

HOSPITALISED PATIENTS WITH COMMUNITY-ACQUIRED PNEUMONIA DUE TO ATYPICAL RESPIRATORY PATHOGENS

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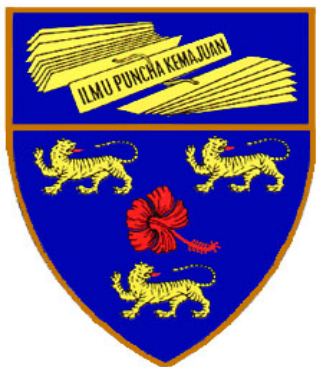
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INTRODUCTION

- The atypical respiratory bacteria *Mycoplasma pneumoniae*, *Chlamydomphila pneumoniae*, and *Legionella* spp. are increasingly recognised as common and important pathogens in community-acquired pneumonia (CAP).
- There is a paucity of published studies on the prevalence of these pathogens as causes of CAP in Malaysia.

OBJECTIVES

- To determine the frequency of atypical respiratory pathogens as a cause of CAP in patients requiring hospitalisation
and
- To define the clinical features of CAP due to these pathogens

PATIENTS AND METHODS ¹

- This was a prospective study
- Consecutive patients aged 12 years and above admitted with CAP to the University Malaya Medical Centre, Kuala Lumpur from August 2000 to December 2002.
- Excluded were patients
 - with no convalescent serum specimens for serological testing
 - with tuberculosis
 - on immunosuppressive therapy
 - with HIV infection

PATIENTS AND METHODS ²

Microbiological data were based on the results of

- blood culture and culture of expectorated sputum or other respiratory tract specimens for bacteria obtained before commencement of antibiotic therapy in hospital
- and
- serological tests for atypical respiratory pathogens on paired acute- and convalescent-phase sera obtained 4-6 weeks apart

PATIENTS AND METHODS ³

Pathogens were considered **definite** aetiological agents of CAP when

- isolated from blood or pleural fluid cultures
- associated with a 4-fold or greater rise in the antibody titre between paired acute- and convalescent-phase sera for
 - *Mycoplasma pneumoniae* (to \geq 1:160)
 - *Legionella pneumophila* (to \geq 1:128) or
 - *Chlamydomphila pneumonia*

PATIENTS AND METHODS 4

Pathogens were considered **probable** cause of CAP if any one of the following conditions was present:

- heavy or moderate growth of a predominant bacterial pathogen on culture of sputum or other respiratory tract specimens collected within 24 hours of admission and prior to the commencement of antibiotic therapy in hospital **together** with the finding on sputum Gram's stain of a bacteria compatible with the culture result
- light growth of a pathogen in which the sputum Gram's stain revealed a bacteria compatible with the culture result
- growth of multiple bacteria in equal magnitude if Gram's stain revealed the presence of multiple organisms consistent with those isolated in culture

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Pathogens were considered **probable** cause of CAP if any one of the following conditions was present:

- an antibody titer of $\geq 1:160$ for *Mycoplasma pneumoniae* in either the acute-phase or convalescent-phase serum specimen
- an antibody titer of $\geq 1:1,024$ for *Legionella pneumophila* in either the acute-phase or convalescent-phase serum specimen
- an IgG antibody titer of $\geq 1:512$ for *Chlamydomphila pneumoniae*

STATISTICAL ANALYSIS

Results are expressed as

- the mean \pm standard deviation for continuous variables or
- as a percentage of the group from which they were derived for categorical variables.

In **univariate analyses**, differences between groups were tested for significance with

- chi-square (χ^2) test with Yates' correction or Fisher exact test where appropriate for categorical variables and
- Student's *t*-test for continuous variables

In **multivariate logistic regression analyses**, variables with *p* values less than 0.15 in univariate analyses were used simultaneously

RESULTS ¹

No. of patients	234
Mean age (SD) (range) yrs	54.0 (19.7) (13 – 97)

Co-morbidity	No. of patients
None	90
Diabetes mellitus	60
Hypertension	55
Bronchial asthma	29
COPD	26
Cardiac (IHD, CCF, CRHD)	18, 5, 1
Bronchiectasis	5
Chronic renal insufficiency	4
Interstitial lung disease	1
Old stroke	1

RESULTS ¹

No. of patients	234
Mean age (SD) (range) yrs	54.0 (19.7) (13 – 97)

