

# Risk factors for adverse outcome in adult patients with invasive pneumococcal disease

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## Objectives

The aim of this study was to identify the microbe- and host-related risk factors associated with adverse outcome in adult patients hospitalized with invasive pneumococcal disease (IPD).

## Materials and Methods

Retrospective study included adult patients in whom *S.pneumoniae* was isolated from blood, CSF or other primary sterile site; subsequent identification of serotype and antibiotic susceptibility testing was performed at the National Institute of Public Health. Continuous variables are described as medians and interquartile ranges (IQR), categorical variables are described as absolute frequencies and proportions. Continuous variables were compared using Mann–Whitney test and categorical variables with Fisher's exact test.

## Results

One hundred and ninety-one cases of IPD have been identified, 114 M and 77 F, with median age 57 years (IQR 45–67). *S. pneumoniae* was isolated from blood in 168 patients, from CSF in 42 and from other sterile site in 10 cases. The most frequent clinical form of IPD was pneumonia (120 cases; 62.8%), followed by meningitis (55; 28.8%), sepsis without focus (6; 3.1%), primary peritonitis (3; 1.6%), septic arthritis (3; 1.6%) and other form in 4 cases (2.1%). The most frequently isolated serotypes included 3 and 4 (both in 20 cases; 10.5%), 7F (18; 9.4%), 8 and 14 (both 13; 6.8%) and 1 (11; 5.8%). The antibiotic resistance among isolated strains was low, there were 12 strains resistant to tetracycline, 7 to erythromycin; however, no strain was resistant to penicillin.

### Clinical characteristics of the study group

	Lethal outcome	Non-lethal outcome	P
Number of cases	47	144	
Age (years)	60 (50-78)	42 (18-56)	0.026
Male	30	84	0.608
Duration of hospital stay	8 (2-15)	11 (1-17)	<0.001
Intensive care	37	70	<0.001
Community-acquired infection	36	133	0.007
Development of septic shock	30	28	<0.001
Pneumonia	25	95	0.122
Meningitis	17	38	0.201
Other clinical form	5	11	0.548

### Comorbidities associated with fatal outcome

	Lethal outcome	Non-lethal outcome	P
Immunodeficiency	15	18	0.004
Haematological malignancy	9	6	0.003
Dyslipidemia	26	54	0.041
Atherosclerosis	26	36	<0.001
Cerebrovascular disease	12	11	<0.001

### Symptoms and clinical findings associated with fatal outcome

	Lethal outcome	Non-lethal outcome	P
Tachycardia at admission	39	85	0.003
Hypotension at admission	23	43	0.022
Hyposaturation at admission	25	38	0.001
Altered mental status	39	56	<0.001
Cyanosis	8	10	0.049

Eighty-three cases of IPD were caused by pneumococcal serotype with high invasive potential and 67 cases by serotype with low invasive potential. The subjects infected by a low invasive strain were older [age median 58 (IQR 47-70) vs. 53 years (37-62),  $p=0.031$ ], more often required intensive care [45 (67.2%) vs. 33 (39.8%),  $p=0.001$ ] and their case fatality ratio was significantly higher [20 (29.9%) vs. 12 (14.5%),  $p=0.028$ ]. In total, there were 47 (24.6%) lethal outcomes in our study group. The statistically significant risk factors associated with adverse outcome are listed in the attached tables.

### Microbe-related risk factors

	Lethal outcome	Non-lethal outcome	P
High-invasive serotype	12	71	0.006
Low-invasive serotype	20	47	0.223
PCV7	16	51	1.000
PCV 13	28	101	0.210

## Discussion

IPD range among significant causes of morbidity and mortality especially in the elderly and immunocompromised. The results of this study show that these patients are vulnerable especially to infection with low invasive serotypes such as 3, 6A/B, 8, 9N, 19F, 23F; however, these infections are associated with poor outcome. Thus the vaccine for the above mentioned risk groups should target in particular these serotypes. The identification of laboratory and clinical markers associated with adverse outcome could contribute to risk stratification during the initial assessment as well.

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