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Research Article

COVID-19 Infection in Egyptian Older Patients: Does it Differ?

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Abstract

The affection of older population was noticed early in COVID-19 pandemic with a less favorable outcome. Differences in mortality and prevalence were observed between countries, which could be explained by various theories. We conducted this study to investigate and compare the clinical characteristics of COVID-19 among elderly with young and middle-aged patients. Descriptive comparative study was conducted on 139 confirmed COVID-19 cases recruited from Ain Shams University Specialized Hospital in Obour City from May 1st to June 15th, 2020. According to age, cases were divided into two groups: the elderly group (≥ 60 years old), with 66 patients, and the middle-aged group (< 60 years old), with 73 patients. The mean age of elderly group was 66 years, while that of young and middle-aged group was 38 years. Besides, the elderly group demonstrated higher CURB65 score than that of young and middle-aged group ($P < 0.01$). In older patients, development of acute respiratory distress syndrome (ARDS) and septic shock was significantly higher than that of young and middle-aged patients. Furthermore, older patients group exhibited significantly higher mortality than the other group, reaching 13 (19.7%) and 3 (4.1%), respectively. The older population remains the most vulnerable group, suffering from significant morbidity and mortality during COVID-19 pandemic.

Keywords: COVID-19; Older Patients; CURB65; ARDS; Mortality

Introduction

The recent outbreak of coronavirus recognized as COVID-19 represents a significant public health threat on a global scale. This rapidly infectious disease, resulted from exposure to a member of coronavirus family, was called acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was first isolated from patients in Wuhan City, China, in December 2019 [1].

Given the rapid spread among countries, on March 11, 2020, the World Health Organization (WHO) declared that SARS-CoV-2 is a global pandemic. As of January 2020, over 132 million COVID-19 cases have been confirmed, with over two million deaths [2].

The Centers for Disease Control and Prevention (CDC) reported that 8 out of 10 deaths in the U.S. occurred in adults aged 65 and older. Compared to younger ages, older population showed that

hospitalizations' rate due to COVID-19 infections was 5x higher and 13x higher for those aged ≥ 65 and ≥ 85, respectively. Besides, mortality rate was 90x higher among those ≥ 65 old, and rates increase dramatically with age. Based on this, it appears that older individuals are more likely to be infected with COVID-19 and have worse health outcomes than the general population [3].

In Egypt, confirmed COVID-19 cases reached approximately 207 thousand people, with over 12 thousand deaths. The Egyptian ministry of health reported that although individuals aged 60 or over comprise 6.7% of the total population, they account for 20% and 7% of COVID-19 infections in the age groups over 60 and 70, respectively. Also, older patients represent 60% of total death rates [4].

Risk factors for disease progression are studied; however, preliminary data suggest that disease severity is more likely to be linked to individuals with older age, male sex, and underlying comorbidities [5]. The fact that higher impact on older persons, in particular, those with a higher comorbidity burden and increased risk from COVID-19 complications, is strongly related to age-related changes in the immune system associated with multimorbidity [6].

The older population showcases immunosenescence, causing immune system disruption as age advances and exhibits a continual process of producing inflammatory mediators and cytokines, known as 'inflamm-aging' phenomenon. This dysregulation in cytokine homeostasis plays a critical role in developing cytokine storm, causing more severe COVID-19 infection and increasing morbidity and mortality in older patients [7].

As mortality and morbidity were observed to be higher among older population in the available data up-to-date, this study aimed to compare clinical features and outcomes between older population and adult COVID-19 patients.

Methods

This study was a retrospective descriptive comparative one, including 139 confirmed COVID-19 cases by nasopharyngeal swab PCR treated in Ain Shams University (ASU) Obour isolation hospital from May 1, 2020 to June 15, 2020. The included cases were divided into older group (≥ 60 years old) and young and middle-aged group (< 60 years old). The Ethical Committee of Human Experimentation of Faculty of Medicine at Ain Shams University approved this study and informed consents were taken.

