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ORIGINAL ARTICLE

Pneumonia in Children with Congenital Heart Disease: Bacterial Spectrum and Risk of Bacteremia

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ABSTRACT

Background: Community-acquired pneumonia (CAP) is widely acknowledged as the leading cause of morbidity and mortality among children worldwide, particularly in developing nations. Children with congenital heart disorders (CHD) are more likely to have pneumonia and require repeated hospitalization. We aim to determine the most frequent microorganism responsible for pneumonia in children with and without CHD, as well as the frequency of bacteremia in such cases, and whether or not CHD raises the risk of bacteremia in children with pneumonia. **Methods** We conducted our prospective cohort study in Department of Pediatrics, Faculty of Medicine, Zagazig University on 50 children who divided equally into 2 groups; group I contained 25 children with pneumonia in patients with CHD, group II contained 25 non cardiac children with pneumonia. All underwent complete blood count (CBC), chest x ray (CXR), echocardiogram (ECHO), sputum culture, and blood culture. **Results:** Patients of CHD had significant more frequent previous hospital admissions by pneumonia. Among the children in group I, the blood culture results revealed no growth in 15 cases (60%), and klebsiella pneumoniae in 3 cases (12%), while in group II, the result revealed no growth in 11 cases (44%), klebsiella pneumoniae in 5 cases (20%) and there was no statistically significant difference between both groups.

Conclusion: Klebsiella pneumoniae was the most prevalent pathogen responsible for pneumonia in children with and without CHD, and linezolid was the most sensitive antibiotic. In children who have pneumonia, CHD might attribute to higher risk of bacteremia, however, we couldn't prove that in our study.

Keywords: Pneumonia; Congenital Heart Disease; Bacteremia; Pediatric

INTRODUCTION

Community-acquired pneumonia (CAP) is still the most common cause of morbidity and mortality in children between the ages of 28 days and 5 years. Although pneumonia is more common and has the highest fatality rate in Sub-Saharan Africa and lower socioeconomic regions where immunizations are less accessible, it affects children worldwide and poses a serious risk to their health as well as a financial strain on healthcare systems [1]. Congenital heart diseases (CHD) represent one of the most common predisposing factors for the development of childhood

pneumonia, which is a clinically severe illness that arises from a complex combination of host and environmental risk factors [2]. CHD with left to right shunt as atrial septal defect (ASD). Ventricular septal defect (VSD), patent ductus arteriosus (PDA), etc characterized by increasing pulmonary blood flow which leads to pulmonary congestion providing a good media for lower respiratory tract infection [3]. Numerous earlier studies have demonstrated that CHD is thought to be the fundamental cause of children's recurrent pneumonia [4]. The most frequent pathogens causing bacteremia in children with CHD and pneumonia are Haemophilus influenza, Stenotrophomonas maltophilia, Klebsiella pneumoniae, and Pseudomonas aeruginosa [5].

Blood cultures are generally not required for children receiving outpatient treatment, but they should be taken into consideration for those who need to be hospitalized, especially for children with risk factors or if they have complicated pneumonia. According to recent research, blood cultures appear to be ineffective and have a low yield of 1 to 3% when taken from children admitted to hospitals due to simple CAP with no associated comorbidities [6]. According to recent studies, the prevalence of bacteremia among hospitalized children with CAP has changed, along with reported changes in the epidemiology and management of pneumonia. The bacteriological profile of CAP varies between nations and changes over time within a single nation, most likely as a result of increased antibiotic use, environmental pollution levels, rising public awareness of the illness, and alterations in life expectancy [7].

So, it is crucial to update the antibiogram for CAP in previously healthy children or in those with CHD. In this study, we aimed to determine the most common pathogens causing pneumonia, and to assess the frequency of bacteremia in children suffering from pneumonia with and without CHD, also to determine whether CHD increases the risk of the development of bacteremia.

