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A year's review of bacterial pneumonia at the central hospital of Lucerne, Switzerland

Balthasar L. Hug, Marco Rossi

Summary

Community acquired pneumonia (CAP) remains an important cause of substantial morbidity and mortality in inhospital patients.

We conducted a retrospective study of all patients hospitalised at our hospital with the diagnosis of bacterial pneumonia according to ICD-10 within one year. Of 360 identified charts, 335 met the requirements and were reviewed regarding risk factors, diagnosis, treatment, and overall mortality.

The typical patient hospitalised with pneumonia was elderly (mean 68 years), male (60%), and suffered from comorbidities or predisposing factors (96.4%). A total of 72.8% of pneumonias were localized in the inferior lobes, and 21.1% had bilateral infiltrates. Etiologic agents were searched for in 297/335 patients (87.5%) and were found positive in 33.4%: of 169 blood cultures 9.5% were positive, of 150 sputum cultures taken 46.6% were positive, of 17 serologies taken 58.8% were positive, and of 9 pleural effusions analysed 22.2% were positive. Encapsulated bacteria were the most common found bacterial etiologies, namely *Streptococcus pneumoniae (S. pneumoniae)* in 30.9% of patients with known bacterial etiology, *Haemophilus* in 24.7%, and *Klebsiella* in 12.4%. Methicillin-resistant *S. aureus* was not found. The three most commonly used antibiotics were amoxicillin/clavulanic acid used in 77.3% of patients, clarithromycin (41.2%), and ceftriaxone (16.6%). Mean duration of treatment was 12.1 days. 245/335 (73.1%) patients had a favourable outcome, 16.7% (56/335) of patients had a protracted illness with delayed resolution (i.e. prolonged hospital stay, need for intensive care, intubation or several of these complications).

Overall mortality in our unit was 8.6%.

Key words: bacterial pneumonia; retrospective study; ICD-10; hospitalised, antibiotics

Introduction

Bacterial pneumonia is an important cause of death. In Switzerland death related to a lung disease (including flu, pneumonia, chronic bronchitis, and asthma) is very common: in 1997 the death rate was 87.9/100,000 inhabitants [1]. Pneumonia caused 27.6 deaths/100,000 inhabitants in 1997 which is comparable to the death rate caused by colon cancer (25.8/100,000). In the US pneumonia is the leading cause of death regarding infectious diseases, and the sixth-leading cause of death overall [2]. A general practitioner or internist makes the diagnosis of pneumonia about ten times a year [3]. It is important to make a quick diagnosis and refer the patient to the adequate treatment in order to minimize complication rates; taking blood cultures within 24 hours and administering antibiotics within 8 hours of hospital admission has been shown to be associated with improved survival [4]. To reach this goal, it is helpful to know which diagnostic procedures are successful, what empiric treatment to install, and which aetiologic agents to suspect.

Methods

We conducted a retrospective chart review at our referring hospital (727 active beds and 24,029 hospitalisations in 1998) of all patients 18 years of age or older who were hospitalised between January 1st and December 31st 1998 with bacterial pneumonia according to ICD-10. The ICD-codes included were A 02.2, 20.2, 22.1, 39.8, 48.0-1, 49.8; B 05.2; J 10.0, 11.0, 13, 14, 15.0-2, 15.4, 15.6, 15.9, 16.0, 17.0, 17.8, 18.0-2, 18.8-9, 69.0, 84.8, 85.1. Diagnosis was established at hospitalisation as well as confirmed and coded by the treating doctors.

Data was collected from patient charts without standardisation questionnaire and included age, sex, and different comorbidities predisposing to bacterial pneumonia. Furthermore, we extracted data regarding diagnostics,

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their success rate, the aetiologic agents identified during hospitalisation, the kind of antibiotic treatment applied, treatment duration, and finally overall mortality.

