Clinical Profile of Elderly Patients with COVID-19 Hospitalized in Indonesia's National General Hospital

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ABSTRAK

Latar belakang: *sebanyak 38.6% kasus kematian pasien COVID-19 di Indonesia terjadi di populasi lansia. Data mengenai profil klinis pasien rawat inap lansia dengan COVID-19 masih tidak ada. Padahal kelompok pasien ini adalah pasien risiko tinggi selama pandemi ini yang memerlukan perhatian lebih.* ***Metode:*** *studi deskriptif ini menggunakan data lengkap pasien lansia dengan COVID-19 yang dirawat inap di Rumah Sakit Umum Pusat Nasional Cipto Mangunkusumo (RSUPN Cipto Mangunkusumo) dari April hingga akhir Agustus 2020. Data termasuk karakteristik klinis, gejala, komorbiditas, multimorbiditas dan luaran mortalitas pasien.* ***Hasil:*** *di populasi pasien lansia (n=44), mayoritas berusia di antara 60-69 tahun (68%), berjenis kelamin laki-laki (66%), dan tidak memiliki riwayat kontak erat dengan pasien COVID-19 sebelumnya (86%). Gejala tersering ialah demam, batuk, dan sesak yang merupakan gejala khas COVID-19, sedangkan penyakit kronis tersering adalah diabetes melitus, hipertensi, dan keganasan. Multimorbiditas ditemukan hanya di 14% pasien lansia, dan para pasien tersebut bertahan hidup pasca infeksi virus SARS-CoV-2. Angka kematian pasien lansia rawat inap dengan COVID-19 di studi ini adalah 23%, dan 90% dari kasus kematian berjenis kelamin laki-laki.* ***Kesimpulan:*** *pasien laki-laki mendominasi kasus terkonfirmasi dan kasus kematian lansia dengan COVID-19. Gejala khas COVID-19 hanya ditemukan di sekitar setengah pasien penelitian. Pasien yang meninggal dunia memiliki persentase gejala khas lebih tinggi. Gejala tidak khas pun mungkin ditemukan di pasien lansia. Immunosenescence dan fungsi imunoregulasi jenis kelamin tertentu dihipotesiskan memiliki peran penting dalam menyebabkan kematian lansia di studi ini.*

Kata kunci: *profil klinis, lansia, pasien geriatri, COVID-19, Indonesia.*

ABSTRACT

Background: *older people contributed to 38.6% of death cases related to COVID-19 in Indonesia. Data regarding clinical profile of hospitalised elderly with COVID-19 in Indonesia were still lacking. Older people are at-risk population in the pandemic, whom we should pay attention to.* ***Methods:*** *this single centre descriptive study utilised complete data of elderly inpatients with COVID-19 in Indonesia's national general hospital from April to late August 2020. The data consisted of clinical characteristics, symptoms, comorbidities, multimorbidity, and mortality outcome.* ***Results:*** *among elderly patients (n=44), a majority of patients were aged 60-69 years (68%), were male (66%), and had no history of close contact with COVID-19 patient (86%). The most common*

symptoms were fever, cough and shortness of breath (classic symptoms of COVID-19), whereas the most common chronic diseases were diabetes mellitus, hypertension, and malignancy. Multimorbidity was only found in 14% of patients, all of whom remained alive following SARS-CoV-2 infection. The death rate among elderly inpatients with COVID-19 in this study was 23%, and male older adults contributed to 90% of death cases. ***Conclusion:*** *male patients dominated both confirmed cases and death cases among elderly with COVID-19. Classic symptoms of COVID-19 were only found in about half of the study patients. Non-survivors had higher percentage of the classic symptoms of COVID-19 than survivors. Atypical COVID-19 presentations are possible in older adults. We postulated that immunosenescence and sex-specific immunoregulatory function play an important role in causing death in this study cohort.*

Keywords: *clinical profile, elderly, geriatric patient, COVID-19, Indonesia.*

INTRODUCTION

Indonesia faced challenges in tackling coronavirus disease 2019 (COVID-19). The pandemic itself is still an ongoing problem in many parts of the world. There is no sign of decrease in number of new cases in Indonesia, which exceeded 3,000 in late August. In late March 2020, the nation's case fatality rate (CFR) reached 8.9%[1], whereas the rate was 4.3% in late August.[2] Despite the decrease, it was still higher than the global case fatality rate.