Methods

This prospective cohort study was carried out in pediatric pulmonology and cardiology units at Department of Pediatrics, Faculty of Medicine, Zagazig University. We included fifty children, twenty-five patients with CHD suffering from pneumonia and twenty-five non cardiac patients who had pneumonia throughout the duration from July 2023 to December 2023. The study was approved by Institutional Review Board of Zagazig University. IRB approval number (10890). Written informed consent was taken from all patients' caregivers. All enrolled children underwent careful history taking, thorough clinical examination, Chest x ray and laboratory investigations including:

- Complete blood count (CBC) that was done using Sysmex xs 500i (System, Japan).
- CRP was done using Cobas 6000-c502 auto analyzer (Roche Diagnostics, Germany, sputum culture and blood culture.
- Sputum culture: Older children who can expectorate have their samples collected in sterile containers. In contrast, sputum production was induced in younger children who cannot expectorate by inhaling a 3% hypertonic saline solution for 5–10 min [8]. To prevent bronchoconstriction, inhaled salbutamol (0.15 mg/kg, maximum dosage 5 mg) was administered via a nebulizer device. In order to get a nasopharyngeal sample and clear the nasopharynx of mucus, a disposable catheter was inserted into the back wall of the nasopharynx and drawn back while suction was applied using an electronic suction device for both nostrils.
- Blood culture: Using meticulous aseptic methods, we extracted blood samples. The media was then incubated in BACTEC/ALERTdevice (BioMerieux Ltd). Bottles were checked for microbiological growth every day for up to seven days. We did subculture on blood agar and chocolate agar when growth was evident. We incubated blood agar plates aerobically and chocolate agar in an anaerobic gas package with carbon dioxide. Using an automated broth microbial system (Vitek; BioMerieux Ltd.), a conventional technique was used to identify the clinical isolates' antimicrobial susceptibility test results.
- Echocardiography (Echo): Reports of ECHO recently performed by a pediatric cardiologist to determine types of congenital heart diseases and assess pulmonary blood pressure.

Statistical Analysis

Version 26 of the SPSS (Statistical Package for the Social Sciences) program was used to analyze the data. The absolute frequencies of the categorical variables were used to describe them, and when necessary, Monte Carlo, and Chi square tests were used to compare the data. Chi square for trend test was used to compare ordinal data between two groups. The Shapiro-Wilk test was employed to confirm the assumptions made for parametric testing. Depending on the type of data, the means and standard deviations or the median and interquartile range were used to characterize quantitative variables. The independent samples t test (for regularly distributed data) and the Mann Whitney test (for non-normally distributed data) were used to compare quantitative data between two groups. P<0.05 was designated as the level of statistical significance. If p≤0.001, a highly significant difference was found.

linezolid was the most frequently used sensitive medication (7 cases, or 70%), followed by vancomycin (6 cases, or 60%). Gentamycin (9 cases, 81.8%) was the most frequently used sensitive medication in group II, followed by vancomycin (8 cases, 72%) and linezolid, which has the same percentage as indicated in Table 5. Table 6 indicates that there was no statistically significant relation between the incidence of bacteremia and the type of CHD

RESULTS

The demographic data of the studied groups are showed in table 1. The median age in group I was 5 months in comparison with group II which was 20 months (p <0.001). Group I gave significantly more frequent history of previous hospital admission due to pneumonia, (80%) when compared to group II (44%) (p<0.009).

The commonest abnormalities detected in Echo among group I were ASD (36%), combined ASD and VSD (20%) and fallot tetralogy (8%). Table 2

According to the result of sputum culture, larger percentage within both groups showed no growth (72% in group I, 76% in group II), among the cultures that yield organisms, the commonest was Klebsiella pneumoniae in both groups as shown in table 3.

In group I, blood culture results showed no growth in 15 cases (60%), Klebsiella pneumoniae was found in 3 cases (12%), staph hemolyticus in 3 cases (12%), coagulase negative staph in 2 cases (8%) and staph aureus in 1 case (4%). in group II, the result was no growth in 11 case (44%), Klebsiella pneumoniae in 5 cases (20%), staph hemolyticus in 4 cases (16%), coagulase negative staph in 2 cases (8%), Strept pneumoniae in 1 case (4%) as presented in table 4.