RESULTS ²

Microbial aetiological agents of CAP

Aetiological agent	No. of patients		
	Definite	Probable	Total
<i>Klebsiella pneumoniae</i>	6	21	27 (11.5%)
<i>Mycoplasma pneumoniae</i>	14	12	26 (11.1%)
<i>Chlamydophila pneumoniae</i>	2	10	12 (5.1%)
<i>Streptococcus pneumoniae</i>	7	4	11 (4.7%)
<i>Haemophilus influenzae</i>	1	9	10 (4.3%)
<i>Legionella pneumophila</i>	3	5	8 (3.4%)
<i>Pseudomonas aeruginosa</i>	-	8	8 (3.4%)
<i>Staphylococcus aureus</i>	3	3	6 (2.6%)
<i>Enterobacter spp</i>	-	4	4 (1.7%)
<i>Escherichia coli</i>	0	3	3 (1.3%)
<i>Acinetobacter baumannii</i>	1	1	2 (0.9%)
<i>Burkholderia pseudomallei</i>	1	0	1 (0.4%)
<i>Citrobacter spp</i>	-	1	1 (0.4%)
<i>Stenotrophomonas maltophilia</i>	-	1	1 (0.4%)
<i>Streptococcus milleri</i>	1	-	1 (0.4%)
None identified			123 (52.6%)

RESULTS ²

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<i>Staphylococcus aureus</i>	3	3	6 (2.6%)
<i>Enterobacter sp</i>			4 (1.7%)
<i>Escherichia coli</i>			3 (1.3%)
<i>Acinetobacter k</i>			2 (0.9%)
<i>Burkholderia pseudomallei</i>	1	0	1 (0.4%)
<i>Citrobacter spp</i>	-	1	1 (0.4%)
<i>Stenotrophomonas maltophilia</i>	-	1	1 (0.4%)
<i>Streptococcus milleri</i>	1	-	1 (0.4%)
None identified			123 (52.6%)

Atypical respiratory pathogens were identified in 46 patients (19.7%)

RESULTS ³

Comparison of clinical features of CAP due to *Mycoplasma pneumoniae* and that of CAP due to other pathogens

Clinical features	Aetiological agent		P value
	<i>M. pneumoniae</i> (n = 26)	Other pathogens (n = 208)	
Mean age (\pm SD), yr	34.4 \pm 18.2	56.2 \pm 18.5	<0.001
Age below 65 yrs	22 (84.6%)	127 (61.1%)	0.018
Smoker	10 (38.5%)	103 (49.5%)	0.287
No underlying co-morbid illness	17 (65.4%)	73 (35.1%)	0.005
Mean duration of symptoms before admission (days)	5.9 \pm 3.8	6.7 \pm 6.9	0.576
Chest radiograph changes			
Lobar consolidation	11 (42.3%)	52 (25.0%)	
Patchy	14 (53.8%)	149 (71.6%)	
Reticulonodular	1 (3.8%)	7 (3.4%)	0.162

Data are presented as mean \pm SD, or No. of patients (%)

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RESULTS 4

Comparison of clinical features of CAP due to *Mycoplasma pneumoniae* and that of CAP due to other pathogens

Clinical features	Aetiological agent		P value
	<i>M. pneumoniae</i> (n = 26)	Other pathogens (n = 208)	
No. of lobe(s) involved on chest radiograph			
One	21 (80.8%)	143 (68.8%)	
Two or more	5 (19.2%)	65 (31.2%)	0.301
Mean TWBC on admission (x 10 ⁹ /L)	11.9 ± 7.8	14.6 ± 6.7	0.060
TWBC on admission ≤11 x 10 ⁹ /L	17 (65.4%)	69 (33.2%)	0.003
Serum sodium on admission (mmol/L)	137 ± 4	135 ± 6	0.0281
Mean PSI score	27 ± 34	65 ± 38	<0.001
Patients in PSI class I or II	23 (88.5%)	113 (54.3%)	0.001

Data are presented as mean ± SD, or No. of patients (%)

TWBC = total white blood cell count

PSI = pneumonia severity index

RESULTS ⁵

Univariate and multivariate analyses of clinical features associated with CAP due to *Mycoplasma pneumoniae*

Clinical feature / No. of patients(%)	Univariate analysis				Multivariate analysis	
	<i>Mycoplasma pneumoniae</i> n = 26	Other n = 208	OR (95% CI)	P value	OR (95% CI)	P value
Aged below 65 years	22 (84.6)	127 (61.1)	3.51 (1.17 – 10.55)	0.018	1.08 (0.28 – 4.19)	0.917
No co-morbid illness	17 (65.4)	73 (35.1)	3.49 (1.48 – 8.23)	0.005	2.86 (1.13 – 7.21)	0.023
Total white blood cell count $\leq 11 \times 10^9/L$	17 (65.4)	69 (33.2)	3.81 (1.61 – 8.97)	0.003	4.07 (1.66 – 9.99)	0.002
PSI class I or II	23 (88.5)	113 (54.3)	6.45 (1.88 – 22.13)	0.001	5.53 (1.28 – 23.99)	0.011

