Children with Myocarditis: Clinical Profile and Electrocardiographic Changes and Their Prognostic Significance: A Prospective Observational Study

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Authors’ contributions

This work was carried out in collaboration between both authors. Author JRG designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Both authors managed the analyses of the study and managed the literature searches. Both authors read and approved the final manuscript.

ABSTRACT

Aims and Objective: To study the clinical profile and electrocardiographic changes in children with myocarditis and their prognostic significance.

Methods: 223 children presented with signs and symptoms of myocarditis from June 2016 to May 2017. Amongst them, 21 children with congenital heart disease or rheumatic heart disease and 166 children with negative cardiac markers were excluded. The remaining 36 patients with myocarditis and elevated levels of both SGOT and CKMB were studied. The patient outcome was recorded as expired or discharged. Data were analyzed using the chi-square test.

Results: Majority (13; 36%) were infants. Post infancy, there was a uniform age distribution of cases. Myocarditis was commonly seen in association with culture-negative (probably viral) pneumonia, and diphtheria. Bradycardia and A-V block, although seen less frequently, were having a significant association with mortality. Congestive cardiac failure (28.6%) and cardiomegaly (25.0%) were not significantly associated with mortality. ECG changes like Sinus tachycardia and T wave inversion (most common) and ST elevation, Q waves and low amplitude (less common) were insignificantly associated with mortality.

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Conclusion: In children, myocarditis should be suspected especially in infants with unexplained breathlessness or fatigue, arrhythmia, or signs of acute cardiac decompensation. It was seen more with bacterial-culture-negative (viral) pneumonia and diphtheria. Continuous ECG monitoring and chest X-ray should be done. Congestive cardiac failure and cardiomegaly, though observed in a quarter of patients were not significantly associated with mortality. Bradycardia and A-V block have a poor prognosis and cardiac pacing should be considered. Echocardiography should be available in-house.

Keywords: Myocarditis; electrocardiograph; cardiomegaly; congestive cardiac failure; children; pneumonia; AV block.

Abbreviations

A-V block: Atrio-Ventricular block;
CCF: Congestive Cardiac Failure;
CHD: Congenital Heart Disease;
CK: Creatine Kinase;
CNP: Culture Negative Pneumonia;
CPP: Culture Positive Pneumonia;
ECG: Electrocardiograph;
RHD: Rheumatic Heart Disease;
SGOT: Serum Glutamic Oxaloacetic Transaminase.

1. Introduction

Although clinical myocarditis is rare in children, subclinical myocarditis is quite common and is responsible for up to 12% of sudden cardiac deaths in children. Myocarditis should be suspected in any child with unexplained breathlessness or fatigue, arrhythmia, or signs of acute cardiac decompensation. Common etiological factors for myocarditis include viruses like coxsackievirus B, enterovirus, influenza, rubella, and adenovirus; bacteria like streptococcus, C. diphtheriae; parasites like Trypanosoma cruzi; drugs like anthracycline; various toxins like ethanol, arsenic, copper and autoimmune conditions like SLE. Diagnostic evaluation includes elevation of cardiac markers such as SGOT (elevated in 85%) and CK MB (elevated in 73%). The most common associated X-Ray finding is cardiomegaly.

Changes in ECG are found in 93-100% cases and include sinus tachycardia, sinus bradycardia, atrioventricular block, T wave inversion, ST-segment elevation, and pathological Q wave. Other diagnostic modalities include echocardiography and cardiac MRI which can clearly define the anatomical and physiological alteration in cardiac status. Prognosis of myocarditis is variable, the majority recover completely without any ill effects.

Objectives: To study the electrocardiographic changes and short term outcomes in children with myocarditis.

2. Materials and Methods

An observational prospective study was conducted at Pediatric wards of Sir T G Hospital, Bhavnagar, Gujarat, India between June 2016 and May 2017. The study was approved by the Institutional Review Board, Human Ethics Committee. Term neonates, infants, and children below 12 years of age presenting with clinical suspicion of myocarditis and with elevated levels of both SGOT and CKMB were included in the study, after obtaining written informed consent. Those with congenital or rheumatic heart disease (CHD/ RHD) were excluded from the study. Detailed clinical evaluation, complete blood count, renal and liver function test, blood culture, SGOT, CKMB, urine examination, ECG, X-ray chest, and other specific tests as per need were carried out in all children. Patients were monitored for the development of congestive cardiac failure (CCF). The final outcome was recorded as expired or discharged.

