Journal of Medical and Health Studies
ISSN: 2710-1452
DOI: 10.32996/jmhs
Journal Homepage: www.al-kindipublisher.com/index.php/jmhs

JMHS
AL-KINDI CENTER FOR RESEARCH AND DEVELOPMENT

| RESEARCH ARTICLE

Evaluating the Efficacy and Safety of Antihypertensive Drugs in the Treatment of Congenital Heart Disease in Paediatric Patients: A Comprehensive Study

Samad Ali[1], Abdus Sobhan[2] and Abhijit Pathak[3] ✉

[1]*Research Assistant, Department of Pharmacy, Varendra University, Rajshahi, Bangladesh*
[2]*Research Assistant, Department of Computer Science and Engineering, Varendra University, Rajshahi, Bangladesh*
[3]*Assistant Professor, Department of Computer Science and Engineering, BGC Trust University Bangladesh, Chattogram, Bangladesh*

Corresponding Author: Abhijit Pathak, **E-mail**: abhijitpathak@bgctub.ac.bd

| ABSTRACT

CHD is the most common of all congenital anomalies causing mortality among children, characterized by structural abnormalities present at birth that vary in severity and complexity. Increased cardiac workload due to CHD may stipulate a growth delay in the affected children. The complexity of treatment is further compounded by medication errors, and hence, rigorous strategies of evaluation and management become necessary. This study was conducted to determine antihypertensive drug consumption patterns and to evaluate their therapeutic efficacy among 92 patients with CHD to meet the evaluation criteria, including appropriateness of treatment for the condition of the patient, adherence to indications, accuracy of dosage, and drug use practice. Females constituted the highest proportion of patients at 53.26 percent, infants were the most common age group at 43.48 percent, and Atrial seal defect accounted for 22.5 percent of the CHD patients. The antihypertensive drugs predominantly prescribed are Furosemide, used by 44.9% of the subjects, followed by Captopril, used by 30.3%, and Spironolactone, used by 10.1%. Therapy was evaluated for its effectiveness; appropriateness, both for the patient's indications and drug usage, was found to be very high, at 98.9% and 97.8%, respectively, whereas adherence to prescribed dosage was relatively lower at 62.7%. This study points toward further challenges in the management of antihypertensive treatment among children with CHD. It needs combined efforts by a pediatric cardiologist, pharmacist, nurse, and caregiver for total care to reduce the risk from treatment. Continuous monitoring and alterations in the plan of treatment, coupled with education, could be significant in optimizing medication adherence to improve long-term health outcomes in CHD children. The research done in this field, at large, improves pediatric cardiology practice to reduce morbidity and mortality rates associated with congenital heart disease around the world.

| KEYWORDS

Congenital Heart Disease (CHD), Antihypertensive Drugs, Clinical Study, Cardiovascular, Pediatric

| ARTICLE INFORMATION

ACCEPTED: 01 August 2024 **PUBLISHED:** 06 August 2024 **DOI:** 10.32996/jmhs.2024.5.3.6

1. Introduction

Congenital Heart Disease (CHD), which is also called congenital cardiovascular disease, is one of the most common congenital disorders in children. Where the defect is related to the heart, this condition can have an extensive and diverse set of features that would manifest themselves. This implies that whereas children with CHD experience physical problems as they grow, they become more complicated as they join adulthood. Among these, the essential and significant risk factors include hypertension, smoking, type 2 diabetes, dyslipidemia, and obesity, which are intensifying continually. These are the problems that affect adults with Congenital Heart Disease (CHD). Hence, among the adult population with CHD, CHD related to heart failure is the most common cause of death.

Nevertheless, there is an influence of the co-morbid factors and the other factors associated with cardiovascular disease to be considered as determinants of mortality in elderly patients. Childhood obesity has been rising at a global rate in the past years. It is also observed in patients having CHD, which is consistent with studies. To this end, high energy-density food intake and a sedentary lifestyle are possible factors that might lead to overweight and obesity in children with CHD. Since a sedentary lifestyle and obesity predisposes an adult to develop CVD, efforts toward managing weight gain should be incorporated into the management of CHD patients.

Children also face numerous challenges with CHD; they include pulmonary hypertension, heart failure, shade III/IV in maximum cases, a tendency towards developing cyanosis, arrhythmia, any growth failure, and mild to moderate exercise capacity. Denovo, though there remain countless challenges of this nature, medical and surgical explorations have enhanced childhood survivorship and even the adolescents and adults, thus leading to an enhanced, improved cohort with CHD who are undergoing repaired or palliated.

Hypertension manifests as an issue affecting CHD patients in childhood, secondary to the abnormal anatomic configuration, persistent volume or pressure loading, and operations like surgical intervention. Hypertension control in these patients plays an essential role in reducing future cardiovascular risk and effective outcomes.

However, children's CHD is hardly manageable and is compounded by medication errors within pediatric hospitals. Research reveals that the proportions of medical administrative mistakes vary between 17. 4% to 33. To summarize, in different countries, the error frequency is 8 percent per 100 opportunities with AI. For example, in Argentina, around 78% of individuals do not follow the advised daily vegetable consumption levels – 5 servings per day. I can personally confirm that according to several studies, medication error is a common issue within neonatal and pediatric intensive care units wherein 5% of all medication administrations lead to an error, which can be attributed to the heightened risk that children have to drug-related mishaps. Likewise, in Ethiopia, studies have also revealed that medication administration errors occurred at a high rate among cases. This is true for all countries in the world, where safe medication practices in pediatric healthcare facilities are hard to achieve.

Even today, it has been a significant source of morbidity and mortality among infants and children despite the recent developments in medical and surgical treatments for the disease. However, of all the complications linked to CHD, hypertension is a pertinent issue of worry as it poses a threatening risk factor that can worsen the situation if not well controlled. Intro paragraph non-first C Moreover, children with CHD are at high risk of medication-related complications in hospitals, which makes their treatment more challenging. In the pediatric population of patients with congenital heart disease, what are the best approaches for determining the effectiveness and the possible adverse effects of the administered antihypertensive medications?

Hypotheses of this analysis are given as follows: The goals of this study are developed to capture all the difficulties and intricacies that are likely to be found when treating children with CHD while having hypertension. First, by identifying the frequency and nature of CHD across the world, the study will set up the theoretical framework of CHD epidemics, as well as widen awareness of the broad range of structural cardiac abnormalities among children.

Secondly, the study aims to identify the challenges that present the most difficulty in managing children with CHD; focus is being made on the aspect of hypertension that is often associated with this condition. Framingham risk, including hypertension, requires further investigation on its prevalence, underlying risk factors, and the cardiovascular risks it poses to this population to formulate appropriate measures that can help reduce these risks.