Among confirmed cases in late August in Indonesia, 11.2% were elderly patients aged 60 years and above. Older people also contribute to 38.6% of death cases related to COVID-19 nationwide.[2] A hospital-based report from Hainan, China, stated that only 5.26% of elderly with COVID-19 died. The most common symptoms were fever and cough. Only a minority of elderly had co-morbidities, such as diabetes and diabetes.[3] However, data regarding clinical profile of hospitalised elderly with COVID-19 in Indonesia were lacking. Older people are at-risk population in the pandemic,[4] whom we should pay attention to. Indonesia's national general hospital is one of COVID-19 referral centres with integrated care and specialised isolation ward for the patients, including elderly inpatients with COVID-19.

We aimed to provide a descriptive study results of clinical profile of elderly inpatients with COVID-19 in Indonesia's national general hospital. This may in turn inform Indonesian physicians of the possible presentations and sex-specific difference in outcome of elderly with COVID-19.

METHODS

This observational descriptive study utilised inpatient data of Cipto Mangunkusumo Hospital, Indonesia's national general hospital, from April to late August 2020. The data of elderly inpatients aged 60 years and older with COVID-19 consisted of clinical characteristics, symptoms, comorbidities, and mortality outcome. The data were inputted and filled in by physicians to electronic and handwritten medical record, respectively. The inclusion criterion was complete data of elderly inpatients with COVID-19.

COVID-19 confirmation was based on gold-standard laboratory test, reverse transcription polymerase chain reaction (RT-PCR). Clinical characteristics consisted of age (classified into 60-69 years; and 70 years and older), sex (female or male), history of close contact with COVID-19 patients, and outcome. We took into account fever, cough, shortness of breath, sore throat, rhinorrhoea, anosmia, nausea, vomitting, diarrhoea, abdominal pain, myalgia and malaise as symptoms reported by the patients. Underlying chronic diseases included diabetes mellitus, hypertension, cardiovascular disease, chronic kidney disease (CKD), malignancy, chronic obstructive pulmonary disease (COPD), asthma, tuberculosis (TB), cerebrovascular disease. We also gathered data in regards to multimorbidity of elderly patients. Multimorbidity was defined as the presence of 2 or more chronic diseases in the same individual. We recorded the data related to history of close contact, symptoms, and comorbidites as "yes" if present and "no" if absent. Descriptive statistical analysis utilised IBM SPSS Statistics Version 20 and the results were subsequently presented as number of cases and percentage.

Table 1. Clinical characteristics and symptoms of elderly patients with COVID-19 hospitalised in Indonesia's national general hospital.

Variables	All elderly patients n (%)	Survivors (n=34) n (%)	Non-survivors (n=10) n (%)
Clinical Characteristic			
Age group			
- 60-69 years	30 (68)	24 (71)	6 (60)
- 70 years and above	14 (32)	10 (29)	4 (40)
Sex, Male	29 (66)	20 (59)	9 (90)
History of close contact with COVID-19 patient			
- No	38 (86)	28 (82)	10 (100)
- Yes	6 (14)	6 (18)	0 (0)
Symptoms			
Fever			
- No	18 (41)	14 (41)	4 (40)
- Yes	26 (59)	20 (59)	6 (60)
Cough			
- No	18 (41)	14 (41)	4 (40)
- Yes	26 (59)	20 (59)	6 (60)
Shortness of breath			
- No	19 (43)	15 (44)	4 (40)
- Yes	25 (57)	19 (56)	6 (60)
Sore throat			
- No	36 (82)	26 (76)	10 (100)
- Yes	8 (18)	8 (24)	0 (0)
Rhinorrhoea			
- No	43 (98)	33 (97)	10 (100)
- Yes	1 (2)	1 (3)	0 (0)
Anosmia			
- No	44 (100)	34 (100)	10 (100)
- Yes	0 (0)	0 (0)	0 (0)
Nausea			
- No	39 (89)	30 (88)	9 (90)
- Yes	5 (11)	4 (12)	1 (10)
Vomitting			
- No	40 (91)	31 (91)	9 (90)
- Yes	4 (9)	3 (9)	1 (10)
Diarrhoea			
- No	37 (84)	30 (88)	7 (70)
- Yes	7 (16)	4 (12)	3 (30)
Abdominal pain			
- No	40 (91)	30 (88)	10 (100)
- Yes	4 (9)	4 (12)	0 (0)
Myalgia			
- No	41 (93)	32 (94)	9 (90)
- Yes	3 (7)	2 (6)	1 (10)
Malaise			
- No	23 (52)	17 (50)	6 (60)
- Yes	21 (48)	17 (50)	4 (40)

The study has been approved by the Ethical Committee of Faculty of Medicine Universitas Indonesia with reference number KET-419/UN2F1/ETIK/PPM.00.02/2020.

