Pneumococcal Pneumonia Increases Risk of End–Stage Renal Disease in Adult Patients: A Nationwide Population-Based Cohort Study in Taiwan

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OBJECTIVES

Although studies of P-HUS and invasive pneumococcal disease in pediatric patients have characterized long-term renal outcomes, the long-term renal effects in adult patients remain unclear. The aim of our current study was to determine the relationship between PP and the subsequent risk for ESRD

METHODS

We conducted a population-based retrospective cohort study of 18,302 cases of PP infection diagnosed between 1998 and 2010 using claims data from the National Health Insurance Research Database (NHIRD) in Taiwan. The comparison cohort contained 73,208 age- and sex-matched patients without PP. The NHI also includes a catastrophic illness program that exempts patients from copayments for the corresponding medical services, and the registry for catastrophic illness patients (HV) includes ESRD patients. The National Health Insurance Research Database (NHIRD) contains comprehensive claims records of outpatient and inpatient care provided by the NHI [14]. The data used in our study were extracted from the NHIRD. We used 3 data sources: the registry of beneficiaries, the HV, and inpatients claims records. The incidence rate ratios (IRRs) and hazard ratios (HRs) of ESRD were calculated.

Table 1. Demographic characteristics and comorbidities in patients with and without a history of pneumococcal pneumonia

Variable	Pneumococcal pneumonia No N=73208	Pneumococcal pneumonia Yes N=18302	*P* value
Sex	n (%)	n (%)	
Female	25068 (34.2)	6267 (34.2)	.99
Male	48140 (65.8)	12035 (65.8)	
Age (mean±SD, y)	65.0±17.8	65.8±17.9	0.001#
Stratified age			
20-35	6047 (8.26)	1513 (8.27)	.99
35-50	8844 (12.1)	2211 (12.1)	
50-65	13956 (19.1)	3489 (19.1)	
65-75	16352 (22.3)	4088 (22.3)	
75↑	28004 (38.3)	7001 (38.3)	
Comorbidity			
Hypertension	11953 (16.3)	5957 (32.6)	<.0001
Diabetes mellitus	5930 (8.10)	3660 (20.0)	<.0001
Hyperlipidemia	2369 (3.24)	1227 (6.70)	<.0001
Coronary artery disease	5991 (8.18)	3191 (17.4)	<.0001

Chi-Squared Test; #2-sample *t*-test

Table 2. Comparison of incidence of ESRD stratified by sex, age and comorbidity between with and without pneumococcal pneumonia patients

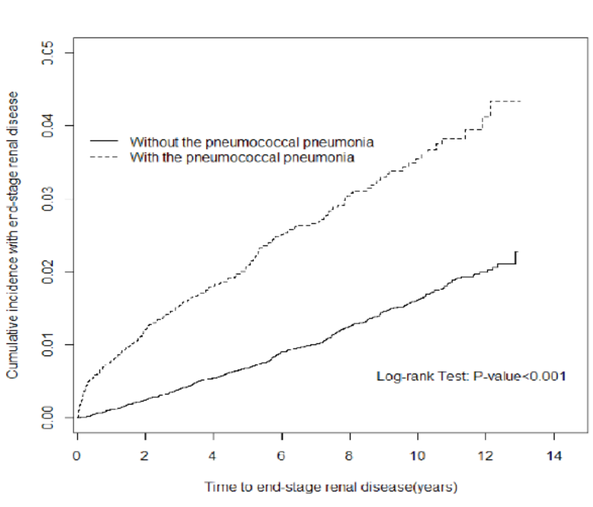
Variables	Pneumococcal pneumonia No ESRD Event	PY	ESRD Rate#	Pneumococcal pneumonia Yes ESRD Event	PY	ESRD Rate#	IRR* (95% CI)
All	609	405158	15.0	290	67706	42.8	2.82 (2.70, 2.95)***
Sex							
Female	221	146156	15.1	120	27178	44.2	2.92 (2.71, 3.15)***
Male	388	251997	15.4	170	40040	42.5	2.76 (2.61, 2.92)***
Stratify age							
20-35	3	38402	0.78	8	9566	8.36	10.7 (8.81, 13.0)***
35-50	25	57567	4.34	29	11888	24.4	5.62 (4.93, 6.40)***
50-65	104	85479	12.2	99	15187	65.2	5.36 (4.87, 5.89)***
65-75	201	99356	20.2	77	15159	50.8	2.51 (2.28, 2.77)***
75+	276	117348	23.5	77	15418	49.9	2.12 (1.96, 2.30)***
Comorbidity							
Hypertension							
No	398	353612	11.3	125	53255	23.5	2.09 (1.97, 2.21)***
Yes	211	44540	47.4	165	13963	118.2	2.49 (2.28, 2.73)***
Diabetes							
No	401	376718	10.6	127	58441	21.7	2.04 (1.93, 2.15)***
Yes	208	21434	97.0	163	8777	185.7	1.91 (1.71, 2.14)***
Hyperlipidemia							
No	558	389103	14.3	243	63825	38.1	2.65 (2.53, 2.78)***
Yes	51	9049	56.4	47	3393	138.5	2.46 (2.04, 2.97)***
CAD							
No	514	375424	13.7	211	59310	35.6	2.60 (2.47, 2.73)***
Yes	95	22728	41.8	79	7908	99.9	2.39 (2.11, 2.70)***