Another essential goal will be a review of current literature about antihypertensive medications in pediatric patients with CHD. This review will summarize the up-to-date findings of some classes of antihypertensive drugs regarding effectiveness and safety profile and explore the existing gaps.

Moreover, it will be done systematically for all the drugs that are commonly used for hypertension management in pediatric patients with CHD in terms of safety and efficacy. The research thus seeks to understand evidence from comparative randomized controlled trials alongside cohort studies and case-control data to understand a tight therapeutic chain that could fit the physiological and clinical features of children with CHD. In conclusion, upon these assessments, the study intends to proffer invaluable guidelines for the best practices when it comes to treating hypertension in children with CHD.

2. Background of the Study

Congenital Heart Disease (CHD) includes a range of structural heart defects present at birth, from minor to severe conditions. Congenital Heart Disease (CHD) includes a range of structural heart defects present at birth, ranging from minor to severe conditions. Major types associated with advanced maternal age (≥35) include coarctation of the aorta, valvular pulmonic stenosis, ventricular septal defect, atrial septal defect, endocardial cushion defect, and hypoplastic left heart syndrome. CHD mutations can affect molecules involved in myocyte specification, differentiation, or cardiac morphogenesis, often by altering gene-protein dosage and causing individual malformations. Symptoms such as abnormal heart sounds, cyanosis, rapid breathing, and poor weight gain may indicate CHD, which echocardiogram, ECG, chest X-ray, and cardiac catheterization confirm. Cardiac malformations can be produced by perturbing molecules involved in myocyte specification, differentiation, or cardiac morphogenesis. Family history and genetic testing are essential in diagnosing and identifying CHD mutations. Common types include coarctation of the aorta, valvular pulmonic stenosis, ventricular septal defect, atrial septal defect, endocardial cushion defect, and hypoplastic left heart syndrome. Family history and genetic testing are essential in identifying CHD-associated mutations.

Pulmonary Hypertension (PAH) is a common complication of CHD occurring in nearly 10% of pediatric patients. Disease-targeted therapies (e.g., bosentan, prostaglandin i2, and vardenafil) are critical aspects of the care intended to improve surgical outcomes and quality of life for individuals with PAH. Commonly, these therapies lower pulmonary vascular resistance and improve hemodynamics, exercise capacity, and survival. PAH management is one of the main goals for symptom control and enhancing Q.O.L. among sinusoidal-sequestration patients receiving liver transplantation, using bosentan, prostaglandin i2, and vardenafil. PDE5 inhibitors decrease pulmonary arterial resistance and favorably alter multiple hemodynamic variables. Bosentan administered orally yielded favorable hemodynamics, exercise capacity, and survival results. The 2017 Clinical Practice Guideline for the Screening and Management of High Blood Pressure in Children and Adolescents states that blood pressure should be measured on three separate visits to ensure accurate classification, using the appropriate cuff size and having the arm supported inappropriately positioned when seated. Auscultatory confirmation of blood pressure is desirable as oscillometric readings often overestimate blood pressure levels. Hypertension in children is usually underreported but has a profound association with the development of cardiovascular and renal disease.

In yet another study, it was noted that antihypertensive treatment on children with CHD was significant for better clinical outcomes and quality of life gains. This management is made possible through the use of antihypertensive drugs to keep blood pressure in check and, in turn, minimize cases of CV incidents and their repercussions. ACE inhibitors, ARBs, beta-blockers, and calcium channel blockers are the usual antihypertensive agents that may be prescribed. It is critical to understand that the use of these drugs, as well as their dosage, should be highly individualized to the physiology of the patient as well as the specifics of his or her cardiac abnormalities. While these medications can improve survival, symptoms, and stabilization, they could interact with cells in the body and cause side effects such as electrolyte alterations and compromised hemodynamics where close monitoring and management are required. Examples include electrolyte disorders whose equalization, if not made, can lead to serious complications such as hypokalemia or hyperkalemia. Lastly, frequently, the advantages mentioned above are considerably more significant than the possible side effects. However, each case needs to be discussed, and a patient needs to be prescribed such drugs to gain maximum positive therapeutic effect.

Specifically, in this paper, the author is concerned with the safety of stimulant medications for ADHD in patients with CHD, and after reviewing extensive literature on the subject area, providing various pieces of information that were presented in the subsequent sections of this paper. Fewer clinical investigations have been designed to evaluate directly whether stimulant agents pose a risk to patients with CHD. However, the studies conducted have implied that the use of stimulant drugs is not ill-advised in the treatment of such patients. However, the long-term safety profiles of most of these products remain unknown, and there is an embarrassment of riches, so more research is needed. As reported possible cardiovascular side effects of stimulant medications, pediatric CHD needs to be closely monitored to ensure a safe and appropriate treatment for ADHD.

The present systematic review suggested the lack of information from the little known about antihypertensive drugs in pediatric patients with CHD. As highlighted by the evidence, there is a need to develop more proactive drugs with specific regard to the concern outlined herein. The current article aims to provide the reader with a brief literature review of the efficacy of the most used medications in pediatric CHD patients following cardiac surgery using cardiopulmonary bypass techniques. An essential part of the latter is that both single-center regression and cohort studies revealed substantial center- and disease-age-dependent variations in drug clearance. One hundred and twenty-seven studies with children, a total of 51,573 and across different medication classes, revealed the wide range of variation and a general age/case condition-dependent way in which children metabolized and used these drugs. Such variations underscore the importance of enhanced patient-focused techniques when it comes to addressing hypertension and other issues that pertain to children with CHD.

According to a study done recently, a child with severe Congenital Heart Disease (CHD) is commonly on antihypertensive agents, more often in the early period of the first year of life. There is also a different trend of children having CVM, which is decreasing with age. First-year children with severe CHD were prescribed CVM at a proportion of 47%, but this rate declined progressively as the child's age advanced. Compared with this study, which uses the entire population of a region, the data may not reflect the use of cardiovascular medications at individual hospitals, although overall use might be higher; nevertheless, the study design may inflate the prevalence of 'off-label' medication use. However, it points out that children with severe CHD are more likely to be prescribed such drugs at an early age, and usage decreases with those at younger ages.

In this paper, the authors are focused on the utilization of interventional therapy for compound congenital heart disease (CCHD) in children. The study pointed out that the most frequently identifiable type of CCHD was atrial septal defect associated with ventricular septal defect, of which the prevalence rate reached 32%. 3% of the patients. Nevertheless, the follow-up period is short, there is no surgery group for comparison, and the study's sample size is not large, which makes doubt its generalizability. Also, it is a retrospective study…. Despite these limitations, we found relatively good generalizability for all the results. The therapy was successfully administered in 97. Thus, the case indicates that therapy can be efficiently delivered through a combination of factors such as technology, communication, and trust. Hence, only 2% of the children are provided 4% of the overall impetus for their education. Mild adverse events, which most subjects could tolerate, were 58%.

