Title: Response letter to COIVD-19 Disease: Tackling a pandemic in 21st Century

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Main text

Dear Sir,

Response letter to COIVD 19 Disease: Tackling a pandemic in 21st Century.
This letter is in response to the letter to the editor by Dr Sahu, Dr Mishra and Dr Lal, which raised concerns about the epidemiologic, clinical features, treatment and prognostic of COVID-19 in Zhejiang, China.[1]

At the time of paper submission, nearly two-thirds of the COVID-19 patients were not discharged, but now all 91 patients are fully discharged without death, including a 96-year-old woman.[2] Moreover, as at 24:00 on March 29th in Zhejiang province, there were 1,255 laboratory-confirmed cases, 1,225 cases were discharged, 29 remain hospitalized and 1 case died. A total of 46,521 close contacts were tracked, and 2,827 people are still under medical observation.[3] The mortality rate between Wuhan and Zhejiang is quite different, where reported mortality rates range from 4.3 to 15% in Wuhan.[4-6] The longer median time for illness onset to hospital admission (9.84 days, however, the median time from visiting doctor to be confirmed was 1 days in Zhejiang), and shortage of health care workers and resources in the early stage, might have contributed to higher mortality in Wuhan.[7]

The bilateral pneumonia in chest computed tomography (CT) scan was an important manifestation of COVID-19. In our study, 67.03% of patients had bilateral pneumonia in CT scan and none of the patients used extracorporeal membrane oxygenation (ECMO).[2] Other studies have presented similar statistics. In Shanghai, which is geographically adjacent to Zhejiang, it was reported that 81.53% of COVID-19 patients had bilateral infiltrations in Shanghai.[8] In an earlier study of Zhejiang patients, Lian et al examined the medical records of 788 patients, at the time of their submission in early February most patients had yet to be discharged, none had died and they concluded that the symptoms of COVID-19 in Zhejiang province were relatively mild given the evidence they had at the time.[7,9] This result might be due to well-resourced treatments administered in Zhejiang and Shanghai. The serious cases reported in Chen et al and Huang et al had high incidences of acute respiratory distress syndrome (ARDS) could be due to that these were cases drawn from Wuhan, and some of the sample were taken from designated hospitals for severe pneumonia. Collectively, the research indicates that there are important differences in COVID-19 case fatality rate in different regions.

In our study, the odds of developing severe COVID-19 is larger amongst those over 60.[2] There were 9 patients (9.89%) that had severe COVID-19. There were 19 (20.88%) patients who were 60 years or older, 5 of them (26.32%) developed severe COVID-19 (Figure). Amongst the 9 severe patients, 8 had hypertension, 4 had Type 2 diabetes mellitus, and one had a history of cancer. Moreover, several studies have reported that hypertension, diabetes, cardiovascular disease, and COPD were associated with severity and admission to intensive care units.[7,10,11]

The clinical features of COVID-19 are of great concern to many. SARS-CoV-2 spreads rapidly through human-to-human contacts. Presymptomatic or asymptomatic patients are infectious.[12] The reproduction number (R0) is lower in SARS-CoV-2 (1.4 to 2.5) compared to SARS-CoV (2 to 5), and also the case fatality rate is lower than SARS-CoV (9.5%) and MERS-CoV (37%).[13]

Fever, cough and fatigue are the most common symptoms reported in our study, which is similar to other cohorts. Interestingly, diarrhoea was presented in 23.8% patients of our study[2] compared to 3% or 2% of other studies.[4,6] In comparison, the proportion of patients of MERS and SARS who had diarrhoea ranged from12.3% to one-thirds.[1,14,15] Moreover, the gastrointestinal symptoms of confirmed subjects were 37% from a Singapore study.[16] On the other hand, diarrhoea was more common in the ICU group.[10] Furthermore, Chen et al reported that the clinical features presented at admission change over time. The percentage of patients that reported fever, fatigue and myalgia were different across two periods: January 16th to January 22nd and January 23rd to January 29th.[17] Therefore, there may be differences and changes in clinical symptoms between different generations of COVID-19. On the other hand, it is particularly important to understand the dynamic changes of patients' symptoms during hospitalization.

Up to date, there is no drug proven effective for treating COVID-19. Recently, Cao et al from China using a sample of 199 patients reported that lopinavir-ritonavir (400mg and 100 mg) twice a day for 14 days did not benefit those with severe COVID-19 (assessed on whether it accelerate clinical improvement, reduce mortality, and diminish throat viral RNA detectability) .[18] However, the median days of ICU length of stay of the treatment group was 9 days compared to 11 days of the control group. At day 14, the proportion of clinical improvement of the treatment group was 45.5% compared to 30% of the standard care group. Double-blind and larger clinical trials are needed in the future. The results of the Gautret et al study on the use of hydroxychloroquine and azithromycin to treat COVID-19 are found to be

controversial by some references.[19,20] Current research suggested that remdesivir (GS-5734) and chloroquine (Sigma-C6628) can effectively inhibit SARS-CoV-2 at cellular level.[21] The current consensus of experts in China is that, Chloroquine 500mg twice a day for 10 days should be administered to COVID-19 patients.[22] Chloroquine might be an effective drug for treating COVID-19.

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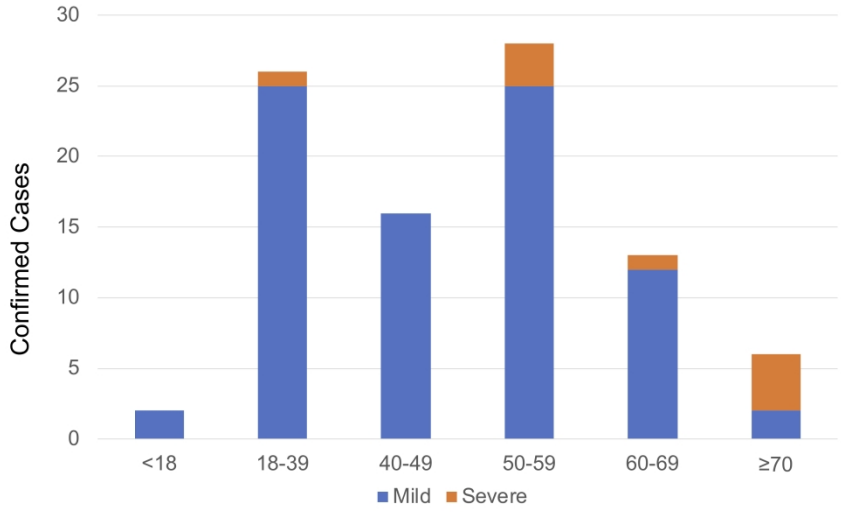
Figure. Age distribution of the 91 COVID-19 patients reported in Qian et al.



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