For categorical data, the chi-square test was used and a p-value of <0.05 was considered significant.

A total of 223 patients with clinical signs and symptoms of acute myocarditis were evaluated during the study period. Twenty-one patients with CHD/RHD were excluded. Of the remaining 202 children, 166 having negative cardiac markers were also excluded. Remaining 36 patients with myocarditis and elevated levels of both SGOT and CKMB were enrolled (Fig. 1).
Following case definitions were used -

**Myocarditis:** Myocarditis was diagnosed in the clinical context of possible myocardial injury with raised biomarkers of cardiac injury.

**Signs and Symptoms suggestive of myocarditis:** Patients with myocarditis may present with chest discomfort, fever, palpitations, easy fatigability, or syncope/near syncope. On examination, respiratory distress, tachycardia, hypotension, gallop rhythm, and cardiac murmur are commonly seen. Associated findings may include a rash or systemic involvement such as hepatitis or aseptic meningitis. In patients with the associated pericardial disease, an audible friction rub may be noted. Chest pain from myocarditis may resemble typical angina.

**Congestive Cardiac Failure:** Patients of myocarditis presenting with tender Hepatomegaly, positive heato-jugular reflux, peripheral edema, and pulmonary findings such as wheeze or rales.

**Cardiomegaly:** Cardiomegaly was diagnosed with cardiomegaly, positive heato-jugular reflux, peripheral edema, and pulmonary findings such as wheeze or rales.

**Positive Serology:** SGOT > 40U/L and CK-MB 25IU/L

**Diphtheria:** Patients presenting with upper respiratory tract illness with a sore throat, fever, an adherent, grey membrane covering the posterior aspect of the pharynx and throat swab culture positive for Corynebacterium.

**Dengue:** Patients with fever along with two of the following symptoms: nausea and vomiting, rash, generalized pains, low white blood cell count, positive tourniquet test, in someone who lives in an endemic area. All cases were confirmed with the detection of NS1 antigen during the febrile
phase or the presence of IgM to NS1 after subsiding of fever.

**Bronchiolitis:** Patients less than two years of age with acute cough, wheeze, poor feeding, lethargy, and shortness of breath, with findings of tachypnea, respiratory distress and rhonchi, and chest x-ray to exclude pneumonia.

**Blood Culture Positive Pneumonia:** Patients with either a cough or difficulty in breathing with high respiratory rate, respiratory distress, or decreased level of consciousness and chest x-ray showing airspace opacities or lobar consolidation with a positive bacterial blood culture.

**Blood Culture Negative Pneumonia:** Patients diagnosed with pneumonia with a negative blood culture. This group includes patients with Viral Pneumonia, Atypical Pneumonia, and Bacterial Pneumonia with false-negative blood cultures.

### 3. OBSERVATION AND RESULTS

Fig. 1 depicts the patients who met the inclusion criteria and those who were excluded from the study. 36 patients of myocarditis were selected and their ECG and chest x-ray were obtained. There were 21 (58.3%) males and 15 (42.7%) females out of which three (14.3%) males and two (13.3%) females died. 13 (36.1%) cases were seen in infants; and there was a uniform age distribution of cases thereafter, post infancy. Two (15.3%) infants expired, while three (13.0%) children expired.

Table 1 depicts the distribution of myocarditis cases in different conditions and the associated deaths. Out of 202 patients screened, the most common factor for the development of acute myocarditis was culture-negative pneumonia (CNP), followed by diphtheria, dengue, bacterial (culture positive) pneumonia (CPP), and bronchiolitis. The highest number of deaths was seen in CNP, followed by diphtheria. There was no death in myocarditis from dengue, CPP, and bronchiolitis.