Variables were included in the logistic regression model for the multivariate analysis when univariate comparisons yielded a level of significance of $p < 0.15$

RESULTS 6

Comparison of clinical features of CAP due to *Chlamydia pneumoniae* and that of CAP due to other pathogens

Clinical features	Aetiological agent		P value
	<i>C. pneumoniae</i> (n = 12)	Other pathogens (n = 222)	
Mean age (\pm SD), yr	68.5 \pm 15.0	53.2 \pm 19.6	0.008
Aged 65 yrs and above	9 (75.0%)	76 (34.2%)	0.010
Smoker	8 (66.7%)	105 (47.3%)	0.241
No underlying co-morbid illness	3 (25.0%)	87 (39.2%)	0.380
Mean duration of symptoms before admission (days)	9.9 \pm 11.1	6.4 \pm 6.3	0.082
Chest radiograph changes			
Lobar consolidation	7 (58.3%)	56 (25.2%)	
Patchy or reticulonodular	5 (41.7%)	166 (74.8%)	0.029

Data are presented as mean \pm SD, or No. of patients (%)

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RESULTS ⁷

Comparison of clinical features of CAP due to *Chlamydia pneumoniae* and that of CAP due to other pathogens

Clinical features	Aetiological agent		P value
	<i>M. pneumoniae</i> (n = 12)	Other pathogens (n = 222)	
No. of lobe(s) involved on chest radiograph			
One	8 (66.7%)	156 (70.3%)	
Two or more	4 (33.3%)	66 (29.7%)	0.755
Mean TWBC on admission (x 10 ⁹ /L)	14.9 ± 6.9	14.3 ± 6.9	0.746
TWBC on admission >11 x 10 ⁹ /L	9 (75%)	139 (62.6%)	0.543
Serum sodium on admission (mmol/L)	134 ± 4	135 ± 6	0.469
Mean PSI score	75 ± 31	60 ± 40	0.197
Patients in PSI class I or II	5 (41.7%)	131 (59%)	0.236

Data are presented as mean ± SD, or No. of patients (%)

TWBC = total white blood cell count

PSI = pneumonia severity index

RESULTS ⁸

Comparison of clinical features of CAP due to *Legionella pneumophila* and that of CAP due to other pathogens

Clinical features	Aetiological agent		P value
	<i>C. pneumoniae</i> (n = 8)	Other pathogens (n = 226)	
Mean age (\pm SD), yr	67.5 \pm 17.7	53.5 \pm 19.6	0.048
Aged 65 yrs and above	6 (75.0%)	76 (34.2%)	0.010
Smoker	3 (37.5%)	110 (48.7%)	0.723
No underlying co-morbid illness	4 (50.0%)	86 (38.1%)	0.488
Mean duration of symptoms before admission (days)	8.9 \pm 9.8	6.5 \pm 6.5	0.324
Chest radiograph changes			
Lobar consolidation	2 (25.0%)	61 (27.0%)	
Patchy or reticulonodular	6 (75.0%)	165 (73.0%)	1.000

Data are presented as mean \pm SD, or No. of patients (%)

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RESULTS ⁹

Comparison of clinical features of CAP due to *Legionella pneumophila* and that of CAP due to other pathogens

Clinical features	Aetiological agent		P value
	<i>M. pneumoniae</i> (n = 8)	Other pathogens (n = 226)	
No. of lobe(s) involved on chest radiograph			
One	6 (75.0%)	158 (69.9%)	
Two or more	2 (25.0%)	68 (30.1%)	1.000
Mean TWBC on admission (x 10 ⁹ /L)	13.6 ± 8.0	14.3 ± 6.8	0.788
TWBC on admission >11 x 10 ⁹ /L	5 (62.5%)	143 (63.3%)	1.00
Serum sodium on admission (mmol/L)	135 ± 5	135 ± 6	0.961
Mean PSI score	63 ± 33	60 ± 40	0.833
Patients in PSI class I or II	5 (62.5%)	131 (58%)	1.000

Data are presented as mean ± SD, or No. of patients (%)

TWBC = total white blood cell count

PSI = pneumonia severity index

CONCLUSIONS

- The atypical respiratory pathogens were identified in 19.7% of patients hospitalised for CAP
- CAP due to *M. pneumoniae* was less severe and was more common in younger patients and those without comorbid medical illnesses
- *C. pneumoniae* and *L. pneumophila* were more likely to cause CAP in patients aged 65 years or older