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COVID-19 INFECTION IN THE ELDERLY. CASE CONTROL STUDY

Ta-Wei Wang[1], Kuan-Chih Kuo[2], Yu-Jang Su[3], Chen-Wang Chang[4]

[1]*MD. Department of Emergency Medicine, Tao-Yuan General Hospital, Taoyuan City, Taiwan.*
[2]*MD. Department of Emergency Medicine, Mackay Memorial Hospital, Hsinchu, Taiwan.*
[3]*MD. Senior Attending physician, Department of Emergency Medicine, Mackay Memorial Hospital, Taipei, Taiwan. Director, Poison Center, Department of Emergency Medicine, Mackay Memorial Hospital, Taipei, Taiwan. Assistant Professor, Department of Medicine, Mackay Medical College, New Taipei City, Taiwan. Assistant Professor, MacKay Junior College of Medicine, Nursing and Management, Taipei, Taiwan. Yuanpei university of medical technology. Hsinchu 300, Taiwan*
[4]*MD, MSc. Senior Attending physician, Department of Medicine, Mackay Medical College, New Taipei City, Taiwan. Assistant Professor, MacKay Junior College of Medicine, Nursing and Management, Taipei, Taiwan. Assistant Professor, Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan. Taiwan*

E-mail: yjsu.md@msa.hinet.net

Abstract

On December 8, 2019, in Wuhan, China, several novel pneumonia cases were found, and then the pathogen was named COVID-19 (coronavirus disease 19) and has been rapidly spreading worldwide till today. For the elderly who are susceptible and vulnerable to the COVID -19 infection. Here we want to recognize more manifestations of COVID-19 in infected elderly patients. A total of 398 patients was diagnosed with COVID-19 from 21st January 2020 to 18th April 2020. We divided the patients into an elderly group 65 and over and a non-elderly group under 65 . The associated data were collected for statistical analysis included travel history, timing of onset of symptoms days of symptom to confirming diagnosis, mortality, intensive care unit (ICU) admission, lung infiltration on chest X-ray (CXR), and symptoms. All statistical tests were 2-tailed, statistical significance was defined as $P < 0.05$. Of 398 patients with COVID-19 infection, the mean age was 38.6 ffi 16.8 years. Notably, elderly patients were also more likely to be admitted to intensive care units (ICU) initially and lung infiltration (3.4% and 25.4% respectively). Regarding the risk factor of mortality, we found that lung infiltration posed a threat to elderly people (odds ratio, OR 10.75, 95% confidence interval, CI: 1.02-112.93, P-value: 0.048.) Elderly patients more often presented with atypical symptoms such as muscle pain and diarrhoea. Moreover, they are more likely to have lung infiltration related to worse outcomes with respect to non-elderly patients, for whom upper respiratory infection symptoms is more common. Non-elderly patients are more likely to have smell and taste dysfunction.

Key words: COVID-19, aged, infectious disease incubation period, signs and symptoms, mortality, elderly, incubation period, symptoms.

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Introduction

A cluster of atypical pneumonia cases was emerging and has spread rapidly from Wuhan, China since December 2019.[1] The first four cases were all linked to Huanan Seafood Wholesale Market, and then the disease spread rapidly there. After analysis of viral sequence, this type of coronavirus was known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and then subsequently formally named coronavirus disease-2019 (COVID-19) by the World Health Organization (WHO).[2,3] As the outbreak was growing rapidly and spreading all around the world, the WHO declared that COVID-19 was a Public Health Emergency of International Concern (PHEIC) on January 30, 2020. Although COVID-19 is highly contagious, it has a broad disease spectrum ranging from asymptomatic to critically ill and even death.[4]

Taiwan is the country where a epidemic was successfully controlled and the earliest to return to playing professional baseball in the world. During the epidemic COVID-19 period, Taiwanese people kept going to work and lived as usual with mask-wearing and social distancing protection, while the students kept going to school. Taiwan is an epitome of the world in endemic COVID-19. COVID-19 cases were imported from Europe (41.7%), America (23.9%), Asia (17%), Africa (3%), Oceania (0.8%) and indigenous cases (13.6%).

From previous studies, we already knew that the elderly have a poor prognosis, and some parameters indicate the progression of the disease.[5,6] However, we want to recognise more manifestations in COVID-19 infected elderly patients and their outcome and prognosis. This article was created to determine the difference in clinical features between elderly and non-elderly patients based on COVID-19 cases in Taiwan.

