BACTERIAL PATHOGEN ASSOCIATED WITH COMMUNITY- ACQUIRED PNEUMONIA IN CHILDREN AGED BELOW FIVE YEARS

By

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ABSTRACT

Background: *Community-acquired pneumonia (CAP) is a significant cause of respiratory morbidity and mortality in children, especially in developing countries.*

Objective: *To detect the causative bacterial pathogen associated with (CAP) in children aged below five years in Egypt &to know the most sensitive antibiotic.*

Patients & Methods: *This cross- section study included 60 children with pneumonia between 1month to 5 years, from Al-zhraa University Hospital (outpatient clinic and inpatient department), selected by simple random method , from August 2020 to Feb 2021. All patients were subjected to complete history taking, clinical examination, and investigations (complete blood count, CRP, ESR, liver, kidney function tests, blood culture, gastric lavage culture, Chest x-ray & CT chest to indicated cases).*

Results: *60 children (age 1.12 ± 1.45years, 35 males (58.3%) and 25 females (41.7%)) from them (51.6%) with positive blood culture & (43.3%) positive gastric lavage culture. The most common bacterial pathogens identified by blood culture were coagulase negative staph (25%) & staph. aureus (10%), other bacterial causes include klebsiella pneumonia (6.6%), pseudomonas (5%), gram positive bacilli (3.3%) & growth of candida spp (1.7%). The most common bacterial pathogens identified by gastric lavage culture were Klebsiella pneumonia (13.3%) & strept. pneumonia (8.3%).*

Conclusion: *The common bacterial pathogens causing CAP in Egyptian children below 5 years detected by blood culture were coagulase negative staph (25%) & staph aurous (10%) & by gastric lavage culture were Klebsiella pneumonia (13.3%) & strept pneumonia (8.3%). Amoxicillin/ clavulanic were the most frequent sensitive antibiotic for different organisms reported by both culture.*

Keywords: *Community Acquired Pneumonia, Blood Culture, Gastric Lavage Culture, Amoxicillin/ Clavulanic, Children.*

INTRODUCTION

Community-acquired pneumonia (CAP) remains an important cause of morbidity and mortality in both industrialized and developing countries. It is considered one of the three most common infectious causes of death worldwide, pneumonia, diarrhea, and measles[1].

The definition of CAP varies between different sources; on a pathological level, pneumonia is considered infection of the lung parenchyma, i.e., lower respiratory tract (LRT) infection by microorganisms[2].

CAP is defined clinically as "the presence of signs and symptoms of pneumonia in a previously healthy child due to an infection which has been acquired outside hospital[3].

Pneumonia killed about 935.000 children younger than 5 years in 2013, accounting for 15% of all deaths of children in that age. It affects children everywhere, but is most prevalent in South Asia and Sub-Saharan Africa[4].

In Egypt, it was estimated that 10% of children deaths below the age of 5 years is likely caused by pneumonia and other acute respiratory infections[5].

SUBJECTS AND MATERIALS

Study design:

The current study is cross section study.

Population:

The present study included 60 children with pneumonia from Al-zhraa University Hospital (outpatient clinic and inpatient department), selected by simple random method from August 2020 to Feb2021. Age of patients ranged between 1 month and 5 years.

Inclusion criteria:

1. Infant and children aged one month to five years (male and female sex).

2. Children diagnosed with CAP clinically & laboratory.

Exclusion criteria:

- Children above 5 years.

- New born infants.

- Children with other type of pneumonia (Hospital acquired pneumonia, Ventilator associated pneumonia or Aspiration pneumonia).

- Children With chronic lung disease.

- Children with congenital lung disease.

- Children with other chronic disease.

Ethical consideration:

- An Informed written consent was obtained from all participants' parents before enrollment into the study and approved by the Ethics committee of Al-Azhar University.

- All data &results of the study are confidential & the patient has the right to keep it.

- The patient has the right to withdraw from the study at any time.

- The author declared that there is no conflict of interest & financial support regarding the study & publication.

