

Profile of community- and hospital-acquired pneumonia cases admitted to Basra General Hospital, Iraq

G.J. Al-Ghizawi,¹ A.A. Al-Sulami¹ and S.S. Al-TaHER¹

مُرْتَسَم حالات الالتهاب الرئوي المكتسبة من المجتمع والمكتسبة من المستشفيات، في مستشفى البصرة العام، في العراق

غيداء جاسم الغزاوي، أمين عبد الجبار السلمي، سعد شاهين الطاهر

الخلاصة: تمّ على مدى أكثر من 18 شهراً، أخذ 485 مسحة من الخلق وعيئة من البلغم، من مرضى أدخلوا إلى مستشفى البصرة العام، بالعراق، على أساس أنهم مصابون سريراً بالتهاب رئوي. وكان لدى معظم المرضى (94%) التهاب رئوي مكتسب من المجتمع؛ بينما كان 6% منهم (29 مريضاً) مصابين بالتهاب رئوي مكتسب من المستشفى. وكان أعلى معدل لوقوع الالتهاب الرئوي بين المرضى الذكور في عمر ≥ 15 عاماً. وتم تحليل الحالات على أساس نمط الالتهاب الرئوي: «الشعبي» (76.3%) مقابل «الفصي»، (23.7%)، والأولي (81%) مقابل الثانوي (19%). وكانت «العقدية الرئوية» هي أكثر الجراثيم المسببة للمرض شيوفاً بين هذه الحالات (43.9%)، تلتها «المفطورة الرئوية» (19.4%)، ثم نسبة بسيطة من أنواع «المتقلبة» (1.2%). وكان لدى عشرين من المرضى عدوى بالمتفطرة السلية.

ABSTRACT Over an 18-month period 485 throat swabs and sputum samples were taken from patients admitted to Basra General Hospital, Iraq, with a clinical diagnosis of pneumonia. Most patients (94.0%) had community-acquired pneumonia; 29 (6.0%) had hospital-acquired pneumonia. Patients aged ≤ 15 years and males had the highest incidence of pneumonia. Cases were analysed by type of pneumonia: bronchial (76.3%) versus lobar (23.7%), and primary (81.0%) versus secondary (19.0%). The most common pathogen was *Streptococcus pneumoniae* (43.9%) followed by *Mycoplasma pneumoniae* (19.4%); a low percentage were *Proteus* spp. (1.2%). Twenty patients were infected with *Mycobacterium tuberculosis*.

Profil des cas de pneumonie communautaire et nosocomiale admis à l'Hôpital général de Bassora en Iraq

RÉSUMÉ Sur une période de 18 mois, 485 prélèvements de gorge et échantillons d'expectorations provenant de patients admis à l'Hôpital général de Bassora (Iraq) sur diagnostic clinique de pneumonie ont été analysés. La plupart des patients (94,0 %) présentaient une pneumonie communautaire et 29 (6,0 %) une pneumonie nosocomiale. La plus forte incidence de la pneumonie a été observée chez les patients âgés de 15 ans ou moins et de sexe masculin. L'analyse des cas par type de pneumonie a fait apparaître 76,3 % d'atteinte bronchique contre 23,7 % d'atteinte lobaire, une pneumonie primaire dans 81,0 % des cas et secondaire dans 19,0 %. L'agent pathogène le plus répandu était *Streptococcus pneumoniae* (43,9 %), suivi de *Mycoplasma pneumoniae* (19,4 %), le pourcentage de *Proteus* spp. s'avérant faible (1,2 %). Vingt patients étaient porteurs d'une infection à *Mycobacterium tuberculosis*.

¹Department of Biology, College of Education, University of Basra, Basra, Iraq (Correspondence to Al-Sulami: aminabdulah@yahoo.com).

Received: 09/02/05; accepted: 05/06/05

Introduction

Pneumonia is an inflammation of the lungs involving the alveolar ducts and alveolar sacs and associated with acute respiratory tract infection and recently developed radiological signs [1,2]. Pneumonia ranks 6th among the causes of death in the world today [3]. There are a number of different kinds of pneumonia: primary pneumonia, which is usually community-acquired, secondary pneumonia, which occurs when the host or lungs are diseased or weakened, hospital-acquired nosocomial pneumonia and aspiration pneumonia [4].

The pathogens causing pneumonia have not changed much over the years, but their relative importance has changed and there are regional differences [5]. Clinicians need to be aware of the major organisms causing community- and hospital-acquired pneumonia, so that therapy may be started with the most cost-effective and appropriate antibiotics [5].

Streptococcus pneumoniae is one of the major causes of bacterial pneumonia [6,7]. Pneumococci are frequently isolated from the nasopharynx of healthy persons but pneumococcal pneumonia develops as a result of the spread of the bacteria to the lower respiratory tract [8]. *Mycoplasma pneumoniae* is the primary cause of atypical pneumonia in young adults and children, second only to *S. pneumoniae* [9]. *S. pyogenes* may cause a variety of illnesses from very common ones such as pharyngitis to less common severe infections including septicaemia and pneumonia [10,11]. *Staphylococcus aureus* accounts for 2.5% of community-acquired pneumonia and 11% of hospital-acquired pneumonia. *Haemophilus influenzae* is often present in the upper respiratory tract, particularly among patients with chronic obstructive pulmonary disease, whereas *Klebsiella pneumoniae*,

Escherichia coli and *Pseudomonas aeruginosa* have emerged as pathogens of major importance with the introduction of potent antibiotics and the proliferation of intensive care units. There are other etiological agents of pneumonia such as viruses and fungi [12,13]. Ruize et al. [14] described the mixed infection of pneumonia caused by more than one pathogen: these cases include typical and atypical pneumonia.

