REVIEW ARTICLE

Cardiac Murmurs in Children: A Challenge For The Primary Care Physician

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Abstract: Congenital heart disease is present in almost 1% of live births and despite current progress in prenatal screening a significant percentage has delayed diagnosis or remain undiagnosed. A cardiac murmur may be the first or unique clinical sign of congenital heart disease in childhood, however, less than 1% of auscultated murmurs are of an organic cause. Distinguishing between an innocent and a pathologic murmur can be challenging and the experience of the examiner is crucial for identifying the distinctive properties of an innocent murmur. Timely diagnosis of underlying cardiovascular pathology is of great significance so that prompt management is provided and morbidity or mortality are restricted. Of similar importance is the avoidance of unnecessary anxiety for the parents and unreasonable referrals to Paediatric Cardiologists. Indications for referral include a medical history suggestive of a cardiac abnormality, such as the presence of relevant symptoms, the identification of abnormal findings on clinical examination, auscultatory findings suggestive of an organic murmur, and very young patient age. ECG and a chest X-ray are not usually part of the diagnostic approach of a child with a cardiac murmur, as they do not increase the success rate of diagnosing heart disease, as compared to a detailed medical history accompanied by a thorough physical examination.

In conclusion, the recognition of suspicious distinctive features of cardiac murmurs is crucial and requires skills based on sufficient training and experience.

Keywords: Cardiac murmurs, congenital heart disease, innocent murmurs, organic murmurs, transthoracic echocardiography, auscultatory, Cardiovascular malformations.

1. INTRODUCTION

Cardiovascular malformations occur in 0.4-1.4% of live births and approximately one fourth represent severe defects that will require expert cardiologic care, surgery or transcatheter intervention, particularly in infancy [1]. Delayed or unsuccessful diagnosis has been reported in 20-30% of cases [2, 3]. In the current era, when prenatal diagnosis of Congenital Heart Disease (CHD) is widely available and is associated with progressively increasing success rates, delayed identification is still noted in more than 10% of severe CHD cases [4].

Undiagnosed CHD is accompanied by severe risk for mortality, morbidity and handicap, most of which are potentially preventable. Timely recognition of significant CHD is crucial in order to provide prompt management and avoid irreversible complications [5]. The main advantage of early diagnosis is that the evaluation of infants will take place whilst they are still haemodynamically stable.

A cardiac murmur may be the first clinical sign of significant cardiac disease [6] and represents the most common condition leading to paediatric cardiology consultation [7]. Furthermore, a cardiac murmur may be the sole clinical sign in children with CHD or it may be accompanied by symptoms, such as feeding difficulties, cyanosis, chest pain, fatigue, palpitations, near-syncope or syncope and failure to thrive.

Cardiac murmurs are audible turbulent sound waves in the range of 20 to 20,000 cycles/second, heard with a stethoscope and emanating from the heart and vascular system [8]. Whereas normal cardiac sounds are produced by the closure of heart valves, murmurs are produced as additional, unexpected sounds by turbulence or disturbance in the flow of blood while it circulates through the heart or at the origin of the major blood vessels. About 50% of children have a cardiac murmur at some time in their life. However, less than 1% have CHD [9]. It has been shown that 60% of the murmurs referred for cardiology evaluation were functional murmurs [10]. Distinguishing murmurs caused by an underlying heart defect from murmurs caused by the flow of blood within a structurally normal heart can be challenging for the primary care physician.
Children seen in the Emergency Department are often found to have a heart murmur, because they suffer from conditions associated with hyperdynamic circulation (fever, anaemia or dehydration) and are usually in an extreme anxiety state; however, the majority of these murmurs are benign, physiological or flow murmurs. Innocent murmurs are produced by the normal flow of blood through the heart and great vessels. These children are usually evaluated by a Paediatric trainee who examines the child for the first time and is relatively inexperienced in cardiovascular examination. It has been observed that the ability of students and trainees to evaluate cardiac sounds and murmurs gets diminished over time. On the contrary, physical examination by an experienced clinician is sufficient for distinguishing innocent from pathologic murmurs [8, 11]. In addition, physical examination performed by a Paediatric Cardiologist has a sensitivity of 96% and a specificity of 95%, according to Smythe et al., in distinguishing an innocent from a pathologic heart murmur [12].