The treatment protocol was applied according to Egyptian national protocol besides the approved drugs by the university hospitals treatment protocols.

The clinical records were revised regarding symptoms characteristics, laboratory results (leukocyte, neutrophil ratio, lymphocyte ratio, C reactive protein (CRP)), imaging, treatment lines, admission to intensive care unit (ICU), mechanical ventilation requirements, hospital stay duration of the two groups and disease outcome. Comparison between both groups of patients regarding pneumonia severity was performed using CURB 65 score (confusion, urea >7 mmol/L, respiratory rate ⩾30/min, and low blood pressure (diastolic blood pressure (DBP) ⩽60 mm Hg or systolic blood pressure (SBP) < 90 mm Hg) and age ⩾ 65). Each present feature was given one point, with values ranging from 0 to 5; higher scores indicated more severe pneumonia. As patients with a CURB65 score of ≥ 3 points have a higher 30-day mortality rate (22%) [8], it was utilized as a cutoff for comparison between both groups.

According to British society of thoracic imaging, the difference between the two groups of patients was classified based on chest slice computed tomography (CT) regarding diagnosis and severity of lung affection [9]:

- **Mild:** Pure ground glass opacities (GGO) + ≤3 focal abnormalities, all are < 3 cm max diameter.
- **Moderate/severe*:** Pure GGO + (>3 focal abnormalities or >3 cm max diameter) or focal GGO + early consolidation (The difference between moderate and severe is subjective to reporters' opinion).
- **Severe:** Diffuse GGO or consolidation with architectural distortion signs.

Statistical analysis

Data were coded and processed with a pre-designed SPSS (Statistical Package for Social Science) version 20 and then checked for data entry errors. Continuous variables with normal distribution as age were expressed as mean ± standard deviation and analyzed using independent t-test to compare data between the two groups. Categorical variables as gender were presented as numbers and percentage and analyzed using Chi-square test to compare data be-

tween the two groups. Post hoc paired comparison was done using Chi-square test for qualitative data. A value of $P < 0.05$ was considered statistically significant.

Variable	Older patients (n = 66, 47.5%)	Young and middle-aged (n = 73, 52.5%)	p-value
Demographic characteristics			
Age (years)	66.47 (60-88)	38.03 (22-55)	< 0.01
Male (n, %)	47 (71.2%)	32 (43.8%)	0.01
Co-morbidities (n, %)			
DM	21 (31.8%)	5 (6.8)%	< 0.01
Hypertension	27 (40.9%)	8 (11%)	< 0.01
Bronchial Asthma	2 (3%)	5 (6.8%)	0.30
Coronary heart disease	12 (18.2%)	1 (1.4%)	< 0.01
COPD	2 (3%)	1 (1.4%)	0.50
Chronic kidney disease	6 (9.1%)	4 (5.5)	0.41
Atrial fibrillation	5 (7.6%)	0	-
Chronic liver disease	3 (4.5%)	0	-
Cerebrovascular stroke	3 (4.5%)	0	-
Clinical manifestations (n, %)			
Fever	52 (78.8%)	52 (71.2%)	0.31
Dyspnea	47 (71.2%)	32 (43.8%)	0.01
Tachycardia	22 (33.3%)	25 (34.2%)	0.91
Confusion	24 (36.4%)	6 (8.2%)	< 0.01
Fatigue	33 (50%)	31 (42.5%)	0.37
Cough	33 (50%)	31 (42.5%)	0.37
Anosmia	8 (12.1)	17 (23.3%)	0.09
Loss of taste	11 (16.7%)	15 (20.5%)	0.56
Diarrhea	10 (15.2%)	8 (11%)	0.46
Hypoxia	46 (69.7%)	27 (37%)	< 0.01
Pneumonia severity Curb65	2.59	0.77	<0.01

Table 1: Comparison of past medical history and basic clinical characteristics between the two groups.

