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RESPONSE TO LETTER

Serum Levels of Tumor Necrosis Factor-α and Vascular Endothelial Growth Factor in the Subtypes of Clinical High Risk Individuals: A Prospective Cohort Study [Response to Letter]

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Dear editor

We thank Authors Lienggonegoro, Dany, and Panjaitan for their thoughtful replies to our article.

Lienggonegoro et al reinforce our initial findings regarding the involvement of inflammatory processes in the pathophysiology of mental illnesses, particularly schizophrenia. They also underscore the significance of tumor necrosis factor-α (TNF-α) and vascular endothelial growth factor (VEGF) in psychiatric disorders, providing valuable insights into subclinical inflammation and neuroinflammation associated with psychosis.

Lienggonegoro et al provided valuable input regarding the role of TNF-α in immunological and physiological processes, particularly its connection with obesity. We conducted further analyses to explore the relationship between BMI and TNF-α levels among our study participants. However, we did not observe significant differences or correlations between these variables. One possible explanation could be that our sample did not receive medication at the time of enrollment, which might have mitigated the impact of medication-induced metabolic syndrome. Past research has indeed demonstrated the influence of antipsychotic medications on TNF-α levels.[1] The interplay among these three factors may be complex, and our cohort is currently undergoing follow-up assessments. Some participants will commence medication treatment, and we intend to report on the relationships between these factors in our future research.

In our study, the primary focus was on examining the differences in TNF-α and VEGF levels among clinical high risk(CHR) for psychosis subgroups with different clinical characteristics, particularly those categorized based on positive and negative symptoms. We appreciate your suggestion and have indeed conducted repeated measures analysis of variance analysis as advised. However, the results did not show any statistically significant effects of Time, Group, or their interaction (Time × Group) on TNF-α and VEGF levels. One potential explanation for this might be related to the data collection process during the longitudinal follow-up. Unfortunately, due to the impact of the COVID-19 pandemic, blood sample collection was completed for only 65 participants, as many patients were unable to attend in-person visits. As we continue our research, we plan to address this issue by collecting blood samples at multiple time points to provide a more comprehensive understanding of these factors.

In our study, we conducted measurements for both serum levels of TNF-α, VEGF, and complement proteins. Our findings indicated that serum complement proteins, rather than inflammatory factors, were effective in predicting psychosis.[2] The serum levels of TNF-α and VEGF for each sample were measured in duplicate using an enzyme-linked immunosorbent assay (ELISA) with the Human HS Cytokine Premixed Kit. This was done following the manufacturer's instructions.

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In summary, our ongoing follow-up within the Shanghai At Risk for Psychosis-extended (SHARP-extended) program[3–5] for at-risk individuals continues to yield valuable insights. Growing evidence suggests that longitudinal data collected at multiple time points may hold significant value in understanding the onset of mental illnesses.

Disclosure

The authors report no conflicts of interest in this communication.

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