Title: No association between polymorphisms/haplotypes of the vascular endothelial growth factor gene and preeclampsia.

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Reviewer: Hege Vefring

Reviewer's report:

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Title: No association between polymorphisms/haplotypes of the vascular endothelial growth factor gene and preeclampsia

The objective of the present study was to investigate the association between single nucleotide polymorphisms (SNP's) in the vascular endothelial growth factor (VEGF) gene and the risk for preeclampsia. Four VEGF SNP's (rs699947, rs1570360, rs2010963 and rs25648) were selected. The study is a case-control study consisting of venous blood from 86 preeclamptic women and 78 normotensive women from Mexico. Although no association was found between the selected VEGF SNP's and preeclampsia, these results may contribute to the elucidation of its aetiology and should therefore be replicated in various ethnic populations.

Major concerns:

1. The authors should explain the selection of the four SNP's (rs699947, rs1570360, rs2010963 and rs25648) in the VEGF gene. The selection should be described in the Methods.

2. The SNP names should be checked against their dbSNP ID and their location relative to the translation start site. The SNP order for VEGF which defines the VEGF haplotype structure should be included as a footnote in actual tables. The authors should check that the VEGF haplotype structure is correctly defined in all tables and throughout the text.

3. No association was found between the investigated VEGF SNP’s or VEGF haplotypes, and the severity of PE. The frequency of alleles, genotypes and haplotypes in women with mild - and severe preeclampsia are given in Table S1. The diagnostic criteria for mild and severe PE should be included in the Methods.

4. Table 1 should include a footnote explaining the nucleotides in bold letters with a reference to the article describing the different genotyping assays.

5. Describe and discuss the power of the study.

6. As a quality control for the genotyping assays, four patient samples were validated by cycle sequencing. At least 10% of the study material should be validated by cycle sequencing.
Minor concerns:
1. The authors refer to a relatively high percentage of preeclamptic pregnancies; 5-8% which depends on the study population as the authors claim. However, they should also describe that the diagnostic criteria for preeclampsia varies and that some of this variation might affect the number of reported preeclamptic pregnancies between studies.
2. The inclusion criteria for study participants were according to the International Society for the Study of Hypertension in Pregnancy and should be followed by a reference; an article or a web-site.
3. In the abstract, page 3, line 10, a definition of the abbreviation “PCR-RFLPs” and “SNP” is necessary.
4. The SNP’s should be identified by their rs-numbers throughout the text, and in all tables. The rs-numbers are missing in Table 4 and Table S2.
5. page 7, line 5: Remove sentence: “All the DNA samples were quantified …”

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests