

Aetiological agent in community acquired pneumonia in patients requiring hospitalization

المسببات الجرثومية لذات الرئة المكتسبة من المجتمع للمرضى الداخليين للمستشفى

Tural Yelderim Baker* Mushrik K. Abood Abdullah Mustafa Qader

*College of Health and Medical Biotechnology
Biotechnology Research Center/ Al-Nahrain University

Abstract

This study was carried out to determine the etiological agents in patients with community-acquired pneumonia (CAP). Ninety-three patients with radiologically confirmed pneumonia admitted to the Medical City, Baghdad Teaching Hospital through the period extended from October 2001 till March 2002. Also to investigate a possible correlation between etiological agents in patients with CAP and comorbid factors including age. The etiological agents were identified from 50 (53.8%) patients with CAP, while no agents were detected in 43 (46.2%) patients. Blood samples were taken from all patients for identification of *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* infection. Sputum samples for culture were taken from 76 (81.7%) patients; bacterial species were isolated from 22 (23.7%) samples. *Streptococcus pneumoniae* was the most frequent typical bacterial pathogen isolated from 17 (18.3%) patients. Atypical pathogens (*C. pneumoniae* and *M. pneumoniae*) using ELISA technique were identified in 22 (23.6%) and 20 (21.5%) respectively. Atypical pathogens were a most common causes of CAP identified from (39.8%) cases. Sixteen (17.2%) of the patients had mixed infections (two pathogens were identified in 12 (75%) and three pathogens in 4 (25%) patients). *C. pneumoniae* and *S. pneumoniae* were the most common mixed organisms found in 6 (37.5%) of patients.

المستخلص

اجريت هذه الدراسة لتحديد المسببات المرضية لدى المرضى المصابين بذات الرئة المكتسبة من المجتمع. كما تم البحث عن وجود علاقة بين المسببات المرضية والعوامل المهنية للإصابة مثل العمر. تم تحديد المسببات المرضية في 50 (53.8%) من المرضى وبذلك يكون عدد المرضى الذين لم تحدد المسببات المرضية لهم 43 (46.2%). وقد اخذت عينات للدم من جميع المرضى لغرض تحديد وجود الإصابة بالبكتريا اللائمطية (*Mycoplasma pneumoniae* and *Chlamydia pneumoniae*). اما عينات القشع فقد جمعت من 76 (81.7%) مريض اعطت 22 (23.7%) عينة منها نتائج موجبة بالزرع المختبري حيث كانت المكورات الرئوية (*Streptococcus pneumoniae*) اكثر انواع

البكتريا النمطية شيوعا فقد عزلت من 17 (18.3%) مريض . و قد اثبتت هذه الدراسة ان البكتريا اللائطية (*Mycoplasma pneumoniae* and *Chlamydia pneumoniae*) و التي تم تحديدها بواسطة طريقة الـ روز المناعي المرتبط بالانظيم (ELISA) هي من اكثر المسببات شيوعا لذات الرئة المكتسب من المجتمع حيث شكلت مجتمعة (39.8%) من مجموع المرضى. تم قياس الاجسام المضادة من نوع (IgM) و التي تؤكد الاصابة الحادة بالـ (*Mycoplasma pneumoniae*) في 22 (23.6%) و بذلك تكون اكثر الجراثيم المحددة شيوعا تتبعها الـ (*Chlamydia pneumoniae*) و التي وجدت في 20 (21.5%) مريض . و قد اظهرت الدراسة ان 16 (17.2%) من المرضى لديهم اصابة مشتركة فقد حدد مسببين مرضيين في 12 (75%) من حالات الاصابات المشتركة و ثلاثة مسببات في اربعة (25%) من المرضى و شكلت اكثر حالات الاصابة المشتركة بين *Chlamydia pneumoniae* و *Mycoplasma pneumoniae* و التي وجدت في 6 (37.5%) من المرضى .