COPD: Chronic Obstructive Lung Disease.

Results

During the study period, 139 patients were evaluated, including 66 older patients (47.5%), with mean age of 66 years (60 - 88) and 73 young and middle-aged patients (52.5%), with mean age of 38 years (22 - 55), showing a statistically significant difference between the two groups ($P < 0.01$).

The both groups experienced prevalent symptoms, including fever, dyspnea, cough, and fatigue. The CURB65 score of older patients group was higher than that of young and middle-aged group ($P < 0.01$). For the former group, CURB65 score ≥ 3 was significantly higher than that of the latter group ($P < 0.01$).

Variable	Older patients (n = 66, 47.5%)	Young and middle-aged (n = 73, 52.5%)	p-value
CT severity score			
Normal	2 (3%)	30 (41.1%)	<0.01
Mild	20 (30.3%)	22 (30.1%)	
Moderate	18 (27.3%)	17 (23.3%)	
Severe	26 (39.4%)	4 (5.5%)	
Laboratory indicators at admission			
Hemoglobin (g/L)	12.26 (± 2.47)	13.42 (± 1.60)	<0.01
Total leukocyte count ($\times 10^9$/L)	8.02 (± 4.17)	5.54 (± 2.23)	<0.01
Neutrophil ($\times 10^9$/L)	6.37 (± 4.06)	3.56 (± 2.27)	<0.01
Lymphocyte ($\times 10^9$/L)	1.20 (± 0.73)	1.59 (± 0.76)	<0.01
Platelets ($\times 10^9$/L)	259.51 (± 85.28)	255.10 (± 79.94)	0.75
ALT (U/L)	46.48 (± 37.59)	35.25 (± 41.39)	0.10
AST (U/L)	43.34 (± 47.31)	29.86 (± 22.86)	0.03
D.dimer (µg/mL)	1007.97 (± 1071.65)	612.10 (± 913.03)	0.02
Ferritin ($\times 10^2$µg/L)	779.46 (± 725.15)	420.76 (± 669.95)	<0.01
Urea (mmol/L)	58.98 (± 36.51)	42.49 (± 25.05)	<0.01
Creatinine (µmol/L)	1.32 (± 1.23)	1.42 (± 4.17)	0.85
CRP (mg/L)	83.64 (± 56.57)	31.18 (± 45.33)	<0.01

Table 2: Differences between CT and laboratory indicators in the chest between the two groups.

ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase.

During the hospitalization period, lung CT scans of 139 patients were performed, resulting in higher proportion of severe lung affection in older patients group and dominant normal CT findings among young and middle-aged patients. The higher-grade or level of CT severity scores is always present in the older patients group and is statistically significant compared to adult group through the paired comparison.

Although older patients group manifested lower proportion of lymphocytes than that of young and middle-aged group (P < 0.01), it showed significantly higher CRP, white blood cell count, neutrophil ratio, urea, d dimer, and ferritin levels. Beside, no significant differences were present in platelet and serum creatinine in both groups.

Variable	Older patients (n = 66, 47.5%)	Young and middle-aged (n = 73, 52.5%)	P value
Complications (n, %)			
ARDS	12 (18.2%)	2 (2.7%)	<0.01
AKI	2 (3%)	2 (2.7%)	0.92
MI	3 (4.5%)	0	-
Shock	12 (18.2%)	2 (2.7%)	<0.01
Myocarditis	0	1 (1.4%)	-
Lines of treatment (n, %)			
Favipiravir	6 (9.1%)	30 (41.1%)	<0.01
Hydroxychloroquine	60 (90.9%)	43 (58.9%)	<0.01
Oxygen	51 (77.3%)	28 (38.4%)	<0.01
Tocilizumab	29 (43.9%)	11 (15.1%)	<0.01
Mechanical ventilation (n, %)			
No need	41 (62.1%)	62 (84.9%)	<0.01
Non invasive	9 (13.6%)	5 (6.8%)	
Invasive	16 (24.2%)	6 (8.2%)	
No ventilation	41 (71.9%)	62 (91.2%)	<0.01
Invasive	16 (28.1)	6 (8.8%)	
ICU admission (n, %)			
Need	38 (57.6%)	14 (19.2%)	<0.01
Not need	28 (42.4%)	59 (80.8%)	
length of hospital stay (in days)	14.17 (5-24)	14.04 (5-25)	0.89
Prognosis (n, %)			
Cured and discharged	53 (80.3%)	70 (95.9%)	<0.01
Deceased	13 (19.7%)	3 (4.1%)	