All studied patients were subjected to the following:

1. Complete history taking (Personal history, Present history, past medical history).

2. Physical examination especially signs of respiratory distress & other systemic evaluation e.g signs of heart failure.

3. Laboratory evaluation as:

   - Complete blood count, using (Sysmex XP, Kobe, Japan).

- CRP: quantitatively by Beckman coulter AU Analyzers (USA).

- ESR.

- Liver & kidney function tests.

- Blood culture: About 2-10 ml/set were added to blood culture bottle =. subcultures of positive Bactec samples were done on blood agar, chocolate agar, & MacConkey agar media and incubated at 37°c for 24 hr. identification of isolated organisms was done by colony morphology, microscopic examination by gram stain and conventional biochemical reactions , it was done by using BD Bactec 9050 Blood Culture System,(USA, Catalog No.445800) instrument.

- Gastric lavage culture: During this procedure, a nasogastric catheter was inserted through the nose and down the stomach after nebulization with hypertonic saline 5% for 10 seconds. Suction was applied for up to 15 seconds to collect the swallowed sputum in a sterile container.

- Chest x-ray.

- CT chest if indicated case.

Statistical Analysis:

Results were collected and analyzed by personal computer and statistical package for social science (SPSS Inc., Chicago, Illinois, USA) version 20.

Parametric data were expressed as mean and standard deviation (SD). Comparing the mean ±SD between the two groups was done using a student t-test. Also, Pearson Correlation Coefficient (r) was used to measure the association between two quantitative variables. The level of significance was set as P-value <0.05.

RESULTS

Our results were demonstrated in the following tables.

Table (1): Demographic data of studied patients

		Studied patients (N = 60)
Age (years)	Mean ± SD	1.12 ± 1.45
	Range	0.1 – 5
Age groups	< 1 year	39 (65.0%)
	(1-2 years)	11 (18.3%)
	(2-4 years)	5 (8.3%)
	> 4 years	5 (8.3%)
Sex	Male	35 (58.3%)
	Female	25 (41.7%)
Residence	Urban	40 (66.7%)
	Rural	20 (33.3%)
Mother occupation	House wife	42 (70.0%)
	Working	18 (30.0%)
Father occupation	Working	45 (75.0%)
	Not working	15 (25.0%)

This table shows that: the mean age of studied patients was 1.12 ± 1.45 years, most them < 1 year, with male sex was predominance, mostly were living in urban areas, their mothers mostly house wives & their fathers mostly working.

Table (1): Clinical finding in studied patients

		Studied patients (N = 60)
Weight (kg) for age	>5th centile	60 (100.0%)
	Mean ± SD	7.9 ± 4.4
	Range	2.5 – 18
	<5th centile	0 (0.0%)
Height (cm) for age	>5th centile	60 (100.0%)
	Mean ± SD	71.2 ± 17.9
	Range	47 – 109
	<5th centile	0 (0.0%)
Symptoms		
Fever (> 38°c)	No	2 (3.3%)
	Yes	58 (96.7%)
Cough	No	10 (16.7%)
	Yes	50 (83.3%)
	Dry	10 (20.0%)
	Wet	40 (80.0%)
Rhinitis	No	15 (25.0%)
	Yes	45 (75.0%)
Signs		
Tachypnea	No	0 (0.0%)
	Yes	60 (100.0%)
Fine crepitation	No	0 (0.0%)
	Yes	60 (100.0%)
Air entry	Normal	10 (16.7%)
	Decreased	50 (83.3%)
Rhonchi	Absent	20 (33.3%)
	Present	40 (66.7%)

This table shows that, normal weight & height for age, fever, and wet cough were the most presenting symptoms & tachypnea, fine crepitation's and diminished air entry were the most common clinical signs among studied patients.