When it came to cases where blood cultures revealed the growth of organisms, in group I,

Table (1): Comparison between the studied groups regarding demographic data:

	Group I N=25 (%)	**Group II N=25 (%)**	**χ^2**	**P**
Gender: **Female** **Male**	 8 (32%) 17 (68%)	 10 (40%) 15 (60%)	0.347	0.556
Consanguinity **Positive**	 9 (36%)	 6 (24%)	0.857	0.355
Previous hospital admission	20 (80%)	11 (44%)	6.876	0.009*
	Median (IQR)	Median (IQR)	Z	P
Age (month)	5(3 – 7)	20(7.5 – 42)	3.596	<0.001**

Z Mann Whitney test, χ^2Chi square test, *p<0.05 is statistically significant, **p≤0.001 is statistically highly significant , IQR (interquartile range) , N (number)

Table (2) Comparison between the studied groups regarding Echocardiographic data:

	Group I N=25 (%)	**Group II N=25 (%)**	**T**	**P**
	Mean ± SD	**Mean ± SD**		
EF (%)	64.52 ± 6.66	68.0 ± 3.81	-2.268	0.028*
	Median (IQR)	Median (IQR)	Z	P
Pulmonary arterial pressure BP (mmHg)	35(29.25 – 60)	30(26.5 – 32.5)	-2.701	0.007*
Abnormalities **Atrial septal defect (ASD)** **Ventricular septal defect (VSD)** **ASD and VSD** **Pulmonary stenosis** **Common atrioventricular canal** **Patent ductus arteriosus(PDA)** **ASD&VSD&PDA** **Fallot tetralogy** **Double outlet right ventricle** **ASD and PDA**	 9 (36%) 2 (%) 5 (20%) 1 (4%) 1 (4%) 1 (4%) 1 (4%) 2 (8%) 1 (4%) 2 (8%)	-	-	-

Z Mann Whitney test, t independent sample t test, *p<0.05 is statistically significant, **p≤0.001 is statistically highly significant

Table (3) Comparison between the studied groups regarding result of sputum culture:

	Group I N=25 (%)	**Group II N=25 (%)**	**χ^2**	**P**
Culture **No growth** **Positive**	 18 (72%) 7 (28%)	 19 (76%) 6 (24%)	0.104	0.747
Organism: **Acinetobacter** **E coli** **Klebsiella pneumoniae** **Pseudomonas** **Staph hemolyticus** **Staph aureus**	 0 (0%) 0 (0%) 5 (20%) 1 (4%) 1 (4%) 0 (0%)	 1 (4%) 1 (4%) 3 (15%) 0 (0%) 0 (0%) 1 (4%)	MC	0.64

χ^2Chi square test, MC Monte Carlo test

Table (4) Comparison between the studied groups regarding result of blood culture:

	Group I N=25 (%)	Group II N=25 (%)	χ^2	P
Culture				
No growth	15 (60%)	11 (44%)	1.282	0.258
Positive	10 (40%)	14 (56%)		
Organism:				
Coagulase -ve staph	2 (8%)	2 (8%)		
Staph hemolyticus	3 (12%)	4 (16%)		
Klebsiellapneumoniae	3 (12%)	5 (20%)	MC	0.8
Staph hominis	0 (0%)	1 (4%)		
Staph epidermidis	0 (0%)	1 (4%)		
Staph aureus	1 (4%)	0 (0%)		
Staph warnei	1 (4%)	0 (0%)		
Strept pneumonia	0 (0%)	1 (4%)		

χ^2Chi square test MC Monte Carlo test

Table (5) Comparison between the studied groups regarding sensitivity of blood culture organisms:

	Group I N=10(%)	Group II N=14(%)	χ^2	P
Sensitive to				
Amikin	0 (0%)	4 (36.4%)	Fisher	0.09
Gentamycin	5 (50%)	9 (81.8%)	Fisher	0.182
Colistin	1 (10%)	2 (18.2%)	Fisher	>0.999
Ceftriaxone	0 (0%)	2 (18.2%)	Fisher	0.476
Ciprofloxacin	5 (50%)	6 (54.5%)	0.043	0.834
Minocycline	0 (0%)	1 (9.1%)	Fisher	>0.999
Meronym	2 (20%)	4 (36.4%)	Fisher	0.635
Tigecycline	6 (60%)	6 (54.5%)	Fisher	>0.999
Levofloxacin	0 (0%)	1 (9.1%)	Fisher	>0.999
Linezolid	7 (70%)	8 (72.7%)	Fisher	>0.999
Vancomycin	6 (60%)	8 (72.7%)	Fisher	0.659

