

Abstract: Generation of Host Genetic Factor Information Known to Associate With Hospitalized Severe Influenza: a Preliminary Analysis

Authors:

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Background

Influenza remains a leading cause of severe respiratory infections worldwide. Emerging evidence indicates that genetic variation of host immunity genes may play a key role in susceptibility to severe influenza. Notably, several ‘risk’ genotypes appear to be more prevalent in Asian population and are associated with high estimated population attributable risks.

Methods

This study was undertaken as a part of 3-year prospective cohort study among adults aged over 65 years hospitalized for influenza A or B at Prince of Wales Hospital, Hong Kong. Host genetic single nucleotide polymorphisms (SNPs) in different genes related to innate immunity and mucosal glycan expression were determined, including interferon-induced transmembrane protein 3 (IFITM3), toll-like receptor 3 (TLR3) and fucosyltransferase 2 (FUT2). These SNP signatures were statistically compared between vaccinated and non-vaccinated groups, incorporating demographic and clinical data.

Results

The study cohort consisted of 100 subjects (61 males and 39 females), with a mean age ($\pm$ SD) of 77.1 ($\pm$ 7.1). Clinical characteristics were shown in Table 1. In univariate analysis, TLR3 rs5743313 CC genotype was shown to be significantly associated with reduced requirement for supplemental oxygen (60.6% in CT/TT genotype vs 34.3% in CC genotype; $P = .013$). In multivariable analysis, TLR3_rs5743313 was the only significant predictor for requirement of supplemental oxygen ($p = .014$). Specifically, individuals with TLR3_rs5743313 CC genotype had significantly lower odds of requiring supplemental oxygen (OR = 0.333) compared to CT/TT type. This represented a 66.7% reduction in odds of oxygen requirement. There were no significant differences of ICU admission, 30-day mortality and in-hospital mortality between different genotypes. (Table 2)

Conclusion

Individuals with TLR3_rs5743313 CC genotype had significantly lower odds of requiring supplemental oxygen. Host genetic factors may influence clinical outcomes. Such findings have important implications on patient care in at-risk populations.

This project is supported by the Health and Medical Research Fund, the Health Bureau, The Government of the Hong Kong Special Administrative Region [INF-CUHK-2].

Table 1

Table 1. Descriptive Data on Clinical Characteristics, Severity, and Outcomes of 100 Chinese Patients with Confirmed Influenza A Infection and Hospitalization

Variable	Hospitalized patients with Influenza A infection (n=100)
Age, mean $\pm$ SD, years	77.1 $\pm$ 7.1
Sex, male (%)	61 (61)
Vaccination (%)	50 (50)
Length of hospitalization, mean $\pm$ SD, days	9.6 $\pm$ 14.1
Charlson comorbidity score (CCI), High score (≥ 4) (%)	81 (81)
Supplemental oxygen use (%)	43 (43)
ICU admission (%)	3 (3)
30-day outcome, death (%)	3 (3)
60-day outcome, death (%) ^a	4 (4)
NAI treatment within 2 days from onset ^b	31 (31)

^aNot include those death number in 30-day outcome

^bNine subjects' data are missing

Table 2

Table 2. Clinical severity and outcomes of hospitalized patients with Influenza

		FUT2_rs1047781			IFITM3_rs12252			IFITM3_rs34481144			TLR3_rs5743313		
Clinical severity/outcomes	Status	TT (%)	AA/AT (%)	P-Value	CC (%)	CT/TT (%)	P-Value	GG (%)	GA (%)	P-Value	CC (%)	CT/TT (%)	P-Value
Supplemental Oxygen	Yes	29.7	70.3	0.963	29.3	70.7	0.718	100.0	0.0	1.000	53.5	46.5	0.013
	No	30.2	69.8		32.7	67.3		98.1	1.9		77.2	22.8	
ICU Admission	Yes	33.3	66.7	1.000	66.7	33.3	0.229	100.0	0.0	1.000	66.7	33.3	1.000
	No	29.9	70.1		30.1	69.9		98.9	1.1		67.0	33.0	
Death (30 days)	Yes	33.3	66.7	1.000	66.7	33.3	0.229	100.0	0.0	1.000	66.7	33.3	1.000
	No	29.9	70.1		30.1	69.9		98.9	1.1		67.0	33.0	
Death (60 days)	Yes	33.3	66.7	1.000	57.1	42.9	0.200	100.0	0.0	1.000	57.1	42.9	0.681
	No	29.8	70.2		29.2	70.8		98.9	1.1		67.7	32.3	
In-hospital Death	Yes	40.0	60.0	0.634	66.7	33.3	0.074	100.0	0.0	1.000	66.7	33.3	1.000
	No	29.4	70.6		28.9	71.1		98.9	1.1		67.0	33.0	