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Community acquired acute bacterial and atypical pneumonia in Saudi Arabia

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Abstract

Background **Rational treatment of pneumonia requires knowledge of the likely aetiological diagnosis in any community. Little is known about the pattern and outcome of pneumonia in Saudi Arabia.**

Methods **A total of 567 pneumonic episodes in adult patients from the Al-Qassim area were reviewed retrospectively.**

Results **Patients had a mean age of 42·7 years, with 103 patients (18%) aged 13 to 20 years and 103 (18%) aged 60 or more. Almost two thirds of the episodes (64%) occurred in men. An aetiological diagnosis was established in 351 (62%) cases, with 145 episodes being due to pneumococcal infection and 129 to *Mycoplasma pneumonia*. Inhospital mortality was 6% (35 patients). Age over 60 years, aspiration pneumonia, and Gram negative infection were the only factors that independently predicted adverse outcome on adjusted mortality analysis.**

Conclusion **This analysis of pneumonia in the Al-Qassim area indicates the pattern and prognosis of acute bacterial and atypical pneumonia that requires admission to hospital in the central region of Saudi Arabia. It should provide a basis for developing rational treatment for community acquired pneumonia in Saudi Arabia.**

Respiratory tract infections are probably the most common infections in otherwise healthy people.[1] Bacterial pneumonia is a chief cause of death and illness, particularly in developing countries, among those who are very young or very old.[2 3]

Little is known about the pattern of respiratory tract infections in Saudi Arabia, and most reports provide only radiological data.[4–7] None of the reports have documented clinical features, microbiological pattern, treatment, or outcome adequately. The only clinically oriented series, reported from Jeddah, comprised only 150 patients.[8]

The lack of information on the clinical and microbiological pattern of community acquired acute bacterial or atypical pneumonia in Saudi Arabia prompted us to analyse various aspects of this common disorder among adult Saudi patients admitted to a referral hospital in the Al-Qassim region.

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Patients and methods

Patients admitted to the 570 bed King Fahd Specialist Hospital, the main tertiary care facility for the Al-Qassim area, were studied. This is a predominantly rural area with some new urban districts. It has two main cities and is located in the central region of Saudi Arabia. Around 550 000 people live in Al-Qassim, of whom some 450 000 are Saudis.

Included in this retrospective analysis were all the Saudi patients over the age of 12 years admitted with the diagnosis of community acquired acute bacterial or atypical pneumonia between July 1987 and December 1990. Patients were identified from the hospital computerised database file according to the *International Classification of Diseases* (9th edition). Eligible patients had to fulfil the criteria for having community acquired pneumonia to be included in the study: a history of lower respiratory tract infection, consistent physical findings, and a chest radiograph showing consolidation of a part of parts of one or both lungs for which antibiotics were prescribed.[9] Patients with nosocomial pneumonia occurring more than three days after admission were excluded, as were those with clinical, radiological, microbiological, immunological, or serological evidence of non-bacterial pneumonia. We also excluded patients with a confirmed diagnosis of pulmonary tuberculosis based on more than one of the following criteria: a supportive clinical history and physical findings, a strongly positive tuberculin reaction, positive Ziehl-Neilsen staining for acid fast bacilli, a positive sputum culture for *Mycobacterium tuberculosis*, a positive diagnostic analysis of pleural fluid and pleural biopsy, and a therapeutic response to antituberculous treatment.

On admission the following were routinely requested: a full blood count and differential white cell count, blood urea, serum creatinine, and electrolyte concentrations, liver function tests, arterial blood gas analysis, and a chest radiograph. The chest radiograph was repeated after about two to three weeks or earlier if indicated. Samples of sputum were also obtained routinely for culture and Gram staining of smears. A set of three blood cultures was obtained on admission from most patients. Laboratory and microbiological investigations were repeated during the hospital stay as indicated by the clinical course.

In this analysis a sputum sample was considered to be of a good quality if it had fewer than 10 epithelial cells and more than 25 leucocytes per low power field and was not

considered to be contaminated or to contain only oropharyngeal flora. A good quality Gram stained smear was defined as having diagnostic value when large numbers of organisms with characteristic staining and morphological features were present. Only the results from such smears were considered in identifying the aetiological diagnosis. A quantitative sputum culture procedure was used when more than 10^6 colony forming units per ml were required to incriminate the pathogen.