As there is no previous study of pneumonia in Basra, Iraq, this study of patients admitted to wards in Basra city centre was carried out to investigate the profile of pneumonia (community and hospital-acquired, primary and secondary, broncho- and lobar) and to identify the main bacterial causative agents of pneumonia and to study the difference in etiology between the groups.

Methods

Studied cases

A total of 485 patients with a clinical diagnosis of pneumonia were included in the study: age range 14 days to 87 years. These were all 456 patients admitted to the medical and paediatric wards of Basra General Hospital over the period September 1998 to March 2000 (community-acquired pneumonia cases). The remaining 29 patients were those admitted to the intensive care unit, the dialysis unit and other surgical wards who developed pneumonia after 48 hours after admission (hospital-acquired pneumonia cases).

The patients' case histories were reviewed by the same physician to confirm the diagnosis of pneumonia; other conditions that cause similar respiratory symptoms were excluded. The selection and diagnostic criteria for primary and secondary pneumonia were a positive chest X-ray and clinical features. Clinical features were cough,

sputum, chest pain, wheeze, haemoptysis, shortness of breath and fever. Primary cases were patients with pneumonia only. Patients with heart failure or pneumonia acquired in hospital, tuberculosis, bronchitis, cancer represented secondary pneumonia.

A further group of healthy patients without respiratory complaints (250 males and 250 females), age range 12 days to 88 years, were selected as a control group to exclude organisms from the normal flora cultured from the mouth and oropharynx.

Cultures

Throat swabs (from 243 patients) and sputum samples (from 242 patients) were obtained for culture. Sputum and throat samples were collected daily during the study period and cultured according to standard methods [15]. Isolates were identified according to their culture, morphological and biochemical characteristics [16].

Results

Of the 485 pneumonia patients 209 were female and 276 male. The age and sex distribution of cases is shown in Table 1. Almost half the cases (48.9%) were aged ≤ 15 years and 40.4% were ≤ 5 years. Significant

differences were found in the distribution by age and sex ($\chi^2 = 6.360$; $P = 0.095$). The rate of pneumonia in males was higher than in females (ratio 1.22:1).

Cough was the most common presenting symptom, followed by wheezing, shortness of breath, fever, sputum production chest pain and haemoptysis. Most patients had duration of illness < 1 month; only 63 patients (13.0%) suffered from illness for ≥ 1 month. Overall 90 cases (18.5%) had other family members with pneumonia.

Causative agents

Figure 1 shows the types of microorganism detected in the whole group of patients with pneumonia. The most common agents were *S. pneumoniae* (43.9% of cases) and *M. pneumoniae* (19.4%). *Proteus* spp. was the lowest percentage (1.2%). The causative agent could not be determined for 6.8%. Tuberculosis (i.e. infection with *M. tuberculosis*) was identified in 20 (4.1%) of patients; these were patients who presented without the typical clinical features of tuberculosis (long duration of fever, night sweat, cough, haemoptysis and typical X-ray findings).

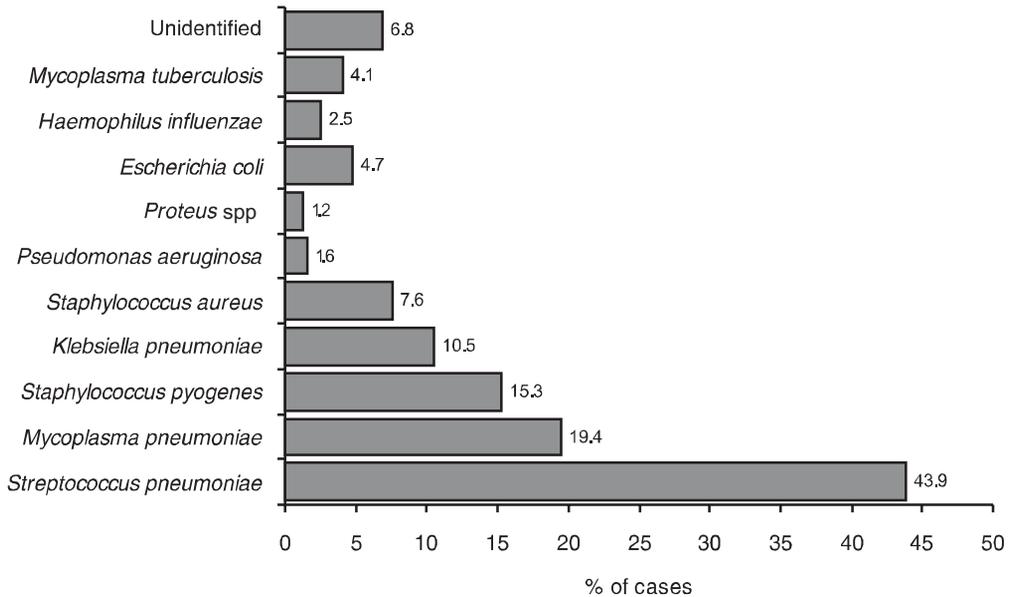
A total of 324 isolates were Gram positive and 100 Gram negative not including *M. pneumoniae* and *M. tuberculosis*. A total

