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CORRESPONDENCE

Response to Li

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We are grateful to the author who shared his comments and suggestions to the editor[1] regarding several issues regarding our meta-analysis.[2] After carefully reviewing the authors' comments and checking the raw data and our original article, we are pleased to reply to and clarify his questions point by point.

First, the author mentioned there were five additional articles that should be included in our meta-analysis.[3–7] After re-searching for articles relating to the association between the C677T polymorphism and pre-eclampsia (PE), we found only two articles mentioned by the author that should have been added to our meta-analysis.[3,7] Another study with incomplete data should not have been included because only data for the allele T and TT genotype was provided.[4] Furthermore, another two articles were not included because they did not refer to the association between the MTHFR C677T polymorphism and PE.[5,6] In addition, the author mentioned that another two studies should have been included in our meta-analysis.[8,9] We agree that it is important when conducting a meta-analysis to search and include as many studies as possible. However, the article by Dissanayake VH and coworkers was published in September 2012, 5 months after we submitted our article (April 2012). And the article by Lykke JA and coworkers was published in July 2012, 3 months after we submitted our article (April 2012). We would like to emphasize here that we had indicated in our article 'An upper date limit of March 2012 was applied and we used no lower date limit.' in the search strategy section. We hope that an updated meta-analysis can be performed in the future that includes these two studies.[8,9]

Second, the author mentioned that there were two articles that did not deviate significantly from the Hardy–Weinberg equation (HWE).[10,11] After re-calculation, we found that these two articles are in HWE ($P=0.066$, $P=0.129$) and that another study[12] was also in HWE ($P=0.078$). Thus, these three articles should have been included in our meta-analysis.

Third, the author mentioned that the population in the Aggarwal study[13] should be defined as of Caucasian ethnicity, while this study was defined as of Asian ethnicity in our meta-analysis. After carefully reading the article by Aggarwal, as the author said, the population from the Aggarwal study should have been classified as being of Caucasian ethnicity.

Finally, the author also pointed out that one article was not in line with the raw data.[14] We re-read this article and found that subjects from the PE group from Grandone *et al.*[14] were CC (25), CT (41) and TT (28).

Taking these issues into account, we performed a new analysis. The pooled results showed that the MTHFR C677T polymorphism was significantly associated with PE ($P=0.01$, odds ratio (OR) = 1.26, 95% confidence interval (CI) = 1.04–1.52, $P_{\text{heterogeneity}}=0.03$, for the dominant genetic model; $P=0.02$, OR = 1.26, 95% CI = 1.04–1.52, $P_{\text{heterogeneity}}=0.001$, for the recessive genetic model; $P=0.004$, OR = 1.34, 95% CI = 1.10–1.64, $P_{\text{heterogeneity}}=0.007$, for the additive genetic model). The results of the subgroup analysis showed that the MTHFR 677T polymorphism had the effect of increasing PE risk for the recessive genetic model ($P<0.0001$, OR = 2.15, 95% CI = 1.66–2.80, $P_{\text{heterogeneity}}=0.16$), the additive comparison ($P<0.0001$, OR = 2.56, 95% CI = 1.88–3.47, $P_{\text{heterogeneity}}=0.24$) and allele contrasts ($P<0.0001$, OR = 1.52, 95% CI = 1.31–1.77, $P_{\text{heterogeneity}}=0.13$) in Asian populations, whereas there was no evidence of an association between the MTHFR C677T polymorphisms and PE observed in Caucasians.

The conclusion from this new analysis agrees with that of our previous study.[2] In summary, the constructive comments provided help our study to reach more persuasive conclusions.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

Wei-wei Chang[1,5], Xiao-ping Xia[2,3,5] and Yun-xia Cao[4]

[1]Department of Preventive Medicine, Wannan Medical College, Wuhu, China; [2]Reproductive Medicine center, The First Affiliated Hospital of Anhui Medical University, Hefei, China; [3]Department of Gynaecology and Obstetrics, the Liu'an People's Hospital, Liu'an, China and [4]Department of Gynaecology and Obstetrics, The First Affiliated Hospital of Anhui Medical University, Hefei, China
[5]These authors contributed equally to this work.
E-mail: aydcaoyunxia@163.com

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