χ^2Chi square test MC Monte Carlo test

Table (6) Relation between bacteremia and echocardiographic data among group I:

	No bacteremia N=15 (%)	Bacteremia N=10 (%)	χ^2	P
Abnormalities				
ASD	4 (26.7%)	5 (50%)		
VSD	1 (20%)	1 (10%)		
ASD&VSD	5 (33.3%)	0 (0%)		
ASD&PDA	1 (6.7%)	1 (10%)		
PDA	0 (0%)	1 (10%)	11.574	0.238
Fallot	2 (13.3%)	0 (0%)		
DORV	1 (6.7%)	0 (10%)		
Common AV canal	0 (0%)	1 (10%)		
Pulmonary stenosis	0 (0%)	1 (10%)		
ASD, VSD&PDA	1 (6.7%)	0 (0%)		

	Mean ± SD	Mean ± SD	T	P
EF (%)	64.2 ± 5.54	65.0 ± 8.37	-0.289	0.775
	Median(IQR)	**Median(IQR)**	**Z**	**P**
Pulmonary arterial pressure (mmHg)	35.5(34 – 60)	28.5(25 – 61)	-1.682	0.093

χ^2Chi square test t independent sample t test Z Mann Whitney test

DISCUSSION

For many years, the most common cause of death in children under five has been pneumonia [9]. It carries out many consequences on child health which may extent to chronic chest problem as chronic bronchitis, lung suppuration and bronchiectasis [10]. Most previous reports showed that CHD is a major risk factor of pneumonia and its recurrence especially when there are two or more pneumonia episodes in a year [5]. Also pneumonia has negative impact on the children of CHD as it may worse their condition, extend hospital stay and complicate the treatment [11]. Antimicrobial resistance has been identified by international health organizations, such as the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), and the European Centre for Disease Prevention and Control (ECDC), as one of the most significant issues for human health with significant negative effects on clinical outcomes and higher costs due to the consumption of healthcare resources [12].

Egypt is as one of many low- and middle-income nations that are especially susceptible to the problem of antibiotic resistance. This is brought about by fewer chances for surveillance and diagnosis and by less restricted use of antibiotics [13]. This prospective cohort study aimed to detect the frequency of bacteremia in children who had pneumonia with and without congenital heart disease, as well as the most prevalent organisms causing pneumonia in those children.

Our study showed male predominance in both groups, group I (68%) and group II (60%), which is consistent with Jat et al. [14] who reported that the gender distribution of children with pneumonia was 56.98% male with a male: female ratio of 1.3:1. Mahapatra A et al. [15] have observed a similar distribution pattern and gender prevalence. Our findings on gender diverge from those of Kiconco et al. [16], who studied the risk factors and prevalence of pneumonia in children under five years old in Uganda.

The median age of children with pneumonia and congenital heart disease (group I) in our study was 5 months, with an IQR ranging from 3 to 7 months, compared to group II, where children's median age ranged from 7.5 to 42 months. Sadoh et al. [5] observed that patients with various forms of CHD had a mean age of 8.57 ± 8.77 months at the time of pneumonia presentation, with 51% of the patients being male. Our pneumonia with CHD were younger , this may be random selection bias come from the fact that cases of CHD who were admitted by lower respiratory tract infections were younger in age this was supported by the result Shah et al. [17]who studied the prevalence of pneumonia with congenial heart disease in Pakistan and found that the highest percentage of children with severe pneumonia infections (39.80%) were those under the age of 1-2 years, followed by those aged 3–4 years (36.04%), 5–6 years (30.87%), 7-8 years (25.58%), and 9–10 years (19.81%).so the risk of sever pneumonia in CHD patients decreases with age .