Materials and methods

A total of 398 patients were diagnosed with COVID-19 from 21st January 2020 to18th April 2020. Data was collected from the information which was released by Taiwan Centers for Disease Control (CDC). The diagnosis was made by positive detection of SARS-CoV-2 via real-time reverse-transcription-polymerase-chain-reaction (real-time RT-PCR) comprised of a throat swab.[7]

We divided the patients into two groups: an elderly group, which contained patients aged 65 and above and a non-elderly group, which contained patients were younger than 65 years. Associated data were collected for statistical analysis included travel history, timing of onset of symptoms, days from symptom to confirming diagnosis, mortality, intensive care unit (ICU) admission, lung infiltration on chest X-ray (CXR), and symptoms including fever and lung infiltration objectively, and shortness of breath, rhinorrhoea, cough, nasal stuffiness, headache, sore throat, anosmia, dysgeusia, muscle pain, general malaise and chest pain subjectively described by patients.

In statistical analyses, continuous data are expressed as mean ffi the standard deviation and compared using Student's t-test. Category data are described as a percentage (followed by the number of patients represented). The $\chi 2$ test was used to analyse categorical data. Because of the ordinal and categorical nature of the data, the Mann–Whitney U test was also applied to compare the data. All the covariates were included in a logistic regression analysis, while multivariate analysis was also conducted to evaluate the predictive factors. All statistical tests were 2-tailed, statistical significance was defined as P ¡ 0.05, and all statistical analyses were conducted using Stata software, version 12.0 (Stata Corp LP, College Station, Texas). The study did not involve the collection of patients' blood samples nor data. The information was released by the CDC in the public media, so it was automatically exempt from an Internal Review Board.

Results

Data was collected from a total of 398 patients with COVID-19 infection from 21st January 2020 and 18th April 2020. The mean age was 38.6 ±16.8 years (mean ffi standard deviation (SD), years), and the male: female ratio was about 0.87: 1 (male, n = 187; female, n = 211). The elderly group comprised 59 patients, and the non-elderly group comprised 339 patients.

A total of 86.4% of all patients had travelled from other countries, mainly from Europe. Notably, the mortality rate was much higher in the elderly group (3.4% versus 0.8%, P ¡ 0.05). Additionally, elderly patients were also more likely to be admitted to the intensive care unit (ICU) initially and lung infiltration (3.4% and 25.4% respectively) (**Table 1**).

Table 1. Comparisons of COVID-19 patients in two groups by age

	Non-elderly (339)	Elderly (59)	Total (398)	p-value
Age	33.4 ± 14.0	68.4 ± 5.8	38.6±16.8	<0.001
Gender(male%)	158 (46.6)	29 (49.2)	187 (47.0)	0.720
Onset of Symptoms	5.6±5.3	4.7±3.3	5.4±5.0 (101)	0.510
Symptom to Diagnosis	7.5±5.6	7.9±6.0	7.5±5.6 (374)	0.630
Mortality (%)	3 (0.9)	4 (6.8)	7 (1.8)	0.001
Initial ICU admission (%)	1 (0.3)	2 (3.4)	3 (0.8)	0.010
Other Diseases				
Diabetes Mellitus (%)	0	2 (3.4)	2 (0.5)	0.001
Hypertension (%)	2 (0.6)	2 (3.4)	4 (1.0)	0.047
Uremia (%)	0	1 (1.7)	1 (0.3)	0.016
Lung infiltration (%)	19 (5.6)	15 (25.4)	34(8.5)	<0.001
Indigenous (%)	45(13.3)	9(15.3)	54(13.6)	0.680
Imported				0.0001*
Europe (%)	152 (44.8)	14 (23.7)	166 (41.7)	
America (%)	82 (24.2)	13 (22.0)	95 (23.9)	
Asia (%)	51 (15.0)	17 (28.8)	68 (17.1)	
Africa (%)	6 (1.8)	6 (10.2)	12 (3.0)	
Oceania (%)	3 (0.9)	0	3 (0.8)	
*Two-sample Wilcoxon rank-sum (Mann-Whitney) test				

Regarding the risk factor of mortality, we found that lung infiltration posed a threat to elderly patients (odds ratio, OR 10.75, 95% confidence interval, CI: 1.02-112.93, P-value: 0.048). We found that no significant difference between subjective symptoms (such as muscle pain, shortness of breath, cough, rhinorrhoea, and fever) and mortality rate. Other less common symptoms, such as general malaise, headache, chest pain, nasal stuffiness, anosmia, dysgeusia, and diarrhoea were not analysed due to small amounts, which were not statistically significant (**Table 2**).

