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REVIEW ARTICLE

Risk Factors and Etiology of Cardiac arrhythmias in Children

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ABSTRACT

Background: Heartbeat abnormalities, such as when it beats too quickly or too slowly, are known as cardiac arrhythmias. Although certain arrhythmias are more common in neonates and young infants compared to older children and adults, all types of arrhythmias can occur. Many are benign and do not cause hemodynamic compromise. Others may compromise cardiac output and cause decreased blood pressure and decreased perfusion. Arrythmias can be due to abnormal structure of the heart, cardiomyopathy, inherited diseases, drugs, infections, inflammation, systemic diseases, autoimmune diseases, mechanical ventilation, central venous line insertion, electrolyte disturbance and others. Not all arrhythmias provide the same risk to the patient, despite the fact that they are frequently seen in critically ill patients. Certain arrhythmias, for instance, can be benign and self-limiting, whereas others might swiftly worsen and become potentially fatal. **Aim**:An overview of the most frequent causes of arrhythmias in children with acquired or structurally congenital cardiac disorders is provided in this article. **Conclusion**: In pediatric patients there are wide range of causes for arrhythmias. May be caused by primarily diseases or acquired factors.

Key words: arrythmia, risk factors, children

INTRODUCTION

This article would explore the various causes and risk factors associated with pediatric arrhythmias. The etiology (causes) and risk factors of pediatric arrhythmias can vary depending on the specific type of arrhythmia. Here are some common etiological factors and risk factors associated with pediatric arrhythmias. Arrhythmias in juvenile patients who are otherwise healthy are not common, but early detection can reduce unnecessary morbidity and death. Patients with a history of congenital heart disease have a much higher prevalence of arrhythmias. A variety of cardiac arrhythmias can manifest in children that can present at any time from fetal life to adolescence [1].

Congenital heart disease has higher risk of developing arrhythmias due to the abnormal heart structure. Additionally, surgical repairs or interventions for congenital heart disease can cause scarring or damage to the conduction system, increasing the risk of arrhythmias

1-Ventricular septal defect repair: Irregular heartbeats are not usually associated with ventricular septal defects, the most common kind of congenital cardiac defect. Since clinically severe Ventricular septal defects are repaired in early childhood, arrhythmias are less common today. Current surgical methods that omit right ventricle incision have significantly decreased the occurrence of ventricular arrhythmias. Patients who have had surgery still have an increased risk of developing a heart block even after significant

correction. When a small, hemodynamically stable, there is no elevated risk of arrhythmia [2].

2. Repair of atrial septal defects account for five to ten percent of all congenital heart defects and are prevalent in 30–50% of infants with other categories of congenital heart disease. Prolonged volume overload and atrial dilatation may result in atrial tachycardias in large defects. Early repair has been shown to improve survival and reduce the incidence of late arrhythmias. Surgery may be necessary to treat injuries to the SA node that cause tachy-brady syndrome, sinus nodal dysfunction, or secondary bradycardia [2].

3. Tetralogy of Fallot: Three to five percent of patients with congenital heart disease have tetralogy of Fallot, the most common cyanotic heart disease. Patients who do not get their cardiac abnormalities fixed or corrected may develop atrial and ventricular arrhythmias. Two to six percent of individuals who were corrected in infancy have abrupt death or arrest. While atrial tachycardias are more common (20–30%), sinus node dysfunction and atrial reentry tachycardias have also been documented. However, ventricular tachycardia is the main concern in tetralogy of Fallot, with a long-term mortality risk estimated at three to six percent [3].

4. Transposition of the great arteries: The so-called "congenitally corrected" or L-transposition of the major arteries affects 1% of all patients with congenital heart disease; this carries a high risk of arrhythmia. In this condition, the right atrium is connected to the left ventricle, which empties into the pulmonary artery, while the left atrium enters the right ventricle and then the aorta. It has been observed that in instances of spontaneous complete heart block, the incidence of intrinsic abnormalities in the His bundle might reach up to 22%[4], D-transposition of the main arteries, the left ventricle's connection to the pulmonary artery and the right ventricle's link to the aorta, occurs significantly more frequently. This disease was invariably fatal prior to corrective surgery. Arrhythmia risk is minimal while employing modern surgical techniques. The most reported arrhythmias are atrioventric ularblock, ventricular arrhythmias and supra ventricular tachycardia following surgical correction [5].