Pathogens were identified using conventional bacteriological techniques (gram stain, culture morphology, biochemistry, and antigen testing) for sputum, blood cultures, and pleural fluid as well as immunological assays for detection of specific antibodies in serum. Sputum, pleural fluid, and positive blood cultures were cultivated on different agar media. Pneumocci were cultivated on Columbia blood agar plates at 5% CO_2, identification was based on gram stain, culture morphology, optochin susceptibility, and bile solubility. Other streptococci were cultured on blood agar and CNA blood agar plates. The strains were then identified by gram stain, culture morphology, and biochemical testing (ATB 32 Strep; Bio Mérieux, France). *Haemophilus influenzae* was grown on chocolate agar plates, and, together with *S. aureus* on blood agar to observe a satelliting phenomenon. Identification included gram stain and evaluation of growth in the presence of V, X, and V+X factor. *Moraxella catarrhalis* was cultured on blood agar plates with subsequent identification by gram stain, oxidase and catalase, and biochemical testing using OF media. *Staphylococcus aureus* was grown on blood agar and CNA agar plates. Identification included gram stain, catalase, clumping factor and free coagulase testing, and biochemical evaluation. Gram negative rods were grown on Mac Conkey agar plates, and further identifiaction was based on fermenting properties. *Enterobacteriaceae* such as *Klebsiella* sp., *Enterobacter* sp., *Citrobacter* sp., *Proteus* sp., and *Morganella* sp. were identified by commercially available biochemical test systems (API 20 E, Bio Mérieux, France). Nonfermenting rods like *Pseudomonas aeruginosa* and *Acinetobacter* sp. were identified by growth on Cetrimide agar and growth at 42°C (*P. aeruginosa*), and gram stain and biochemical testing for *Acinetobacter* sp. (API 20 NE, Bio Mérieux, France).

Serological testing for *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* was accomplished by complement fixation method (Virion, Switzerland), whereas *Legionella* antibody titers were assessed by indirect immmunofluorescence technique (SCIMEDX, USA).

Legionella serology was considered positive with a single titer of 1:256 or more according to Stout [5], *Chlamydia pneumoniae* serology was considered positive if IgM alone or IgG and IgM were both positive.

Table 1

Comorbidities and predisposing factors to pneumonia (n = 335).

	n	%
Chronic obstructive pulmonary disease	81	24.2
Carcinoma ever	70	20.9
Smoking*	59	17.6
Coronary heart disease	37	11
Diabetes mellitus	37	11
Cardiopathies (non coronary heart disease)	25	7.5
Aspiration*, difficulty swallowing	23	6.9
Cerebrovascular insult	18	5.4
Alcoholism	17	5.1
Chronic renal insufficiency, Hemodialysis	13	3.9
Dementia	10	3
Chronic heart failure	8	2.4
M. Parkinson	5	1.5
Immunosuppression		
HIV pos. (men only)	4	1.2
Renal transplant	2	0.6
Chronic lymphatic leukemia	2	0.6
Heart transplant	1	0.3

* smoking and aspiration are considered as predisposing factors not comorbidities

Table 2

Diagnostic features (n = 293). Legionella serology was considered positive with a single titer of 1:256 or more according to Stout [5].

Etiologic agents assigned	33.4%	(98/293)
Blood cultures taken	57.7%	(169/293)
Positive blood cultures	9.5%	(16/169)
Sputum cultures taken	51.2%	(150/293)
Positive sputum cultures	46.6%	(70/150)
Serologic testing taken	6%	(17/293)
Positive serology	58.8%	(10/17)
Pleural effusion analyse	3%	(9/293)
Positive pleural effusion	22.2%	(2/9)

Results

Of 360 identified charts, 25 had to be excluded because diagnosis of pneumonia could not be confirmed according to the documented data, or because of ambulatory setting. A total of 335 medical records were finally included in the study.

Of these 201 (60%) were male. Median age was 68 years (range 18–97 years).

