ISSN: 2320-5407
ISSN NO. 2320-5407
International Journal of Advanced Research
Publisher's Name: Jana Publication and Research LLP
www.journalijar.com

REVIEWER'S REPORT

Manuscript No.: IJAR-54645 Date: 4/11/2025

Title: Cerebral Vasoreactivity to Carbon Dioxide Assessed by Transcranial Doppler Ultrasound in Post–COVID-19 Patients: A Moroccan Comparative Study

Recommendation:
Accept as it is .....
✓ Accept after minor revision.....
Accept after major revision .....
Do not accept (*Reasons below*) .....

Rating	Excel.	Good	Fair	Poor
Originality		✓		
Techn. Quality		✓		
Clarity		✓		
Significance		✓		

Reviewer Name: Dr. S. K. Nath Date: 5/11/2025

Reviewer's Comment for Publication:
The study convincingly demonstrates that individuals recovered from moderate to severe COVID-19 exhibit impaired cerebral vasoreactivity, likely reflecting ongoing endothelial dysfunction. These findings underscore the need for vigilant cerebrovascular assessment in post-COVID-19 follow-up care. However, limitations such as small sample size and lack of longitudinal data suggest that further research is necessary for definitive conclusions.

Reviewer's Comment / Report

Strengths:
1. **Timely and Relevant Topic:** The study addresses the important issue of cerebrovascular dysfunction in post-COVID-19 patients, which is a growing concern in medical research.
2. **Clear Objective and Methodology:** The use of transcranial Doppler ultrasound (TCD) to assess cerebral vasoreactivity (CVR) and breath-holding index (BHI) is well-established, and the study's methodology is straightforward and reproducible.
3. **Comparative Approach:** Including both post-COVID-19 patients and controls enhances the validity of findings and allows for meaningful comparisons.
4. **Clinical Implications:** The findings suggest that endothelial dysfunction persists after recovery, emphasizing the importance of monitoring cerebrovascular health in COVID-19 survivors.

Weaknesses:
1. **Limited Sample Size:** The study includes only 75 participants (50 post-COVID-19 and 25 controls), which may reduce the statistical power and the generalizability of the results.
2. **Lack of Detail on Severity and Duration:** The manuscript does not specify the severity of COVID-19 infections or the time elapsed since recovery, which could influence CVR outcomes.
3. **Potential Confounding Factors:** Although some comorbidities are noted, a more detailed analysis controlling for other risk factors (e.g., hypertension, diabetes) would strengthen the conclusions.
4. **Insufficient Discussion on Mechanisms:** While the study points to endothelial dysfunction, a deeper discussion regarding pathophysiological mechanisms would enhance the interpretability.
5. **Limited Data on Long-term Outcomes:** The cross-sectional nature of the study does not allow assessment of whether CVR impairment persists long-term or improves over time.

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Recommendations for the Authors:

- **Address Sample Size and Power:** Clarify how the sample size was determined and discuss potential limitations.
- **Include Additional Participant Details:** Specify the duration since COVID-19 recovery and the severity of initial infection.
- **Control for Confounders:** Incorporate multivariate analysis to adjust for comorbid conditions affecting cerebrovascular health.
- **Deepen Mechanistic Discussion:** Expand on possible pathophysiological pathways linking COVID-19 to endothelial dysfunction.
- **Consider Longitudinal Follow-up:** If possible, include or suggest follow-up studies to assess the persistence or reversibility of CVR impairment.

Typographical and Grammatical Observations:

- The manuscript is generally well-written. Minor typographical adjustments are recommended:
- In the abstract and text, ensure consistent formatting of measurements (e.g., "CVR" and "BHI").
- Correct minor spacing issues and unify abbreviations throughout the document.