Parents who are informed about the detection of a cardiac murmur by the paediatric trainee at the Emergency Department usually assume that their child suffers from severe disease [6]. Therefore, it is crucial that the physician acquires the skills to distinguish an innocent from an organic murmur so that the family does not suffer from unreasonable anxiety and unnecessary referrals are avoided [13]. It is of note that the availability of new technologies, the inefficient training on clinical examination, and the fear of legal consequences of medical omissions, contribute to reduced self-confidence and the increasing number of specialist referral.

2. CHARACTERISTICS OF A CARDIAC MURMUR

Important properties of a cardiac murmur are: timing in the cardiac cycle, location, quality, intensity, shape, radiation and pitch, and the presence or absence of a click. There are four main “auscultation points” of the heart on the chest, which determine the possible origin or the aetiology of a murmur. The right upper sternal border represents the aortic valve area, the left upper sternal border is the pulmonic valve area, the left lower sternal border is the tricuspid valve and the apex represents the mitral valve area. A murmur may radiate to more than one auscultation sites. The shape of a murmur describes the change of intensity throughout the cardiac cycle. Murmurs may be crescendo, decrescendo, crescendo-decrescendo or uniform. The intensity of a murmur is determined by the volume and the velocity of blood flow, as well as the distance between the stethoscope and the lesion. The pressure gradient across a lesion determines if a murmur is high pitched or low pitched. The intensity of a systolic heart murmur is graded from I to VI. Grade I murmurs are barely audible; grade II murmurs are soft but can be heard immediately; grade III murmurs can be heard easily and are moderately loud; grade IV murmurs are heard easily over a wide area and have a palpable thrill; grade V murmurs are loud and also have a precordial thrill; and grade VI murmurs are loud enough to listen with the stethoscope raised off the chest.

Based on their clinical importance and the etiology, cardiac murmurs are divided as innocent or functional and organic or pathologic. An innocent murmur is characterised by the following distinctive features (the seven S’s):

It is Systolic, Small (nonradiating to the precordium), Soft (mild), Short (not holosystolic), Single (with no other pathological auscultatory findings), Sweet (not harsh) and Sensitive (it changes with altering of the position/declines at a standing position) [14].

Whereas innocent murmurs are of short duration, crescendo-decrescendo type, have low intensity, are poorly transmitted in the precordium, occur in early systole and are best heard when the child is supine, an organic murmur is usually loud (≥3/6 intensity, and thus may be associated with a thrill), diastolic, holosystolic, harsh, occur late in systole, increase in intensity in the standing position and may be associated with an abnormal S2 or a click [15, 16]. Nearly all innocent murmurs auscultated in childhood are classified in one of the following distinguishable types: vibratory Still’s murmur, the physiological pulmonary flow murmur, the aortic flow murmur, the supraclavicular or arterial bruit, the venous hum and peripheral pulmonary artery stenosis of infancy (Figs. 1 and 2). Apart from the venous hum, which is a continuous murmur, the rest of the innocent murmurs are all systolic.

![Image](image_url)

Fig. (1). Innocent murmurs in children.
Brachiocephalic murmur or carotid bruit, venous hum, aortic flow murmur, pulmonary flow murmur, still’s vibratory murmur.
2.1. Vibratory Still’s Murmur

It is a musical, vibratory, low frequency murmur, confined to early systole, generally grade 2, auscultated maximally at the lower left sternal edge extending to the apex. It is usually noted after infancy and its peak incidence is at the age of 3 to 7 years. It is generally loudest in the supine position, but changes in character and diminishes in intensity with upright positioning. Valsalva maneuver also reduces the intensity of the murmur.

2.2. Pulmonary Flow Murmur (Physiological Pulmonary Systolic Ejection Murmur)

It is an early systolic crescendo-decrescendo, ejection murmur heard at the second and third intercostal space at the left sternal border. It is of low intensity (grade 2-3), heard best with the diaphragm and transmits to the pulmonary area. It is louder in the supine position and during inspiration, fever or exercise. This murmur must be differentiated from the murmur of an atrial septal defect or pulmonary stenosis. The murmur of an atrial septal defect is attributable to the increased flow through the pulmonary outflow tract and may be indistinguishable from the innocent pulmonary flow murmur. Patients with an atrial septal defect are usually asymptomatic and the murmur may be classified as “innocent”. However, a hyperdynamic right ventricular impulse, a mid-diastolic rumble and most importantly a fixed wide splitting of the pulmonary component of S2 may enable clinical diagnosis. The abnormalities due to an atrial septal defect on physical examination and ECG may be too subtle to detect. Although it is well known that variations can occur in the clinical signs and symptoms typical of an atrial septal defect, dependence on classical physical and or ECG findings may result in the underdiagnosis of a significant number of patients [17].

