The Correlation Between Congenital Heart Disease and The Risk of ADHD in Children

Nadira Putri Nastiti¹, Abraham Dharmawan¹, Afifur Rafi Hilmi Aziz¹, Yunias Setiawati¹*, Ratih Dewi Anggraini Jubair Hagemur¹, Andronikus Dharmawan¹, and Salva Yurista²

¹Faculty of Medicine, Airlangga University, Surabaya, Indonesia
²Heart, Vascular and Thoracic Institute, Cleveland Clinic, Cleveland, OH, USA

E-mail: nadhiraputri23@gmail.com; abrahamdharmawan15@gmail.com; afifurrafi23@gmail.com; yunias.setiawati@fk.uniar.ac.id; ratihdwewi23@gmail.com; androd5453@gmail.com; salvayurista23@gmail.com

*Corresponding author details: Yunias Setiawati; yunias.setiawati@fk.uniar.ac.id

ABSTRACT
Congenital Heart Disease (CHD) is the most common birth defect in the world, and patients are more prone to intellectual functioning deficits, developmental issues, and academic performance issues. Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder and is associated with coronary heart disease (CHD). While cardiac patients with ADHD symptoms are frequently misdiagnosed and, as a result, undertreated, this study examines the association between CHD and the risk of ADHD, including the effect of cardiac surgery on children. The data for this study was compiled by searching multiple databases using pertinent keywords. Through school age and adolescence, children with CHD have an elevated risk of neurodevelopmental impairment, specifically ADHD. In children with surgically corrected ADHD, inattention becomes the predominant subtype, and scores were significantly increased. However, the severity of the symptoms is reduced if cardiac surgery is performed at a young age. This association leads to alterations in behavior associated with hypoxic-ischemic mechanisms that occur in oxygen-sensitive regions. To improve the quality of life of children with CHD, surveillance, screening, evaluation, and management strategies for ADHD should be promoted regardless of their specific cardiac diagnosis.

Keywords: congenital heart disease; attention deficit/hyperactivity disorder; children; cardiac surgery

INTRODUCTION
Congenital heart disease (CHD) is the most prevalent birth defect in the world, affecting millions of infants each year (1). Between 1970 and 2017, the global mean prevalence of CHD was 8.22 per 1000. Globally, the prevalence of CHD increased by 10% every five years (2). Children with CHD are more susceptible to intellectual functioning deficits, developmental problems, and academic performance issues (3). Children with congenital heart disease are at increased risk for several cognitive disorders, including inattention, which can interfere with school-based learning (2). Previous studies have reported unfavorable effects of chronic and intermittent hypoxia on development, behavior, and academic achievement in children with CHD.

It has been reported that children with congenital heart disease have a 30% higher risk of inattention and hyperactivity disorder compared to healthy individuals. Importantly, despite the fact that nearly half of surgically treated patients require remedial school services when they reach adolescence, cardiac patients with ADHD symptoms are frequently underdiagnosed and, as a result, undertreated (5).

Attention deficit hyperactivity disorder (ADHD) is an important neurodevelopmental outcome because it is a treatable disorder. The morbidity associated with undiagnosed and untreated ADHD is substantial (6). Hansen et al. found that DSM-IV estimated the prevalence of ADHD to be between 3% and 5% (7). ADHD is also associated with maternal anxiety, but it is advantageous to administer ADHD medication if its severity is detected early (8). There are numerous screening instruments available for detecting ADHD. The Swanson, Nolan, and Pelham IV (SNAP-IV) Teacher and Parent Rating Scale is a 20-item questionnaire based on the Diagnostic and Statistical Manual of Mental Disorders, fourth revision diagnostic criteria for ADHD.

Hansen et al. estimated a correlation of 41.2% between CHD and ADHD parent ratings based on the SNAP-IV (7). Consequently, the purpose of this study is to examine the association between CHD and the risk of ADHD, as well as the effect of pediatric cardiac surgery. Through our review of the literature, we hope to improve the quality of life for children with CHD and ADHD.

METHOD
The correlation between congenital heart disease and the risk of childhood attention deficit hyperactivity disorder (ADHD) was the subject of this literature review, which was compiled using data from PubMed, Science Direct, Research Gate, and other databases.
The following keywords are used in conjunction with "Congenital Heart Disease", "Attention Deficit Hyperactivity Disorder" and "Children". The AND, OR, and NOT boolean operators were also used to narrow the search results.

The final article is from April 2022. The reviewed literature is written in English or Indonesian for the authors’ convenience.