Pneumococcal capsular antigens were not determined. *Mycoplasma pneumoniae* infection was diagnosed from supporting clinical and radiological evidence and by determining IgM cold agglutinins and by complement fixation tests with an enzyme linked immunosorbent assay (ELISA). Complement fixation was considered to be positive if it showed an antibody titre of 1:128 with a fourfold or greater rise in the titre in a repeat test. In a few patients in whom non-mycoplasma atypical pneumonia was suspected two paired samples were tested for antibodies to chlamydia and rickettsia and by indirect immunofluorescence for antibody to *Legionella pneumophila*. Antibodies to influenza A and B, parainfluenza, and respiratory syncytial viruses were also sought. Patients were excluded from the analysis if a fourfold rise in the titre was shown in association with a supportive clinical course on the basis that the pneumonia had a viral cause.

Deaths were attributed to pneumonia when the clinical course was consistent with this interpretation and no other concurrent or intercurrent disease process was incriminated as responsible for the patient's death. No necropsies were performed.

DATA ANALYSIS AND STATISTICAL METHODS

Medical records and microbiological and radiological data were reviewed retrospectively. A computerised database was constructed to contain all relevant information. Comparisons of proportions were made with a χ^2 test of homogeneity with Yates' correction when appropriate or with Fisher's exact test. Comparisons of means of continuous variables were made with a two tailed t test and one way analysis of variance. When the assumptions of normality and equal variance were not met as detected by Levene's test, the non-parametric test of Kruskal-Wallis was used. The stepwise binary logistic regression method was used to identify factors that independently predicted in-hospital mortality.[10] A two sided $p < 0.05$ was considered to be significant. All data analyses were carried out with the P1D, P4F, P3D, P7D, and PLR programs of the BMDP statistical package.[11]

Results

A total of 567 patients were eligible for the study. Nineteen patients (3·4%) had more than one episode of pneumonia; only the first episode was included in our analysis. Patients' mean age was 42·7 (SD 21·9) years; 103 (18%) patients were aged between 13 and 20 years and another 103 (18%) were older than 60. Almost two thirds of the patients (64%; 361) were male, and 206 (36%) were female. In 305 patients (54%) a total of 324 coexisting diseases were present (table 1).

AETIOLOGICAL DIAGNOSIS

An aetiological diagnosis was established in 351 (62%) patients (table 2). In most cases organisms were identified by Gram stained sputum smears and by sputum or blood culture, or both; bronchoalveolar lavage was used in 12 patients and transbronchial lung biopsy in five. *Streptococcus pneumoniae* and *M pneumoniae* infections were the most common, occurring in 274 patients, while *Haemophilus influenzae* and *Staphylococcus aureus* infections accounted for 49 episodes (table 2). Gram negative enteric pathogens were the sole organisms causing pneumonia in seventeen patients and they occurred with other pathogens in a further six patients.

Table 3 shows the results of bacteriological investigations. A high diagnostic yield was attained from properly collected sputum samples. Positive blood culture was achieved in only 92 (19%) of those examined; of the patients with pneumococcal pneumonia, 56 (38%) had bacteraemia. Among the 129 patients with *M pneumoniae* the diagnosis was made only from supporting clinical manifestations and the disease course (129 patients), suggestive radiological data (61 patients; 47%), testing for IgM cold agglutinins (positive in 60 out of 116 patients tested; 52%) and complement fixation tests by ELISA (positive in 72 out of 104 patients tested; 69%). Non-mycoplasma atypical pneumonia was suspected in only 23 patients (8%), in whom serological tests showed *Chlamydia trachomatis* (positive in one out of 11 patients), no rickettsia antibodies (nine patients), and no *Legionella pneumophila* antibodies (nine patients).

CLINICAL FEATURES

The clinical, laboratory, and radiological differences between *S pneumoniae* and *M pneumoniae* infections are given in table 4. Significant differences were noted for age and haematological measures between the two groups. The expected difference in the prevalence of cold agglutinins was found.

