

Original Article

Congenital Heart Disease Does Not Increase Risk of Bacteremia In Children With Pneumonia

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Abstract:

Background: Pneumonia is a major cause of childhood morbidity and mortality worldwide. It can be complicated by bacteremia. Congenital heart diseases (CHD) that cause increased pulmonary blood flow are a common predisposing factor for pneumonia in children.

Aim of the Work: We aimed to identify if children with pneumonia suffer from bacteremia and to identify the most common organisms causing bacteremia in cases of pneumonia with and without congenital heart disease and to study role of CHD in influencing type of bacteremia in pneumonia.

Patients and Methods: We conducted a pilot prospective study at Pediatric Hospital, Cairo University on 55 children with pneumonia (group 1) and 55 children with pneumonia and CHD (group 2). They all underwent complete blood counts, blood cultures and chest x-ray.

Results: The frequency of bacteremia was 56.4% in children with pneumonia and no CHD and 38.2% in those with pneumonia and CHD. In group with pneumonia and no CHD blood culture results showed no growth in 24 cases (43.6%), *Klebsiella* spp. growth 11 cases (20%), Coagulase negative staphylococci (CONS) in 6 cases (10.9%), Methicillin Resistant *Staphylococcus aureus* in 4 cases (7.3%), *Candida albicans* in 2 cases (3.6%) and *Pseudomonas* spp. in 2 cases (3.6%). While the blood cultures in the group with pneumonia and CHD showed no growth in 34 cases (61.8%), *Klebsiella* spp. in 10 cases (18.2%), CONS in 5 cases (9.1%) and *Candida albicans* in 3 cases (5.5%) and no statistically significant difference was found.

Conclusion: Frequency of bacteremia in children with pneumonia with and without congenital heart disease were not significantly different, the most common organism causing bacteremia in cases of pneumonia with or without congenital heart disease is *Klebsiella* spp. and the most sensitive antibiotic is polymyxin.

Level of Evidence of Study: IIA (1).

Keywords: pneumonia; congenital heart disease; bacteremia; pediatric; children.

Abbreviations: CAP: community-acquired pneumonia; CHD: congenital heart disease; CONS: Coagulase negative staphylococci; spp.: species; MRSA: methicillin resistant staphylococcus aureus.

Introduction

Pneumonia is a major cause of childhood morbidity and mortality worldwide (2). Congenital heart diseases (CHD) that cause increased pulmonary blood flow are a common predisposing factor for pneumonia in children (3). In the acyanotic CHD because of a left to right shunting of blood, via a septal defect or the arterial duct, there is pulmonary over circulation and pulmonary oedema (4). The pulmonary oedema leads to congestive heart failure and becomes a nidus of infection for the lower respiratory tract (5). The patients with CHD with increased pulmonary blood flow thus present with pneumonia and congestive cardiac failure amongst other features. Pneumonia and congestive heart failure may be the first signs of an underlying CHD. Most previous reports identified CHD as an underlying cause of recurrent pneumonia, when there are two or more pneumonia episodes in a year (3).



Most common cause of bacterial pneumonia in congenital heart disease are *Haemophilus influenzae*, *Stenotrophomonas maltophilia*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* (6). Blood cultures are often performed in the diagnostic evaluation of children hospitalized with community-acquired pneumonia (CAP). Recent clinical practice guidelines for the management of pediatric CAP recommended performing routine blood cultures in children requiring hospitalization for moderate or severe CAP, but the quality of evidence supporting this recommendation is low (7). We aim to identify if children with pneumonia suffer from bacteremia and to identify the most common organisms causing bacteremia in cases of pneumonia with and without congenital heart disease and to study role of CHD in influencing type of bacteremia in pneumonia.

Subjects and Methods

This was a prospective study conducted at Cairo University Pediatrics Hospital between March and August 2020. It included patients diagnosed with pneumonia who presented to the emergency room and the Pulmonology Clinic or were admitted to the general ward or in the intensive care unit during the six months period. The study was approved by the Pediatrics Department, Committee for Higher Research and Research Ethics Committee of Faculty of Medicine.

Participants

A total of hundred and ten children were included in the study, 55 cases with pneumonia without CHD (group I) and 55 cases with pneumonia and CHD (group II).