Table 1 Distribution of pneumonia cases by age and sex

Age (years)	Male		Female		Total	
	No.	%	No.	%	No.	%
≤ 15	150	54.3	87	41.6	237	48.9
> 15–30	41	14.9	49	23.4	90	18.6
> 30–45	26	9.4	29	13.9	55	11.3
> 45–60	26	9.4	27	12.9	53	10.9
> 60	33	12.0	17	8.1	50	10.3
Total	276	100.0	209	100.0	485	100.0

$\chi^2 = 6.360$; $df = 3$; $P = 0.095$.

a) All cases (n = 485)



b) Cases with complications (n = 41)

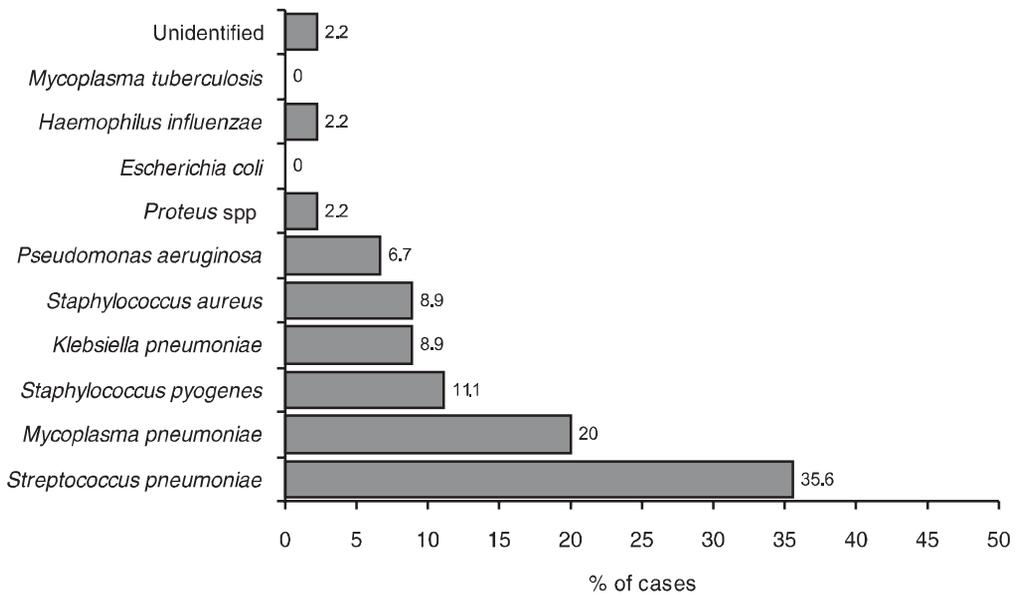


Figure 1 Distribution of pneumonia cases by causative agent (some cases were infected with more than 1 organism)

of 370 cases were single infections and 80 mixed infections. The remaining 35 cases were unidentified.

Throat swabs taken from the 500 control patients showed that normal bacterial species isolated were *S. viridans*, *Neisseria catarrhalis*, *S. albus*, *M. orale*, *M. salivarium* and *M. buccale*.

Relationship of pneumonia infection with complications

In this study 41 patients (8.5%) suffered complications, including death or co-morbidity, heart failure, lung abscesses and pleural effusion (Table 4). The mortality rate was 1.3% (for inpatients follow-up only). There were no significant differences in the pattern of complications by age ($\chi^2 = 2.855$; $P > 0.05$) or sex ($\chi^2 = 0.307$; $P > 0.05$). The highest rate of complications was with *S. pneumoniae* infection (35.6%) (Figure 1).

Community- and hospital-acquired cases

The majority of cases of pneumonia (456, 94.0%) were community-acquired. Of these, 348 were single infections, 74 mixed infections and 34 of unknown etiology. Nosocomial pneumonia was recorded in 29 patients (6.0%) with 22 single infections, 6 mixed infections and only 1 case of unknown etiology. The relationship between causative agents and both kinds of pneumonia is shown in Figure 2.

Broncho- and lobar pneumonia

Bronchopneumonia was diagnosed in 370 (76.2%) patients, while lobar pneumonia was diagnosed in 115 (23.7%) patients. The difference between the types of pneumonia were not statistically significant in relation to age ($\chi^2 = 0.004$; $P = 0.99$), sex ($\chi^2 = 0.001$; $P = 0.99$) or causative agent ($\chi^2 = 4.59$; $P = 0.7$) (Table 2). Unidentified agents accounted for 66 cases of bronchopneumonia

(17.8%) and 3 cases of lobar pneumonia (2.6%).

Primary and secondary pneumonia

Primary pneumonia was recorded in 393 (81.0%) patients and secondary pneumonia in 92 (19.0%) patients. A higher proportion of primary pneumonia was found in the younger age groups (≤ 15 years) but for secondary pneumonia the higher proportion was in older age groups (> 15 years) ($\chi^2 = 12.8$; $P < 0.003$) (Table 3). More males than females had secondary pneumonia but the difference was not statistically significant ($\chi^2 = 1.4$; $P = 0.235$). However, the difference was statistically significant in relation to both types of pneumonia and causative agent ($\chi^2 = 40.67$; $P < 0.00001$). *S. pneumoniae* and *K. pneumoniae* were the commonest pathogens causing secondary pneumonia. Unidentified agents accounted for 67 (17.0%) cases of primary pneumonia and 14 (15.2%) cases of secondary pneumonia.