In this study, the number of severe patients in the CP+ group was smaller than in the CP- group in terms of central SBP measured from the cuff. Atrial fibrillation, cardiac operation, hypertension medication as well as taking anticoagulant, antiplatelet, and antibacterial drugs also acted as exclusion criteria, and the overall sample size was small, with only 60 patients in the CP+ and CP- groups. These means suggested that the investigational subjects in the CP+ group experienced reduced central SBP than the CP- counterparts. This bespoke that CP drugs may have the potential to prevent future cardiovascular disease in patients with Congenital heart disease (CHD).

3. Methodology

This present study employed an observational approach with a descriptive research design and method; data were gathered through record review, mainly of the patient's medical files. The study participants were all referred patients who were 0-18 years of age with CHD and incepted in with antihypertensive agents in the calendar years 2020 and 2022. These patients were from two hospitals in Chattogram and Dhaka, a sub-division of Bangladesh. The sample comprised the entire population encountered during the research period.

3.1 Data Analysis

Data reflecting patient identification information, age and gender, diagnosis, and details about the antihypertensive treatment – name of the antihypertensive, dose prescribed, and method of administration are provided descriptively. The types of antihypertensive drugs may include all classes of antihypertensives, depending on the cyanotic and non-cyanotic types of congenital heart diseases. Assessment of patient medication reconciliation looked at the compatibility of the specific medications that the doctor recommended with the medical condition diagnosed by the doctor on the patient's body (Tuloli et al., 2019). This evaluation matched the literature source: Drug Information Handbook, 17th Edition (2009), the BNF for Children 2020-2021, Clinical Practice Guidelines, Cardiovascular Pathway Clinical 2016, and The National Drug Information Center Philippines- PIONAS, 2015.

Therapeutic indication deals with the entire process of administering a drug and pharmacological treatment without considering other factors apart from the medical need. The diagnosis determines the medication choice depending on the distinctive symptoms emerging from the disease. If the diagnosis is wrong, then the substance administered is not the one capable of eliciting the desired outcome (Sumawa, 2015). Investigators determined that the actual doses administered were conformable to those recommended by the BNF 2020-2021 and the Drug Information Handbook, 17th Edition (2009). Some of the dose accuracy discretions are the frequency of doses given, the recommended dose, and the particular dosing route. When the dosage is in the prescribed dosage range and the minimum and recommended daily doses, then the prescription is exact. The fair administration of the drugs is established if the chosen drug has the consideration of benefits and risks.

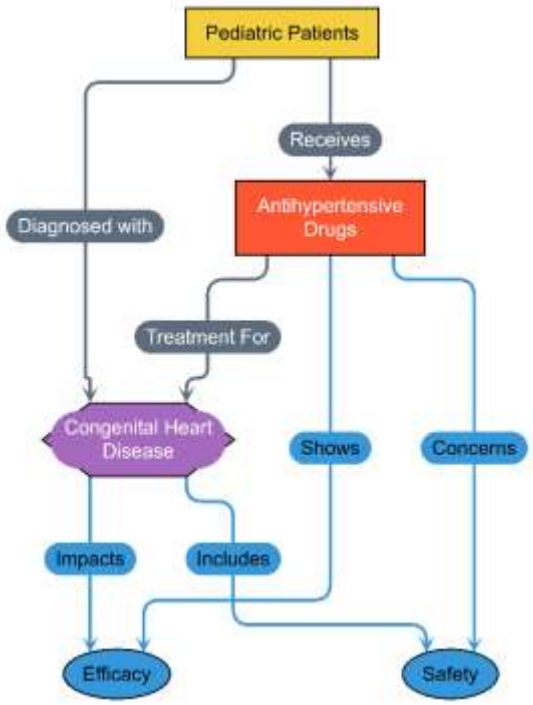

Figure 1: Overview of Antihypertensive Drug Use in Pediatric Patients with Congenital Heart Disease

The algorithm suggested in the work (Figure 1) shows the treatment process of children with congenital heart disease (CHD) and the use of antihypertensive preparations. This starts with identifying patients of the pediatric population who have been diagnosed with CHD and was done with a focus on the specialized medical attention such patients require. Antihypertensive drugs constitute an essential aspect of the treatment plans for such patients and are prescribed to enable effective control of their hearts. Reading the flowchart, one can identify that the administration of antihypertensive drugs affects the risks and benefits of the treatment. The efficiency issues relate to the extent to which these drugs are effective in maintaining CHD, which must be closely monitored. At the same time, safety issues are highly significant, and the focus should be paid to the protection of children's rights while receiving medical care. Collectively, the flowchart gives an understandable chronology of the management plan, illustrating that the treatment intent for congenital heart disease with antihypertensive drugs in children entails both effectiveness and safe delivery.

The symptoms and conditions are presented in detail in Table 1, which is relevant for the further development of the subject and for understanding the problem area of congenital heart disease in children. An understanding of these symptoms is still vital to assess the effectiveness and side effects of antihypertensive drugs taken by pediatric CHD patients since these drugs affect cardiovascular outcomes and may alter the expression of these symptoms as well.

Table 1: Common Symptoms and Conditions Associated with Congenital Heart Disease in Pediatric Patients

Symptom	Description
Growth Delay	They are commonly observed in children with CHD.
Risk of Being Underweight	It is increased with the severity of CHD.
Risk of Being Overweight/Obese	Higher in children with mild or moderate CHD.
Reduced Sports Activity	Frequency decreases with increasing severity of CHD.
Height Reduction	Statistically significant reduction in height z-score in children with a univentricular heart defect.