Methods

All enrolled children underwent:

- Careful history taking and clinical examination.
- Laboratory investigations including blood culture on day 1 before initiation of antibiotic therapy.
- Blood culture samples were withdrawn by peripheral venipuncture on BD BACTEC™ PEDS PLUS™ bottles and processed by BD BACTEC 9050 automated blood culture system. Positive blood culture bottles were inoculated on routine blood agar, chocolate agar and MacConkey agar media. Identification of Gram negative bacteria was performed by routine biochemical reactions on Triple sugar iron agar, lysine decarboxylase, urease agar, Simmons citrate agar and Motility-Indole-Ornithine semisolid media. Identification of *Staphylococci* was done by Gram stain, catalase test, mannitol salt agar and DNase agar media. *Enterococci* identification was done by Gram stain, catalase test and Bile Esculin agar media. *Candida* spp. identification was done by Gram stain and CHROMagar™ *Candida* (8). Antibiotic susceptibility was done by disc diffusion method on Mueller Hinton agar media according to CLSI 2020 guidelines (9). Antifungal susceptibility was done by fluconazole E-test strips.
- Imaging:
 - Chest x ray radiography posteroanterior view to assess cardiac size, pulmonary infiltrate and pulmonary vasculature.
 - Echocardiography using General Electric GE Vivid 5 system with probe 3 or 8 according to the age of the patient to assess type of congenital heart disease and to exclude vegetations.

Statistical Analysis

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). Data were summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between qualitative variables were done using the non-parametric Mann-Whitney test (10) and Chi square (χ^2) test. Exact test was used instead when the expected frequency is less than 5 (11). P values less than 0.05 were considered statistically significant.



Results

The median age in pneumonia group was 2 years in comparison with CHD group which was 5 months ($p < 0.001$). In pneumonia group, most of cases presented with first time pneumonia in comparison to CHD group, where most of cases presented with recurrent pneumonia ($p < 0.001$) and had higher CRP ($p < 0.001$). (Tables 1-3). The blood cultures revealed no growth among 58 cases (52.7%) and growth of organism from 52 cases. *Klebsiella* spp. was the highest organism reported, it was isolated from 21 patients which represented (19.1%) of cases. *CONS* was the second one reported, it was isolated from 11 patients (10%) followed by *Candida albicans* which was reported from 5 cases (4.5%). In group with pneumonia and no CHD blood culture results showed no growth in 24 cases (43.6%), *Klebsiella* spp. growth 11 cases (20%), *CONS* in 6 cases (10.9%), *MRSA* in 4 cases (7.3%), *Candida albicans* in 2 cases (3.6%) and *Pseudomonas* spp. in 2 cases (3.6%). While the blood cultures in the group with pneumonia and CHD showed no growth in 34 cases (61.8%), *Klebsiella* spp. in 10 cases (18.2%), *CONS* in 5 cases (9.1%) and *Candida* in 3 cases (5.5%) and no statistically significant difference was found. (Tables 4 and 5).

Table (1): Ages of studied children with pneumonia according to presence of underlying CHD.

| | Age(years) | | | | | P value |
|--------------------------------|------------|------|--------|---------|---------|---------|
| | Mean | SD | Median | Minimum | Maximum | |
| Group I (55 cases) | 2.72 | 3.00 | 2.00 | 0.16 | 12.00 | < 0.001 |
| Group II (55 cases) | 0.91 | 1.79 | 0.40 | 0.20 | 12.00 | |

Group I: children with pneumonia and no underlying congenital heart disease. Group II: children with pneumonia and underlying congenital heart disease.

Table (2): Recurrences of pneumonia among studied children with pneumonia according to presence of underlying CHD.

| Pneumonia | Group I | Group II | P value |
|-----------|-------------|-------------|---------|
| Single | 45 81.8% | 22 40.0% | < 0.001 |
| Recurrent | 10 18.2% | 33 60.0% | |

Group I: children with pneumonia and no underlying congenital heart disease. Group II: children with pneumonia and underlying congenital heart disease.

Table (3): CRP values among studied children with pneumonia according to presence of underlying CHD.

| | Age(years) | | | | | P value |
|--------------------------------|------------|-------|--------|---------|---------|---------|
| | Mean | SD | Median | Minimum | Maximum | |
| Group I (55 cases) | 71.87 | 59.73 | 50.00 | 1.30 | 240.00 | < 0.001 |
| Group II (55 cases) | 37.09 | 45.47 | 15.00 | 0.40 | 190.00 | |

Group I: children with pneumonia and no underlying congenital heart disease. Group II: children with pneumonia and underlying congenital heart disease.