Comorbidities and predisposing factors

Some 96.4% of patients were suffering from comorbidities and factors predisposing to pneumonia, 3.6% (12) had no comorbidities. Comorbidities and predisposing factors are listed in table 1. The three most important comorbidities with implications on survival included chronic obstructive pulmonary disease (COPD) in 24.2% of patients, carcinoma in 20.9%, and smoking as predisposing factor in 17.6%. Coronary heart disease and diabetes mellitus with 11% each were quite common. Immunosupression of any kind was the least common underlying disease: four male patients were HIV positive (1.2%), two were renal transplant recipients (0.6%), two were patients with chronic lymphatic leukemia (CLL) under immunosuppressive drug therapy (0.6%), and one was a heart transplant recipient (0.3%).

Localisation of pneumonia

Pneumonic consolidation documented either clincally, radiologically or both were most commonly found in the inferior lobes (72.8%). The superior lobes were affected in 20% of the patients, and 21.1% (71 patients) had bilateral pneumonic infiltrates.

Diagnostic procedures

Specific etiologies were searched for in 87.5% of patients (293/335) and could be assigned in 33.4% (98/293) of patients (see table 2). A total of 12.5% of patients were diagnosed having pneumonia according to clinical and radiologic aspects without any further diagnostic tests such as blood cultures, sputum or serology. Blood cultures were drawn in different numbers in 57.7% (169/293) of patients; 9.5% of blood cultures grew an organism (16/169). Sputum cultures were taken in 51.2% (150/293) of patients and were positive in 46.6% (70/150). Serology was performed in 6% (17/293) and was positive in 58.8% (10/17). Pleural effusions were analyzed in 9/293 patients (3%) and yielded a positive result in two cases (22.2% of all effusions).

Bacteriology

The most common etiology found was ordinarily encapsulated bacteria: *S. pneumoniae* in 30.9% of patients (n = 97), *Haemophilus* in 24.7% with subspecies *H. influenzae* 75% and *H. parainfluenzae* 25% (see table 3). *S. pneumoniae* was followed by *Klebsiella* 12.4% with *K. pneumoniae* 83%, and *K. oxytoca* 17%. *Pseudomonas* accounted for 12.4% of CAP, thereof 66% *P. aeruginosa* and 33% others like *P. fluorescens* and related bacteria such as *Stenotrophomonas maltophilia*.

Non-encapsulated grampositive bacteria were identified in 9.3% of the patients, including *viridans streptococci* 44% (of these *S. milleri (anginosus)* 33% and others 22%) and *Staphylococcus aureus* 8.6%. No methicillin-resistant *S. aureus* (MRSA) was found.

So-called atypical bacteria like *Legionella pneumophila* (serology =1:256) accounted for 7.5%, and *Chlamydia pneumoniae* for 3.1% of all pneumonias with identified bacterial etiology.

Gramnegative bacteria were rather rare: *Moraxella catharralis* in 5.4%, *Enterobacter* sp. in 4.3%, *Citrobacter* in 3.1%, of these *C. freundii* 66% and *C. diversus* 33%. *Acinetobacter baumanni* accounted for 2.1%, *Proteus vulgaris* for 2.1% and *Morganella morgani* for 1% of known etiologies.

Treatment

An antibiotic treatment was administered to 330 of 335 patients (98.5%), and 1.5% were not treated because of terminal illness. Monotherapy was installed in 45.4% (150/330) patients, two or more antibiotics were given to 54.6% (180/330) patients.

The three most commonly prescribed antibiotics were amoxicillin/clavulanic acid in 77.3%, clarithromycin in 41% and ceftriaxone in 16.6%. The antibiotics are completely listed according to their frequency of prescription in table 4.

Macrolides other than clarithromycin were used only rarely (<1%).

If an aminoglycoside had to be added gentamicin was preferred over tobramycin (3.6 vs. 0.6%). Other aminoglycosides were not used.

