Risk factors and pneumococcal serotypes associated with severe invasive pneumococcal disease in adults in France, the SIIPA study

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Background

Invasive pneumococcal diseases (IPD) remain a major cause of morbi-mortality worldwide. Despite the overall decrease in circulation of the conjugate vaccine serotypes, the decline in disease incidence in adults was lower than expected. From 2015, we observed an increase in the incidence of infections associated with serotypes 3 and 8 in adults over 65 years. However, thanks to this evolution, little is known about factors associated with severity. The aim was to identify factors associated with severe presentations of IPD including host factors and serotypes.

Methods

We conducted a longitudinal prospective cohort study, from 2014 to 2022, in 25 French centers, including adults patients with nonmeningitis IPD (NCT03983616). Demographic, clinical and microbiological data, including serotypes, were prospectively collected. Severe cases were defined as those with severe sepsis, or intensive care unit admission. Factors associated with severe IPD were identified using a logistic regression with a multivariable fractional polynomial model.

Table: characteristics of IPD patients according to the severity, 2014-2022, SIIPA, CNR-ORP, France

	No severe cases	Severe cases	Univariate	Multivariate	
	n= 1005	n= 913	p value	OR [95% CI]	p value
Age (years old)			**0.001**		**0.001**
≥ 65	661 (65,8)	587 (64,3)		2.66 [1.49-4.75]	
Sex			**0.016**		
Male	533 (53,0)	534 (58,5)			
Site of infection			**0.012**		
Pneumonia or pleuresia	770 (76,6)	750 (82,1)		1	
Isolated Bacteriema	137 (13,6)	100 (11,0)		0.76 [0.57-1.02]	0.065
Other	85 (8,5)	54 (5,9)		0.68 [0.46-1.00]	0.048
Risk level			**<0.005**		
Healthy	187 (18,6)	108 (11,8)			
At risk	325 (32,3)	375 (41,1)			
High risk	358 (35,6)	316 (34,6)			
At risk criteria					
Heart failure	143 (14,2)	187 (20,5)	<0.005	1.56 [1.19-2.04]	0.001
Coronary insufficiency	88 (8,8)	112 (12,3)	0.012		
Broncho-pulmonary pathology	187 (18,6)	219 (24)	0.004		
Chronic liver disease	55 (5,5)	78 (8,5)	0.008		
Chronic renal failure	89 (8,9)	127 (13,9)	<0.005	1.60 [1.16-2.21]	0.004
Diabetes	177 (17,6)	207 (22,7)	0.005	1.30 [1.02-1.66]	0.031
Others criteria					
Denutrition	127 (12,6)	142 (15,6)	0.065		
Alcoholism	103 (10,2)	146 (16,0)	<0.005	1.60 [1.20-2.15]	0.002
Smoking	186 (18,5)	194 (21,2)	0.129		
Previous PID or pneumococcal pneumonia	20 (2)	35 (3,8)	0.016	1.92 [1.06-3.46]	0.031
Neurological at-risk pathology	66 (6,6)	70 (7,7)	0.345		
Auto-immune disease	44 (4,4)	32 (3,5)	0.330		
Serotypes			**<0.005**		
PCV13 vaccine	210 (20,9)	285 (31,2)			
2-add. PCV15 vaccine	98 (9,8)	57 (6,2)			
5-add. PCV20 vaccine	266 (26,5)	207 (23,7)			
PPSV23 no PCV13 vaccine	464 (46.2)	356 (39.0)			
Non vaccine serotypes	299 (29,8)	229 (25,1)			
Individual Serotypes					
serotype 3	114 (11,3)	167 (18,3)	<0.005	1.91 [1.46-2.50]	<0.005
serotype 19A	40 (4,0)	56 (6,1)	0.025	1.73 [1.13-2.67]	0.012
serotype 19F	16 (1,6)	29 (3,2)	0.019	2.38 [1.25-4.54]	0.008

Conclusion

Both host factors and vaccine serotypes were associated with severe forms of IPD. If new conjugate vaccines are expected in France in 2024, efforts should be made to improve vaccination coverage in at-risk populations.