Introduction

Despite advances in the management of severe infectious diseases, community-acquired pneumonia (CAP) remains the major cause of mortality and the six most common cause of death overall [1, 2]. The disease is a common cause of hospital admission and presents challenge to physicians because a causative microorganism can be only found in about 50% of cases [3]. Despite more than a century of microbiological investigations, there is still uncertainty about the relative importance of the various organisms that cause pneumonia [4]. The urgent challenge in the management of CAP is the selection of appropriate antibiotic therapy. However, CAP can be caused by a myriad of pathogens with differing antimicrobial susceptibilities, and no sufficiently rapid

Materials and Methods

This study included 93 patients with CAP. They were 54 males (58%) and 39 females (42%). The age range was 15-86 years

and accurate battery of diagnostic tests for the cause of CAP is available presently. Furthermore, it has proved to be difficult to predict the etiology of CAP on the bases of presenting clinical and radiographic features [5,6]. Thus, initial antibiotic selection usually must be empirical and is based on the results of numerous studies of CAP etiology conducted [7]. The understanding of the pathogens most frequently involved is a key consideration in the choice of empirical antibiotic therapy [1]. A prospective study was conducted in order to determine the etiological agents of community-acquired bacterial pneumonia in adult population requiring hospitalization to guide the empirical antibiotic therapy.

with mean 45 years. Patients were admitted to the Medical City, Baghdad Teaching Hospital between October 2001

and March 2002. Diagnosis of pneumonia was made depending on clinical and radiological findings. Blood samples were collected from all patients, while sputum samples were collected from 76 (81%) of them. 60 (79%) sputum samples were suitable for culture (considering > 25 neutrophils and < 10 epithelial cells as a valid specimen, evaluated by gram-stain

Results

Out of 93 patients studied, the etiological agents were identified in 50 (53.8%) patients either by isolation of the causative organisms on culture media or by detection of the host's specific immune response by serology. While no etiologic agents were detected in 43 (46.2%) patients of the total population studied.

Typical bacterial species causes of pneumonia were isolated from 22 (23.7%) of patients figure (1). The most frequently

and culture). A total of 50 patients with age ≥ 15 years, attend to hospital complaining diseases other than pneumonia, were examined as a control group. ELISA technique (PLATELIA, Sanofi, Japan) was used for evaluation presence a specific IgM-anti *Chlamydia pneumoniae* and IgM-anti *Mycoplasma pneumoniae* antibodies in serum samples.

isolated organism was *S. pneumoniae* which was isolated from 17 (18.3%) patients table (1). Atypical pathogens (*M. pneumoniae* and *C. pneumoniae*) were identified in 37 (39.8%) out of patients (all diagnosed serologically by detection of specific IgM antibodies) as shown in figure (1). Table (1) revealed that *M. pneumoniae* identified in 22 (23.6%), while *C. pneumoniae* was identified in 20(21.5%).

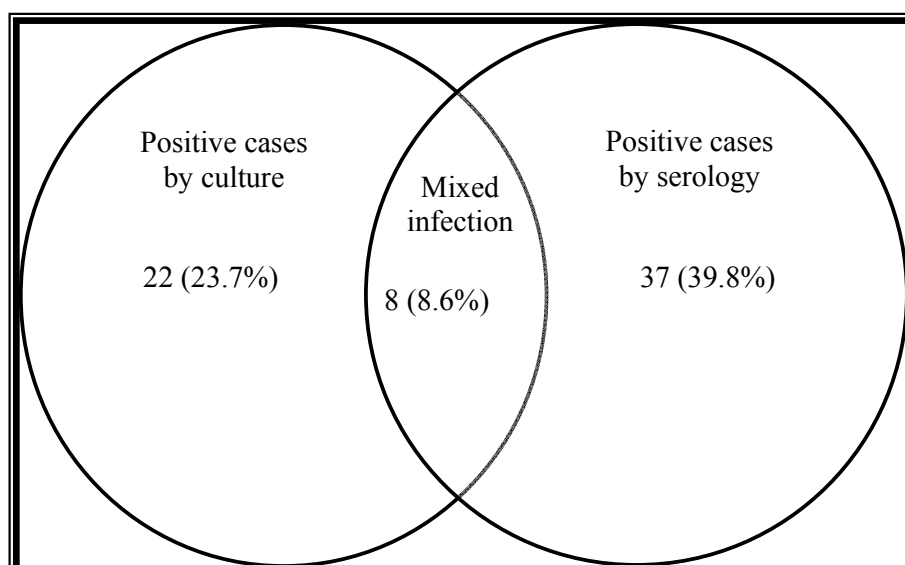


Figure (1): Major etiologic groups of 93 patients with community-acquired pneumonia requiring hospitalization.