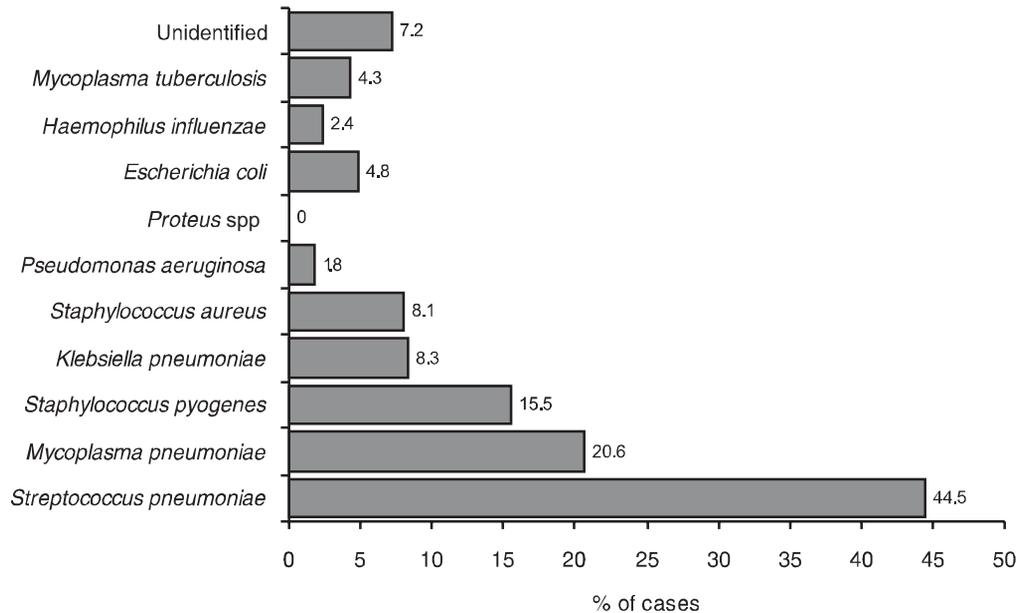
Seasonal variation of pneumonia during the study period

Figure 3 shows the common causative agents in each month of the year. During the study period of 19 months (Figure 3), a high frequency of pneumonia was seen in the winter months especially in February, while August had the fewest admissions. *M. pneumoniae* was not recorded in the early months of the study period and but the frequency rose in the final months of the study. *S. pneumoniae* was the most common pathogen in most months of the study.

Discussion

Basra General Hospital is one of the main referral hospitals in Basra Governorate with multi-specialty services for adults and children. This allows the inclusion of

a) Community acquired (n = 456)



b) Hospital acquired (n = 29)

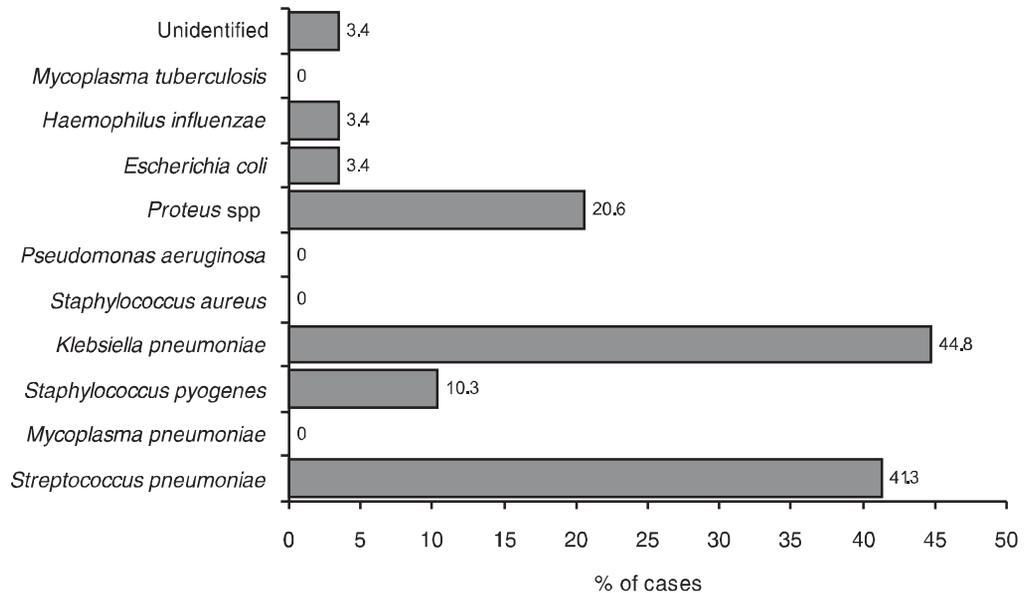


Figure 2 Distribution of community- and hospital-acquired pneumonia cases by causative agent (Some cases were infected with more than 1 organism)

Table 2 Distribution of bronchopneumonia and lobar pneumonia cases by age, sex and causative agent

Variable	Broncho-pneumonia (n = 370)		Lobar pneumonia (n = 115)	
	No.	%	No.	%
Age (years)				
≤ 15	177	47.8	60	52.1
> 15	193	52.2	55	47.8
Sex				
Male	213	57.6	63	54.7
Female	157	42.4	52	45.2
Organism				
<i>Streptococcus pneumoniae</i>	166	44.9	47	40.8
<i>Mycoplasma pneumoniae</i>	68	18.3	26	22.6
<i>Streptococcus pyogenes</i>	60	16.2	14	12.1
<i>Klebsiella pneumoniae</i>	38	10.2	13	11.3
<i>Staphylococcus aureus</i>	33	8.9	4	3.4
<i>Escherichia coli</i>	18	4.8	5	4.3
<i>Hemophilus influenzae</i>	9	2.4	3	2.6
Unidentified ^a	66	17.8	3	2.6

n = total number of cases.