Table (2): laboratory findings in studied cases

	Studied patients (N = 60)		
	Mean	±SD	Range
Hb (g/dl)	10.3	1.5	7 – 15.4
RBCs (x10^6/ul)	3.8	0.7	2.5 – 5.6
PLTs (x10^3/ul)	402.6	166.2	110 – 885
WBCs (x10^3/ul)	10.7	4.7	2.1 – 22.6
Neut. (x10^3/ul)	6.6	4.62	0.5 – 24.4
Lymph (x10^3/ul)	4.03	2.4	0.7 – 11.9

This table shows that laboratory findings in our studied patients.

Table (3): CRP & ESR in studied patients

		Studied patients (N = 60)	
CRP	**< 6 mg/L**	17	28.3%
	6 mg/L	6	10%
	12 mg/L	5	8.3%
	24 mg/L	18	30%
	48 mg/L	10	16.7%
	96 mg/L	2	3.3%
	192 mg/L	2	3.3%
ESR (mm/h)	**Mean ±SD (Range)**	24 ± 15.9 (5 – 80)	

This table shows that, most cases with positive CRP & the mean ESR of studied patients was 24 ± 15.9 mm/hour with minimum ESR of 5 mm/hour and maximum ESR of 80 mm/hour.

Table (4): Relation between blood culture results and (ESR & CRP)

		Blood culture				Stat. test	P-value
		Negative (N = 29)		Positive (N = 31)			
ESR (mm/h)	**Median**	15		30		**MW = 233**	**0.001 S**
	IQR	10.5 – 20		15 – 48			
CRP (mg/L)	**Negative**	13	44.8%	4	12.9%	**X^2 = 7.5**	**0.006 S**
	Positive	16	55.2%	27	87.1%		

MW: Mann Whitney test, S: p-value < 0.05 is considered significant, X2: Chi-square test.

This table shows: Statistically significant (p-value < 0.05) increased ESR in patients with positive blood culture results, statistically significant (p-value < 0.05) positive CRP results in patients with positive blood culture result.

Table (5): Blood culture results in studied patients

		Studied patients (N = 60)	
Blood culture results	**No growth**	29	48.3%
	Coagulase negative staph	15	25%
	Staph aurous	6	10%
	gram +ve bacilli	2	3.3%
	Pseudomonas	3	5%
	Klebsiella pneumonia	4	6.7%
	growth of candida spp.	1	1.7%

This table shows that, the most common organism was the coagulase negative staph (25%), staph aurous (10%) and there was no growth in 29 patients (48.3%).

Table (6): Results of gastric lavage culture in studied patients

		Studied patients (N = 60)	
Gastric lavage culture results	**No growth**	34	56.7%
	coagulase negative staph	1	1.7%
	staph aurous	4	6.7%
	Pseudomonas	4	6.7%
	Klebsiella pneumonia	9	15%
	fungal growth	3	5%
	Strept. Pneumonia	5	8.3%

This table shows that, the most common organism was the Klebsiella pneumonia (13.3%), strept pneumonia (8.3%) and there was no growth in 34 patients (56.7%).

Table (7): Antibiotic sensitivity results for gram positive organisms detected by both blood culture & gastric lavage culture in studied patients

		Patients with bacterial growth (N = 32)	
Anti-biotics	**Amoxicillin/clavulanic**	14	43.7%
	Ampicillin/sulbactum	10	31.2%
	Azithromicin	9	28.1%
	Vancomycine	8	25%
	Ciprofloxacine	7	21.8%

The sensitive antibiotics for gram positive organisms detected by both culture were amoxicillin/clavulanic (43.7%), ampicillin/sulpactum (31.2%), azithromycin (28.1%), vancomycin (25%), ciprofloxacin (21.8%).

Table (8): **Antibiotic sensitivity results for gram negative organisms detected by both blood culture & gastric lavage culture in studied patients**

		Patients with bacterial growth (N = 32)	
Anti-biotics	**Imipenem**	10	31.2%
	Polymixine b	9	28%
	Colstine	9	28%
	Gentamicine	7	21.8%
	Amickacin	6	18.7%
	Amoxycilline/clavulanic	5	15.6%
	Ampicilline/sulbactum	5	15.6%
	Pipracilline	4	12.5%

The sensitive antibiotics for gram negative organisms detected by both culture were imipenem (31.2%), polymixine (28%), colstine (28%), gentamicin (21.8), amikacin (18.7%), amoxicillin/clavulanic (15.6%), ampicilline/ sulbactume (15,6%), pipracilline (12.5%).