<table>
<thead>
<tr>
<th>No.</th>
<th>Author (Year)</th>
<th>Country</th>
<th>Sample Characteristics</th>
<th>Outcome Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cober (2021)</td>
<td>Hungary</td>
<td>School aged (10.5 ± 3.3)</td>
<td>ADHD Prevalence for children who had undergone open-heart surgery before 1 year of age.</td>
</tr>
<tr>
<td>2</td>
<td>Razzagh (2015)</td>
<td>USA</td>
<td>6 - 17</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Tsao (2017)</td>
<td>Taiwan</td>
<td>&lt;18 (2.21 ± 0.08)</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>DeMaso (2017)</td>
<td>USA</td>
<td>10-19 (14.5 ± 3.0)</td>
<td>61%</td>
</tr>
<tr>
<td>5</td>
<td>Yaranda (2013)</td>
<td>Canada</td>
<td>7-15</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>Hamza (2012)</td>
<td>USA</td>
<td>7-15 (23.6)</td>
<td>63%</td>
</tr>
<tr>
<td>7</td>
<td>Holte (2020)</td>
<td>Denmark</td>
<td>10-16 (13 ± 1.8)</td>
<td>55%</td>
</tr>
<tr>
<td>8</td>
<td>Shabta (2021)</td>
<td>Iran</td>
<td>&lt;18 (59 ± 91.7 years)</td>
<td>78.70%</td>
</tr>
<tr>
<td>9</td>
<td>Lubben (2022)</td>
<td>England</td>
<td>3-21 (16.6)</td>
<td>56.8%</td>
</tr>
<tr>
<td>10</td>
<td>Gonzales (2021)</td>
<td>USA</td>
<td>4-17</td>
<td>56.8%</td>
</tr>
<tr>
<td>11</td>
<td>Wang (2020)</td>
<td>Taiwan</td>
<td>6-15 (10 ± 2.43)</td>
<td>53.3%</td>
</tr>
<tr>
<td>12</td>
<td>Shillingford (2008)</td>
<td>USA</td>
<td>5-40 (17.9 ± 1.3)</td>
<td>67%</td>
</tr>
<tr>
<td>13</td>
<td>Guadet (2021)</td>
<td>Canada</td>
<td>5-35 (20.26)</td>
<td>53.7%</td>
</tr>
</tbody>
</table>

**TABLE 1** : Studies included to this review.

**OVERVIEW**

Congenital Heart Disease (CHD) is a heart defect present at birth. Congenital heart disease (CHD) is also referred to as congenital heart defects, which is a general term for abnormalities in the structure of the heart and great blood vessels that are present at birth, are frequently observed, and are the leading cause of death among all types of congenital abnormalities (9). Due to cardiac abnormalities, hemodynamic disturbances can produce symptoms that characterize the severity of the abnormality. The presence of growth retardation, cyanosis, decreased exercise tolerance, frequent recurrent respiratory tract infections, and the ability to hear heart sounds may be early indicators of heart defects in infants and children (10).

Two possible causes of congenital heart disease are genetic and environmental factors. Genetic factors include heredity or a family history of disease, as well as Down syndrome and other syndromes caused by an abnormal number of chromosomes. Maternal rubella virus infection, use of teratogenic drugs during pregnancy, and excessive alcohol consumption are environmental factors (11).

Important basic investigations for CHD include chest X-rays, electrocardiography, and routine laboratory tests, whereas important follow-up examinations include echocardiography and a cardiac catheterization procedure.
The combination of two advanced examinations for visualization and confirmation of the morphology and path-anatomy of each type of congenital heart disease allows for a near-perfect diagnosis (12).

In general, the treatment of congenital heart disease includes both non-surgical and surgical methods. Nonsurgical management includes medical management and interventional cardiology. Generally, medical management is secondary due to complications from the heart disease or other accompanying disorders (13).

Congenital Heart Disease (CHD) is the most common birth defect in the world, and patients are more prone to intellectual functioning deficits, developmental issues, and academic performance issues.

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder and is associated with coronary heart disease (CHD). While cardiac patients with ADHD symptoms are frequently misdiagnosed and, as a result, undertreated, this study examines the association between CHD and the risk of ADHD, including the effect of cardiac surgery on children.

The data for this study was compiled by searching multiple databases using pertinent keywords. Through school age and adolescence, children with CHD have an elevated risk of neurodevelopmental impairment, specifically ADHD. In children with surgically corrected ADHD, inattention becomes the predominant subtype, and scores were significantly increased. However, the severity of the symptoms is reduced if cardiac surgery is performed at a young age. This association leads to alterations in behavior associated with hypoxic-ischemic mechanisms that occur in oxygen-sensitive regions.

To improve the quality of life of children with CHD, the surveillance, screening, evaluation, and management strategy for ADHD should be promoted regardless of their specific cardiac diagnosis.

Attention Deficit/Hyperactivity Disorder (ADHD)

Multiple tests are utilized to diagnose children with ADHD. Additionally, sleep disturbances, anxiety, depression, and learning disorders all share the same symptoms. ADHD is diagnosed using the Diagnostic and Statistical Manual, Fifth Edition (DSM-5) from the American Psychiatric Association. DSM-5 is applicable from early childhood to adulthood. Patients with ADHD exhibited persistent patterns of inattention and hyperactivity (14).