RESULTS

We collected data from 44 elderly patients in this study. The death rate among this cohort was 23%. Among all elderly patients, a majority of patient were aged 60-69 years (68%), were male (66%), and had no history of close contact with COVID-19 patient (86%). (**Table 1**) The classic COVID-19 symptoms of fever, cough and shortness of breath were only present in 59%, 59%, and 57% of elderly patients, respectively. Nearly half of the patients had malaise. Most elderly patients did not complain of sore throat, rhinorrhoea, anosmia, nausea, vomitting, diarrhoea, abdominal pain, and myalgia.

There was a higher proportion of elderly aged 70 years and older among non-survivors compared to the survivors (40% vs 30%). Ninety percent of non-survivors were male patients. Diarrhoea were also present in 30% of non-survivors, whereas it was reported by only 11.8% of survivors.

Multimorbidity was only found in 14% of patients, all of whom remained alive following SARS-CoV-2 infection. The most common chronic diseases found in elderly inpatients with COVID-19 were diabetes mellitus (11%), hypertension (14%), and malignancy (7%). (**Table 2**).

Table 2. Chronic diseases of elderly patients with COVID-19 hospitalised in Indonesia's national general hospital.

Variables	All elderly patients n (%)	Survivors (n=34), n (%)	Non-survivors (n=10), n (%)
Diabetes mellitus			
- No	39 (89)	29 (85)	10 (100)
- Yes	5 (11)	5 (15)	0 (0)
Hypertension			
- No	38 (86)	28 (82)	10 (100)
- Yes	6 (14)	6 (18)	0 (0)
Cardiovascular disease			
- No	43 (98)	33 (97)	10 (100)
- Yes	1 (2)	1 (3)	0 (0)
Chronic kidney disease			
- No	42 (95)	32 (94)	10 (100)
- Yes	2 (5)	2 (6)	0 (0)
Malignancy			
- No	41 (93)	32 (94)	9 (90)
- Yes	3 (7)	2 (6)	1 (10)
Chronic obstructive pulmonary disease			
- No	44 (100)	34 (100)	10 (100)
- Yes	0 (0)	0 (0)	0 (0)
Asthma			
- No	44 (100)	34 (100)	10 (100)
- Yes	0 (0)	0 (0)	0 (0)
Tuberculosis			
- No	42 (95)	33 (97)	9 (90)
- Yes	2 (5)	1 (3)	1 (10)
Cerebrovascular disease			
- No	43 (98)	33 (97)	10 (100)
- Yes	1 (2)	1 (3)	0 (0)
Multimorbidity (≥2 chronic diseases in the same individual)			
- No	38 (86)	28 (82)	10 (100)
- Yes	6 (14)	6 (18)	0 (0)

DISCUSSION

The death rate among hospitalised older adults with COVID-19 in this study was much higher than the national COVID-19 case fatality rate among Indonesian elderly (23% vs 14.9%).[2] Not only was male sex predominant among confirmed cases of COVID-19 in elderly population in this study, 90% of non-survivors were also of male sex. A study utilising data of 17,278,392 adults suggested that male sex itself is associated with COVID-19-related death (hazard ratio (HR) 1.59, 95% CI 1.53 to 1.65). The study also showed that estimated HR for COVID-19-related death also increases in older age groups.[4]

There were several mechanisms that could possibly explain the link between male sex and unfavourable disease outcome. Both ACE2 and transmembrane serine protease-2 (TMPRSS2) are crucial for SARS-CoV-2 viral entry in human cells.[5] Since ACE2 gene is located on the X chromosome, alleles that confer resistance to COVID-19 may be present, explaining the lower adverse outcome among female patients.[6] Different outcome of the disease based on sex category can also be explained by different immunoregulatory functions of testosterone and oestrogen sex hormones.[7] In general, there is different response to many DNA and RNA viral infections in males compared to females.[8] Testosterone's control of TMPRSS2 expression has been suggested to contribute to male predominance in terms of unfavourable outcomes in COVID-19. Androgen receptor activity is required for the transcription of TMPRSS2 gene.[9] Furthermore, immune system of male individuals respond to the infection less robustly. Ageing males have a more dramatic decrease in total amount of B and T cells compared to females. In addition, ageing males experience higher increases in senescent CD8+ T effector memory cells. Similar to COVID-19 data, epidemiological data of SARS-CoV-1 and MERS-CoV infection also suggested different disease outcome based on sex category.[8]