Cyanosis	Bluish discoloration of the lips, tongue, and extremities; associated with cyanotic heart diseases like Tetralogy of Fallot and Truncus arteriosus.
Shortness of Breath	This could indicate cardiac involvement or fluid overload.
Fatigue	Excessive tiredness or lack of energy.
Abnormal Heart Sounds (Heart Murmur)	Detected by a physician during cardiac examination.
Heart Failure	Impaired heart function leads to fluid accumulation and symptoms like edema.
Poor Blood Circulation	Manifests as cool extremities, delayed capillary refill time, or pallor.
Fast Breathing	Increased respiratory rate is often a sign of respiratory distress.
Chest Indrawing	Visible inward movement of the chest wall during breathing.
Cough	Persistent cough, possibly due to fluid buildup in the lungs.
Poor Weight Gain	Difficulty gaining weight despite adequate caloric intake.
Feeding Problems	Difficulty feeding, possibly due to fatigue or respiratory distress.
Anemia	Low red blood cell count, leading to fatigue and pale skin.
Clubbing of Fingers	Abnormal enlargement of the fingertips due to chronic lack of oxygen.
Easy Fatigability	Tires easily during physical activities.
Recurrent Chest Infections	Frequent respiratory infections, possibly due to compromised respiratory function.
Angina	Chest pain or discomfort, often during exertion.
Palpitations	The sensation of rapid, fluttering, or pounding heartbeats.
Dizziness or Light-headedness	Feeling faint or dizzy, especially during physical exertion or stress.
Nausea	Occasionally experienced, often associated with chest discomfort.
Sweating	Unexplained sweating, especially if cold and clammy.
Pain/Discomfort in Other Areas	Pain, discomfort, or numbness in arms, shoulders, back, neck, or jaw.
Edema	Swelling in the legs, abdomen, or around the eyes due to fluid retention.
Syncope	Fainting or loss of consciousness due to inadequate cardiac output or arrhythmias.
Pulmonary Edema	Fluid accumulation in the lungs causes coughing, wheezing, or difficulty breathing.
Arrhythmias	Abnormal heart rhythms cause palpitations, dizziness, or chest discomfort.

Elevated Liver Enzymes	Due to liver congestion caused by impaired blood flow through the heart.
Delayed Development	Developmental delays due to chronic hypoxia and limited energy.

3.2 Gender Distribution across Different Age Groups of Pediatric Patients with Congenital Heart Disease

Table 2 below provides a detailed description of the gender distribution among pediatric patients with congenital heart disease (CHD) across various age groups. This distribution helps in understanding the demographic patterns and potentially tailoring treatment approaches to the specific needs of different age and gender groups.

Table 2: Gender Distribution Across Different Age Groups of Pediatric Patients with Congenital Heart Disease

Age Group	Male (%)	Female (%)
Neonates	44.5	55.5
Infants	41.1	58.9
Toddlers	21.1	78.9
Preschoolers	20.5	79.5
School-age	10.3	89.7
Adolescents	2.3	97.7

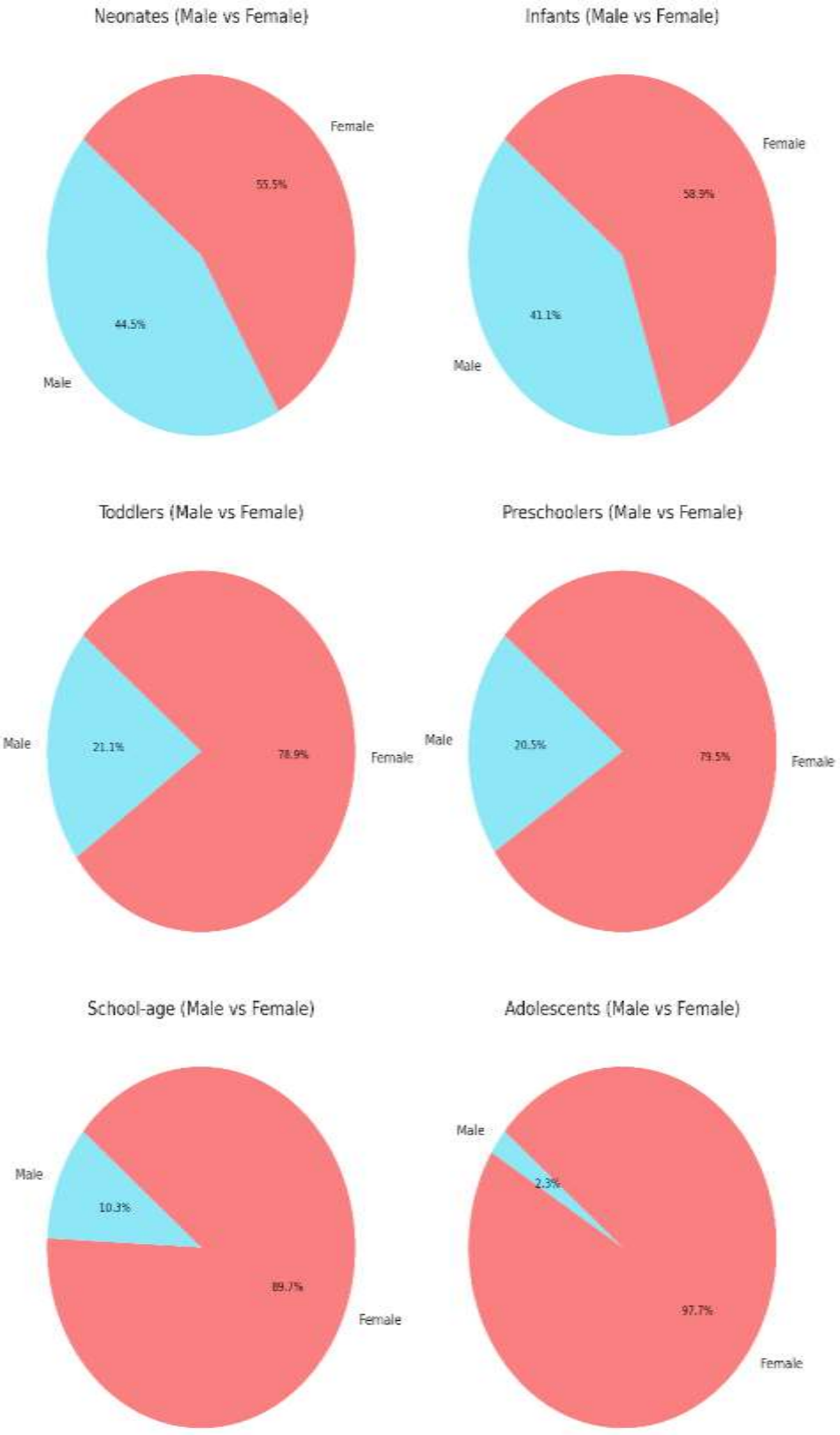

Figure 2: Gender distribution across different age groups of pediatric patients with Congenital Heart Disease (CHD)

3.3 Age Group Descriptions for Pediatric Patients with Congenital Heart Disease

Understanding the different age groups is essential for evaluating the efficacy and safety of antihypertensive drugs in pediatric patients with Congenital Heart Disease (CHD). Each age group has unique developmental characteristics and healthcare needs.