Rate#, incidence rate, per 10,000 person-years; IRR*, incidence rate ratio
*p<0.05, **p<0.01, ***p<0.001

Table 3. Cox model with hazard ratios and 95% confidence intervals of ESRD associated with Pneumococcal pneumonia and covariates

Variable	Crude HR (95%CI)		Adjusted† HR (95%CI)	
Stratify age				
20-35	1	(Reference)	1	(Reference)
35-50	3.39	(1.77, 6.48)***	3.14	(1.64, 6.01)***
50-65	8.81	(4.80, 16.2)***	6.22	(3.38, 11.4)***
65-75	10.7	(5.83, 19.5)***	6.35	(3.46, 11.7)***
75↑	11.8	(6.48, 21.5)***	6.79	(3.70, 12.5)***
Sex(female vs male)	0.97	(0.85, 1.11)***	-	-
Baseline co-morbidities (yes vs no)				
Pneumococcal pneumonia	2.79	(2.43, 3.21)***	2.03	(1.75, 2.34)***
Hypertension	5.19	(4.54, 5.95)***	1.86	(1.58, 2.20)***
Diabetes	10.6	(9.22, 12.1)***	5.52	(4.71, 6.48)***
Hyperlipidemia	4.45	(3.61, 5.50)***	1.28	(1.02, 1.60)*
CAD	3.43	(2.90, 4.05)***	1.10	(0.91, 1.32)

†Adjusted HR: multivariable analysis including for Stratify age, sex, hypertension diabetes, hyperlipidemia, and CAD
*p<0.05, **p<0.01, ***p<0.001



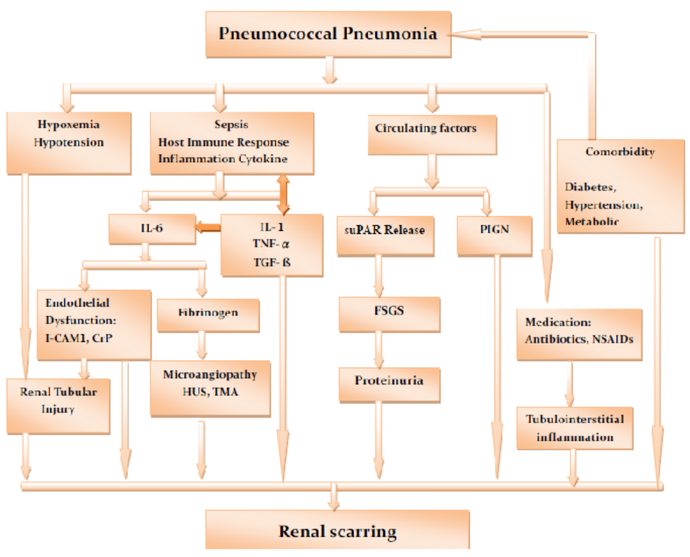


Figure 2: CrP, C-reactive protein ; FSGS, focal segmental glomerulosclerosis; HUS, hemolytic uremia syndrome; ICAM-1,intercellular adhesion molecule-1; IL-1, interleukin-1; IL-6, interleukin-6; NSAIDs, nonsteroidal anti-inflammatory drugs; PIGN, post-infection glomerulonephritis; suPAR, soluble urokinase-type plasminogen activator receptor; TMA, thrombotic microangiopathy; TNF-α, tumor necrosis factor-α; TGF- β, transforming growth factor-β .

RESULTS

The incidence rate of ESRD in the PP cohort was 2.82-fold (95% CI, 2.70-2.95) higher than that of the control cohort. The IRR of ESRD among the PP cohort members younger than 35 years of age was much greater (IRR, 10.7; 95% CI = 8.81-13.0) than that of the age-matched controls. After adjusting for age, sex, and the comorbidities, the HR of ESRD in the PP cohort was 2.03 (95% CI, 1.75-2.34, P < .001). The ESRD cumulative incidence curve showed that the PP cohort had a significantly higher risk of ESRD than the non-PP cohort (P < .001 by log-rank test).

CONCLUSIONS

Pneumococcal pneumonia not only reflects the underlying comorbid conditions but also is considered as an independent risk factor for ESRD in adult patients. The underlying pathophysiological mechanisms contributing to this relationship may be multifactorial. The effect of one episode of PP can have clinically significant long-term effects, and long-term follow-up of renal function is recommended in adult patients with a history of PP.

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