Source :
Crit Care. 2021 Jan 10;25(1):24
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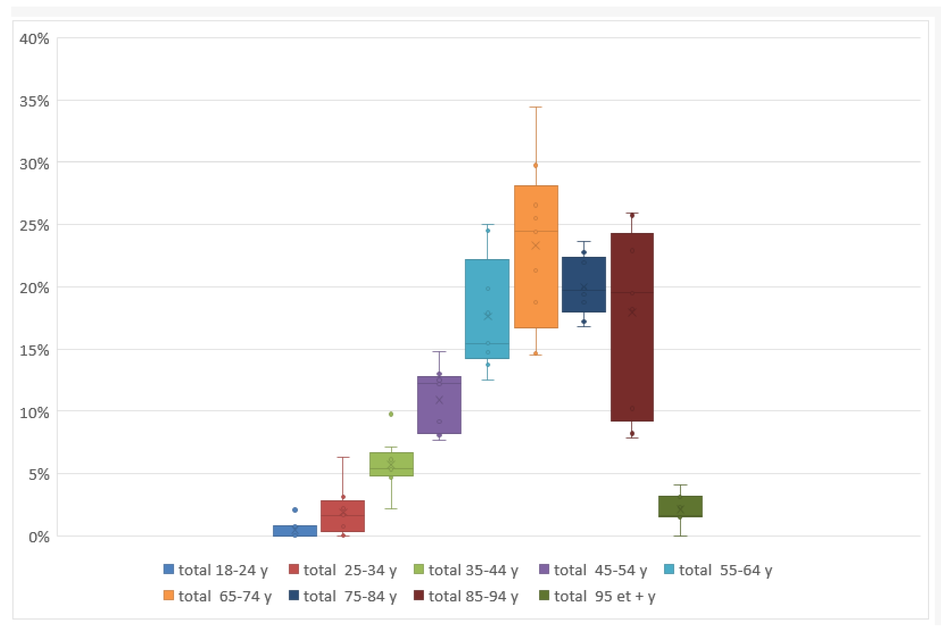
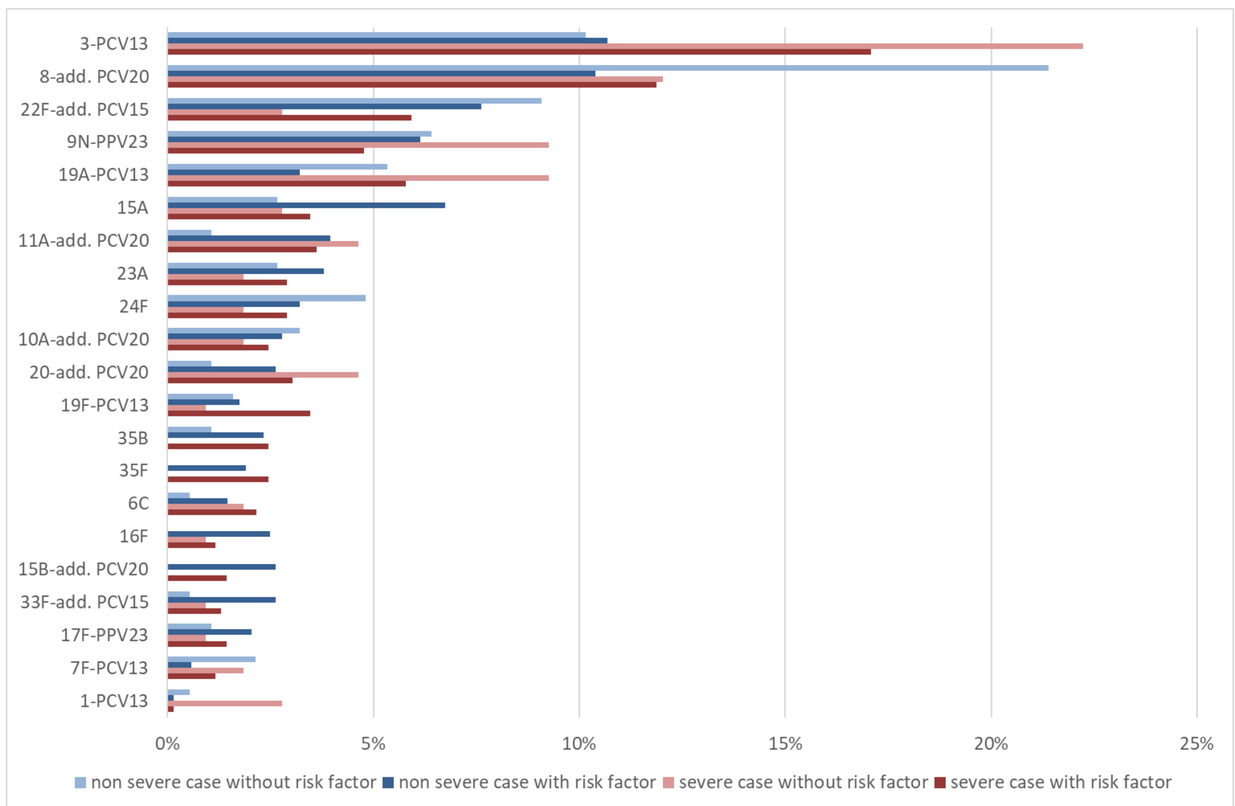
Results

Over the period 2014-2022, 1 931 cases of IPD without meningitis were diagnosed, 55.6% were males and 65.1% were over 65 years old (median 70). These IPD were severe for 913 patients (47.3%) and 391 (20.2%) died. In the 12 months previous their hospitalization for IPD, 1560 patients (80.8%) had consulted a practitioner. The part of vaccinated cases was low (7.3%), in a similar way according to severity. At-risk patients accounted for 86.4% of severe patients (versus 78.5% of no severe patients, p<0.005) among the cases with known risk status. The risk of developing a severe IPD is 3 times higher for patients aged 65 years and over compared to younger ones (2.66, 95%CI [1.49-4.75], p=0.001). Patients with risk factors have a higher risk of serious illness, particularly heart failure (1.56, 95%CI [1.19-2.04], p=0.001) and chronic renal failure (1.60, 95%CI [1.16-2.21], p=0.004). Serotypes 3 (1.91, 95%CI [1.46-2.50], p<0.005), 19A (1.73, 95%CI [1.13-2.67], p=0.012) and 19F (2.38, 95% CI [1.25-4.54], p=0.008) were significantly associated with severe IPD.

Distribution of severe IPD cases by age, 2014-2022, SIIPA, CNR-ORP, France



Proportion of serotypes for cases of invasive pneumococcal infections (excluding meningitis) by severity and risk status, 2014-2022, SIIPA, CNR-ORP, France



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