5. Ebstein’s anomaly: The tricuspid valve leaflets in Ebstein's anomaly, an extremely rare condition, have an aberrant attachment that forces the valve into the right ventricle. People have a higher chance of developing supra ventricular tachycardia, which can happen up to 42% of the time. It may be difficult for patients to tolerate tachycardias if they have severe tricuspid regurgitation and/or atrial septal anomalies. Patients with Ebstein's anomaly are more likely to experience atrial fibrillation and flutter due to their larger right atrium [6].

Inherited arrhythmias syndromes: Syndromes associated with hereditary arrhythmias: Mutations in genes encoding proteins or ion channels can cause disruptions in these channels' normal function, which can result in aberrant rhythms. Some arrhythmias are genetically based. Familial atrial fibrillation, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, and familial Long QT syndrome are a few examples. Affected people and their family members may be able to detect these syndromes with the use of genetic testing [7].

Cardiomyopathies: A class of illnesses known as cardiomyopathies impair the structure and function of the heart muscle. Often, the etiology runs in the family. Certain cardiomyopathies, such as hypertrophic and dilated cardiomyopathies, may make children more prone to arrhythmias. While these conditions can also result from acquired causes including infections or exposure to toxins, hypertrophic cardiomyopathyhas an asymmetrically enlarged heart, which increases the risk for ventricular tachycardia and sudden arrest. Dilatedcardiomyopathy has dilatedpoorlycontractile ventricles increasing the risk for supra ventricular tachycardia,

ventricular tachycardia, Sudden arrest. Fibrofatty replacement of the right ventricular wall myocyte sand patchy areas of fibrosis with progressive right ventricle dysfunction and enlargement increasing the incidence for ventricular tachyarrhythmias with variable response to betablockers and to catheter ablation [8].

Acquired causes of arrhythmia

Medication and Drugs: Prescription drugs for conditions other than heart problems may unintentionally alter the heart's electrical circuitry. For example, certain antiarrhythmic medications contain proarrhythmic side effects that might induce or worsen arrhythmias in people who are vulnerable. Arrhythmias can also occur in children and teenagers who use illegal drugs, such as stimulants or pleasure compounds [9].

[Medications that could make sinus bradycardia greater]:

-Acetylcholinesterase inhibitors, which include neostigmine and donepezil, increase the activity of the parasympathetic nervous system and decrease the reactivity of sinus nodes.

-Beta blockers and some antihypertensive medications like verapamil and diltiazem can cause arrhythmias.

-Anesthetic medications, such as propofol, reduce sympathetic activity.

-Inotrope medications. For example, digoxin, enhances the vagal tone.

-Adenosine levels rise as a result of vasodilator and antiplatelet medications, such as dipyridamole, which directly stimulates the sinoatrial and atrioventricular nodes.

-Antiarrhythmic inhibitors medications of the sinoatrial and atrioventricular nodes, such as Ivabradine, Amiodarone, and Adenosine [10].

[Drug-inducedsupraventriculararrhythmias]:

-Anti-inflammatory**:** diclofenac,Cyclooxygenase-2 inhibition like etoricoxib and corticosteroids(methylprednisolone);may increase the risk for atrial fibrillation (AF) and atrial flutter.

-Bronchodilator**:** β2-adrenergic agonist likealbuterol, terbutaline and metaproterenol, anticholinergic like Ipratropium bromide and phosphodiesterase inhibition liketheophylline,aminophylline all increase the risk for supraventriculararrhythmias.

-Catecholamin: β-adrenergic agonist dopamine, dobutamine and epinephrine

-Antiemetic:Ondanstron

-Opioids: Morphine increase intracellular calcium, activates protein kinase C, open mitochondrial KATP channels

-Antiarrhythmic: adenosine can decrease atrial effective refractoryperiodwavelength and increase pulmonary vein ectopic activity while amiodarone may cause thyrotoxicosis [11].

