

Reviewer's report

Title: Obstetric prognosis in sisters of preeclamptic women - implications for genetic linkage studies

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Reviewer: Dr Svein Rasmussen

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Unable to decide on acceptance or rejection until the authors have responded to the compulsory revisions

The manuscript has its potential, but should be extensively rewritten.

Below, please find some suggestions for editing the text. Reviewers are asked to divide their revisions into discretionary and compulsory. Complying to all suggestions below may be considered necessary, except for a few obviously minor points. Suggested deletions are within [brackets].

However, complying to these suggestions is not sufficient. First, the authors should put considerable effort into making formulations clear and concise for the average reader. Second, if necessary, the authors should find someone, or an editing service, to help them rewrite the manuscript.

ABSTRACT

Methods:

"In 530 cases". There were rather 530 pairs. Throughout the text, the use of the word "case" is often not quite appropriate.

"...[deliveries] pregnancies (the reference group) "

Conclusion: "Unaffected sisters ... [chronic] utero-placental"

"Basically, sisters of preeclamptic women should be screened for hypertension and proteinuria, but otherwise there is no need to initiate special antepartum surveillance". Suggestion: It is sufficient only to state that they do not need special antepartum surveillance.

BACKGROUND

The authors state that others have found evidence that there is an interplay between genes and environment in the development of preeclampsia. But they do not inform whether earlier studies provide data on pregnancy outcomes other than preeclampsia among relatives of women with preeclampsia. Generally, when authors raise a question, they should also provide information whether it has been dealt with before.

The sentences from "This trait may be described" through ".....left in relation to the proband but to the right of the general obstetric population." are rather unnecessary.

"This ...outcome. This data..... purposes." The authors should state briefly the objective and not implementations .

MATERIALS AND METHODS

The definition of preeclampsia should be referred, e.g. National High Blood Pressure Education

Program Working Group. High blood pressure in pregnancy. Am J Obstet Gynecol 1990;163:1691712. Was proteinuria defined as excretion of 0.3 g or more per day estimated using a urine reagent strip?

No information on reference material for the birth weight percentiles is given .

RESULTS

"[It is also noteworthy that only] 1.59% of the women in study group I and 0.57% in the reference group had pregnancy-induced hypertension. Otherwise, the pregnancy characteristics were similar in these groups." I was not able to find the numbers in the table.

DISCUSSION

"Basically, no differences were noted [recorded] in reproductive risk factors between the groups studied."

Suggestion: Among affected sisters, the rate of prematurity, low birth weight, and small-for-gestational age infants were increased, as expected. Although a trial of this size cannot reliably detect differences in rare complications such as neonatal death ascribable to familial risk, the number of cases in the present study is [high enough] sufficient to make statistically valid comparisons with regard to commonly used outcome variables.

"Clinically, affected versus unaffected status appears to be clear-cut in first-degree relatives regardless of their genetic susceptibility to preeclampsia, although in affected pregnancies atherotic changes have been shown to be present in the placental bed early in the first trimester, before clinical onset of the disease."

It is not clear what the authors mean by "although ... onset of the disease." Have the authors found any atherotic changes in first-degree relatives, or do they merely mean to state that acute atherosclerosis can be present before the clinical signs of preeclampsia. This should be made more clear .

"In the [present] current study, only one (1.59%) of the unaffected women with a first-degree relative with [affected by] preeclampsia developed pregnancy-induced hypertension." Perhaps "affected" should more often be substituted by e.g. "with preeclampsia". This result is mentioned in the Results section, but not in the tables and no significance level is given. Besides, I am not able to recognize a clear link between this result and the following line : "Accordingly, Caruso et al. demonstrated in their study of pregnant women with gestational hypertension and preeclampsia that only the former were characterized by metabolic features similar to those of patients with insulin resistance syndrome, such as lower insulin sensitivity, and higher levels of triglycerides and nonesterified fatty acids". Neither, the average reader would find the following line meaningful in this contexts: "On the other hand, preeclampsia phenotypes defined by other criteria such as glomerular endotheliosis are difficult to assess in routine clinical work."

"Preeclampsia is a heterogeneous disorder and women with various underlying medical condition are at risk of developing the disease." -misspelling

"Many of these conditions are known to be governed by some genetic components, e.g. essential hypertension and diabetes mellitus, and mitochondrial abnormalities, which in turn, are characterized by microvascular disease." Essential hypertension and diabetes mellitus is hardly a genetic component, although they may have genetic origin.

"Nevertheless, in this study the contribution of chronic illness was of little importance in the overall predisposition to preeclampsia or its occurrence in first-degree relatives." This statement implies that the results provide direct basis for this conclusion, which is not obvious.

"[The current data] Our results may be useful in counselling patients and their first-degree relatives. "

"Genetic susceptibility to preeclampsia has minor effects, if any, on pregnancy outcome in first-degree relatives of index patients, if they do not develop the disease, Basically, routine [prenatal] antenatal care in which blood pressure and urine dipstick are checked each visit is sufficient for women with an affected sister and there is no need to initiate special fetal monitoring in these pregnancies." Are these conclusions based on the present study? As written, they merely appear as statements not linked to the results.

The authors state that " In other words, this observation provides further justification to stratify pregnant women into the categories of affected and unaffected individuals." Has this been supported by earlier studies?

What exactly do the authors mean by that their results have implications for genetic linkage? Are they able to provide any exact advises based on their results. The implications are rather vaguely formulated.

It would be interesting to know whether this conclusion directly supported in other studies?

The summary given in the paragraph which precedes "Conclusions" does not only serve as a summary but provides discussion items.

Both a summary- and conclusion section is superfluous.

The subtitle "implications for genetic linkage studies" - In the conclusions such implications are not mentioned.

REFERENCES

The references should be consistently formatted.

Competing interests:

None declared.