Se levels at any time of gestational period in both pregnant women with gestational hyperglycemia or GDM and healthy pregnant women as their control group were enrolled in the current systematic review and meta-analysis.

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