The admission rates for pneumococcal and

Table 1 Coexisting disorders in 305 patients with pneumonia

Disease	*No of patients*
Asthma	61
Diabetes mellitus	76
Cardiovascular disease	35
Chronic obstructive lung disease	39
Neurological disorders	31
Liver disorders	24
Carcinoma:	
Non-pulmonary	21
Bronchogenic	19
Renal failure	17
Major surgery	1

Table 2 Aetiological diagnosis in 567 episodes of bacterial and atypical pneumonia

Aetiological diagnosis	*No of patients (%)*
Streptococcus pneumoniae	145 (26)
Mycoplasma pneumoniae	129 (23)
Haemophilus influenzae	37 (6·5)
Staphylococcus aureus	12 (2)
Klebsiella pneumoniae	9 (1·6)
Pseudomonas aeruginosa	4 (0·7)
Escherichia coli	3 (0·5)
Infection:	
Mixed	6 (1)
Other	6 (1)
Total	351 (62)
No pathogen identified	153 (27)
No microbiological investigations	63 (11)

mycoplasmal pneumonia during the short winter season (December to February) was compared with that during the rest of the year, when the temperature is generally hot with little variability. Of 145 admissions for pneumococcal pneumonia 43 (30%) occurred during the winter months compared with 35 out of 129 (27%) admissions for mycoplasma pneumonia.

Aspiration pneumonia accounted for 18 episodes (3%). The mean age (53·4 years) of this group was significantly greater than that of the other groups, and it consisted mainly of men (68%); in addition, Gram negative infections accounted for the majority of the episodes (67%).

TREATMENT

Initial antibiotic treatment included benzylpenicillin (277 episodes), ampicillin or amoxycillin (102 episodes), erythromycin (91 episodes), tetracycline (62 episodes), cotrimoxazole (52 episodes), aminoglycosides (23 episodes), extended spectrum penicillin (16 episodes), cephalosporins (nine episodes), and others (12 episodes). Combined treatment was mainly used as initial treatment in the management of aspiration and Gram negative pneumonias. Antibiotic sensitivity data were poorly documented and could not be analysed.

OUTCOME

Thirteen patients (2·3%) experienced non-fatal complications and 35 patients (6%) died of their pneumonia. Table 5 gives the unadjusted mortality data classified according to categorised variables. Older age, coexisting illness, non-mycoplasma pneumonia, aspiration pneumonia, and Gram negative infection were associated with higher death rates. Adjusted mortality analysis carried out with a stepwise inclusion of all the variables in table 5 as independent variables identified older age (60 years and over), aspiration pneumonia, and Gram negative infection as the only factors that independently predicted an adverse outcome ($p < 0{\cdot}002$, $< 0{\cdot}035$, and 0·037, respectively).

Table 3 Results of microbiological investigations

Method	*No tested (No of good quality)*	*No positive (%*)*
Sputum Gram stain	567 (345)	198 (57)
Culture:		
Sputum	567 (345)	203 (59)
Blood	489 (489)	92 (19)
Pleural fluid	52 (52)	11 (21)
Bronchoscopic bronchoalveolar lavage	12 (12)	10 (83)
Transbronchial lung biopsy	5 (5)	4 (80)

*Of good quality investigations.

Discussion

In our predominantly adult population about a fifth of patients were older then 60. This age pattern together with the predominance of men could be due to the high frequency of pneumococcal infection and its possible high prevalence among those in whom no pathogen was identified or satisfactory microbiological investigation carried out. The younger mean age of our patients reflects the age distribution of the population of Saudi Arabia.

The occurrence of coexisting diseases in our patients (54%) was greater than that in a large British study (43%), in which only 22% needed hospital admission.[12] A recent study from France reported coexisting disease in 55% of patients with community acquired pneumonia,[13] and a high concomitant illness rate was noted in 68% of patients with pneumonia from the western region of Saudi Arabia.[4]

Despite our inability to test for pneumococcal capsular antigen and the infrequent use of invasive diagnostic procedures, an aetiological diagnosis was made in 62% of episodes, which compares favourably with the results of other studies.[12 13] This high microbiological isolation rate may be due to the small number of patients receiving antibiotics before admission to hospital, although this could not be ascertained in a retrospective study. Other pathogenic agents may not have been identified because they were screened for infrequently, such as those causing non-mycoplasma atypical pneumonia, but this probably did not influence the overall validity of our data to a great extent. In a prospective epidemiological study of community acquired pneumonia *L pneumophila* was identified in five patients and chlamydia in one patient out of 116 investigated serologically.[13]

The high frequency of pneumococcal pneumonia in our study conforms with the high prevalence of this infection worldwide.[2 9 12-15] Similarly, a high frequency of mycoplasma pneumonia was also noted, confirming earlier studies.[16 17] Analysis of seasonal variability failed to show the reported predilection of pneumococcal pneumonia for the winter months and mycoplasma pneumonia for the summer season.[2 9] The extremely long and hot summer in Saudi Arabia may account for the lack of any specific pattern.

