Feb 17, 2020

The prognostic role of serum uric acid levels in preeclampsia: a meta-analysis

Ioannis Bellos[1], Vasilios Pergialiotis[1], Dimitrios Loutradis[1], Georgios Daskalakis[1]

[1]National and Kapodistrian University of Athens

1 Works for me dx.doi.org/10.17504/protocols.io.bcndiva6

Ioannis Bellos

ABSTRACT

The present meta-analysis will assess the possible association of serum uric acid with the development of preeclampsia. Preeclampsia represents a serious pregnancy complication with increased fetal and maternal morbidity and mortality rates. Its incidence is estimated at approximately 5-8% of pregnancies, although presenting wide variance worldwide. Its pathophysiology is complex; however, it is hypothesized that the combination of poor trophoblast invasion with the release of angiogenic and pro-oxidant mediators into maternal circulation leads to generalized endothelial dysfunction. Prediction of the disease is necessary in order to provide measures of prevention, especially the administration of aspirin; nonetheless, the optimal screening model remains under investigation. All the available literature evidence regarding the prognostic utility of serum uric acid in preeclampsia is planned to be evaluated, by applying no date or language restrictions during the literature search. Result will be pooled by a quantitative meta-analytic approach, planning to subgroup outcomes on the basis of pregnancy trimester, disease severity and onset. The credibility of evidence will be evaluated under the GRADE framework.

1 Review title: The prognostic role of serum uric acid levels in preeclampsia: a meta-analysis

2 Review question: The meta-analysis aims to clarify whether uric acid levels are altered in preeclampsia compared to normotensive pregnant women. Also, it will be evaluated whether uric acid levels differ in the severe form of the disease, as well as whether they are able to predict adverse maternal outcomes, such as eclampsia, cesarean section, low birth weight and neonatal death.

3 Searches: MEDLINE, Scopus, CENTRAL, ClinicalTrials.gov and Google Scholar will be systematically searched from inception by two authors independently. No language or date restrictions will be applied. Key-words will include: uric, urate, preeclampsia, pre-eclampsia, eclampsia, gestational hypertension.

4 Condition or domain being studied: The present meta-analysis will assess the possible association of serum uric acid with the development of preeclampsia. Preeclampsia represents a serious pregnancy complication with increased fetal and maternal morbidity and mortality rates. Its incidence is estimated at approximately 5-8% of pregnancies, although presenting wide variance worldwide. Its pathophysiology is complex; however, it is hypothesized that the combination of poor trophoblast invasion with the release of angiogenic and pro-oxidant mediators into maternal circulation leads to generalized endothelial dysfunction. Prediction of the disease is necessary in order to provide measures of prevention, especially the administration of aspirin; nonetheless, the optimal screening model remains under investigation.

5 Participants/population: Preeclamptic cases should be defined as new-onset hypertension (BP >140/90 mmHg) after the 20th week of pregnancy combined with either proteinuria or signs of maternal organ dysfunction. Early-onset preeclampsia should be defined as preeclampsia occurring before the 34th week of pregnancy. Exclusion criteria: pre-existing hypertension, diabetes mellitus or gestational diabetes mellitus, chronic kidney disease, any cardiovascular disease, any autoimmune disease.

6 Intervention(s), exposure(s): -Measurement of serum or plasma uric acid levels in preeclamptic and healthy pregnant women. -Measurements of all trimesters will be examined. -No restrictions regarding laboratory assay will be applied. -Outcome will be expressed in mg/dl.

7 Comparator(s)/control(s): The control group will consist of healthy normotensive pregnant women without proteinuria or any other signs of pregnancy complications.

8 Types of study to be included: All observational studies (prospective cohort, retrospective cohort, case-control and cross-sectional) will be eligible for inclusion. Case reports, small case series (<10 cases), conference proceedins, posters, review articles and animal studies will be excluded. Studies with only the abstract available will also be excluded, as they ineviably will lack essential information for data analysis.

9 Main outcome(s): Outcomes: serum uric acid levels (as a continuous variable expressed in mg/dl), diagnostic accuracy (in terms of sensitivity and specificity) of serum uric acid for preeclampsia and its complications.

10 Data extraction (selection and coding): Study selection will be conducted consecutively in 3 stages. At first, the titles and abstracts of all electronic papers will be screened to evaluate their potential eligibility. Subsequently, all articles presumed to meet the criteria will be retrieved as full-texts. Finally, all observational studies reporting the outcomes of interest will be held eligible. Small case series (<10 patients), case reports, conference abstracts or posters, review articles and animal studies will be excluded. Data extraction will be made by two reviewers independently. Any potential discrepancies concerning retrieval of articles and statistical analyses will be resolved by the consensus of all authors. The extracted data will include the following parameters: name of first author, year of publication, eligibility criteria, study design, country, timing of measurement, cut-off value, assay method, use of serum or plasma, maternal age, gestational age, cesarean section rate, eclampsia, birth weight and neonatal death.

11 Risk of bias (quality) assessment: The methodological quality of the included studies will be evaluated with the Newcastle-Ottawa Scale (NOS) score. Case-control studies will be evaluated regarding the risk of bias on the domains of selection of cases and controls, comparability of the two groups, ascertainment of exposure and non-response rate. The risk of bias in cohort studies will be judged by assessing the selection and comparability of the exposed and non-exposed cohorts, as well as the assessment of outcome and the adequacy of the follow-up period. Risk of bias evaluations will be conducted by two authors independently and any discrepancies will be resolved through the consensus of all authors.

12 Strategy for data synthesis: A qualitative synthesis will be initially used for all outcomes. Quantitative synthesis will be used if the included studies present homogeneity and express serum uric acid levels in terms of mean and standard deviation, implying a normal distribution of the data. In addition, a diagnostic accuracy analysis will be performed if the included studies provide the sensitivity and specificity of the examined test. Statistical analysis will be perfromed with Review Manager 5.3, Open Meta-Analyst and R-3.4.3.

13 Analysis of subgroups or subsets: Subgroup analysis is planned to be conducted concerning the following parameters: preeclampsia onset (early vs. late onset), severity (mild vs. severe preeclampsia), timing of measurement (1st, 2nd or 3rd trimester of pregnancy).