Table (1): Numbers and percentages of pathogens detected in 93 adult patients with community-acquired pneumonia requiring hospitalization.

Pathogens	Number	%
Bacterial pathogens	28	30.1
<i>S. pneumoniae</i>	17	18.3
<i>H. influenzae</i>	2	2.15
<i>S. aureus</i>	1	1.07
<i>S. pyogens</i>	1	1.07
<i>M. catarrhalis</i>	1	1.07
Aerobic GNB*	6	6.5
<i>K. pneumoniae</i>	2	2.15
<i>E. coli</i>	2	2.15
<i>P. aeruginosa</i>	2	2.15
Atypical pathogens	42	45.16
<i>M. pneumoniae</i>	22	23.6
<i>C. pneumoniae</i>	20	21.5
Total	70	75.3

In this study only a single identified pathogen was verified in 34 (36.6%) patients, and 16 (17.2%) patients had two or more etiologic agents (mixed infections) table (2). This table also shows that 11 (55%) of 20 *C. pneumoniae* infections were mixed and the most frequent identified pathogen mixed to others.

This study shows that the majority of bacterial pathogens causing pneumonia were identified more frequently (24.7%)

among patients at age 15-24 years, while at least frequent pathogens identified (3.2%) at age 35-44 years. ($p < 0.001$).

Table (3) shows the association between specific microorganisms and specific age group. For the first interval of age (15-24 years) only *M. pneumoniae* plays a highly significant role ($p < 0.001$). For a second interval 25-34 years, only *C. pneumoniae* plays highly significant role ($p < 0.001$).

Table (2): Numbers and percentages of pathogens in 50 patients with identified cause of community-acquired pneumonia requiring hospitalization.

Organism	Single infection No (%)*	Mixed infection with other organism No (%)*	Total No (%)
Typical bacterial pathogens	10 (35.7)	18 (64.3)	28
<i>S. pneumoniae</i>	7 (41.2)	10 (58.8)	17
<i>H. influenzae</i>	-	2 (100)	2
<i>S. aureus</i>	-	1 (100)	1
<i>S. pyogenes</i>	1 (100)	-	1
<i>M. catarrhalis</i>	1 (100)	-	1
<i>K. pneumoniae</i>	-	2 (100)	2
<i>E. coli</i>	-	2 (100)	2
<i>P. aeruginosa</i>	1 (50)	1 (50)	2
Atypical pathogens	24 (70.6)	18 (50)	42
<i>M. pneumoniae</i>	15 (68.2)	7 (31.8)	22
<i>C. pneumoniae</i>	9 (45)	11 (55)	20
Total	34 (48.6)	36 (51.4)	70

* (%) is calculated to the total number of pathogen identified.

Table (3): Impact of age on microbial etiology of community-acquired pneumonia requiring hospitalization.

Age group	Number of patients	Microbial etiology	Proportion of patients with corresponding etiology	Odds ratio	p value
15-24	21	<i>S. pneumoniae</i>	3/17 (17.6%)	0.7	0.590
		<i>C. pneumoniae</i>	2/20 (10%)	0.31	0.230
		<i>M. pneumoniae</i>	16/22 (72.7%)	35.2	<0.001
25-34	16	<i>S. pneumoniae</i>	3/17 (17.6%)	1.03	0.957
		<i>C. pneumoniae</i>	9/20 (45%)	7.7	<0.001
		<i>M. pneumoniae</i>	4/22 (18.2%)	1.09	0.889
35-44	8	<i>S. pneumoniae</i>	1/17 (5.9%)	0.6	0.658
		<i>C. pneumoniae</i>	1/20 (5%)	0.49	0.517

45-54	13	<i>S. pneumoniae</i> <i>C. pneumoniae</i>	2/17 (11.8%) 3/20 (15%)	0.78 1.11	0.771 0.882
55-64	16	<i>S. pneumoniae</i> <i>C. pneumoniae</i>	3/17 (17.6%) 3/20 (15%)	1.03 0.81	0.957 0.768
≥ 65	19	<i>S. pneumoniae</i> <i>C. pneumoniae</i> <i>M. pneumoniae</i>	5/17 (29.4%) 2/20 (10%) 2/22 (9%)	1.84 0.36 0.31	0.310 0.192 0.131