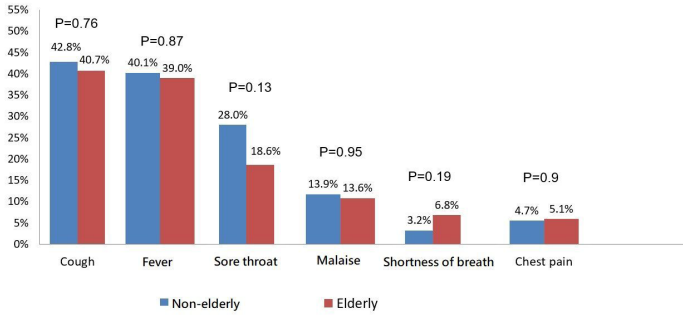
Table 2. Risks of mortality in the elderly patients.

Variables	Univariate		Multivariate	
	OR (95%CI)	p-value	OR (95%CI)	p-value
Indigenous	6.86(0.83-56.80)	0.070	6.86(0.28-164.21)	0.240
Lung infiltration	10.75(1.02-112.93)	0.048	3.52(0.20-63.75)	0.390
Fever	5.25(0.51-53.90)	0.160	14.91(0.36-609.68)	0.150
Rhinorrhea	8.17(0.97-69.10)	0.054	29.11(0.43-599.35)	0.080
Cough	1.5(0.20-11.45)	0.700	0.27(0.01-9.67)	0.470
SOB	5.78(0.45-73.62)	0.180	15.2(0.42-555.57)	0.140
Muscle pain	1.33(0.13-14.09)	0.810	0.25(0.01-10.96)	0.480
* The cases of other symptoms (such as malaise, headache, nasal stuffiness, chest pain, anosmia, dysgeusia, diarrhoea) were too small to analyse.				

With respect to the difference of clinical presentation between two groups, the elderly group was more likely to have atypical symptoms, such as muscle pain and diarrhoea than non-elderly one (20.3% versus 10.6%, P = 0.03 and 15.3% versus 6.5%, P = 0.02 respectively). However, the

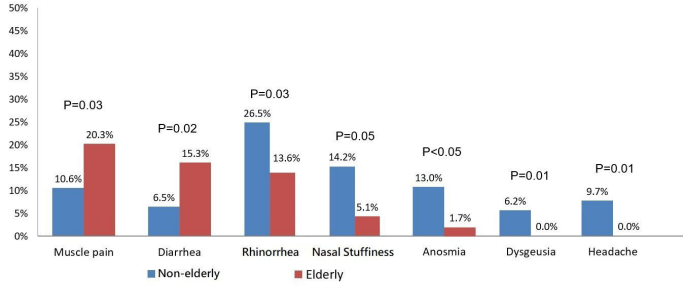
non-elderly group had more rhinorrhoea, nasal stuffiness, headache, anosmia, and dysgeusia **Figure 1**.

Fig. 1. : Comparisons in symptoms of COVID-19 patients by age with statistical differences.



Some symptoms, which showed no difference in frequency between the two groups, are shown in **Figure 2**.

Fig. 2. : Comparisons in symptoms of COVID-19 patients by age without statistical differences.



Discussion

Lung infiltration is 4.5 more - common in COVID-19 elderly patients than non-elderly ones.

Elderly patients who suffered from infectious disease are more debilitated than non-elderly patients, and COVID-19 is no exception. Elderly people are thought to have more comorbidity and poor immunity and thus are more vulnerable to infectious disease.[6] Many clinical features are observed in this group. We are trying to find out which is more related to mortality or morbidity.

Our study reveals that the presence of lung infiltration in elderly COVID-19 patients is 4.5more likely compared to the non-elderly group (25.4% versus 5.6%, $P < 0.001$). Besides, lung infiltration poses a threat to elderly patients (OR 10.75, 95% CI: 1.02-112.93, p-value: 0.048.). As we mentioned above, though both groups may have an upper respiratory infection, elderly patients are likely not to have the ability to maintain airway hygiene and thus more susceptible to the progression of the disease.[4] As a result, the rate of initial ICU admission is much higher (11.3-fold) in the elderly group (3.4% versus 0.3%, $P < 0.05$). We suggest that if patients have chest X-rays with lung infiltration or pneumonia, the prognosis is expected to be worse than a patient whose chest X-ray is unexceptional.

Elderly COVID-19 patients have more muscle pain and diarrhoea than non-elderly ones

Many kinds of research already studied the most prominent symptoms of COVID-19 infection such as fever, cough, sputum production, sore throat, and shortness of breath.[4,5,7,8] We found that for the symptoms of malaise and chest pain there are no statistical differences between elderly and non-elderly patients. In our study, the elderly COVID-19 patients had more atypical symptoms like muscle pain and diarrhoea and less rhinorrhoea, nasal stuffiness, anosmia, dysgeusia, and headache than non-elderly patients.

Fever, cough, and fatigue were the most common symptoms of COVID-19 in China.[5,9] In our study, the top five symptoms in the elderly COVID-19 patients are cough (40.7%), fever (39.0%), muscle pain (20.3%), sore throat (18.6%), and diarrhoea (15.3%). However, neither in Europe nor China were muscle aches mentioned in elderly patients.[9,10].

