



## LETTERS TO THE EDITOR

## A letter to the editor: “The association between congenital heart disease and the risk of autism spectrum disorders or attention-deficit/hyperactivity disorder among children: a meta-analysis”



Dear editor,

We have read with great interest the excellent paper “The association between congenital heart disease and the risk of autism spectrum disorders or attention-deficit/hyperactivity disorder among children: a meta-analysis” by Jenabia et al.<sup>1</sup> The study showed that congenital heart disease could lead to neurodevelopmental abnormalities in children. We want to make a few contributions to further scientific discourse.

It is unclear what duration of fetal hypoxia results in autism spectrum disorders (ASD) and attention-deficit/hyperactivity disorder (ADHD) and what the critical period of gestational during which hypoxia affects the fetus’ oxygen-sensitive central nervous system area. The risk factors such as preeclampsia, smoking, Alcohol Use Disorder, viral infections, medications, thyroid deficiency, Toxoplasmosis, Rubella, Chlamydia, Herpes and Syphilis infections, anemia, hypertension, or any other factors can cause oxygen-deficient status in the mother resulting in hypoxia in the fetus and can lead to adverse neurodevelopmental outcomes.<sup>2,3</sup> Congenital anomalies in the offspring that could temporarily cause intrauterine hypoxia can directly affect the development of ASD<sup>2</sup> and ADHD<sup>3</sup> in the baby. Not having done subgroup analysis on the type of chronic heart disease (CHD) (cyanotic or acyanotic) was acknowledged as a limitation by the authors. Still, the severity of hypoxemia (mild Ventricular Septal defect (VSD) vs. moderate VSD, muscular versus membranous) could determine the extent of neurodevelopmental outcomes, which could be the future direction for researchers. Likewise, conditions like transient tachypnea of the newborn or complications like cord compression can be confounders as they—like CHD, could cause hypoxia. Further, the timely management of CHD in the baby may affect the level and duration of hypoxia and the risk of developing ASD and ADHD and should be factored into the association between CHD and ASD and ADHD.<sup>4</sup>

We know that some genetic causes and syndromes may underlie a cluster of CHD and, ASD, ADHD. In

velocardiofacial syndrome, the psychotic disorder may change the association between CHD and ASD and ADHD in complex yet not understood ways.<sup>5</sup>

We believe future directions would be for studies to consider all these aspects to inform clinical care by pediatric cardiologists and child and adolescent psychiatrists.

### Ethical considerations

None.

### Funding

None.

### Conflict of Interest

None.

### References

- Jenabi E, Bashirian S, Fariba F, Naghshtabrizi B. The association between congenital heart disease and the risk of autism spectrum disorders or attention-deficit/hyperactivity disorder among children: a meta-analysis. *Eur. J. Psychiatry*. [Internet]. 2022;36(2):71–6. Available from: <https://doi.org/10.1016/j.ejpsy.2021.10.001>.
- Modabbernia A, Velthorst E, Reichenberg A. Environmental risk factors for autism: an evidence-based review of systematic reviews and meta-analyses. *Mol. Autism*. [Internet]. 2017;8(1):13. Available from: <https://doi.org/10.1186/s13229-017-0121-4>.
- Guney E, Cetin FH, Iseri E. The role of environmental factors in etiology of attention-deficit hyperactivity disorder. *ADHD - new directions in diagnosis and treatment*. InTech; 2015.
- Wernovsky G, Licht DJ. Neurodevelopmental outcomes in children with congenital heart disease—what can we impact? *Pediatr. Crit. Care Med*. [Internet]. 2016;17:S232–42. Available from: <https://doi.org/10.1097/pcc.0000000000000800>.
- Furniss F, Biswas AB, Gumber R, Singh N. Cognitive phenotype of velocardiofacial syndrome: a review. *Res. Dev. Disabil*. [Internet]. 2011;32(6):2206–13. Available from: <https://doi.org/10.1016/j.ridd.2011.05.039>.

<https://doi.org/10.1016/j.ejpsy.2022.07.002>

0213-6163/© 2022 Asociación Universitaria de Zaragoza para el Progreso de la Psiquiatría y la Salud Mental. Published by Elsevier España, S.L. U. All rights reserved.

Aashraya Ramu<sup>a,1,\*</sup>, Sushma Srinivas<sup>b,1</sup>, Alex Honest<sup>c,1</sup>,  
Zeeshan Mansuri<sup>d,1</sup>, Shailesh Jain<sup>e,1</sup>

<sup>a</sup> *Mount Sinai Beth Israel, New York, United States*

<sup>b</sup> *A.J. Institute of Medical Sciences and Research Centre,  
Mangalore, India*

<sup>c</sup> *AllianceHealth Durant Family Medicine Residency, United  
States*

<sup>d</sup> *Harvard Medical School, Boston, USA*

<sup>e</sup> *Texas Tech University Health Sciences Center, Lubbock,  
United States*

\* Corresponding author.

E-mail address: [aash12012@gmail.com](mailto:aash12012@gmail.com) (A. Ramu).

Received 21 June 2022; Accepted 7 July 2022

Available online 29 September 2022

---

<sup>1</sup> These authors contributed equally to this work.