Table 3: Age Group Descriptions

Age Group	Description
Neonates	Newborns up to 1 month old. Characterized by rapid physiological changes as they adapt to life outside the womb. Vulnerable to CHD complications and require close monitoring and immediate medical intervention.
Infants	1 month to 1 year old. Significant growth and development, achieving milestones like sitting up, crawling, and possibly standing. CHD can impact growth rates and overall development.
Toddlers	1 year to 3 years old. Highly active, begin to walk, run, and explore. Marked by rapid physical, cognitive, and emotional development. CHD can limit activity levels, cause feeding difficulties, and poor weight gain.
Preschoolers	3 years to 6 years old. Develop advanced motor skills, language abilities, and social interactions. Engage in structured play and learning activities. CHD may lead to reduced sports activity and height reduction.
School-age	6 years to 12 years old. It involves academic learning, social skill development, and increasing independence. Children with CHD might face challenges in physical activities and sports and may have affected height and weight.
Adolescents	12 years to 18 years old. Characterized by puberty, growth spurts, and complex social life. Adolescents with CHD might experience symptoms like fatigue, palpitations, and dizziness, impacting physical and social activities.

Understanding these age-specific characteristics (Table 3) helps in tailoring treatment plans and ensuring that antihypertensive drugs are administered safely and effectively to pediatric patients with CHD, considering their developmental stage and specific health needs.

Table 4: Common Medications Used in the Treatment of Congenital Heart Disease (CHD) in Pediatric Patients

Medication Class	Medications	Age Group	Typical Use (%)
Diuretics	Furosemide (Lasix)	All ages	70-80%
	Spironolactone	All ages	20-30%
ACE Inhibitors	Enalapril, Lisinopril	School-age and older	40-50%
Beta-Blockers	Propranolol, Carvedilol	School-age and older	30-40%
Digoxin	Digoxin	All ages	30-40%
Anticoagulants/Antiplatelets	Aspirin, Warfarin	School-age and older	20-30%
Prostaglandin E1 (PGE1)	Alprostadil (Prostin VR)	Neonates	10-20%
Vasoactive Medications	Dopamine, Dobutamine	Neonates, ICU	10-20%
Antiarrhythmics	Amiodarone, Sotalol	School-age and older	10-20%
Nutritional Supplements	Iron supplements, Multivitamins	All ages	40-50%
Other	Antibiotics (prophylactic)	All ages	10-20%
	Oxygen therapy	Neonates, Infants	20-30%

Table 4 provides an overview of common medications used to treat CHD in pediatric patients, including information on medication classes, specific drugs, typical age groups, and usage percentages. The age group represents the typical age range for the use of each medication class based on clinical guidelines and practice. For example, diuretics like Furosemide (Lasix) and Spironolactone are prescribed across all age groups, whereas ACE inhibitors such as Enalapril and Lisinopril are generally used in school-age children and older.

4. Results and Discussion

4.1 Characteristics of Patients

This study shows that the proportion of female child patients with Congenital Heart Disease (CHD) and using antihypertensive treatment is higher (53.26%) (Table 5). This may be influenced by biological differences in the structure of blood vessels. The diameter of arteries in females is smaller compared to males. This condition can increase the risk of vascular endothelial dysfunction associated with cardiovascular diseases, including congenital heart disease (Fedora, Utamayasa, and Purwaningsih, 2019).

The most common age characteristic of the study sample is the age group of infants 1 month to 2 years (43.48%). This indicates that CHD can be detected in the first year of life. This result is not much different from other studies, which show that children with CHD are more commonly found in the first year of life, amounting to 56.4% (Ain, Hariyanto, and Rusdan, 2015). Generally, congenital heart disease can be detected from birth, but symptoms often do not appear until a few weeks or months after birth (Kalalo, Pateda, and Salendu, 2016). From the research results, there are three final conditions of hospitalization for pediatric patients with Congenital Heart Disease (CHD), with the most common outcome being improved conditions at 82.61% (Table 5). Patients with congenital heart disease (CHD) whose condition improved showed a stable state. Early detection and management are crucial components for the survival of CHD patients (Amal and Ontoseno, 2017).

There were 7.61% of patients who died under the age of 1 month. This could be due to the disease not being detected early enough and not being properly managed. If untreated, 50% of deaths occur within the first month of life. In developed countries, almost all types of CHD are detected before the age of 1 month, whereas in developing countries, many cases are only detected after the child is older. Therefore, in some severe cases of CHD, patients may have died before being diagnosed (Hermawan, Hariyanto, and Aprilia, 2018).

Table 5. Profile Characteristics of Patients

Characteristics	Number of Patients (N=92)	Percentage (%)
Gender		
Male	43	46.74
Female	49	53.26
Age		
Neonatal (0 days – 28 days)	16	17.39
Infants (1 month - 2 years)	40	43.48
Children (2 years - 11 years)	27	29.35
Adolescents (12 years - 18 years)	9	9.78
Final Condition of Hospitalization		
Improved	76	82.61
Discharged against medical advice	9	9.78
Deceased	7	7.61

Table 6. Profile of Diagnoses in Congenital Heart Disease Patients

Diagnosis of CHD	Total (N=102)	Percentage (%)
Atrial septal defect	23	22.5
Asianotic congenital heart disease	22	21.6
Ventricular septal defect	22	21.6
Cyanotic congenital heart disease	12	11.8
Patent ductus arteriosus	8	7.8
Tetralogy of Fallot	5	4.9
Atrioventricular septal defect (AVSD)	4	3.9
Transposition of the great arteries (TGA)	3	2.9
Congenital heart disease (Unidentified)	2	2.0
Double outlet right ventricle	1	1.0

Note: *One patient can have more than one diagnosis.*

Based on Table 6, which profiles the diagnoses of congenital heart disease (CHD) in pediatric patients, one patient can have more than one diagnosis. The most common type of cyanotic CHD diagnosis is Atrial Septal Defect (ASD), accounting for 22.5% of cases. A study by Bermudez et al., 2015, reported that the most frequent CHD diagnosis was Atrial Septal Defect (ASD), with 254 cases (42.1%). ASD is a congenital heart disease characterized by a hole (defect) in the interatrial septum resulting from the failure of the septum to fuse during fetal development (Firdaus et al., 2016). There are several anatomical types of atrial septal defects, including primum, secundum, sinus venosus, and coronary sinus types (Maramis, Kaunang, and Rompis, 2009).

Most secundum atrial defect patients are asymptomatic, particularly infants and young children unless they frequently suffer from respiratory infections. If the shunt is large enough, the patient may experience shortness of breath. The prevalence percentage in Asia for ASD CHD is 13 per 1000 live births (Kumala, Kartika Yantie, and Hartawan, 2018).

Proper medication usage aligns with the therapeutic algorithm for CHD patients and avoids drugs that may exacerbate cardiac workload. The goal of antihypertensive medication is to reduce patient mortality and morbidity, improve heart function, and prevent heart failure. The general objective of treating pediatric heart failure is to minimize symptoms until surgical intervention can be performed (Dedieu & Burch, 2013). Management principles for pediatric heart failure include identifying and eliminating precipitating factors, correcting the underlying cause, and managing pulmonary or systemic congestion. Pediatric heart failure therapy typically adopts findings from adult studies, with commonly used pharmacological therapies including antihypertensives (Willim et al., 2020).