Table (9): **Relation between blood culture results and age categories in studied patients**

		Age categories							
		< 1 years (N = 40)		1 – 2 years (N = 11)		2 – 4 years (N = 4)		> 4 years (N = 5)	
Blood culture results	**No growth**	21	52.5%	4	36.4%	3	75%	1	20%
	Coagulase negative staph	11	27.5%	2	18.2%	0	0%	2	40%
	Staph aurous	1	2.5%	3	27.3%	0	0%	2	40%
	gram +ve bacilli	1	2.5%	0	0%	1	25%	0	0%
	Pseudomonas	1	2.5%	2	18.2%	0	0%	0	0%
	Klebsiella pneumonia	4	10%	0	0%	0	0%	0	0%
	growth of candida spp.	1	2.5%	0	0%	0	0%	0	0%

The most common organism in patients < 1 year was coagulase negative staph (27.5%), in patients 1- 2 years was staph aurous (27.3%), in patients 2-4 years was gram +ve bacilli (25%) & in patients > 4 years were coagulase negative staph (40%) & staph aurous (40%).

Table (10): Relation between gastric lavage culture results and age categories in studied patients

		Age categories							
		< 1 years (N = 40)		**1 – 2 years (N = 11)**		**2 – 4 years (N = 4)**		**> 4 years (N = 5)**	
Gastric lavage culture results	**No growth**	23	57.%	6	54.5%	1	25%	4	80%
	Coagulase negative staph	0	0%	0	0%	1	25%	0	0%
	Staph aurous	0	0%	2	18.2%	0	0%	0	0%
	Pseudomonas	1	2.5%	1	9.1%	0	0%	0	0%
	Klebsiella pneumonia	8	20%	0	0%	0	0%	0	0%
	Gram -ve bacilli	1	2.5%	1	9.1%	0	0%	1	20%
	Fungal growth	1	2.5%	1	9.1%	1	25%	0	0%
	Strept pneumonia	4	10%	0	0%	1	25%	0	0%
	MRSA	2	5%	0	0%	0	0%	0	0%

This table shows that, the most common organism in patients < 1 year was Klebsiella pneumonia (20%) & the most common organism in patients 1 - 2 years was staph aurous (18.2%), in patients 2-4 years was strept pneumonia (25%) & in patients > 4 years was gram – ve bacilli (20%).

DISCUSSION

Community-acquired pneumonia (CAP) is a significant cause of respiratory morbidity and mortality in children, especially in developing countries (**Hayes et al., 2012**)[7].

In developed countries, the burden of the disease is also high, despite better nourishment and higher levels of all immunizations (**Chetty et al., 2007**)[8].

The present study included 60 children with pneumonia Age of patients ranged between 1 month to 5 years with Mean±SD (1.12 ± 1.45 year).

Our study reported that, male gender (58.3%) was predominance than female (41.7%).

Similar to our results, male sex predominance among infants and children with pneumonia was evident in many previous studies, as *Juven et al., (2003)* who found that 56% of hospitalized infants (mean age 2.8 years) because of pneumonia in Finland were males[9] & **Bose et al., 2006** found that approximately 70% of hospitalized infants (less than 2 years of age) because of pneumonia in India were males[10].

El Seify et al. (2016) study showed that about 56.7% of her cases with CAP were males[5].

Our study showed that fever (96.7%), cough (83.3%) were the most presenting symptoms & tachypnea, fine consenting crepitation's and diminished air entry were the most common clinical signs among studied patients.