On the other hand, in the non-elderly group in Europe, the most common symptoms were headache, anosmia, nasal obstruction, cough, and rhinorrhoea which were consistent with our study.[10] We found that the clinical characteristics in Taiwan COVID-19 patients were more like those in Europe because cases imported from Europe accounted for a large share of them(41.7% of all COVID-19 in Taiwan).

Special symptom in COVID-19 patients: asymptomatic

There was another special clinical presentation: Asymptomatic. Diamond Princess Cruise, carrying over three thousand passengers, was boarded by an 80-year-old passenger from Hong Kong. However, this passenger was diagnosed with COVID-19 six days after leaving the ship. This was astonishing news then. All passengers were quarantined onboard. Until 16th March 2020 at least 712 passengers were tested positive for COVID-19. Then, one study was conducted to estimate the asymptomatic proportion of COVID-19 on this ship. In this study, 17.9% of patients with COVID-19 were asymptomatic, and the author believed the actual numbers of asymptomatic patients were even higher.[11] We also found research from China, which collected data in Chongqing. They found the local cases, who directly contacted with confirmed patients who had not left Chongqing before illness onset, had more probability of asymptomatic infection.[12] In a report from Bangladesh on January 2021 described 10.9% of COVID-19 patients were asymptomatic[13].

In our study, we only found that the proportion of asymptomatic patients was higher in the elderly group (6.8%) without statistical difference. Though a recent study revealed relatively the transmissibility of asymptomatic cases could be significantly smaller than that of the symptomatic cases, it still poses a threat to public health potentially.[14]

Anosmia and dysgeusia

Notably, our study includes symptoms of anosmia and dysgeusia, which may be a unique symptom in patients with

COVID-19. The exact mechanism is thought to be due to the inflammatory reaction of the nasal mucosa or invasion of coronaviruses into the brain via the olfactory nerve or bulb or both [15]; it is not uncommon in COVID-19 and another coronavirus.[16] In our study, we found that anosmia and dysgeusia were more common in the non-elderly group (13% versus 1.7%, P < 0.05; 6.2% versus 0%, P: 0.01, respectively).

We reviewed reports from China, and we found that the description of olfactory and taste dysfunction was not mentioned.[16] In contrast, in one study, about 33.9% of patients with COVID-19 complained of smell or taste dysfunction in Italy. They also concluded that younger patients were more likely to have these complaints.[17] Furthermore, another study from multiple centres in Europe also found that 85.6% of patients had olfactory dysfunction, and 88.8% of them had taste dysfunction. Beyond the expectation, 79.7% of patients suffering from anosmia denied complaints of nasal stuffiness and rhinorrhea.[16] Regarding cases in the United States, smell and taste loss were reported in 68% and 71% of COVID-19-positive subjects, respectively, compared to 16% and 17% of COVID-19-negative patients.[18]

In one study, investigating virus evolution, they found that the sequence of the surface protein in the European virus strain was mutated.[19] Thus, they proposed a hypothesis that the mutation of virus sequence could influence the clinical features in the different continents. As we mentioned above, in Taiwan, the prevalence of smell and taste maybe because most non-elderly patients were infected with the virus strain that was imported from Europe.

Prognosis

In China, we found that fever and shortness of breath were related to mortality.[6] Though they did not discuss lung infiltration, we could infer that shortness of breath might be due to lung involvement. Some independent risk factors such as old age, male gender, or having a history of diabetes mellitus, persistent lymphopenia, d-dimer greater than 1 μg/mL, severe acute respiratory dyspnoea syndrome, refractory shock, anuric acute kidney injury, and higher Sequential Organ Failure Assessment (SOFA) score caused a poor outcome from the COVID-19 infection.[20, 21, 22, 23.]

Conclusion

COVID-19 is still spreading all over the world, and elderly patients are more vulnerable to infection and worse outcomes. Critically ill patients might result in a large number of medical costs. Thus, figuring out clinical features and risk factors of mortality is important. Elderly patients presented more often with atypical symptoms such as muscle pain and diarrhoea than non-elderly ones. Moreover, they are more likely to have lung infiltration related worse outcome with respect to non-elderly patients; symptoms of upper respiratory infection are more common. Non-elderly patients are more likely to have smell and taste dysfunction. Because nearly half of the non-elderly patients were infected with a strain which was imported from Europe into Taiwan; clinical features are more like those in Europe. In summary, we suggest paying attention to chest radiography in elderly patients and being cautious with atypical symptoms, such as diarrhoea and muscle pain, as these might be the common features of COVID-19 in Taiwan.

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