Reviewer's report

Title: Meta-analysis of diabetic nephropathy associated genetic variants in inflammation and angiogenesis involved in different biochemical pathways

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Reviewer: Geetha Chittoor

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The purpose of this manuscript is to conduct meta-analysis and determine any earlier investigated/established genetic variants in biological pathways are significantly associated with the development of diabetic nephropathy, and also to explore the functional relevance of these genes/variants. To carry out the meta-analysis, data from 34 relevant studies with 55 genetic variants in 18 genes of inflammatory cytokines and angiogenesis associated with diabetic nephropathy are included. The authors conclude that they have identified 11 genetic variants in or near 9 genes (VEGFA, CCR5, CCL2, IL-1, MMP9, EPO, IL-8, ADIPOQ, and IL-10) significantly associated with diabetic nephropathy.

1. Major Compulsory Revisions:
   a. Authors should include details on estimates of effect sizes and pooled mean effect sizes considered for this study.
   b. Authors should elaborate on how the meta-analysis technique adjusted for the potential susceptibility differences between cases and controls. Also, should specify the matching criteria for cases and controls.
   c. It will be also interesting to discern the genes/genetic variants (if any) and pathways between cases and controls in the results.
   d. Any attempt made to adjust for covariates as several variables considered for data extraction (for example, population stratification as the data is coming from several ethnicities) should be addressed!
   e. Author’s way of mentioning articles, studies, and/or populations is confusing. This should be elucidated for easy understanding as they are different entities.

2. Minor Essential Revisions:
   a. Results section, page 6, line 2: should mention the list of 9 genes.
   b. All genes and/or pathways in the manuscript when mentioned for the first time should be fully elaborated and after that can be used in abbreviation. Also, all gene names should be italicized.
   c. Figure legends are given upfront, but the titles, and font should be uniform.
   d. Figure 1, and 2: it’s not clear why the column heading is given as ‘study name’ when the SNPs and/or genes are listed.

3. Discretionary Revisions:
a. It will be interesting to further explore and elucidate the functional relevance of these genes in the pathogenesis of diabetic nephropathy based on type and duration of diabetes and how it differs in various ethnic populations. The conclusion from this article gives some insights on genes/variants coming from different biological pathways and their involvement with diabetic nephropathy. As indicated in comments above, there are some methodological and analytical issues that should be explained further.

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

Quality of written English: Acceptable

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