Letter to the Editor

Analysis of an outbreak of COVID-19(alpha-variant) with rapid progression to mortality in Taipei, Taiwan

Dear editor,

Many patients diagnosed with COVID-19 (alpha variant) suffered from rapid progression to death in an outbreak between April and June 2021 in Taipei, Taiwan. It is important to identify risk factors leading to rapid deterioration and death.[1,2] This study aims to identify the characteristic symptoms in predicting the rapid progression to mortality in newly diagnosed patients with COVID-19 using a comprehensive analysis of all 636 COVID-19 related deaths from Taiwan's Center for Disease Control database. Predisposing factors related to the rapid death since symptom onset and rapid death were analyzed using multivariate logistic regression analysis

Patient demographics and descriptive statistics

The analysis includes 636 (411 male, 64.6%; 225 female, 35.4%) mortality cases of during the period of April 1st to June 30th, 2021. The mean age of participants was 68 ± 12.1 for females and 71 ± 12.3 for males, and 88% of the participants had one or more comorbidities.

Of the 636 enrolled cases, 64(10%) did not display apparent symptoms or signs, while the others presented with at least one of the listed symptoms of fever/chills, cough, rhinorrhea, sore throat, olfactory dysfunction, or dyspnea, as shown in Table 1. The average time from a confirmed COVID-19 diagnosis to death and from the symptom onset to death was measured to be 8.6 ± 8.5 days and 13.2 ± 9.3, respectively. The average interval from symptom onset to a confirmed COVID-19 diagnosis averaged was 4.6 ± 3.8 days.

Table 1
Characteristics in predicting the rapid progression from symptoms onset to mortality.

	Odds Ratio	P value	95.0% C.I.for EXP(B)	
			Lower	Upper
Gender	0.822	0.379	0.532	1.272
age	1.004	0.671	0.986	1.021
comorbidity	0.605	0.369	0.202	1.810
fever / chillness	1.636	0.026*	1.062	2.519
cough	3.103	0.000*	1.869	5.149
rhinorrhea	0.684	0.625	0.149	3.131
sore throat	0	0.997	0	.
anosmia	0	0.999	0	.
dyspnea	0.776	0.250	0.504	1.195
				***p < 0.05**

Table 2
Characteristics in predicting the rapid progression from a confirmed COVID-19 diagnosis to mortality.

	Odds Ratio	P value	95.0% C.I.	
			Lower	Upper
age	1.014	0.046*	1.000	1.028
symptomless	2.045	0.023*	1.101	3.798

*$p < 0.05$, insignificant variables excluded from the multivariate logistic regression.

Characteristics in predicting the rapid progression from symptoms onset to mortality

Upon logistic regression analysis, the symptoms of fever/chillness and cough appear to be negative predictors of rapid progression from symptom onset to mortality (OR= 1.636& 3.1.3, $p = 0.026$ & 0.000, respectively). Conversely, gender, age, the presence of comorbidity, and symptoms of rhinorrhea, sore throat, anosmia, and dyspnea were found to be statistically insignificant.

Upon logistic regression analysis, the absence of symptoms at diagnosis and older age appeared to be positive predictors of rapid progression from a confirmed COVID-19 diagnosis to mortality (OR=2.045 & 1.014, $p = 0.023$&0.046, respectively) in Table 2. Insignificant variables were excluded from the multivariate logistic regression.

Discussion

In this study, we have demonstrated that the symptoms of fever/chillness and cough at early onset are associated with a lower chance of rapid progression to mortality, while the factor of age, gender, and the presence of medical comorbidities remained statistically insignificant. After a confirmed diagnosis of COVID-19, increased age and the absence of symptoms at diagnosis are associated with a rapid progression to mortality. These findings provide evidence implying that specific clinical presentation phenotypes might be associated with higher alert to COVID-19, leading to a lower chance of rapid progression before healthcare services are accessed. More importantly, identifying those of older age and without symptoms upon diagnosis might provide additional information for healthcare providers to consider more aggressive and prompt evaluation of these patients.

Quite a portion of the patients diagnosed with COVID-19 suffer from rapid progression where mechanical ventilation and aggressive life-sustaining measures are undertaken, and thus identifying risk factors leading to rapid deterioration and death becomes crucial.[3,4] Evidence has suggested that older age, male gender, underlying comorbidities such as hypertension, diabetes, obesity, chronic lung diseases, heart, liver, and kidney diseases, tumors, clinically apparent immunodeficiencies such as early-type I interferon secre-

tion capacity, and pregnancy, are all associated with elevated risks of severe outcomes.[5,6] Associated serum inflammatory biomarkers (abnormal lymphocyte counts, liver function, procalcitonin levels) were also found to be correlated with progression to critical illness.[5–8] Few studies have focused on the pattern of symptoms in distinguishing potential patients who would rapidly deteriorate from relatively stable individuals. Smell and taste have been used in predictive models for COVID-19 diagnosis but not in disease progressions.[5–8] In the study done by Chang et al. regarding the risk prediction of rapid progression to COVID-19 Pneumonia, the symptom of fever was identified to be significantly associated with disease progression of COVID-19 pneumonia in addition to laboratory findings.[7,8] This is also supported by another study describing fever as one of the prognostic factors to identify the progression of COVID-19 patients with mild or moderate type.[7] In congruence to our study, a meta-analysis of 76 studies reported fever to be associated with a lower estimated risk for both mortality and severity.[8]

Except for the "pre-hospital" factors like age, symptoms, comorbidities, which could serve as precautions to the public health system, the findings of elevated risk for rapid progression to death for the elderly patient presenting without initial symptoms at the confirmed COVID-19 diagnosis become particularly important. With the global outbreak of coronavirus, there is increasing evidence that a significant portion of COVID-19 victims is asymptomatic, and many of them do not seek medical assistance due to no obvious clinical signs.[5–8] Nevertheless, the phenomenon of silent hypoxemia in COVID-19 patients should be reminded as it is associated with poor outcomes.[1,2] Pulmonary embolism is also not an infrequent cause of sudden or rapid death by eliciting perturbations in coagulation through exaggerated immune responses with a prevalence of up to 14.3% among aged patients.[1,2,7] Gao et al. reported that viral shedding duration of the asymptomatic cases was comparable to those with symptoms initially, and the reduced awareness of the condition itself might lead to delayed access to medical care.[3] It has been proposed that instructing asymptomatic patients to stay home until symptoms become apparent may be problematic.[3,4,5,8] More aggressive measures such as routine monitoring of oxygen saturation and following up chest radiologic examination should be considered.

In conclusion, this study demonstrated that the symptoms of fever/chillness and cough at early onset are associated with a lower chance of rapid progression to mortality. After a confirmed diagnosis of COVID-19, old aged and the absence of symptoms at initial diagnosis are associated with a rapid progression to mortality. Physicians may consider taking this information into consideration of more aggressive measures such as routine monitoring of oxygen saturation and following up chest radiologic examination if dyspnea.

Declaration of Competing Interest

The authors have no competing interests to declare.

Ethics approval

Ethics approval was not required for this study.

Reference

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