The glycopeptid antibiotic vancomycin was prescribed in 1.8% of patients. There was no methicillin-resistant *S. aureus* found or treated.

Duration of therapy

Thirty-three out of 330 (10%) treated patients had to be excluded because of missing data. The remaining 297 (90%) patients were treated with a mean duration of 12.1 days (range 1–42).

Outcome

A total of 245/335 (73.1%) patients had a favourable outcome and were discharged in good condition. Around 16.7% (56/335) of patients had a protracted illness with delayed resolution and either prolonged hospital stay, need for intensive care, intubation, or several of these complications. Five out of 335 (<1%) patients could not be categorized because of unspecific documentation, or transfer to other hospitals.

Overall mortality due to pneumonia or other illnesses was 8.6% (29/335 patients).

Table 3

Bacteriology (n = 97).

	%	n
1. Bacterial etiologies (listed according to frequency)		
S. pneumoniae	30.9	30
Haemophilus spp.	24.7	24
– *H. influenzae*		18
– *H. parainfluenzae*		6
Klebsiella spp.	12.4	12
– *K. pneumoniae*		10
– *K. oxytoca*		2
Pseudomonas spp.	12.4	12
– *P. aeruginosa*		8
– others *(Stenotrophomonas m., P. fluorescens* u.a.)		4
Streptococci	9.3	9
– *S. viridans*		4
– *S. milleri (anginosus)*		3
– others		2
*S. aureus**	8.2	8
Moraxella catharralis	5.4	5
Enterobacter sp.	4.3	4
Citrobacter spp.	3.1	3
– *C. freundii*		2
– *C. diversus*		1
Acinetobacter baumanni	2.1	2
Proteus vulgaris	2.1	2
Morganella morgani	1	1
2. So-called "atypical bacteria"		
*Legionella pneumophila***	7.5	7
Chlamydia pneumoniae	3.1	3

* Methicillin-resistant Staphylococci were not found
** Titer = />1:256

Table 4

Antibiotic treatment* (n = 330).

	%	n
Amoxicillin/Clavulanic acid	77.3	255
Clarithromycin	41.2	136
Ceftriaxone	16.6	55
Gentamicin	3.6	12
TMP/SMX	3	10
Ciprofloxacin	2.1	7
Penicillin	1.8	6
Vancomycin	1.8	6
Amoxycillin	1.8	6
Metronidazol	1.5	5
Clindamycin	1.2	4
Cefuroxim	1.2	4
Cefepime	0.9	3
Ceftazidim	0.6	2
Doxycyclin	0.6	2
Tobramycin	0.6	2
Erythromycin	0.3	1
Azithromycin	0.3	1

* According to frequency of prescription

Discussion

The typical patient hospitalised with pneumonia was elderly (mean 68 years), a male (60%), and suffered in 96.4% of the cases from comorbidities such as COPD, carcinoma, cardiovascular disease or others. These findings are in line with the population based study by Marston et al. [6]: the annual incidence of CAP was highest among the elderly (>65 years) amounting to 993/100,000 inhabitants compared to the middle-aged (45–64 years) with 248/100,000 inhabitants.

The annual incidence of CAP found by Marston [6] was significantly higher in men than women (291.4/100 000 vs. 244.8/100 000, p <0.001) with highest rates among elderly males (56% higher than elderly females).

The prevalence of at least one comorbid illness is relatively high in our study population compared to the study by Meehan et al. (1997; 96.4% vs. 58.2%). This difference seems to be explained by the fact that Meehan [4] did not include predisposing comorbidities like diabetes or immunosuppression. Comorbidities such as history of cancer, which applied to 21% of our patients may lead to higher mortality. In their study including 18,016 in-hospital patients with pneumonia and history of cancer, Iezzoni et al. [7] found a significantly raised mortality of 16.7% with an odds ratio of 2.32 (95% CI 2.04–2.65, p <0.001), i.e. mortality in these patients was twice as high compared to the overall mortality in our study.

