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

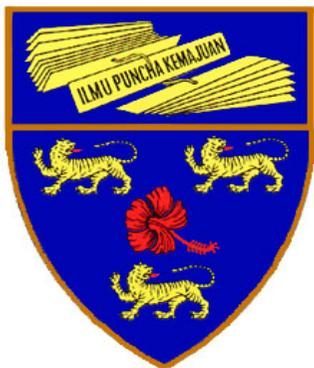**Chong-Kin LIAM, Yong-Kek PANG, Shyamala POOSPARAJAH**

Department of Medicine

Faculty of Medicine / University Malaya Medical Centre

University of Malaya

Kuala Lumpur

Malaysia

INTRODUCTION

- The atypical respiratory bacteria *Mycoplasma pneumoniae*, *Chlamydophila 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.

Ngeow YF *et al*. An Asian study on the prevalence of atypical respiratory pathogens in community-acquired pneumonia. *Int J Infect Dis* 2005; 9:144-53

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
  - *Chlamydophila 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

Continue ….

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 *Chlamydophila pneumoniae*

STATISTICAL ANALYSIS

Results are expressed as

- the mean ± 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 ($\chi 2$) 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
Klebsiella pneumoniae	6	21	**27 (11.5%)**
Mycoplasma pneumoniae	14	12	**26 (11.1%)**
Chlamydophilia pneumoniae	2	10	**12 (5.1%)**
Streptococcus pneumoniae	7	4	**11 (4.7%)**
Haemophilus influenzae	1	9	**10 (4.3%)**
Legionella pneumophila	3	5	**8 (3.4%)**
Pseudomonas aeruginosa	-	8	**8 (3.4%)**
Staphylococcus aureus	3	3	**6 (2.6%)**
Enterobacter spp	-	4	**4 (1.7%)**
Escherichia coli	0	3	**3 (1.3%)**
Acinetobacter baumanii	1	1	**2 (0.9%)**
Burkholderia pseudomallei	1	0	**1 (0.4%)**
Citrobacter spp	-	1	**1 (0.4%)**
Stenotrophomonas maltophilia	-	1	**1 (0.4%)**
Streptococcus milleri	1	-	**1 (0.4%)**
None identified			**123 (52.6%)**

RESULTS [2]

Microbial aetiological agents of CAP

Aetiological agent	No. of patients		
	Definite	Probable	Total
Klebsiella pneumoniae	6	21	**27 (11.5%)**
Mycoplasma pneumoniae	14	12	**26 (11.1%)**
Chlamydophilia pneumoniae	2	10	**12 (5.1%)**
Streptococcus pneumoniae	7	4	**11 (4.7%)**
Haemophilus influenzae	1	9	**10 (4.3%)**
Legionella pneumophila	3	5	**8 (3.4%)**
Pseudomonas aeruginosa	-	8	**8 (3.4%)**
Staphylococcus aureus	3	3	**6 (2.6%)**
Enterobacter spp			**4 (1.7%)**
Escherichia coli			**3 (1.3%)**
Acinetobacter b...			**2 (0.9%)**
Burkholderia pseudomallei	1	0	**1 (0.4%)**
Citrobacter spp	-	1	**1 (0.4%)**
Stenotrophomonas maltophilia	-	1	**1 (0.4%)**
Streptococcus milleri	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

	Aetiological agent		
Clinical features	*M. pneumoniae* (n = 26)	Other pathogens (n = 208)	*P value*
Mean age (± SD), yr	34.4 ± 18.2	56.2 ± 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 ± 3.8	6.7 ± 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 ± SD, or No. of patients (%)

Continue on next slide ….

RESULTS [4]

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

	Aetiological agent		
Clinical features	*M. pneumoniae* (n = 26)	Other pathogens (n = 208)	*P value*
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 $\pm$ 7.8	14.6 $\pm$ 6.7	0.060
TWBC on admission $\leq$11 x 10^9/L	17 (65.4%)	69 (33.2%)	0.003
Serum sodium on admission (mmol/L)	137 $\pm$ 4	135 $\pm$ 6	0.0281
Mean PSI score	27 $\pm$ 34	65 $\pm$ 38	<0.001
Patients in PSI class I or II	23 (88.5%)	113 (54.3%)	0.001

Data are presented as mean $\pm$ 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	
	Mycoplasma pneumoniae 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 x 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 *Chlamydophilia pneumoniae* and that of CAP due to other pathogens

	Aetiological agent		P value
Clinical features	*C. pneumoniae* (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 (%)

RESULTS [7]

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

Clinical features	Aetiological agent		P value
	M. pneumoniae (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 $\pm$ 6.9	14.3 $\pm$ 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 $\pm$ 4	135 $\pm$ 6	0.469
Mean PSI score	75 $\pm$ 31	60 $\pm$ 40	0.197
Patients in PSI class I or II	5 (41.7%)	131 (59%)	0.236

Data are presented as mean $\pm$ 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

	Aetiological agent		
Clinical features	***C. pneumoniae* (n = 8)**	**Other pathogens (n = 226)**	*P value*
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 (%)

RESULTS [9]

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

	Aetiological agent		
Clinical features	*M. pneumoniae* (n = 8)	Other pathogens (n = 226)	*P value*
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 $\pm$ 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