2.3. Supraclavicular/Brachiocephalic Systolic Murmur/ Carotid Bruit

This low-pitched crescendo-decrescendo systolic murmur is audible maximally above the clavicles and radiates to the neck, but may present to a lesser degree on the superior chest. The murmur is present with the patient both supine and sitting, but the murmur diminishes or disappears altogether by hyperextension of the shoulders.

2.4. Aortic Flow Murmur

It is an ejection systolic murmur maximally audible in the aortic area. It may become apparent under circumstances associated with hyperdynamic circulation, such as extreme anxiety, anemia, hyperthyroidism, dehydration or fever. It is detected in older children, adults and athletes. It is often difficult to be certain of the cause of this murmur, thus referral and further investigations may be indicated.

2.5. Venous Hum

It is a high frequency, soft, continuous murmur, noted mostly between 3 and 8 years of age. It is most audible at the low anterior neck just lateral to the sternocleidomastoid muscle, but often extends to the infraclavicular area. It is most prominent on the right than on the left, often resolves or changes in character when the patient lies down and may be eliminated or diminished by gentle compression of the ipsilateral internal jugular vein or by turning the patient’s head towards the side of the murmur. A venous hum is common and not pathological. This murmur should be differentiated from a patent arterial duct. The patent arterial duct murmur is not diminished in supine position and cannot be obliterated by compression of the internal jugular vein.

2.6. Mammary Artery Soufflé

It occurs most frequently late in pregnancy and in lactating women, but may rarely occur in adolescence. It arises in systole, may extend into diastole and is audible on the anterior chest wall over the breast.

2.7. Physiological Peripheral Pulmonic Stenosis

It is a short midsystolic ejection murmur of medium intensity, audible in the pulmonic area and the axillae. During fetal life, most of the blood flow from the right ventricle passes through the arterial duct. Only about 20% of the total cardiac output enters the lungs via the branch pulmonary arteries, and hence, their diameters are relatively small compared to that of the pulmonary trunk. After birth, the arterial duct closes and all the blood from the right ventricle should
pass through these relatively narrow branch pulmonary arteries producing a murmur, which becomes audible in the late neonatal period. This transient innocent murmur is a moderately pitched early- to mid-systolic ejection murmur at the left second intercostal space with radiation at the back, which is audible between the clavicles. Infants with this transient heart murmur have mild underdevelopment of the pulmonary artery branches with significantly smaller diameters and faster flow velocities. After a few months, these smaller diameters become normal and the heart murmur disappears [18]. The cause of this transient stenosis of the branch pulmonary arteries can be explained by the changes from fetal to neonatal circulation [8, 19] (Fig. 3).

2.8. Non-physiological Peripheral Pulmonic Stenosis

In most cases, peripheral pulmonary artery stenosis is an innocent finding. However, non-physiological (i.e. anatomic) stenosis of the main or peripheral pulmonary artery branches is uncommon, but a well described entity. It can be associated with other congenital heart defects, such as Tetralogy of Fallot, and in the isolated form with clinical syndromes, such as Alagille, Williams, cutis laxa, Ehlers Danlos, Noonan, and Silver Russell syndrome. Thus, it is prudent to repeat echocardiography in all neonates with “physiological” peripheral pulmonary stenosis to verify normalisation of pulmonary artery flow and diameter and review the infant’s phenotype, which may sometimes be atypical for the presence of a syndrome in the early neonatal period [19-21].

Once it is determined whether the murmur is systolic or diastolic, the timing of the murmur within systole or diastole also becomes important when characterising a murmur. Systolic murmurs can be classified as early systolic (protosystolic), midsystolic (ejection systolic), holosystolic (pansystolic), or late systolic. A midsystolic murmur begins just after the first heart sound (S1) and terminates just before the second heart sound (S2), so S1 and S2 will be distinctly audible. Conversely, a holosystolic murmur begins with or immediately after S1 and extends up S2, making them difficult, if not impossible, to hear. A mid-late systolic systolic murmur begins significantly after S1 and may or may not extend up to S2.