A microorganism considered as etiologic was found in 33.4% of our patients comparable to the results of Gilbert et al. [8], who found a bacterial etiology in 29.9% of 1328 in-patients. Including both bacterial and viral etiologies Almirall et al. (2000) found in a mixed in- and out-patient setting (n = 232) an identifiable etiology in 44.8% of patients.

In our study serology was taken in 6% of diagnosed patients (17/293) and had a high yield of 58.8% (10/17) positive results; sputum cultures were taken in 57.7% (169/293) of diagnosed patients and yielded positive results in 9.5% of patients (16/169). Pleural effusions yielded a positive result in 22.2% and blood cultures in 9.5%.

Sputum with Gram's staining and culture are generally recommended provided that cytologic screening confirms the presence of lower-airway secretions and that the specimens are obtained before antibiotic treatment [9]. A recent study [10] showed a high sensitivity and specificity of gram's stain for pneumonia caused by *S. pneumoniae* (57% and 97%) and *H. influenzae* (82% and 99%). Good quality samples of sputum (<10 squamous cells and >25 leukocytes/low-power field) were obtained in 39% of patients.

The frequency of positive blood cultures is consistent with a cumulative frequency of 11% in 12 series including 2,935 patients [9]. Meehan et al. [4] found that blood cultures drawn within the

first 24 hours of hospital admission were associated with lower than 30-day mortality (OR 0.90, 95% CI, 0.81–1.00). Positive blood cultures may be associated with a slightly, but not significantly ($p = 0.44$) higher mortality: Iezzoni et al. [7] found a mortality rate of 14.4% (OR 1.08, 95% CI 0.88–1.32) in patients with positive blood cultures, suggesting that a positive blood culture may indicate a more severe or prolonged bacteremia. Blood cultures are more frequently positive in pneumococcal pneumonia (25%) associated with a poor prognosis [11].

Drainage of pleural effusions is indicated in patients with significant effusion, enigmatic pneumonia, or failure to respond to therapy [9, 11]. Usually pH, glucose, protein, lactate dehydrogenase and white blood cell counts are measured.

Although serology was positive in almost 60% of our samples the cost-benefit ratio of serology for *Legionella* species, *Mycoplasma* spp. and *Chlamydia* spp. may be low because of missing impact on decision making [6]. Another unsolved problem is the interpretation and cut-off levels of serology titer results. Serology is therefore generally not advised. Urinary antigen detection of *Legionella pneumophila* serogroup 1 has good sensitivity and specificity but may require up to five days to become positive [11].

As expected encapsulated bacteria like *S. pneumoniae* was the most common etiologic agent. Marston et al. [6] found in their population-based study of 2,776 patients hospitalised for pneumonia a rate of 12.6%, Bartlett [9] identified 5 to 18% (USA) *S. pneumoniae* compared to 31% in our study. The higher pneumonia rate probably derives from the fact that Marston included viral as well as bacterial etiologies. Another possibility is geographical differences in the incidence of pneumococcal disease.

H. influenzae ranges as second most common bacterial etiology with 24.7% of known etiologies compared to 6.6% in the study of Marston and 3 to 10% in the survey of Bartlett. Almirall et al. [12] found in their population-based study in Barcelona, Spain, only one case of *H. influenzae* pneumonia in 114 causative agents identified. Methodological bias or geographical parameters might cause this difference: Whereas all of our patients were hospitalised, 38.6% of patients in the study of Allmirall et al. were not. Therefore incidence of *H. influenzae* pneumonia might be more common in hospitalised patients with CAP and be an indicator of more severe illness.

Klebsiella species accounted for 12.4% of our patients hospitalised with CAP compared to 1% in the study of Marston et al. including definite, probable, and possible bacteriologic diagnosis.