^aViruses, Chlamydia spp., etc.

Table 3 Distribution of primary and secondary pneumonia cases by age, sex and causative agent

Variable	Primary (n = 393)		Secondary (n = 92)	
	No.	%	No.	%
Age (years)				
≤ 15	210	53.4	27	29.3
> 15	183	46.5	65	70.6
Sex				
Male	219	55.7	57	61.9
Female	174	44.2	35	38.0
Organism				
<i>Streptococcus pneumoniae</i>	178	45.2	35	38.0
<i>Mycoplasma pneumoniae</i>	87	22.1	7	7.6
<i>Streptococcus pyogenes</i>	65	16.5	9	9.7
<i>Klebsiella pneumoniae</i>	32	8.1	19	20.6
<i>Staphylococcus aureus</i>	34	8.6	3	3.2
<i>Escherichia coli</i>	17	4.3	6	6.5
Unidentified ^a	67	17.0	14	15.2

n = total number of cases. Some cases were infected with more than 1 organism.

^aViruses, Chlamydia spp., etc.

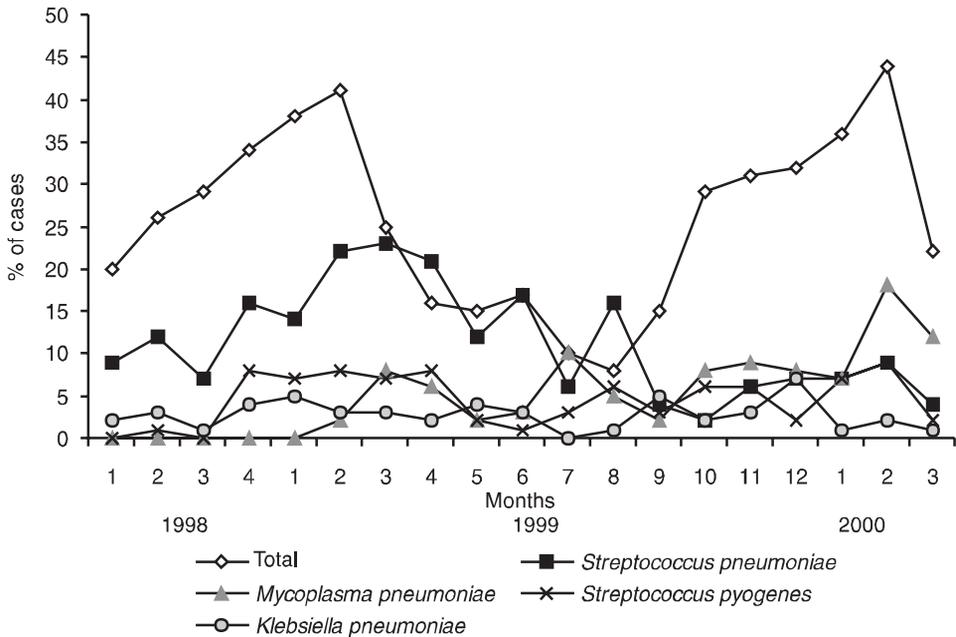


Figure 3 Seasonal variations of pneumonia and common causative agents

cases of pneumonia in different age groups. Although the studied cases did not represent all cases of pneumonia in Basra over the period of study, they are unlikely to be different from the pneumonia cases in the general population. The bias which results from such a selection is probably not big enough to distort the results and conclusions of the study.

A total of 485 cases with pneumonia were seen during this study. The present study revealed a high incidence of pneumonia among young people, especially children < 5 years (40.4%). A significant difference was present between age groups, which agrees with finding reported by others [3, 14]. In the present study the incidence of pneumonia in males was higher than in females (1.22:1) possibly because of a difference in social status between the sexes. This finding is in agreement with that

reported by others, e.g. in the United States of America and Thailand [3, 17].

Clinical findings in conjunction with appropriate laboratory tests will almost always provide an accurate diagnosis of the cause of pneumonia pending results of definitive pathogenic bacterial diagnostic test. Among clinical symptoms, cough was the most frequent symptom in this study, followed by wheezing, shortness of breath, fever, sputum production, chest pain and haemoptysis, similar to that found by others [18, 19]. Hallander et al. showed a duration of cough presentation of 100 days or more for pneumonia [20]; also Grayston reported a duration of cough for 21 days or more [21]. In this study most patients had duration of illness less than 1 month; only 13.0% patients suffered from illness for over 1 month.

Table 4 Complications among pneumonia cases by age and sex

Variable	No. of cases	Death No.	Lung abscesses No.	Complications			Total	
				Heart failure No.	Pleural effusion No.	Others No.	No.	%
<i>Age (years)</i>								
≤ 15	237	3	3	2	3	3	14	5.9
> 15	248	3	10	7	4	3	27	10.9
<i>Sex</i>								
Males	209	3	7	4	4	3	21	10.0
Females	276	3	6	5	3	3	20	7.2
Total	485	6	13	9	7	6	41	8.5

$\chi^2 = 2.855$; $P > 0.05$.