Discussion

The major goal of this study was to establish the microbiological identification of CAP in hospitalized patients. The percentage of patients with positive identified agents was (53.8%), while those with unidentified microbial agents were (46.2%). In the literature, the pathogens responsible for CAP were discovered in < 50 to 70% of patients [8,9,10,11] depending on the types of diagnostic tests. The differences in the results is likely to be a reflection of a number of factors, including using different laboratory tests and various invasive procedures, or difficulty to make a precise diagnosis of the microbial agents causing pneumonia. There were a number of reasons that made difficulty in the identification of microbial agents in this study. First, 53.8% of patients had received antimicrobial treatment before hospitalization, and this obviously lowered the identification yield. Second, the presence of unusual pathogens that go unrecognized (*Legionella*, *Coxiella burnettii* and fungi), the presence of viral infection or anon infection mimic of CAP. Finally, there may have been the presence

of pathogens that are currently not identified or recognized.

In the current study, *S. pneumoniae* was the most frequently isolated bacteria identified as the cause of pneumonia in (18.3 %) patients. In most studies *S. pneumoniae* was the most frequent etiology in adult patients with CAP [12,13,14]. Present study come in contrary with this finding In fact *S. pneumoniae* was identified as the third most frequent pathogen after *M. pneumoniae* and *C. pneumoniae*. Some studies [9,15], reported that there was a change attributable to the increase in the number of patients who are older or who have underlying disease, the development of more sensitive diagnostic technique, and the consideration of *C. pneumoniae* as a respiratory pathogen.

Atypical microbial pathogens (*C. pneumoniae* and *M. pneumoniae*) were identified in (39. 8%) patients with CAP in this study. In contrast to this result higher percentage was reported by different studies [1,6,16, 17,18] might be due to the presence or absence of epidemics of atypical microbial infections. Both *C.*

pneumoniae and *M. pneumoniae* infections occurs in cycles of several years [19, 20]. Another explanation might be due to the use of different serologic techniques and interpretative criteria.

The present study revealed that cases with mixed infections were identified in (17.2%) of patients. The present study disagrees with [14, 17,21]. The difference may be attributed to a high number of the patients who had received prior antibiotics therapy. EL-Solh et al., [18] reported that the cases with mixed infections were more

likely to be identified in those who had not received preadmission antimicrobial treatment.

It is clear from this study that mixed infections most frequently found between typical and atypical pathogens. Atypical pathogens may predispose patient to a second infection is easily seen by their pathological effect on ciliated epithelium. Both infectious pathogens cause cilia stasis which makes the host more susceptible to infection by other more virulent pathogen such as *S. pneumoniae* [22,23].

References

- 1- Falguera M, Sacristán O, and Nogues A (2001). Nonsever Community-acquired pneumonia. Correlation Between Cause and Severity or Comorbidity. *Arch Inter Med*; 161: 1866-72.
- 2- Paganin F, Lilienthal F, Bourdin A, Lugagne N, Tixier F, Ge´nin R, Yvin J-L (2004). Severe community-acquired pneumonia: assessment of microbial aetiology as mortality factor. *Eur Respir J* 2004; 24: 779–785.
- 3- González AR, Falguera M, Nogues A, and Rubio-Caballero M. (1999). Is *Streptococcus pneumoniae* the Leading Cause of Pneumonia of Unknown Etiology? A Microbiological Study of Lung Aspirate in Consecutive Patients with Community-acquired Pneumonia. *The American J of Medicine*; 106: 358-390.
- 4- Jokinen C, Heiskinen L, Junonen H, Kallinen S, Kleemola M, Koskela M, Leinonen M, Saikku P, Stén M, Tarkiainen A, Tukiainen H, Pyörälä K, and Mäkelä. (2001). Microbial Etiology of Community-acquired Pneumonia in the Adult Population of 4 Municipalities in Eastern Finland. *Clin Infect Dis*; 32: 1141-54.
- 5- Niederman MS (1994). Empirical therapy of community-acquired pneumonia. *Semin Respir Infect*; 9: 192-8.
- 6- Park DR, Shetbin VL, and Goodman MS (2001). The etiology of community-acquired pneumonia at an Urban Public Hospital: Influence of Human Immunodeficiency Virus Infection and Initial Severity of Illness. *J of Infectious Diseases*; 184: 268-77.