Geographical variations can make it difficult to compare the incidence of bacterial etiologies and antibiotic recommendations for CAP treatment. One vivid example is the prevalence of penicillin-resistant *S. pneumoniae*, which show highest rates in South Africa, the Far East, and Southern Europe. Even within one single country dramatic variations may be found [13].

The three most commonly used antibiotics were amoxicillin/clavulanic acid, clarithromycin and, ceftriaxone. Because of the above-mentioned geographical variations in bacterial etiologies for CAP and resistance patterns, evidence-based recommendations for therapy are scarce. Read [13] suggests that aminopenicillins, macrolides, fluoroquinolones, and some cephalosporins may have equivalent efficacy in the treatment of mild to moderate CAP. For the choice of treatment of severe pneumonia there is little data. In our study, gentamicin was given as the fourth most used antibiotic; this is comparable to the multicenter, prospective study of Gilbert et al. [8] where it was the third most used antibiotic after cefuroxime and erythromycin.

The mean duration of antibiotic therapy was 12.1 days in our study. Because of the above-mentioned restrictions regarding local distribution and resistance patterns of microorganisms there exist no strict recommendations. All the same, treatment duration seems to be comparable in different countries. In the prospective multicenter cohort study by Gilbert et al. [8] of 927 out-patients and 1,328 in-patients the median treatment durations were 12 days for out-patients and 14 days for in-hospital including upon-discharge treatment.

Marston et al. [6] found in their study of 2,776 in-patients with CAP an overall mortality rate of 8.8% which resembles our results with an overall mortality of 8.6%. Studies including out-patients like the survey of Almirall et al. [12] show lower mortality rates (5%). In-patients with CAP may show mortality rates of up to 10 to 25% [9].

There are several restrictions to this study that have to be mentioned. First, it is retrospective and not prospective. Data had to be extracted on the basis of medical charts, which implied partially incomplete answers to questions such as how pneumonia was exactly diagnosed. Second, diagnosis was made by attending doctors without structured diagnostic procedure but on clinical grounds. This approach reflects local hospital practice. Third, bacteriological spectra may differ from one geographical area to another. It therefore may be difficult to compare study results from different areas and antibiotic therapy recommmendations.

In conclusion we found the typical patient with CAP to be elderly and male and suffering from comorbidities. Drawing blood cultures and sputum Gram's stain are the most common diagnostic procedures, and are recommended to identify and treat properly a possible causative microbial agent after initial empiric antimicrobial therapy. Encapsulated bacteria are a dominant cause of pneumonia beeing treated most often with amoxicillin/clavulanic acid, clarithromycin, or ceftriaxone. With an overall mortality of 8.6% in our survey, pneumonia remains an important cause of death in patients requiring hospitalisation.

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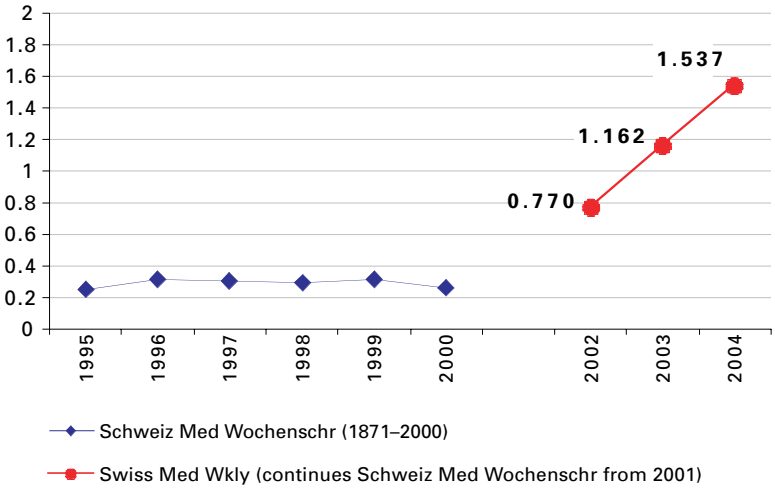

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