Table 2 depicts the incidence of ECG changes (31), CCF (7), cardiomegaly (12), and associated death (5). The most common ECG abnormalities were - sinus tachycardia, T wave inversion, sinus bradycardia, low amplitude QRS complexes, ST inversion, A-V blocks, and Q wave (Fig. 2). CCF and cardiomegaly were associated with death *non-significantly*. All five deaths occurred in children with ECG abnormality. The presence of sinus bradycardia and A-V block was a *significant* risk factor for death; ST elevation,

### Table 1. Distribution of myocarditis and deaths in different conditions

<table>
<thead>
<tr>
<th>Disease</th>
<th>Total</th>
<th>Myocarditis n(%)</th>
<th>Deaths n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>27</td>
<td>6 (22.0)</td>
<td>1/6 (16.7)</td>
</tr>
<tr>
<td>Culture Negative Pneumonia</td>
<td>60</td>
<td>21 (35.0)</td>
<td>4/21 (19.1)</td>
</tr>
<tr>
<td>Culture Positive Pneumonia*</td>
<td>23</td>
<td>3 (13.0)</td>
<td>0</td>
</tr>
<tr>
<td>Bronchiolitis</td>
<td>70</td>
<td>2 (2.8)</td>
<td>0</td>
</tr>
<tr>
<td>Dengue</td>
<td>22</td>
<td>4 (18.2)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>202</td>
<td>36 (17.8)</td>
<td>5/36 (13.9)</td>
</tr>
</tbody>
</table>

*2 Streptococcal pyogenes; 1 Streptococcus agalactiae

### Table 2. Incidence of ECG changes, CCF and Cardiomegaly

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>Deaths n(%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachycardia</td>
<td>25</td>
<td>2 (8.0)</td>
<td>0.1235</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>6</td>
<td>3 (50.0)</td>
<td>0.0051*</td>
</tr>
<tr>
<td>A-V Block</td>
<td>5</td>
<td>3 (60.0)</td>
<td>0.0013*</td>
</tr>
<tr>
<td>Low Amplitude</td>
<td>6</td>
<td>1 (16.7)</td>
<td>0.8293</td>
</tr>
<tr>
<td>S-T Elevation</td>
<td>6</td>
<td>2 (33.3)</td>
<td>0.1314</td>
</tr>
<tr>
<td>T wave inversion</td>
<td>12</td>
<td>2 (16.7)</td>
<td>0.7333</td>
</tr>
<tr>
<td>Q wave</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total ECG changes</td>
<td>31</td>
<td>5 (16.1)</td>
<td></td>
</tr>
<tr>
<td>CCF</td>
<td>7</td>
<td>2 (28.6)</td>
<td>0.2107</td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>12</td>
<td>3 (25.0)</td>
<td>0.1728</td>
</tr>
</tbody>
</table>
Table 3. Comparison of present study with other studies

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Reference study</th>
<th>Present Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>To KK-33.3% [1] H J Why -13/120 (10.8%) [2]</td>
<td>5/36 (13.6%)</td>
</tr>
<tr>
<td>Viral Pneumonia</td>
<td>To KK -21.7% [1] 33.3% expired Binila Chacko - 43.7% [3]</td>
<td>21/60 (35.0%). 4/21 expired (19.0%)</td>
</tr>
<tr>
<td>Bronchiolitis</td>
<td>Kazem Sakha -3/148 (2.0%) [4] None expired</td>
<td>2/70 (2.8%). None expired</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Alakes Kumar Kole -70/100 (70%), 5/70 expired (7.1%) [5]</td>
<td>6/27 (22.0%). 1/6 expired (16.7%)</td>
</tr>
<tr>
<td>Dengue</td>
<td>Li Y- 201/1782 (11.2%). 2/201 expired (1.0%) [7]</td>
<td>4/22 (18.2%). None expired</td>
</tr>
<tr>
<td>Bacterial Pneumonia</td>
<td>Roberto Cangemi -55/301 (18%), 28/55 expired (51%) [8]</td>
<td>3/23 (13.0%). None expired</td>
</tr>
<tr>
<td>CCF</td>
<td>Kuhn B -11/28 developed CCF (39.2%) [9]</td>
<td>7/36 developed CCF (19.4%). 2/7 expired (28.3%)</td>
</tr>
<tr>
<td>Sudden Cardiac Arrest</td>
<td>B A Stockings -11/46 expired from sudden cardiac arrest (23.9%) [10]</td>
<td>3/29 expired from sudden cardiac arrest (10.3%)</td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>Shirley Press -5/7 (71.4%). 2/5 expired (40.0%) [11]</td>
<td>12/36 (33.0%). 3/12 expired (25%)</td>
</tr>
<tr>
<td>ECG changes</td>
<td>B A Stockings -6/ 46 had bradycardia (13.0%), 15/46 had A-V block (32.6%) [10]</td>
<td>Bradycardia 6/36 (16.7%). A-V block 5/36 (13.4%).</td>
</tr>
<tr>
<td></td>
<td>C Ukena et al- 20/214 had A-V block (10.7%), 11/214 had ST elevation (6.1%), 66/214 had T wave inversion (36.9%), 23/214 had Pathological Q waves (12.3%), 16/214 had Low voltage ECG (8.6%) [13]</td>
<td>ST elevation 6/36 (16.7%). T wave inversion 12/36 (33.3%). Pathological Q waves 1/36 (2.8%). Low amplitude ECG 6/36 (16.7%)</td>
</tr>
<tr>
<td></td>
<td>Di Bella et al-46/81 had ST elevation(57%), 7/81 had T invasion (9%), 4/81 had A-V block (6%) [14]</td>
<td></td>
</tr>
<tr>
<td>A-V block and mortality</td>
<td>Chien -1/9 with A-V block expired (11.1%), 1/9 required permanent pacemaker (11.1%) [15]</td>
<td>2/5 with A-V block expired (60.0%)</td>
</tr>
<tr>
<td></td>
<td>A S Batra -2/40 with A-V block expired (5.0%), 11/40 required permanent pacing (27.5) [16]</td>
<td></td>
</tr>
</tbody>
</table>
Fig. 2. ECG changes in myocarditis