3. DIAGNOSTIC APPROACH OF A CARDIAC MURMUR

The diagnostic approach of children with a cardiac murmur includes: a detailed prenatal and postnatal medical history, a complete physical examination, and, in specific cases, a cardiac ultrasound. Chest X-ray and ECG do not usually improve the sensitivity or specificity of detecting structural heart lesions, in the basis of a proper history and physical examination. These investigations serve to identify the severity of already suspected disorders. In the case of uncertainty about the innocence of a murmur, after a proper medical history has been obtained and a careful clinical examination has been performed, the child should be referred to a Paediatric Cardiologist. Parental anxiety and the age of the child should also be taken into consideration while making the decision about referring to a Paediatric Cardiologist. Neonates require a prompt referral, whereas older, asymptomatic children can safely wait for a scheduled assessment.

A cardiac ultrasound is not a first-line diagnostic test. It is not part of the routine screening of children with a murmur, knowing that 60% of the referred individuals have a functional murmur and the cooperation with the patient is difficult, particularly of young age. However, it should be ordered in neonates with a cardiac murmur, even when no symptoms are present. A low threshold for referral is recommended, because the incidence of structural heart malformations is higher in this population [22-25].

When performed by adult Cardiologist laboratories a cardiac ultrasound may be of poor quality or non-diagnostic. Indeed, paediatric echocardiograms performed in adult cardiology practices were unnecessary in 30% of patients, were of inadequate quality in 32% and resulted in an erroneous impression of the nature or presence of pathology in 32% of children [26].
4. PHYSICAL EXAMINATION

The patient’s vital signs should be assessed according to age-established reference values. Tachycardia, tachypnoea, hypoxia or arrhythmia may indicate structural heart disease or congestive heart failure. Unusually bounding pulses or a hyperdynamic precordium may indicate the presence of a patent arterial duct.

The brachial artery represents the best site to assess pulse rate, volume and character, as it has the same distance from the heart as the femoral artery. Hence, simultaneous palpation of the right brachial artery and the femoral artery to check for pulse volume difference and delay represents the best way to check for possible aortic coarctation. Left brachial artery should not be used for peripheral pulse evaluation, as in some patients left subclavian artery may originate distally to the coarctation site [27]. Delayed and weak or absent femoral pulses compared to brachial pulses or a discrepancy in blood pressure of more than 20 mmHg, indicate severe coarctation of the aorta.

Capillary refill time should be less than three seconds. A precordial bulge or a hyperdynamic heart impulse may suggest ventricular hypertrophy. Palpating a thrill on the precordium is indicative of an organic murmur. When palpating the chest, the left ventricular impulse, which normally is at left mid-clavicular line in the fourth or fifth intercostal space, should always be checked.

The heart should be auscultated over the tricuspid, pulmonary, mitral, and aortic areas with the bell and diaphragm of the stethoscope while the patient is supine, sitting, and standing [8].

The clinical evaluation of the second heart sound is very important in Paediatric patients and has been called the "key to auscultation of the heart". It includes an assessment of splitting and a determination of the relative intensities of the aortic (A2) and pulmonary (P2) components. Normally aortic closure occurs prior to the pulmonic closure, and thus the interval between the two components of S2 (splitting) widens on inspiration and narrows on expiration. With quiet respiration, A2 will normally precede P2 by 0.02 to 0.08 seconds [28].

Thus, the finding of audible expiratory splitting in both the recumbent and upright positions is a very sensitive screening test for heart disease, even in the absence of a murmur [17]. A single second sound, however, is usually due to inability to auscultate a relatively soft pulmonic component. The second sound may also be single in a variety of congenital heart defects and other pathologic conditions, such as pulmonary hypertension [29].

Dysmorphic features should be inspected for and careful examination of the cardiovascular, respiratory and gastrointestinal systems should also be performed. Abnormal bruits or heart sounds, irregular respiratory pattern or venous distension should be searched for. Added respiratory sounds, such as crackles or wheezing, liver enlargement or signs of ascites should be evaluated as possible signs of congestive heart failure. The abdominal examination should include careful assessment of the liver position and distance of the edge relative to the costal margin.

After obtaining a detailed personal and family medical history and conducting a thorough clinical examination, specific findings may raise concerns about the severity of a cardiac murmur.

4.1. Red Flags from Personal History
- Feeding difficulties.
- Failure to thrive.
- Respiratory symptoms or cyanosis, frequent lower respiratory infections (associated with left to right shunting).
- Precordial pain.
- Syncope.
- Reduced exercise capacity.
- In utero exposure to infections, medications or alcohol.