Regarding cases with blood cultures showing organism growth, in pneumonia group, the most common sensitive drug was polymyxin B (10 cases) (32.3%), the second most common sensitive drug was vancomycin (9 cases) (29%), the least common sensitive drugs were fluconazole, piperacillin-tazobactam and doxycycline in comparison to CHD group, the most common sensitive drug was polymyxin B (9 cases) (42.9%), the 2nd most common sensitive drug was fluconazole (3 cases) (14.3%), the least common sensitive drugs were meropenem, tigecycline and ciprofloxacin. This was statistically insignificant. Echocardiography done revealed no vegetations in both groups of patients and no evidence of infective endocarditis in the two studied groups. All children with positive culture received the antibiotic according to culture and sensitivity.

**Table (4):** Blood culture yield among studied cases (n=110)

| Blood culture | Total cases | | Group I | | Group II | | P value |
|---------------------------|-------------|-------|---------|-------|----------|-------|---------|
| | Number | % | Number | % | Number | % | |
| No growth | 58 | 52.7% | 24 | 43.6% | 34 | 61.8% | 0.295 |
| <i>Klebsiella</i> spp. | 21 | 19.1% | 11 | 20.0% | 10 | 18.2% | |
| <i>Salmonella</i> spp. | 1 | 0.9% | 1 | 1.8% | 0 | 0.0% | |
| <i>Pseudomonas</i> spp. | 2 | 1.8% | 2 | 3.6% | 0 | 0.0% | |
| <i>MRSA</i> | 4 | 3.6% | 4 | 7.3% | 0 | 0.0% | |
| <i>Acinetobacter</i> spp. | 2 | 1.8% | 1 | 1.8% | 1 | 1.8% | |
| <i>Enterococci</i> | 3 | 2.7% | 1 | 1.8% | 2 | 3.6% | |
| <i>CONS</i> | 11 | 10.0% | 6 | 10.9% | 5 | 9.1% | |
| <i>Candida albicans</i> | 5 | 4.5% | 2 | 3.6% | 3 | 5.5% | |
| <i>Serratia</i> spp. | 1 | 0.9% | 1 | 1.8% | 0 | 0.0% | |
| <i>Proteus mirabilis</i> | 1 | 0.9% | 1 | 1.8% | 0 | 0.0% | |
| <i>Enterobacter</i> spp. | 1 | 0.9% | 1 | 1.8% | 0 | 0.0% | |

Group I: children with pneumonia and no underlying congenital heart disease. Group II: children with pneumonia and underlying congenital heart disease.

Table (5): Antibiotic sensitivity in blood culture results

| Antibiotic Sensitivity | Group I | | Group II | | P value |
|-------------------------|---------|-------|----------|-------|---------|
| | Count | % | Count | % | |
| Polymyxin B | 10 | 32.3% | 9 | 42.9% | 0.528 |
| Amikacin | 1 | 3.2% | 1 | 4.8% | |
| Vancomycin | 9 | 29.0% | 2 | 9.5% | |
| Levofloxacin | 4 | 12.9% | 2 | 9.5% | |
| Ciprofloxacin | 1 | 3.2% | 1 | 4.8% | |
| Piperacillin-tazobactam | 1 | 3.2% | 0 | 0.0% | |
| Doxycycline | 1 | 3.2% | 0 | 0.0% | |
| Co-trimoxazole | 1 | 3.2% | 0 | 0.0% | |
| Meropenem | 2 | 6.5% | 1 | 4.8% | |
| Imipenem | 0 | 0.0% | 0 | 0.0% | |
| Fluconazole | 1 | 3.2% | 3 | 14.3% | |
| Tigecycline | 0 | 0.0% | 1 | 4.8% | |

Group I: children with pneumonia and no underlying congenital heart disease. Group II: children with pneumonia and underlying congenital heart disease.

Discussion

Globally, pneumonia is a leading cause of death in children accounting for 15% of all deaths under age of 5 (2). Despite advances in antimicrobial therapies, microbiological diagnostic tests and prevention measures, pneumonia remains the main cause of death from infectious diseases in the world (12).