As one ages, disruption of both innate and adaptive arms of the immune system has been reported.[10] Ageing is characterised by a progressive dysfunction of several compartments of the immune system, namely immunosenescence, including immunodeficiency and smouldering inflammation.[11] Immunosenescence of COVID-19 patients may in turn promote viral-induced cytokine storm leading to systemic problems, and life-threatening respiratory failure.10 In addition, abnormal ciliary function may impair SARS-CoV-2 viral particle clearance in the elderly.[12]

The disease has been widespread in Indonesia. There was increasing evidence that several patients with COVID-19 have only mild symptoms or are asymptomatic. However, there are difficulties in detecting the asymptomatic infections.[13] Since almost all elderly in this study had no history of close contact with confirmed cases, older adults as well as their caregivers and relatives should really take extra precautions against COVID-19. Moreover, family cluster has been reported in Indonesia and asymptomatic person may potentially transmit the virus.[14]

In this study, only approximately 50% elderly inpatients with COVID-19 presented with classic symptoms of COVID-19 (fever, cough, and shortness of breath). In addition, it should be noted that the percentages of patients complaining of fever, cough, and shortness of breath were higher in non-survivors. This highlights the possibility of atypical presentation of COVID-19 among older adults. Albeit possible, the most common symptoms of COVID-19 in both elderly and non-elderly patients are still fever and cough.[3] Older people are generally already at risk for higher morbidity and mortality due to infection. However, as a cardinal sign of infection, fever may be absent or blunted in elderly patients. The absence of or blunted response to fever may result in diagnostic delay in this population.15 The delay in diagnosis may in turn cause further spread of COVID-19.[16]

The most common chronic diseases of confirmed cases and death cases in older adults in this study were similar to the overall national data, namely hypertension and diabetes mellitus.2 Similarly, hypertension (43.8%) and diabetes mellitus (25.7%) were also the most common underlying chronic diseases in elderly patients with COVID-19 according to a multicentre study in China.[17] A hospital in Hainan, China,

reported that only 27.78% of elderly with COVID-19 had hypertension, whereas it was 16.67% for diabetes.[3] Most underlying chronic diseases were associated with increased risk for death of COVID-19 patients, including diabetes mellitus, cardiovascular disease, kidney disease, respiratory disease (including severe asthma) and history of malignancy.[4] Based on our study and the previous reports, the co-morbidities were found only in a minority of elderly with COVID-19.

An analysis of adult data from UK Biobank (n=428,199) suggested that multimorbidity, especially cardiometabolic multimorbidity, was associated with increased risk for developing COVID-19.[18] As multimorbidity was not the prominent feature of non-survivors in our study, we postulated that immunosenescence and sex-specific immunoregulation play an important role in causing death in this study cohort.

To date, we believe that our study is the first descriptive study focusing on the clinical profile of elderly inpatients with COVID-19 in Indonesia. It is also among the first descriptive studies with similar topic in Southeast Asia. On the other hand, we acknowledge the limitations of this study. The number of patients in this study was still limited. The preliminary data were not consecutive nor randomised. This study relied on successful collection of complete data of patients from the medical record. However, we believe that there may not be remarkable differences between the data presented in this study and the data gathered with extension of data collection period. This article may act as a thought-provoking manuscript to increase the awareness and possibilities pertaining to elderly inpatients with COVID-19. Future studies with similar focus and larger sample size have yet to be conducted.

CONCLUSION

The death rate among elderly inpatients with COVID-19 in this study was 23%, dominated by male patients. Fever, cough, and shortness of breath were only found in about half of elderly with COVID-19, but non-survivors had higher percentage of the classic symptoms of COVID-19 than survivors. The most common underlying chronic diseases were diabetes mellitus and hypertension. We postulated that immunosenescence and sex-specific immunoregulatory function play an important role in causing death in this study cohort.

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