For example, maternal rubella infection is associated with a patent arterial duct and peripheral pulmonary stenosis. Selective serotonin reuptake inhibitors are associated with ventricular septal defects and a bicuspid aortic valve. Lithium exposure may be associated with Ebstein anomaly of the tricuspid valve. Valproate is associated with coarctation of the aorta and hypoplastic left heart syndrome. Fetal alcohol syndrome is associated with atrial and ventricular septal defects, as well as tetralogy of Fallot.

- Kawasaki disease is associated with coronary artery aneurysm and stenosis.
- Acute rheumatic fever is associated with rheumatic heart disease.
- Preterm delivery is associated with persistent patency of the arterial duct.
- Turner syndrome is associated with increased risk of coarctation of the aorta, aortic valve stenosis, left ventricular hypertrophy and hypertension.
- Trisomy 21 is associated with an increased risk of cardiovascular defects. 40% of patients with trisomy 21 have CHD and half of the cases involve an atrioventricular septal defect. Therefore, all neonates with trisomy 21 warrant a cardiac ultrasound in the neonatal period [30].

4.2. Red Flags from Family History
- Sudden cardiac death.
- Marfan syndrome is associated with mitral valve prolapse, aortic root dilation and aortic insufficiency.
- Congenital heart disease in a first degree relative. For example, having a sibling with a ventricular septal defect results in a recurrence risk of 6% [31].
- Maternal diabetes mellitus is associated with transient hypertrophic cardiomyopathy, tetralogy of Fallot, truncus arteriosus and double-outlet right ventricle.

4.3. Red Flags From Physical Examination
- Syndromic neonate-infant.
- Failure to thrive.
• Peripheral oedema.
• Hyperdynamic procardium.
• Delayed – weak femoral pulses.
• Abnormal S2.
• Intense (≥3/6) cardiac murmur.
• Harsh quality murmur.
• Systolic click.
• Diastolic or holosystolic murmur.
• Increased intensity in standing position.
• Ascites.
• Hepatomegaly [32].

5. CORRELATION BETWEEN CARDIAC POSITION AND THE POSITION OF ABDOMINAL ORGANS

Levocardia and normal position of abdominal organs are associated with <1% incidence of CHD. Total organ reversal, which represents a mirror image appearance compared to normal subjects, is associated with CHD in 3-5% of the cases. Almost 100% of the cases of reversed abdominal organs and levocardia have CHD, which is usually severe and can be associated with heterotaxia and asplenia syndrome (which may be accompanied by immunodeficiency) or polysplenia [33].

Indications for referral:

a. Presence of additional findings on physical examination (apart from the murmur).

b. Presence of characteristic auscultatory features of an organic murmur (Fig. 4).

c. Presence of symptoms.

d. Positive history of suspicious features for structural heart disease.

e. Neonatal period.

The incidence of CHD is elevated in neonates/infants [34]. Paediatric cardiologists can detect asymptomatic CHD with greater accuracy in neonates and, therefore, can guide Paediatricians towards investigation and management of cases with a suspicious murmur [35]. The sensitivity of the detection of a pathological murmur has been described between 80.5-94.9% and the specificity between 25-92% [36].

Investigation of neonates with a murmur may include pulse oxymetry after the first 24 hours of life. Clinical investigation of asymptomatic neonates with a murmur has a sensitivity of 46% for the detection of CHD with clinical examination alone and increases to 77% when pulse oxymetry is added. If the clinical estimation of the murmur is uncertain, the neonate has to be referred to a Paediatric Cardiology Specialist. In any case, referral to a Specialist confirms the diagnosis and reduces the family’s anxiety [37, 38].

CONCLUSION

The identification of a pathological murmur, which is associated with heart disease, is crucial and requires significant skills in clinical examination. The findings from a detailed medical history and a properly and thoroughly conducted clinical examination can identify children at increased risk for heart disease and will determine which child with a cardiac murmur should be referred to a Paediatric Cardiology Specialist.

Attention should be paid to suspicious clinical signs or symptoms. CHD is more likely when the murmur is holosystolic, diastolic, ≥III/VI in intensity, is accompanied by a sys-
tolic click, is harsh and increases in standing position (Fig. 5).

In neonates and young infants, the threshold for referral should be low because of the high prevalence of CHD [32, 39]. The cooperation with the family and the level of their anxiety should also be taken into consideration when the decision for referral has to be made. Increased education of physicians can improve their clinical skills and certainty and will help to minimize parental anxiety and unnecessary laboratory investigations.

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REFERENCES