$\chi^2 = 0.307$; $P > 0.05$.

Both bacteria and viruses which are transmitted by contact with infected respiratory secretions can infect a large number of persons in institutional settings or crowded places where close person-to-person contact is common. In this study 90 cases (18.5%) had other family members with pneumonia.

All 29 patients with hospital-acquired pneumonia had serious illnesses with *K. pneumoniae* as the commonest isolated pathogen followed by *S. pneumoniae*, *S. pyogenes*, *Proteus* spp. (which appeared only in nosocomial cases) and *E. coli*, distributed in single and mixed infections. These results agree with those reported by some investigators [22,23] but do not with those who reported *P. aeruginosa* as the most common pathogen in nosocomial cases [24,25].

Definite evidence of the mixed infection with more than 1 organism was shown in 80 cases of community- and hospital-acquired pneumonia. The reported rate of multiple infections in other pneumonia studies have varied widely, for example Fang et al. reported no instance of multiple infection [26]. On the other hand, Marrie et al. found that multiple infections were common (20.5%) [27]. The frequency of

mixed infection is an important consideration for determining appropriate therapy in pneumonia [13].

There were no differences among patients according to sex or age of each type of pneumonia. The most common pathogen was *S. pneumoniae* followed by *M. pneumoniae* then *S. pyogenes* in both types of pneumonia (broncho- and lobar pneumonia). Kauppinen et al. [28] reported similar results in their study of X-ray findings of pneumonia in Finland. Aderele et al. mentioned a similar finding in their report about lower respiratory diseases in hospitalized pre-school children in Nigeria [29]. Miyazaki stated that *H. influenzae* was a common pathogen causing bronchopneumonia [30].

To study the disease from different aspects, the primary and secondary pneumonia cases were analysed. The results showed a high proportion of primary pneumonia cases (81.0%) compared with secondary pneumonia (19.0%). Differences were found in the causative agent. The most common pathogen causing primary pneumonia was *S. pneumoniae* followed by *M. pneumoniae*. In secondary pneumonia the commonest causative agent was *S. pneumoniae* followed by *K. pneumoniae*.

Ruiz et al. reported many kinds of secondary pneumonia in their study which included pulmonary disease associated with community-acquired pneumonia due to *S. pneumoniae*, Gram-negative bacilli and *P. aeruginosa* [14]. In accordance with Ruiz et al. secondary pneumonia was significantly more common in older patients and males more than females, although not significantly so [31]. Gil et al. [32] and Hahn and Golubjatnikov [19] found that adult-onset asthma was frequently associated with *M. pneumoniae* and *C. pneumoniae*. Also, in a prospective study of the etiology of adult community-acquired cases in Singapore Hui et al. found more than half of the patients had pre-existing illness, the most common being diabetes mellitus (21%) [33].

Pneumonia has been studied extensively in many regions of the world, with variable results in regard to the incidence of causative agents and mortality rate. High rates (35.6%, 20.0%) of complications were produced from infection by *S. pneumoniae* and *M. pneumoniae* and low rates of complications were produced by other causative agents. This contrasts with other studies in which approximately 15% of the patients with pneumonia showed complications including dermatologic, renal, musculoskeletal, cardiovascular, gastrointestinal and immunologic manifestations [34–40]. Complications occurred among different ages and in both sexes with no significant differences. The mortality rate in our study was 1.3%. The fatality rate cited in various studies ranged from 1.8%–95% [41–44].

The distribution of all pneumonia patients on a monthly base during the study period revealed that February was the peak month and August had the fewest admissions. The interval from October until February had a relatively high rate of pneumonia admissions. On the other hand, the

most common etiology of pneumonia for each month was *S. pneumoniae*, followed by *M. pneumoniae*. Lieberman et al. [44] and Marston et al. [3] noticed that winter, with its low temperature, is the main reason for the development of community-acquired pneumonia, with the exception of *M. pneumoniae* which has no seasonal predilection. This contrasts with Renner et al. who stated that *M. pneumoniae*, *L. pneumophila* and *H. influenzae* had seasonal variation [45]; also Feikin et al. found a high incidence of *M. pneumoniae* in the summer season [46].

S. pneumoniae was the most common pathogen (43.9%), followed by *M. pneumoniae* (19.4%), whereas *H. influenzae*, *P. aeruginosa* and *Proteus* spp. were responsible for low rates of pneumonia infection. Several investigators have demonstrated that *S. pneumoniae* is the most common pathogen, with *M. pneumoniae* ranking second in children and young adults [13,47–51]. Both *M. pneumoniae* and *S. pyogenes* had a high incidence compared with *S. pneumoniae*, *K. pneumoniae* and *E. coli*. These results agree with other reports [25,52–54]. *Staph. aureus* was present in 7.6% of cases.

The incidence of tuberculosis was low in this study because the cases of tuberculosis with typical history and chest X-rays were excluded from the start, but 20 patients had atypical presentation with atypical pneumonia during the study period. They initially received treatment on the basis of diagnosis of common bacterial pneumonia. They were then referred to hospital and were found to have tuberculosis by acid-fast stain of sputum samples. *M. tuberculosis* was the most common pathogen (21%) in the prospective study of the etiology of adult community-acquired bacterial pneumonia needing hospitalization in Singapore [33]. Also, Ishida et al. found similar results in Japan [55].