According to the Chinese Guidelines for Prevention and Treatment of Hypertension 2018, the recommended classes of antihypertensive drugs for children are CCBs, ACEIs, ARBs, diuretics, and β-blockers. All these classes of antihypertensives are recommended for maintaining pediatric heart health, and medication use should be set on the patient's clinical condition.

Based on Table 7, 178 antihypertensive medications were used for pediatric congenital heart disease patients. One patient may receive more than one type of antihypertensive therapy. The most frequently used antihypertensive in therapy is Furosemide, a diuretic, accounting for 44.9% of cases. Furosemide can be administered orally or by injection, and it is used in the treatment of congenital heart disease to manage heart failure symptoms. Furosemide also has vasodilatory effects and increases systemic venous capacitance, thereby reducing preload (Saxena, 2009).

Table 7. Profile of Antihypertensive Drug Usage

Name	Usage (n=178)	Percentage (%)
Furosemide	80	44.9
Captopril	54	30.3
Spironolactone	18	10.1
Propranolol	14	7.9
Sildenafil	10	5.6
Ramipril	2	1.1

Note: *One patient can consume more than one drug.*

The second most frequently reported drug in this study is captopril, either used as monotherapy or in combination with other drugs, reported in 30. 3%. Captopril is often prescribed for children in pediatric practice, mostly neonates and infants (Saxena, 2009). ACE inhibitors are vasodilators applied in congenital heart disease all types rather than Tetralogy of Fallot and for congestive heart failure in children (Firdaus et al., 2016).

β-blocker is another drug that is given to patients, and this one is called propranolol. This class of drugs antagonizes beta-adrenoceptors in the heart, peripheral blood vessels, bronchi, pancreas, and liver. β-blocking agents are prescribed in treating congenital heart disease, especially Tetralogy of Fallot, according to BNF 2020-2021. Another vasodilator utilized in the patient is sildenafil. In this study, sildenafil was given because patients had VSD, which is a contraindication for the development of pulmonary hypertension and right heart dysfunction. Sildenafil targets the function of the heart as it moves. Furthermore, some patients had pulmonary hypertension as one of the associated features, and sildenafil was a component of the treatment. The USFDA 2012 came out with a warning concerning the administration of high doses of sildenafil to children with pulmonary hypertension because sildenafil use in infants and children requires further investigation (Benjamin et al., 2017; Jiang et al., 2018).

4.2 Evaluation of Drug Usage

4.2.1 Patient Accuracy Evaluation

The results of this study show that the accuracy of patient selection for medications is 98.9% for all drugs, including furosemide, captopril, propranolol, spironolactone, and sildenafil (Table 4). The inappropriate use of medication was observed with ramipril, as it is not recommended for the treatment of heart disease in patients under 18 years of age despite being categorized as a vasodilator. The recommended ACE-I vasodilators for pediatric cardiac treatment are captopril and enalapril (Saxena, 2009). Currently, vasodilators used in pediatric patients aim to supplement standard therapy, which includes diuretics and digitalis to prevent hypokalemia (Sofyani, 2016).

Table 8. Evaluation of Patient Accuracy

Drug	Correct Patient Use	Percentage (%)
Furosemide	Yes	100
Spironolactone	Yes	100
Captopril	Yes	100
Ramipril	No	0
Propranolol	Yes	100
Total Correct	-	**98.9**
Incorrect	-	**1.12**

In this evaluation (Table 8):

- Furosemide, Spironolactone, Captopril, and Propranolol were used correctly in 100% of cases.
- Ramipril was not used correctly in any cases (0%).
- Overall, 98.9% of medications were administered correctly according to patient indications, while 1.12% were administered incorrectly, primarily due to the inappropriate use of ramipril, which is not indicated for congenital heart disease treatment in pediatric patients.

4.2.2 Evaluation of Indication Accuracy

From the analysis in Table 9, it is observed that 98.9% of prescribed medications are aligned with the diagnosis of congenital heart disease in pediatric patients based on the pathological and physiological conditions derived from medical records. There is a 1.12% inappropriate use of ramipril, which does not have indications for congenital heart disease management.

Table 9. Evaluation of Indication Accuracy

Drug	Indication Accuracy	Percentage (%)
Furosemide	Yes	100
Spironolactone	Yes	100
Captopril	Yes	100
Ramipril	No	0
Propranolol	Yes	100
Total Correct	**-**	**98.9**
Incorrect	**-**	**1.12**

4.2.3 Evaluation of Dose Accuracy

Based on the analysis in Table 6, referring to the British National Formulary (BNF) for Children 2020-2021, the accuracy of furosemide usage (both injection and oral) reaches 62.7%. In cases where the dose was incorrect, one patient received an overdose combination of Captopril + Sildenafil + Furosemide, resulting in deterioration during hospitalization. Upon investigation, it was found that the patient, who was less than one year old, received an overdose of sildenafil (the maximum dose should be 30 mg/day, but the patient received 37.5 mg/day). Additionally, this patient also received an underdose of injectable furosemide, which should have been administered three times daily but was given only once. Administration of sildenafil to children, especially those under one year old, requires special attention, as does ensuring correct dosing for all medications, particularly in complex combinations like those observed in this case.

The US Food and Drug Administration (USFDA) issued a safety alert in 2012 regarding children who were taking excessive doses of sildenafil. Another concern that has been recorded in the works, such as the study on STARTS-2 by Li Jiang in 2018, is that controversy regarding the use of high-dose sildenafil has tended to lead to higher mortality incidents than in low and moderate doses. Subsequently, more studies are required because of this controversy (Jiang et al., 2018). Medication mistakes are a three-fold higher rate among children than among adult patients. On the other hand, antihypertensive therapy is considered standard among children with cardiovascular diseases, including congenital heart disease, either in monotherapy or combination therapy (Woo et al., 2015).

4.2.4 Evaluation of Correct Medication Use

In this evaluation of correct medication use, whether used singly or in combination, 97.8% of therapies were appropriately administered (Table 10). The inappropriate use of medication included combinations involving ramipril, which is not recommended

for treating heart disease in individuals under 18 years old despite being a vasodilator. ACE inhibitors recommended for pediatric cardiac treatment are captopril and enalapril. However, enalapril's use is rare due to its potential to cause kidney dysfunction, making captopril the preferred choice in pediatric practice, especially in neonates and infants (Saxena, 2009).