[Ventricular arrhythmias may result from medications] such as:

-Anticonvulsant:Lacosamide

-Antiplatelet:Dipyridamole

-Digoxin is an inotrope. Ventricular ectopic activity and subsequent depolarizations are caused by inhibition of the sodium-potassium-adenosine triphosphate pump, which raises intracellular calcium concentrations. On the other hand, ventricular ectopic activity is caused by dobutamine due to stimulation of β2-receptors[12].

Infections and inflammation: that disturb the normal electrical conduction pathway, such as myocarditis or endocarditis. Rheumatic fever and other inflammatory diseases can cause the myocardium or heart valves to fibrose and scar, which raises the risk of arrhythmias[13].

-Infectious Diseases and Postoperative Infections: Infections can directly impact the heart's electrical system and cause arrhythmias in children who are severely sick and admitted to the PICU because of severe infections[14].

-Sepsis: Severe systemic illness known as sepsis can cause cardiac dysfunction among other organ dysfunctions. Sepsis-induced inflammation can interfere with the heart's regular electrical conduction and cause arrhythmias[15].

-Bacterial Endocarditis:An infection of the heart valves and inner lining is known as bacterial endocarditis. Arrhythmias may arise from vegetation development and damage to the heart valves, which can obstruct normal electrical transmission. Infectious bacterial endocarditis is more common in patients with central venous lines and congenital heart disease [١5].

-Viral Myocarditis and endocarditis: Myocarditis is an inflammation of the heart muscle, while endocarditis is an infection of the heart's inner lining that is frequently brought on by a virus. Children in the PICU may be affected by viral myocarditis, which can damage heart tissue or induce inflammation that prevents normal electrical conduction. The immune system's reaction to the infection can also damage heart tissue and interfere with its electrical activity[١6].

-Central Line-Associated Bloodstream Infections: Central venous catheters are frequently used to provide fluids and medications to children in the pediatric intensive care unit. Sepsis and bloodstream infections from infections involving these central lines can raise the risk of arrhythmias[١5].

-Coronavirus disease 2019(COVID-19) related myocarditis: Children initially appeared with a mild flu-like condition, which can develop into multi-organ failure, fulminant pneumonia, and Sever Acute Respiratory distress syndrome Coronavirus 2 (SARS-CoV-2),all of which have the potential to be fatal. Severe Acute Respiratory Syndrome Coronavirus 2 primarily targets the respiratory tract, but it can also interact with the cardiovascular system through many mechanisms to cause cardiac injury and increase morbidity[17]. Thus, cardiovascular involvement is emerging as one of the most significant and life-threatening complications of Severe Acute Respiratory Syndrome Coronavirus 2infection in both, previously healthy patients and those with underlying cardiovascular conditions [18].

Heart affection mechanisms in COVID-19: Through the usage of the Angiotensin-converting enzyme 2 receptor, a human cell receptor with a great binding affinity to the virus spike protein (primarily expressed in the heart), coronavirus may directly cause cardiac injury by entering cardiomyocytes [17]. Additionally, the virus can induce cardiac inflammation by causing active CD8+ T cells to move to cardiomyocytes and employ cell-mediated cytotoxicity.An unregulated immune response characterized by a greater neutrophil-lymphocyte ratio, decreased levels of T helper and T suppressor cells, and increased expression of pro-inflammatory cytokines that are released into the circulation may result from SARS-CoV-2 infection. The cardiovascular system is harmed by this cytokine storm syndrome, which can lead to multi-organ failure, multi-system inflammation, direct cardiotoxicity, rapidly developing severe cardiac dysfunction, hemodynamic instability, and vascular leakage with peripheral and pulmonary edema[19].

Myocardial injury, myocytes hypoxia and necrosis result from the disparity between oxygen supply and demand due to a severe acute respiratory distress syndrome and systemic hypotension with myocardial hypo-perfusion in association with increased cardio metabolic demand in the myocardial tissue [20].