- 7- Huchon G, Woodhead M, and Gialdroni-Grassi G (1998). Management of adult community-acquired lower respiratory tract infections. *Eur Respir Rev*, 8: 391-426.
- 8- Ishida T, Hashimoto T, Arita M, et al. Etiology of community-acquired pneumonia in hospitalized patients: a 3-year prospective study in Japan. *Chest* 1998; 114:1588-1593.
- 9- Marrie TJ, Peeling RW, Fine MJ, et al. Ambulatory patients with community-acquired pneumonia: the frequency of atypical agents and clinical course. *Am J Med* 1996; 101:508-515.
- 10- Bochud PY, Moser F, Erard P, et al. Community-acquired pneumonia: a prospective outpatient study. *Medicine (Baltimore)* 2001; 80:75-87.
- 11- Wattanathum A, Chaoprasong C, Nunthapisud P, Chantaratchada S, Limpairojn N (2003). Community-Acquired Pneumonia in Southeast Asia: The Microbial Differences Between Ambulatory and Hospitalized Patients. *Chest* 2003;123;1512-1519.
- 12- Bothe R, VanFurth R, and VanderBrock PT (1995). Etiology of community-acquired pneumonia: A prospective study among adults requiring admission to hospital. *Thorax*; 50: 543-547.
- 13- Sopena N, Sabria M, Pedro-Botet ML, Manterola JM, Matas L (1999). Prospective study of community-acquired pneumonia of Bacterial etiology in adults. *Eur J Clin Microbiol Infect Dis*; 18: 852-858.
- 14- Roux AD, Ewig S, Garcí'a E, Marcos MA, Mensa J, Lode H, Torres A (2006). Mixed community-acquired pneumonia in hospitalised patients. *Eur Respir J*; 27: 795-800.
- 15- Allmirall J, Morato I, Riera F, Verdaguer A, Priu R, Coll P, Vidal J, Murgi L, and Valls CF (1993). Incidence of community-acquired pneumonia and *Chlamydia pneumoniae* infection: A prospective multi center study. *Eur Res Jour*; 6: 14-18.
- 16- Macfarlane JT, Lim WS, Boswell M, Harrison TG, Rose D, Leinonen M and Saikku P (1997). Study of community-acquired pneumonia etiology in adults admitted to hospital: Implications for management guidelines. *Thorax*; 56 (4): 296-301.
- 17- Macfarlane J, Holmes W, Gard P, Macfarlane R, Roe D, Weston V, Leinonen M, Saikku P and Myint S (2001). Prospective study of the incidence, etiology and outcome of adult lower respiratory tract illness in the community. *Thorax*; 56 (2): 109-114.
- 18- El-Solh AA, Sikk P, Ramadan F, and Davies J (2001). Etiology of sever pneumonia in the very elderly. *Am J Resp Crit Care Med*; 163: 645-651.

- 19- Grayston JT (1992). Infections caused by *Chlamydia pneumoniae* strain TWAR. *Clin Infect Dis*; 15: 757-763.
- 20- Clyde WA (1993). Clinical overview of typical *Mycoplasma pneumoniae* infections. *Clin Infec Dis*; 17: 32-36.
- 21- Ruiz M, Ewig S, Torres A, Arancibia F, Marco F, Mensa J, Sanchez M, and Martinez JA (1999). Severe community-acquired pneumonia: Risk factors and follow-up epidemiology. *Am J Res Crit Care Med*; 160: 923-929.
- 22- Sarosi GA (1999). Atypical pneumonia, why this term may be better left unsaid. *Postgraduate Med*; 105 (4): 1-8.
- 23- Madhi SA, Klugman KP, Vaccine Trialist Group. A role for *Streptococcus pneumoniae* in virus-associated pneumonia. *Nat Med* 200 4; 10: 811-813.