In our study, we reported that 80% of patients in group II had a history of prior hospital admission due to pneumonia, compared to 44% in groups I. Abdelmegeid et al [18] also mentioned that recurrent pneumonia was present in 60% of patients with underlying cardiac disease and 18.2% of patients without CHD. In addition, Singh PK et al. [19] reported that 43 % of his patients with recurrent lower respiratory tract infection (LRTI) had CHD. Rahayuningsih et al. [20] published that Left to right shunt congenital heart disease considered a risk factor of recurrent pneumonia in under five-year-old children.

The Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) have established guidelines that state that sputum from adult patients who need to be admitted to the intensive care unit because of pleural effusion or because their outpatient antibiotic therapy isn't working should be routinely cultured and Gram stained [21]. Routine sputum analysis has not been advised for children with pneumonia because young children cannot generate sufficient sputum samples and because healthy children frequently have nasopharyngeal colonization with pneumonia-causing bacteria.[22]

In our study, we attempted to get around this problem by using hypertonic saline inhalation to induce sputum production. The majority of CAP children were able to obtain a high-quality sputum specimen using this method, but the children found the repeated nasopharyngeal aspirations and hypertonic saline inhalation to be unpleasant, so our findings do not support the routine use of induced sputum analysis for all CAP children. Additionally, empirical antibiotic therapy was successful in treating the majority of patients. According to the result of sputum culture, larger percentage within both groups was no growth (72% in group I ,76% in group II), among the cultures that yield organisms; the commonest in both groups was Klebsiella pneumonia and the second common organism in group I was pseudomonas, and in the second group was acinetobacter and staph aureus. According to a study conducted in Egypt [23], the most often isolated organism in children with bacterial CAP was Staphylococcus aureus (37.2%), which was followed by klebsiella pneumonia (30.2%), streptococcus pyogenes (14%), pseudomonas (14%), and enterococci (2.3%). There is disagreement with Honkinen et al. [24], who discovered that streptococcus pnemoniae was the most frequently found microorganism, and with other studies conducted globally, including in Finland [25], Japan [26], and certain Chinese cities [27], which revealed streptococcus pneumonia to be the most common bacterial agent in children with CAP. We suggest that the introduction of a pneumococcal vaccine may have contributed to the low prevalence of streptococcus pneumonia. When the pneumococcal vaccine was administered in England, the incidence of streptococcus pneumonia decreased by 88% [28]. Additionally, compared to pre-vaccine times, there was an 81% reduction in the annual incidence of pneumococcal pneumonia in children in Japan [29].

In our study, blood culture revealed that higher percentage of the organisms in both groups showed no growth in terms of their existence and kind. The frequency of bacteremia was 56% in children with pneumonia and no CHD and 40% in those with pneumonia and CHD. In group I, Klebsiella pneumoniae and Staph hemolyticus were the most prevalent growths (12% each), where as in group II, Klebsiella pneumoniae was the most common growth (20%). In our analysis, the most frequently used sensitive antibiotic in group I (patients with blood cultures demonstrating organism development) was linezolid (7 cases, 70%), followed by vancomycin (6 cases, 60%). On the other hand, Gentamycin was the most frequently used sensitive antibiotic in group II (9 cases, 81.8%), followed by vancomycin (8 cases, 72%), and linezolid with the same percentage. According to a study from Egypt [18], the most prevalent bacterium found in both groups (20% in those without CHD and 18.2% in those with CHD) was Klebsiella pneumoniae and the CHD group had the highest sensitivity to polymyxin (32.3%), followed by vancomycin (29%) and levofloxacin (12.9%). Polymyxin (42.9%), fluconazole (14.3%), vancomycin (9.5%), and levofloxacin (9.5%) were administered to the pneumonia group. Also according to Şahan et al. [30], the most prevalent microorganisms were Pseudomonas aeruginosa, Klebsiella pneumoniae, and Haemophilus influenzae.

Our study **was limited** by its relatively small sample size especially when evaluating different age groups and CHD categories. Large multicenter studies are frequently needed to evaluate the culture results and configure local antibiogram for different groups at risk for pneumonia.

CONCLUSION

Klebsiella pneumoniae was the most frequent pathogen responsible for bacterial pneumonia in children with and without congenital heart

disease, and linezolid was the most sensitive antibiotic. CHD might attribute to higher risk of bacteremia, however, we couldn't prove that in our study.

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