These results were in agreement with those of **Juven et al. (2003)[9]** who studied symptoms and signs of CAP in hospitalized children in Finland and found that fever was the most frequent symptom (96%), followed by cough (76%), rhinorrhea (48%) and dyspnea (37%). Children with bacterial pneumonia are often febrile, but those with viral pneumonia or pneumonia caused by atypical organisms may have a low-grade fever or may be afebrile (**Cruz and Wunderlink, 2017**)[11].

Our study showed that, statistically significant relation between increased ESR, CRP & positive blood culture result.

These findings are in agreement with **Lakhani et al. (2013)** who found that, all the patients with positive blood culture had high levels of, ESR & CRP. So these findings can help us in making probable inter pretation, that with increased sepsis, the chances of getting positive blood cultures increases in case of CAP[12].

Our study showed that, the most common organisms identified by blood culture were coagulase negative staph (25%) & staph. aureus (10%), Other bacterial causes include klebsiella pneumonia (6.6%), pseudomonas (5%), gram positive bacilli (3.3%) & growth of candida spp (1.7%).

El Seify et al. (2016) found that only two organisms were isolated by blood culture for studied patients were Klebsiella pneumoniae (3.3%) and Staph. aureus (3.3%)[5].

Leung et al., (2018) found that Streptococcus pneumoniae is the most common bacterial cause across all age groups. Other

important bacterial causes in children younger than 5 years include Haemophilus influenzae, Streptococcus pyogenes, Staphylococcus aureus, and Moraxella catarrhalis[13].

The difference in the results of different studies could be explained by different microbial prevalence and different socioeconomic classes between populations & their vaccination status.

Our stiudy showed that, the commonest organisms identified by gastric lavage culture were Klebsiella pneumonia (13.3%) & strept. pneumonia (8.3%).

These findings were in agreement with (**Taylor et al., 2017**) who studied pneumonia among Chinese children younger than 5 ys found that most frequently identified pathogens were Klebsiella pneumoniae (5.4%), Streptococcus pneumoniae (5.2%), Escherichia coli (5.2%), Staphylococcus aureus (3.9%), Haemophilus influenza (3.6%) and Haemophilus parainfluenzae (3.3%)[14].

Our study showed that, the most frequently sensitive antibiotic for different organisms in both cultures was amoxicillin/ clavulanic acid.

Harris et al. (2011), showed that Amoxicillin is recommended as first choice for oral antibiotic therapy in all children because it is effective against the majority of pathogens which cause CAP, is well tolerated and cheap. Alternatives are co-amoxiclav, cefaclor, erythromycin, azithromycin and clarithromycin. Macrolide antibiotics may be added at any age if there is no response to first-line empirical therapy. Macrolide antibiotics should be used if either mycoplasma or chlamydia pneumonia is suspected or in very severe disease[15].

As regard relation between blood culture results and age categories in studied patients our study showed that, The most common organism in patients < 1 year was coagulase negative staph (27.5%), in patients 1 - 2 years was staph aurous (27.3%), in patients 2-4 years was gram +ve bacilli (25%) & in patients > 4 years were coagulase negative staph (40%) & staph aurous (40%).

While gastric lavage results showed that, the most common organism in patients < 1 year was Klebsiella pneumonia (20%), in patients 1 - 2 years was staph aurous (18.2%) & pseudomonas (18.2%), in patients 2-4 years was strept pneumonia (25%) & in

patients > 4 years was gram –ve bacilli (20%).

Kligman et al. (2020) his study showed that, the causative bacterial pathogens of pneumonia in children between 3 weeks to 3 months were S. pneumonia, H.influanzae & in children between 4 months to 4 years were S.pneumoniae, H.influanzae, mycoplasma pneumonia & group A streptococcus[16].

CONCLUSION

- The common bacterial pathogens causing CAP in Egyptian children below 5 years detected by blood culture were coagulase negative staph (25%) & staph aurous (10%) & by gastric lavage culture were Klebsiella pneumonia (13.3%) & strept pneumonia (8.3%).

- Blood culture had no superiority upon gastric lavage culture or the opposite.