References

1. Pathogenesis of infectious diseases In: Atlas RM, ed. *Principles of microbiology*, volume 13, 1st ed. St Louis, Mosby Year Book, 1995:509.
2. Andreoli F et al. Infections of the lower tract. In: Plum F et al., eds. *Cecil Essentials of medicine*, 4th ed. Pennsylvania, WB Sanders, 1997:699–707.
3. Marston BJ et al. Incidence of community-acquired pneumonia requiring hospitalization. Results of a population-based active surveillance Study in Ohio. The Community-Based Pneumonia Incidence Study Group. *Archives of internal medicine*, 1997, 157:1709–18.
4. Crompton G, Haslett C. Diseases of the respiratory system. In: Edwards C et al., eds. *Davidson's principles and practice of medicine*, 7th ed. New York, Churchill Livingstone, 1995:348–58.
5. Cunha BA. Update on community-acquired pneumonias. *Resident and staff physician*, 1998, 44:27–38.
6. Gillespie SH. Aspects of pneumococcal infection including bacterial virulence, host response and vaccination. *Journal of medical microbiology*, 1989, 28:237–48.
7. Marrie T. Bacteraemia pneumococcal pneumonia: a continuously evolving disease. *Journal of infection*, 1992, 24:247–55.
8. Musher DM. Infections caused by *Streptococcus pneumoniae*: clinical spectrum, pathogenesis, immunity and treatment. *Clinical infectious diseases*, 1992, 14:801–9.
9. Duffy MF, Walker ID, Browning GF. The immunoreactive 116 kDa surface protein of *Mycoplasma pneumoniae* is encoded in an operon. *Microbiology*, 1997, 143:3391–402.
10. Rotta J. Streptococcal diseases. *APMIS supplementum*, 1998, 3:3–7.
11. Hoge CW et al. Changing epidemiology of invasive group A streptococcal infections and the emergence of streptococcal toxic shock-like syndrome. A retrospective population-based study. *Journal of the American Medical Association*, 1993, 269:384–9.
12. Goolam-Mahomed A et al. Does primary *S. viridans* pneumonia exist? *South African medicine journal*, 1992, 8:432–34.
13. Kauppinen MT et al. The etiology of community-acquired pneumonia among hospitalized patients during a *Chlamydia pneumoniae* epidemic in Finland. *Journal of infectious diseases*, 1995, 172:1330–5.
14. Ruiz M et al. Etiology of community-acquired pneumonia: impact of age, comorbidity, and severity. *American journal of respiratory and critical care medicine*, 1999, 160:397–405.
15. Collee J et al. Laboratory strategy in diagnosis of infective syndrome. In: Mackie & Macartney *practical medical microbiology*. New York, Churchill Livingstone, 1998.
16. Holt J et al. *Bergey's manual of determinative bacteriology*, 9th ed. Baltimore, William & Wilkins, 1994.
17. Puthavathana P et al. Incidence of *Mycoplasma pneumoniae*, *Chlamydia trachomatis*, and viral infections in pneumonia cases under six months of age, Bangkok, Thailand. *Southeast Asian journal of tropical medicine and public health*, 1994, 25:657–63.
18. Sillis M, Harrison B. Clinical aspects of *Mycoplasma pneumoniae* infection. *Lancet*, 1992, 339:301–2.
19. Hahn DL, Golubjatnikov R. Asthma and chlamydial infection: a case series. *Journal of family practice*, 1994, 38:589–95.