The combination of ACE inhibitors with diuretics, such as Captopril + Furosemide + Spironolactone, is beneficial for addressing fluid and salt retention to reduce fluid volume in patients, thereby reducing pulmonary edema and lung congestion. However, diuretics alone cannot reduce mortality, so they are often combined with ACE inhibitors. Captopril is administered to treat myocardial dysfunction in congenital heart disease.

Table 10. Evaluation of Dose Accuracy

Drug	Total	Correct Dose	Percentage (%)	Incorrect Dose	Percentage (%)	Unknown	Percentage (%)
Captopril	54	51	94.4	2	3.7	1	1.9
Ramipril	2	0	0.0	2	100.0	0	0.0
Furosemide	95	53	55.8	40	42.1	2	2.1
Propranolol	14	7	50.0	6	42.9	1	7.1
Spironolactone	18	5	27.8	12	66.7	1	5.6
Sildenafil	10	5	50.0	5	50.0	0	0.0
Total	**193**	**121**	**62.7**	**67**	**34.7**	**5**	**2.6**

Note: *Each patient may receive more than one type of medication.*

In Table 10, the evaluation of dose accuracy for various medications used in pediatric congenital heart disease treatment shows the following:

- **Captopril:** 94. 4 percent of the doses delivered were proper, a 3 percent. 7% incorrect and 1. 9% unknown.
- **Ramipril:** No correct doses were seen (100. 0%), as ramipril is contraindicated in cases of children.
- **Furosemide:** 55. Eight percent of doses were correct, 42 percent of doses were intramuscular administrations, and 37 doses were given to females. 1% incorrect, and 2. 1% unknown.
- **Propranolol:** 50. Therefore, none of the doses were correct, and the lowest percentage of 42% was achieved. 9% incorrect, and 7. 1% unknown.
- **Spironolactone:** 27. 8% of the doses that were administered were correct, 66. 7% incorrect, and 5. 6% unknown.
- **Sildenafil:** 50. Specifically, 0% of doses were correct, and 50%. 0% were incorrect.

All in all, it was found that the evaluation turned out to be at the percentage level of 62. When the medication was introduced to the patient, the correct administration was at 7%, with variable results depending on the specific medication.

Table 11. Evaluation of Medication Accuracy

Therapy Type	Drug Combination	Correct	Total	Percentage (%)
Single Therapy	Captopril	2	2	100.0
	Furosemide	13	14	92.9
	Spironolactone	1	1	100.0
	Propranolol	7	7	100.0
Combination Therapy	Ramipril + Sildenafil	0	1	0.0
	Captopril + Sildenafil + Furosemide	7	7	100.0
	Captopril + Furosemide	39	39	100.0
	Spironolactone + Sildenafil	1	1	100.0
	Furosemide + Ramipril	0	1	0.0
	Propranolol + Furosemide	2	2	100.0
	Spironolactone + Furosemide	10	10	100.0
	Captopril + Furosemide + Spironolactone	2	2	100.0
	Propranolol + Furosemide + Spironolactone	2	2	100.0
	Propranolol + Furosemide + Captopril	2	2	100.0
	Spironolactone + Furosemide + Captopril + Sildenafil	1	1	100.0
	Spironolactone + Furosemide + Captopril + Propranolol	1	1	100.0
Total		**90**	**92**	**97.8**
Incorrect		**2**	**92**	**2.2**
Grand Total		**92**	**92**	**100.0**

Notes: *Each patient may receive more than one combination of drugs.*

In Table 11, the evaluation of medication accuracy shows the following:

- **Single Therapy**: Captopril, Furosemide, Spironolactone, and Propranolol were administered correctly in all cases.
- **Combination Therapy**: Various combinations were evaluated, with most combinations (90 out of 92) being administered correctly.
- **Incorrect Therapy**: One case involved the combination of Ramipril and Sildenafil, which was inappropriate.

The data indicates a significant level of compliance with drug regimens in the treatment of juvenile congenital heart disease, with 97.8% of therapy combinations being administered correctly.

5. Conclusion

The investigation of the utilization of antihypertensive medications in the treatment of coronary heart disease (CHD) in children yielded pivotal discoveries and suggestions. Furosemide dominated, used during the treatment course in 44.9%, followed by captopril and spironolactone applied in 30.3%, propranolol in 7.9%, Sildenafil in 5.6%, and ramipril in 1.1%. Furosemide is a highly effective diuretic medication that effectively treats edema and aids in the management of symptoms associated with heart failure. Administering the ACE inhibitor, captopril efficiently reduces blood pressure and improves cardiac function, reducing the likelihood of congestive heart failure. A potassium-sparing diuretic, spironolactone, manages fluid retention without causing hypokalemia. As a beta-blocker, propranolol would be used for arrhythmias and hypertension. However, Sildenafil, which is a vasodilator, can be mainly used to treat pulmonary hypertension, a disease that is one of the various problems associated with CHD. Ramipril, however, is not generally recommended for use in pediatric patients below 18 years because of insufficient data on its establishment of safety and efficacy. Inappropriate therapy, was high, with 98.9% of cases having the correct indication and patient selection, and 97.8% having the correct medication choice. The appropriateness of correct dosing was present in only 62.7% of cases. This leads to subtherapeutic effects if the dosage is too low or to increased risk of adverse effects in case it is too high. This implies continuous monitoring of the therapy and its side effects, whereby the patient's response to medication must be assessed regularly and watched for adverse reactions. There has to be a tremendous enhancement in the adherence to guidelines concerning dosing, more in children, so as not to bring in devastating outcomes, which can be supported by additional professional education for health practitioners and executed dosing calculators and other aids. Taking into consideration the variability of metabolic and physiological responses in children for medications, individual treatment plans for the child concerning his age, weight, and disorders/conditions are much needed. Further studies in this regard are necessary to get more clarity related to dose specifics in pediatric patients, especially for drugs like Sildenafil that proved controversial results and increased risks at some dosages. It can investigate the use of other antihypertensive drugs or their combinations that could bring in better results with fewer side effects for a pediatric patient having CHD. This means that the appropriateness of antihypertensive drug use among

children having CHD showed high rates for proper patient selection and proper medication but reflected high challenges of incorrect dosing. Individualized treatment plans that are appropriately monitored enhance the outcome and minimize the risk.