Pneumonia currently accounts for about 40% of hospital deaths and ranks among the 10 leading causes of death in the United States.[18] Mortality is higher in developing countries.[2 9] In our series in-hospital mortality was 6% with only a 3% mortality in patients with pneumococcal pneumonia. The mortality for pneumococcal pneumonia is comparable with that reported recently in England[12] and lower than

Table 4 Clinical, laboratory, and radiological differences between patients with S pneumoniae and those with M pneumoniae

Variable	S pneumoniae	M pneumoniae	p value
No of patients (%)	145 (26)	129 (23)	—
Mean age (SD) (years)	42·1 (1·7)	36·9 (1·4)	0·03
Sex:			0·40
No (%) men	92 (63)	89 (69)	
No (%) women	53 (37)	40 (31)	
No of associated diseases (No of patients)	116 (84)	79 (56)	0·9
Mean (SE) white cell count ($\times 10^9$/l)	14·6 (0·8)	6·8 (0·4)	<0·0001
Mean polymorphs (SE) (%)	71·4 (1·1)	65·4 (1·2)	0·0003
Mean band (SE) (%)	5·5 (0·5)	3·3 (0·5)	0·07
Mean lymphocyte (SE) (%)	16·7 (0·9)	21·5 (1·1)	0·001
Cold agglutinins (%):			<0·0001
Not done	100 (69)	13 (10)	
Positive	5 (3)	56 (43)	
Negative	40 (28)	60 (47)	

Table 5 Unadjusted mortality data on 567 patients

Variable	Alive No (%*)	Died No (%*)	p value
Age (years)			<0·0001
⩽20	100 (98)	2 (2)	
21–40	191 (97)	5 (3)	
41–60	138 (95)	6 (5)	
>60	103 (83)	22 (18)	
Sex			0·90
Male	339 (94)	22 (6)	
Female	193 (94)	13 (6)	
Coexisting disease			0·0002
Not present	239 (98)	4 (2)	
Present	293 (90)	31 (9)	
PNEUMONIA			
Pneumococcal *v* others			0·20
Pneumococcal	140 (97)	5 (3)	
Others	392 (93)	30 (7)	
H influenzae v others			0·90
H influenzae	34 (92)	3 (8)	
Others	498 (94)	32 (6)	
Mycoplasmal *v* others			0·002
Mycoplasmal	129 (100)	0 (0)	
Others	403 (92)	35 (8)	
Aspiration *v* others			<0·0001
Aspiration	6 (33)	12 (67)	
Others	526 (96)	23 (4)	
Gram negative *v* others			<0·0001
Gram negative	12 (55)	10 (45)	
Others	520 (95)	25 (5)	

*Row percentage.

other quoted rates of 5% to 19%.[9] None of our patients with mycoplasma pneumonia died. A high mortality was linked to Gram negative and aspiration pneumonias.

Multivariate analysis identified only three variables that independently predicted a higher pneumonia related mortality. Age over 60 was associated with a mortality of 18% and confirmed the results of other studies.[19] The second independent variable was aspiration pneumonia with an estimated mortality of 67%. Patients in this category were also older and predominantly men. Aspiration of upper gastrointestinal contents is a well recognised risk factor for the development of the adult respiratory distress syndrome, which has a poor outcome.[20 21] The third variable to influence the model was Gram negative infection, which carried a mortality of 45% and confirms results in other countries.[22] Our results suggest that patients with one or more of these risk factors should receive optimal supportive care and a combination of broad spectrum antibiotics.

The analysis of 567 community acquired pneumonic episodes occurring in the Al-Qassim area showed the characteristics of this disease in central Saudi Arabia.

The analysis was retrospective and restricted to Saudi adults who needed to be admitted to hospital. It provides data that should help in choosing empirical treatment for such patients. A prospective study to validate our data is warranted.

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