In Indonesia, there are two screening instruments for ADHD. Parents and teachers can complete both the Skala Penilaian Perilaku Anak Hipervaktid Indonesia (SPPAH) and the Abbreviated Conner’s Teacher Rating Scale (ACTRS). If the score exceeds the threshold, the child can be identified as a child at high risk (14). Children with ADHD are more likely to exhibit oppositional behavior, academic failure, family conflict, forgetfulness, impulsive behavior, difficulty adapting, and poor learning achievement. These accomplishments require psychomotor (activity), cognitive (knowledge), and behavioral (emotional) components (15).

In school-aged children with dextro-transposition of the great arteries (D-TGAs), deficits in executive functions (EF) have been reported. On the Behavior Rating Inventory of Executive Functions (BRIEF), parents and educators of children with congenital heart disease (CHD) demonstrated significant difficulties, particularly in working memory. Calderon et al. also reported EF deficits in preschool and school-aged children (16).

Current Evidence on the Association of CHD and ADHD

On the basis of a literature search in multiple databases using pertinent keywords, fourteen works of literature that met the inclusion and exclusion criteria were identified. The majority of studies utilized school-aged participants. As the symptoms of ADHD become more apparent in patients, it becomes possible to assess and establish the diagnosis. Six studies used a sample of all CHD patients who underwent cardiac surgery, and the majority of them were young.

Comparing the prevalence, incidence, or odds of CHD in children to those of healthy controls, the vast majority of the studies pooled for this literature review indicate a statistically significant increase. A large cohort study conducted in Taiwan gives results of the overall prevalence of probable ADHD in all patients with CHD was 12.4%. There is a significantly higher prevalence of the inattention-predominant subtype among CHD patients, particularly in patients with cyanotic heart disease and those with a history of attention deficit hyperactivity disorder who have undergone cardiac surgery (17). However, the predominant subtypes of hyperactivity/impulsivity did not differ significantly (17). Several studies have yielded dissimilar prevalence results. The prevalence of subjects with a positive screening score for ADHD was much higher in the CHD group, at 29%, according to a Canadian cohort study (18). The prevalence of ADHD in the CHD population was found to be 31.6% (2). In the most recent study, conducted by Lobelien et al., the prevalence of patients diagnosed with ADHD was significantly higher than in the general population (9.04%) (19).

According to a previous cross-sectional study (7), a significant proportion of children with CHD exhibited symptoms of ADHD. This association led to behavioral changes associated with hypoxic-ischemic damage to the brain’s white matter (20). Patients born with CHD are exposed to physiological stressors that continue to evolve as they mature. One of the stressors is the level and duration of hypoxia that occur in highly oxygen-sensitive regions, which are the prefrontal cortex and corpus striatum of the brain. This region is presumed to be connected to the executive control network of attention (7; 20). CHD patients have risk factors for the inattention-predominant subtype, which include postoperative seizure and a number of cardiopulmonary bypass surgeries, as the greatest risk, cyanotic CHD, prior use of ECMO, and male sex (17). Preoperative hypoxemia in infants with cyanotic CHD is associated with a higher risk of attention deficits compared to acyanotic CHD and healthy infants (20).

In the high severity index, the inattention-predominant subtype of ADHD has the highest prevalence. However, there was no difference in the prevalence of hyperactivity/impulsivity-related symptom severity (17; 7). This high prevalence was observed in children with cyanotic CHD, those who underwent cardiac procedures, and those with an elevated disease severity index (17). ADHD symptoms were more severe in CHD patients treated surgically at or above 3 years of age compared to both the control group and those treated surgically at a younger age (21). Consistent with the findings of other studies, children with Transposition of the Great Arteries who undergo CHD surgery more than
two weeks after birth exhibit impaired brain growth and delayed language development compared to children treated within the first two weeks (20).

Anxiety, depression, and post-traumatic stress were frequently observed with significantly elevated scores in children with CHD and ADHD (22; 23). Achievements in school, education, or work functioning can be disrupted in ADHD patients. Recent research (20) indicates that children with CHD and additional ADHD have a lower quality of life score. Then, neurodevelopmental disorders, particularly ADHD, should be evaluated in all children at high risk for CHD (19).

CONCLUSION
Through school age and adolescence, children with congenital heart disease (CHD) have an increased risk of neurodevelopmental impairment, particularly Attention Deficit Hyperactivity Disorder (ADHD). On the basis of prevalence rates, inattention symptoms become the predominant type of ADHD and are significantly more prevalent hypoxia-induced ischemia. The ADHD scores of surgically corrected CHD children were significantly higher. However, the symptoms are less severe if cardiac surgery is performed at a young age.

To improve the quality of life of children with CHD, the surveillance, screening, evaluation, and management strategy for ADHD should be promoted regardless of their specific cardiac diagnosis. Other neurocognitive and psychiatric evaluations are advised throughout a child’s development.

Acknowledgment
The authors would like to thank Airlangga University and everyone that supports this study.

Conflict of interest
The authors declared there to be no conflict of interest in this study.

Funding disclosure
This study did not receive any funding.

Author contribution
YS carried out the idea of this study and revision. NPN, ARHA, and RDAJH contribute to the design of the study, interpreted the results, and arrangement of the manuscript.

REFERENCES