Congenital heart diseases (CHD) that cause increased pulmonary blood flow are a common predisposing factor for pneumonia in children (3). International health organizations, including the European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC), have highlighted the rapid emergence and spread of antibiotic resistance, which according to WHO has significant adverse impacts on clinical outcomes and higher costs due to consumption of healthcare resources (13).

The increasing antibiotic resistance problems, largely due to wide spread and irrational use of antimicrobial agents in hospitals and community is of great concern, especially in developing countries. Reliable statistics on antibiotic resistance that are mandatory to control spread of resistant pathogens are available from the developed nations. These data are derived from large surveillance studies in countries such as the USA, Europe, Australia, etc. However, such data are sparse in developing countries -like Egypt- due to the lack of large-scale meta-analytic studies. Hospital antibiograms are commonly used to help guide empiric antimicrobial therapy and are an important component of detecting and monitoring trends in antimicrobial resistance (14).

This was a prospective study conducted at Pediatric Hospital Cairo University that included children with pneumonia with and without congenital heart disease. The aim of the study was to



identify the most common organisms causing bacteremia in cases of pneumonia with and without congenital heart disease and to study role of CHD in influencing type of bacteremia in pneumonia.

The frequency of bacteremia was 56.4% in children with pneumonia and no CHD and 38.2% in those with pneumonia and CHD. Among blood cultures that yielded organism growth, *Klebsiella* spp. was the commonest organism reported in both groups (20% in those without CHD and 18.2% in those with CHD). The Children's Hospital of Philadelphia in 2013 reported that the most common pathogen causing bacteremia was *S. pneumoniae*, the remaining pathogens included *H. influenzae* and *Staphylococcus aureus* (15). A study from Turkey reported that *Haemophilus influenzae*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* were the commonest organisms (6). There is no unanimous agreement on type of organism. It might be related to factors (e.g. variations in geographic area) and others that are not currently clear.

Antibiotic sensitivity results in group I showed the highest sensitivity to polymyxin (32.3%), then to vancomycin (29%) and to levofloxacin (12.9%). While in group II, it was to polymyxin (42.9%), then to fluconazole (14.3%) then to vancomycin (9.5%) and to levofloxacin (9.5%). In both groups we have increasing resistance to carbapenems. Fluconazole was the second drug among group II. This might be explained by the recurrent pneumonia in this group that makes them frequently exposed to many trials of antibiotics. All isolates tested were susceptible to levofloxacin, 18% were resistant to meropenem. All methicillin-resistant *Staphylococcus aureus* isolates were susceptible to clindamycin and vancomycin. The *H. influenzae* isolate did not exhibit β -lactamase production. It is not known if the wide compulsory vaccination of neonates in Egypt against *H. influenzae* since 2015 changed the type of organisms among the children with pneumonia.

Most previous reports identified CHD as an underlying cause of recurrent pneumonia, when there are two or more pneumonia episodes in a year (3). In our study we found that among those with underlying CHD, 33 cases (60%) presented with recurrent pneumonia and in those without CHD 10 cases (18.2%) with recurrent pneumonia, it was statistically significant. While CHD explains the repeated pneumonias (16), those with recurrent pneumonia and no CHD need to be investigated for other causes of recurrence of pneumonia e.g. investigated for immune deficiency, or aspiration, etc.

We cannot explain why in the current study we encountered higher CRP levels among children with pneumonia without CHD. Maybe children with CHD seek medical attention more promptly.

The current study is limited by lack of enough epidemiologic data of patients. The effect of bacteremia on clinical march and outcome was not studied as they were out of scope of this study.

The study is limited by lack of further bacterial species identification using automated identification systems as VITEK2 system. The lack of simultaneous sputum culture in our studied patients for typing of microorganisms and knowing if the bacteria causing pneumonia was the same organisms causing the bacteremia is another limitation of our study.

Conclusion

Frequency of bacteremia in children with pneumonia with and without congenital heart disease were not significantly different, the most common organism causing bacteremia in both groups is *Klebsiella* spp. and the most sensitive antibiotic is polymyxin.

Author Contributions: All authors searched medical literature, databases, conceptualized, conducted the case review and reviewed the final manuscript. All authors have read and agreed to the published version of the manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in connection with the reported study. Authors declare veracity of information.



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