- Amoxicillin/clavulanic was the most frequent sensitive antibiotic for different organisms reported by both culture.

RECOMMENDATION

- Multicenter large studies on national bases are needed to identify most common

pathogens causing CAP in our community.

- Studying risk factors of CAP in our community to help in establishing a national program for CAP prevention.

- Multiple diagnostic approach combining microbiology, serology, and biochemical assays is essential to identify causes of CAP in children.

- Amoxicillin/clavulanic, is recommended as most frequent sensitive antibiotic for treatment of CAP as it is effective against the majority of pathogens witch cause CAP in this age group, is well tolerated &cheap.

Acknowledgment:

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دراسة عن مسببات الامراض البكتيرية المرتبطة بالالتهاب الرئوي المكتسب من المجتمع في الاطفال الذين تقل أعمارهم عن خمس سنوات

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الخلفية: الالتهاب الرئوي المكتسب من المجتمع (CAP) هو سبب مهم لنتشار المرض وحدوث الوفاه الخاصه بالجهاز التنفسى عند الأطفال، وخاصة في البلدان النامية.

الهدف من الدراسة: دراسة البكتريا المسببة للالتهاب الرئوى المكتسب من المجتمع لدى الأطفال الذين تقل أعمارهم عن خمس سنوات في مصر والكشف عن أكثر المضادات الحيوية فعالية.

المرضى والطرق: شملت هذه الدراسة المستقطعة 60 طفلاً مصابًا بالتهاب رئوي تتراوح أعمارهم بين شهر واحد و 5 سنوات، من مستشفى الزهراء الجامعى (المرضى الخارجيون والداخليون)، من أغسطس 2020 إلى فبراير 2021. خضع جميع المرضى لأخذ التاريخ الكامل والفحص السريري، والفحوصات (صوره الدم الكامله، والبروتين التفاعلى سى ومزرعه الم ومزرعه غسيل المعده، تصوير الصدر بالأشعة العاديه والتصوير المقطعي للحالات المستدعيه ذلك.

النتائج: 60 طفلاً (عمر 1.12 ± 1.45 سنة، 35 ذكر (58.3٪) و 25 إناث ((41.7٪)) منهم (51.6٪) بمزرعه دم إيجابية و (43.3٪) بمزرعه غسيل معدي إيجابية. أكثر مسببات الأمراض البكتيرية شيوعًا التي تم تحديدها

بواسطة مزرعــة الــدم هـي العنقوديـات الســالبة للتخثر (25٪) والمكـورات العنقودية الذهبية (10٪)، والأسباب البكتيرية الأخرى تشمل الالتهاب الرئوي كليبســيلا (6.6٪)، الزائفــة (5٪)، العصــيات موجبــة الجـرام (3.3٪) ونمــو المبيضات (1.7٪). أكثر مسببات الأمراض البكتيرية التي تم تحديدها بواسطة زراعة غسيل المعدة هي الالتهاب الرئوي (13.3٪) Klebsiella والعقدية. الالتهاب الرئوي (8.3٪).

الخلاصــة: كانـت الميكروبــات الأكثـر شـيوعًا التـي تـم اكتشـافها عـن طريـق مزراعــة الــدم هـي العنقوديـات الســالبة للـتجلط (25٪)، العنقوديـات الذهبيــة (10٪) و كانـت الميكروبـات الأكثـر شـيوعًا التـي تـم اكتشـافها بواسطة مزراعـة غسيل المعدة هي الكلبسيله الرئويه (13.3%) والعقديه الرئويـة (8.3%). كـان الأموكسيسيلين/ الكلافولانيـك هـو المضـاد الحيـوي الأكثـر حساسية للكائنـات الحية المختلفة التي أبلغت عنها كلتا المزرعتين.

الكلمات الدالة: الالتهاب الرئوي المكتسب من المجتمع، مزرعه الدم، مزرعـه غسل المعدة، أموكسيسيلين/ كلافولانيك، الأطفال.