In addition to causing endothelial dysfunction and raising blood procoagulant activity, the systemic inflammation brought on by the cytokine storm can also lead to the production of occlusive thrombi over a ruptured coronary plaque and multi-organ microthrombi[17].

Off-label medications for COVID-19 therapy have the potential to cause AV block, QT prolongation with ventricular arrhythmia, severe systemic hypotension, and myocardial dysfunction [21]. Patients who already have heart conditions are more likely to experience morbidity and death. It is also assumed that patients with underlying heart conditions who have low cardiopulmonary reserve are

vulnerable to cardiac injury. Patients with COVID-19 are more likely to experience myocardial ischemia or infarction, left ventricular systolic dysfunction, or ventricular arrhythmia, which could ultimately result in a sudden deterioration [20].

Mechanical ventilation: Another potential source of cardiovascular side effects in critically unwell children is mechanical ventilation. These consequences can include diminished left ventricular elasticity, decreased venous return to the right heart, and decreased cardiac output as a result of these conditions. Mechanical ventilation with high positive end-expiratory pressure might exacerbate the increased right ventricular after-load caused by the lung infection, which can result in right ventricular failure and subsequent myocardial injury. When hypoxemic, inotropes might increase the demand for cardiometabolic processes [٢1]. Ventilated critically ill children commonly receive sedative and analgesic drugs (Intravenous opioids such as morphine and fentanyl) and benzodiazepines (suchasmidazolam) to easetheirmentalburden, anxiety and pain, induced by frightening or painful interventions and environmental factors in the pediatric intensive care unit. Tolerance and physiological dependence may develop during long-term administration. Discontinuation of medication in dependent patients leads to symptoms of withdrawal, autonomic phenomena related to cardiovascular system such as increased heart rate, and blood pressure in relation to the normal values for the child's ageand disease[٢2].

Autonomic Nervous System Dysfunction: Arrhythmias may result from dysregulation of the autonomic nerve system, which regulates heart rate and rhythm. A number of illnesses, including neurocardiogenic syncope and postural orthostatic tachycardia syndrome, can impair autonomic function and cause irregular cardiac rhythms[٢3].

Electrolyte disturbance*:* Abnormal amounts of potassium, calcium, or magnesium, for example, can upset the normal electrical activity of the heart and cause disturbances in electrolyte levels, which can lead to arrhythmias in children. For instance, abnormalities such as hypokalemia, hyperkalemia, and hypocalcemia might affect the heart's capacity to produce and transmit electrical signals. Arrhythmia risk can be raised by conditions that disturb electrolyte balance, such as renal failure, electrolyte imbalances, or certain drugs[٢4].

Metabolic Disorders: Heart rate and rhythm regulation is greatly influenced by the thyroid gland, which can be negatively impacted by disorders such as hyperthyroidism or hypothyroidism. Arrhythmia risk can also be increased by other metabolic problems that impact cardiac electrical conduction, such as diseases involving the storage of glycogen or disorders related to the metabolism of fatty acids[٢5].

Systemic Illnesses: Arrhythmias in children can be predisposed by a number of systemic disorders. For example, rheumatoid arthritis and systemic lupus erythematosus (SLE) are examples of autoimmune disorders. A systemic illness is a medical disorder that affects more than one organ or system in the body. It can produce inflammation and damage to the heart muscle, which can interfere with the heart's normal electrical conduction or alter the heart's regular conduction pathways[٢6].

***Systemic Lupus Erythematosus: A** chronic autoimmune illness that affects the heart can cause endocarditis, pericarditis, or myocarditis. AmongSystemic Lupus Erythematosus patients, sinus tachycardia (15–50%), atrial ectopic beats, and atrial fibrillation (AF) are the most common heart rhythm abnormalities[27].

***Rheumatoid Arthritis:** primarily a joint disease can also affect the cardiovascular system, including the heart. Inflammation associated with rheumatoid arthritis can lead to pericarditis. The most frequent arrhythmia among RA patients is AF, especially in young females with sedimentationr ates>60mm/hor

anti-tumor necrosis factor-α antibodies [28].