20. Hallander HO et al. *Bordetella pertussis*, *Bordetella parapertussis*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and persistent cough in children. *Scandinavian journal of infectious disease*, 1999, 31:281–6.
21. Grayston JT. *Chlamydia pneumoniae* (TWAR) infections in children. *Pediatric infectious diseases journal*, 1994, 13:675.
22. Al-Alusi FA, Rashid W K. Hospital based study of community-acquired and nosocomial pneumonia. *Journal of the Faculty of Medicine of Baghdad*, 2000, 42:18–23.
23. Bauernfeind A, Petermuller C, Schneider R. Bacteriocins as tools in analysis of nosocomial *Klebsiella pneumoniae* infections. *Journal of clinical microbiology*, 1981, 14:15–9.
24. McNeil M et al. Nosocomial *Pseudomonas pickettii* colonization associated with a contaminated respiratory therapy solution in a special care nursery. *Journal of clinical microbiology*, 1985, 22:903–7.
25. Baltimore RS et al. Epidemiology of pharyngeal colonization of infants with aerobic gram-negative rod bacteria. *Journal of clinical microbiology*, 1989, 27:91–5.
26. Fang G et al. New and emerging etiologies for community-acquired pneumonia with implications for therapy: a prospective multicenter study of 329 cases. *Medicine*, 1990, 69:307–17.
27. Marrie TJ et al. Community-acquired pneumonia requiring hospitalization: 5-year prospective study. *Reviews of infectious diseases*, 1989, 11:586–99.
28. Kauppinen MT, Lahde S, Syrjala H. Roentgenographic findings of pneumonia caused by *Chlamydia pneumoniae*. A comparison with streptococcus pneumonia. *Archives of internal medicine*, 1996, 156:1851–6.
29. Aderelle WI et al. Respiratory syncytial virus-associated lower respiratory diseases in hospitalised pre-school children in Ibadan. *Africa journal of medicine and medical sciences*, 1995, 24:47–53.
30. Miyazaki S. New murin model of bronchopneumonia due to cell bond *H. influenzae*. *Journal of infectious diseases*, 1997, 176:205–9.
31. Ruiz M et al. Severe community acquired pneumonia: risk factors and follow-up epidemiology. *American journal of respiratory and critical care medicine*, 1999, 160:923–9.
32. Gil JC et al. Isolation of *Mycoplasma pneumoniae* from asthmatic patients. *Annals of allergy*, 1993, 70:23–5.
33. Hui KP et al. Prospective study of the etiology of adult community acquired bacterial pneumonia needing hospitalisation in Singapore. *Singapore medical journal*, 1993, 34:329–34.
34. Levy M, Shear N. *Mycoplasma pneumoniae* infections and Stevens-Johnson syndrome. Report of eight cases and review of the literature. *Clinical pediatrics*, 1991, 30:42–9.
35. Friedman MA et al. Inhibition of the scarlet fever exanthema in concurrent varicella and group A streptococcus infection. *Journal of clinical infectious diseases*, 1993, 16:286–7.
36. Agustin ET, Gill V, Cunha BA. *Mycoplasma pneumoniae* meningoencephalitis complicated by diplopia. *Heart and lung*, 1994, 23:436–7.
37. Terada K et al. [Double infection of *C. pneumoniae* and *Mycoplasma pneumoniae* in children.] *Kansenshogaku zasshi*, 1996, 70:1176–80 [in Japanese].
38. Larsen P, Crisp D. Acute bilateral striatal necrosis associated with *Mycoplasma pneumoniae* infection. *Pediatric infectious disease journal*, 1996, 15:1124–6.
39. Handley O, Gray L. The incidence of *Mycoplasma pneumoniae* pneumonia.

- Journal of the American Board of Family Practice*, 1997, 10:425–9.
40. Talkington D F et al. Diagnosis of *Mycoplasma pneumoniae* infection in autopsy and open-lung biopsy tissues by nested PCR. *Journal of clinical microbiology*, 1998, 36:1151–3.
 41. Antela A et al. Neumonias extrahospitalarias: estudio prospectivo de 101 pacientes adultos e inmunocompetentes durante un año. [Community-acquired pneumonia: prospective study of 101 adult, immunocompetent patients for 1 year.] *Enfermedades infecciosas y microbiología clínica*, 1993, 11:525–30.
 42. Ostlergard L, Anderson P. Etiology of CAP. Evaluation by transtracheal aspiration, blood culture, or serology. *Chest*, 1993, 104:1400–7.
 43. Neill AM et al. Community acquired pneumonia: aetiology and usefulness of severity criteria on admission. *Thorax*, 1996, 51:1010–6.
 44. Lieberman D et al. Multiple pathogens in adult patients admitted with community-acquired pneumonia: a one year prospective study of 346 consecutive patients. *Thorax*, 1996, 51:179–84.
 45. Renner E et al. Coinfections of *Mycoplasma pneumoniae* and *Legionella pneumophila* with influenza A virus. *Journal of clinical microbiology*, 1983, 17:146–8.
 46. Feikin DR et al. An outbreak of acute respiratory disease caused by *Mycoplasma pneumoniae* and adenovirus at a federal service training academy: new implications from an old scenario. *Clinical infectious diseases*, 1999, 29:1545–50.
 47. Robins-Brown RM et al. Detection of pneumococci in the upper respiratory tract comparison of media and culture techniques. *Journal of clinical microbiology*, 1983, 16:1–3.
 48. Mackintosh ME et al. Evidence for *Streptococcus pneumoniae* as a cause of respiratory disease in young thoroughbred horses in training. In: Powell DG, Lexington KY, eds. *Equine infectious diseases: proceedings of an international conference*. Kentucky, University Press of Kentucky, 1988:41–4.
 49. Ghosh K, Clements GB. Surveillance of *Mycoplasma pneumoniae* infections in Scotland 1986–1991. *Journal of infection*, 1992, 25:221–7.
 50. Meyer RD, Finch RG. Community-acquired pneumonia. *Journal of hospital infection*, 1992, 22:51–9.
 51. Landyshev S. Changes in the microflora of the sputum and the bronchoalveolar fluid in patients with acute and protected pneumonias. *Problemy tuberkuleza*, 1996, 4:41–3.
 52. Hoffman S. Lack of reliability of primary grouping of beta-hemolytic streptococci. *Journal of clinical microbiology*, 1985, 22:497–500.
 53. Hoffman AM. Sensitivity and specificity of bronchoalveolar lavage and protected catheter brush methods for isolating bacteria from foals with experimentally induced pneumonia caused by *Klebsiella pneumoniae*. *American journal of veterinary research*, 1993, 54:1803–7.
 54. Ieven M et al. Detection of *Mycoplasma pneumoniae* by two polymerase chain reactions and role of *M. pneumoniae* in acute respiratory tract infections in pediatric patients. *Journal of infectious diseases*, 1996, 173:1445–52.
 55. Ishida T et al. Etiology of community-acquired pneumonia in hospitalized patients. A 3-year prospective study in Japan. *Chest*, 1998, 114:1588–93.