T wave inversion, and low voltage complexes were not significant for expiry. Among 31 patients with ECG changes, 12 had cardiomegaly. 5/12 patients developed CCF, and 2/5 expired. 1/7 patient of cardiomegaly without CCF expired. The patients who developed CCF with cardiomegaly had higher mortality rate than those who did not develop CCF (2/5 vs 1/7).

4. DISCUSSION

The present study evaluated various ECG findings of myocarditis in children, to help in early diagnosis and prognostic significance of these ECG changes. We also assessed the risk of developing myocarditis in different infections and the prognosis in children who developed myocarditis with or without CCF.

Table 3 compares the present study with past studies. The incidence of myocarditis in different diseases was similar. Incidence of ECG changes, CCF, cardiomegaly and associated expiry in different studies was variable but comparable to the present study. Higher expiry from A-V block was seen in our study, as compared to studies that employed cardiac pacing. Cardiac pacing appears to reduce mortality in patients with A-V block.

5. CONCLUSION

Childhood myocarditis is most commonly seen in association with culture-negative (viral) pneumonia and diphtheria; and least commonly with bronchiolitis and bacterial pneumonia. Congestive cardiac failure and cardiomegaly develop in a quarter of patients but were not significantly associated with deaths.

Electrocardiographic changes are present in the majority of patients. Deaths were significantly increased in the presence of bradycardia and A-V block when pacing is not available.

6. RECOMMENDATIONS

- Myocarditis should be suspected early in pediatric patients with viral pneumonia and diphtheria.
- Continuous ECG monitoring should be available for suspected cases.
- Cardiac pacing should be considered in children with bradycardia and A-V block to reduce mortality.

7. LIMITATIONS OF THE STUDY

- The study was conducted with a small sample size.
- 2 D ECHO in-house was not available.
WHAT IS ALREADY KNOWN

Myocarditis is most often a result of viral pneumonia and diphtheria. There are two Indian studies on myocarditis with influenza and diphtheria. Congestive cardiac failure and sudden cardiac death are the main reason for death. A-V block is associated with a worse prognosis.

WHAT THIS STUDY ADDS

One-third of cases of myocarditis in children are seen in infancy. Bradycardia with or without A-V block was associated with significantly higher mortality in the absence of cardiac pacing. Cardiomegaly in itself was not associated with higher mortality; cardiomegaly with CCF had higher mortality.

CONSENT

Consent was obtained from the guardians in local language.

ETHICAL APPROVAL

The study was approved by the Institutional Review Board, Human Ethics Committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

15. Chien SJ, Liang CD, Lin IC, Lin YJ, Huang CF. Myocarditis complicated

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