***Diabetes mellitus:** Arrhythmias such as atrial fibrillation (AF) are among the most well-documented in type 1 diabetes mellitus patients, particularly in young females. Males and females with DM1 have a 9–13% and 26–50% respectively increased risk of AF, respectively, and DM2 has been linked to QT interval prolongation[29].

***Graves' Disease**: hyperthyroidism brought on by thyrotropin receptor antibodies in the blood. AF is the most prevalent heart rhythm abnormality in Graves' Disease patients. Additionally, one case of ventricular arrhythmias in Graves' Disease patients has been reported [30].

***Celiac Disease:**A lifelong gluten sensitivity that is autosomal dominant and genetically predisposed, celiac disease typically affects the small intestine but may also have an impact on other organ systems [31]. A reported prevalence of atrial fibrillation, the most prevalent cardiac arrhythmia among celiac disease patients, is 30% greater than in the general population. There has also been evidence of an increased risk of ventricular arrhythmias, which include recurrent and multiform premature ventricular contraction. [٣2].

Otherriskfactors:

1-Obesity*:* The risk of arrhythmias has been linked to childhood obesity. Being overweight increases the workload on the heart and interferes with normal cardiac function, which can result in arrhythmias. Moreover, metabolic irregularities and sleep disturbances are common risk factors associated with obesity, which further contributes to the development of arrhythmias. It was noted that children with obesity had higher blood pressure, heart/vessel widths, and wall thicknesses in addition to higher body weight and body mass index[33].

2-Disorders of Sleep:A sleep apnea, can raise a child's risk of arrhythmias. The hallmark of sleep apnea is irregular breathing during the night, which causes sporadic reductions in oxygen saturation. These periods of oxygen deprivation, especially in kids with underlying cardiac issues, can cause arrhythmias or exacerbate pre-existing ones[34].

3-Exercise-Induced Arrhythmias: Children, especially those with underlying cardiac problems, may experience arrhythmias when engaging in intense physical activity or exercise. Arrhythmogenic right ventricular cardiomyopathy, hypertrophic cardiom= yopathy, and coronary artery abnormalities are among the diseases that might result in exercise-induced arrhythmias. It's critical that kids with established cardiac issues receive the proper evaluation and guidance on any suggested or restricted activity regimens **[**35].

4- Psychological Factors: Children's heart rhythm can be affected by psychological factors. An elevated sympathetic response brought on by stress, worry, and emotional disturbance can cause arrhythmias to develop or worsen already existing ones. Arrhythmia development may be influenced by illnesses like anxiety disorders, panic attacks, or post-traumatic stress disorder [36].

5-Environmental conditions: There is a chance that children may develop arrhythmias if they are exposed to certain environmental conditions. For instance, exposure to chemicals or poisons like lead or specific drugs might interfere with the heart's natural electrical conduction and function. Certain acquired arrhythmias may be influenced by environmental variables, which may also aggravate pre-existing problems [37].

6-Nutritional elements: Nutritional imbalances or inadequacies can impact the electrical system of the heart, causing arrhythmias. For example, deficits in some vitamins or minerals, such as potassium, magnesium, or thiamine, might interfere with the heart's proper electrical conduction. Children who have poor eating habits or improper nutrition may be more susceptible to arrhythmias[38].

7- Chemotherapy or radiation: Children who have received specific types of chemotherapy or radiation therapy for the

treatment of malignancy may be more susceptible to arrhythmias. Arrhythmias may result from these treatments' harm to the heart's tissue or interference with the electrical system[39].

CONCLUSION

Cardiac dysrhythmias or abnormal heart rhythms are uncommon in pediatrics but may be caused by structural abnormalities. infection and inflammation, structural lesions, metabolic abnormalities, drugs, systemic diseases and intrinsic conduction abnormalities.it is critical to identify these etiologies and risk factors for early prediction and management strategies.

CONFLICTS OF INTEREST

No conflicts of interest

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