Funding: This research received no external funding.
Conflicts of Interest: The authors declare no conflict of interest.
ORCID iD: https://orcid.org/0000-0001-7734-0271

References

[1] Ain, N., Hariyanto, D., & Rusdan, S. (2015). Karakteristik penderita penyakit jantung bawaan pada anak di RSUP dr. M. Djamil Padang periode Januari 2010–Mei 2012. *Jurnal Kesehatan Andalas*, 4(3), 928-932.
[2] Alexander, D. C., Bundy, D. G., Shore, A. D., Morlock, L., Hicks, R. W., & Miller, M. R. (2009). Cardiovascular medication errors in children. *Pediatrics*, 124(1), 324–332.
[3] Abhijit P and Arkajyoti P (2017). Insilico molecular docking analysis of isolated compounds of Ocimum sanctum against two related targets to diabetes. Pharma Innovation 2017;6(9):148-151.
[4] Amal, I., & Ontoseno, T. (2017). Tatalaksana dan rujukan awal penyakit jantung bawaan kritis. *Cermin Dunia Kedokteran*, 44(9), 667–669.
[5] Balogh, E. P., Miller, B. T., & Ball, J. R. (2015). *Improving diagnosis in health care*. Committee on Diagnostic Error in Health Care; Board on Health Care Services; Institute of Medicine; The National Academies of Sciences, Engineering, and Medicine. Doi: 10.17226/21794.
[6] Cernadas, J. M. C., Bogado, L., Rolón, F. E., & Galletti, M. F. (2019). Voluntary and anonymous reporting of medication errors in patients admitted to the Department of Pediatrics. *Archivos Argentinos de Pediatria*, 117, e592–e597. doi: 10.5546/aap.2019.eng.e592.
[7] Custer, J. W., Winters, B. D., Goode, V., Robinson, K. A., Yang, T., Pronovost, P. J., & Newman-Toker, D. E. (2014). Diagnostic errors in the pediatric and neonatal ICU: A systematic review. *Pediatric Critical Care Medicine*, 16. doi: 10.1097/PCC.0000000000000274.
[8] Carlos, D and Trinidad-Calderón. (2022). Congenital Heart Disease: The State-of-the-Art on Its Pharmacological Therapeutics. *Journal of Cardiovascular Development and Disease*, doi: 10.3390/jcdd9070201
[9] Chung, L.M and Gopakumar, H. (2023). Safety of stimulant medications for attention deficit hyperactivity disorder in pediatric congenital heart disease. *Journal of Paediatrics and Child Health,* doi: 10.1111/jpc.16380.
[10] Danielle S. B and Joseph W. R. (2019). Significant mortality, morbidity, and resource utilization associated with advanced heart failure in congenital heart disease in children and young adults. *American Heart Journal*, doi: 10.1016/j.ahj.2018.11.010.
[11] Dedieu, N., & Burch, M. (2013). Understanding and treating heart failure in children. *Paediatrics and Child Health*, 23(2), 47–52.
[12] Elizabeth, J., Thompson., Henry, P., Foote., Caitlin, E, King., Sabarish, Srinivasan., Elizabeth, C, Ciociola., Dennis, Leung., Alexandre, T., Rotta., Kevin, D., Hill., Michael, Cohen-Wolkowiez., Christoph, P., Hornik. (2021). A systematic review of the evidence supporting post-operative medication use in congenital heart disease. Cardiology in The Young, doi: 10.1017/S1047951121001463.
[13] Fedora, K., Utamayasa, I. K. A., & Purwaningsih, S. (2019). Profile of acyanotic congenital heart defect in children at Dr. Soetomo General Hospital Surabaya period of January–December 2016. *JUXTA: Jurnal Ilmiah Mahasiswa Kedokteran Universitas Airlangga*, 10(2), 79–82.
[14] Firdaus, I. (2016). *Panduan Praktik Klinis (PPK) dan Clinical Pathway (CP) Penyakit Jantung dan Pembuluh Darah*. PERKI, Jakarta, Indonesia.
[15] Glanzmann, C., Frey, B., Meier, C. R., & Vonbach, P. (2015). Analysis of medication prescribing errors in critically ill children. *European Journal of Pediatrics*, 174(10), 1347–1355.
[16] Hermawan, B., Hariyanto, D., & Aprilia, D. (2018). Profil penyakit penyakit jantung bawaan di Instalasi Rawat Inap Anak RSUP dr. M. Djamil padang periode Januari 2013–Desember 2015. *Jurnal Kesehatan Andalas*, 7, 142. doi: 10.25077/jka.v7.i1.p142-148.2018.
[17] He Q, Lin X, Zhou Z, (2024). Failure to thrive in pediatric patients with congenital heart disease: a cross-sectional study of 13,256 patients. *Lancet Reg Health West Pac*. 2024;44:101002. Published 2024 Jan 29. doi:10.1016/j.lanwpc.2023.101002
[18] Jiang, L., Sun, W., Zhang, K., Zhou, B., & Kong, X. (2018). Perioperative sildenafil therapy in pediatric congenital cardiac disease patients: A meta-analysis. *International Heart Journal*, 17–548.
[19] Kuntal R and Nandita S (2020). Clinical Presentation and Complications of Different Congenital Heart Disease in Children. Am. J. Pediatr. 2020, 6(4), 481-487. doi: 10.11648/j.ajp.20200604.26.
[20] Mads, D., Stine, K U and Joan, K., M. (2022). Prescription of cardiovascular medication in children with congenital heart defects across six European Regions from 2000 to 2014: data from the EUROlinkCAT population-based cohort study. BMJ Open, doi: 10.1136/bmjopen-2021-057400.
[21] O'Connor MJ and Davies RR, (2020). Early experience with the HeartMate 3 continuous-flow ventricular assist device in pediatric patients and patients with congenital heart disease: A multicenter registry analysis. *J Heart Lung Transplant*. 2020;39(6):573-579. doi:10.1016/j.healun.2020.02.007.
[22] Pathak, A., Asma Gani, M., Tasin, A.H., Sania, S.N., Adil, M., Akter, S. (2021). Chronic Kidney Disease (CKD) Prediction Using Data Mining Techniques. In: Vasant, P., Zelinka, I., Weber, GW. (eds) Intelligent Computing and Optimization. ICO 2020. Advances in Intelligent Systems and Computing, vol 1324. Springer, Cham. https://doi.org/10.1007/978-3-030-68154-8_82.
[23] Ran., T and Ling-ying, F. (2023). Clinical analysis and medium-term follow-up of simultaneous interventional therapy for compound congenital heart disease in children: a single-center retrospective study. Frontiers in Pediatrics, doi: 10.3389/fped.2023.1193136.
[24] Tomoaki, M, Yoko, H and Shigeru, T. (2022). Cardiac protection therapy can prevent the elevation of central blood pressure in adult patients with congenital heart disease. *Journal of Hypertension*, doi: 10.1097/01.hjh.0000837872.93541.67
[25] Zoller, T., Prioli, M.A., Clemente, M., Pilati, M., Sandrini, C., Luciani, G.B., Deganello Saccomani, M., Ficial, B., Gaffuri, M., Piacentini, G. (2022). Congenital Heart Disease: Growth Evaluation and Sport Activity in a Paediatric Population. *Children*, *9*, 884. https://doi.org/10.3390/children9060884.