Table 3: Complications and treatment measures after admission in the two groups.

AKI: Acute Kidney Injury; MI: Myocardial Infarction.

The development of ARDS and shock in older patients group was significantly higher than that in young and middle-aged group.

Using hydroxychloroquine, favipiravir, and tocilizumab was statistically different in both groups. Need for oxygen therapy and ICU admission were significantly higher among older patients group (P < 0.01).

Comparing patients who required invasive mechanical ventilation to those who did not, we found a statistically significant difference between older patients group and young and middle-aged group (older patients (28.1%) who required invasive ventilation are significantly higher than adults (8.8%), (P < 0.01)).

Extracorporeal membrane oxygenation had been used for only one patient in the study group aged 53, and the patient subsequently died.

The average number of hospital stay days in both groups was 14 days with no significant difference, and regarding prognosis and outcome, deaths' percentage was significantly higher among older patients group than young and middle-aged group (P < 0.01).

Figure 1: CURB 65 score differences among study groups.

The figure shows that patients with CURB65 score ≥ 3 were more prevalent among older group than young and middle-aged one.

Discussion

COVID-19 infection has shown a distinctive behavior among older patients compared with children and young adults, inducing severe infections including pneumonia and ARDS [10].

Among 139 patients with COVID-19 infection, we observed that men are much more severely affected than women in the older patients group, similar to MERS-CoV and SARS-CoV [11]. Besides, older patients with chronic diseases, mainly cardiovascular diseases and diabetes mellitus (DM), had significantly higher prevalence than in young and middle-aged patients, similar to MERS-CoV [12]. Therefore, SARS-CoV-2 seems to be more likely to infect adult men with chronic comorbidities due to their weaker immune functions, which was corroborated by findings from a Chinese study which included 59 patients [13].

In this study, most SARS-CoV-2 patients had fever, dyspnea, dry cough, and easy fatigability, implying close similarity to SARS-CoV and MERS-CoV [14]. The current results agreed with the Chinese study with patients having mainly fever, cough, dyspnea, and fatigue [15]. Few patients with SARS-CoV-2 had anosmia, taste loss, and some intestinal symptoms (e.g., diarrhea), in contrast to MERS-CoV or SARS-CoV in which about 20-25% of patients had diarrhea [14]. According to CURB65 scoring system, older SARS-CoV-2 patients demonstrated significantly higher pneumonia severity scores than young and middle aged group denoting more severe pneumonia and worse clinical conditions, consistent with Liu K., *et al*. study [13].

Also, in the current study above 60 years old patients, CURB65 score was significantly higher in deceased patients than cured patients (means 4.08 and 2.23, respectively) ($P < 0.01$). This was similar to other studies, which reported that patients with CURB65 score ≥ 3 had higher mortality [8].

Regarding laboratory tests, lymphocytes count proportion was significantly lower in older patients than that of young and middle-aged ones. Besides, number of white blood cells and neutrophils in older patients was much higher than that in young and middle-aged group, suggesting that older infected patients are more vulnerable to have a secondary bacterial infection.

This result proposes that SARS-CoV-2 mainly acts on lymphocytes, especially T lymphocytes, as observed with SARS-CoV. Typically, virus particles spread across respiratory mucosa and infect other cells producing a series of immune responses and a cytokine storm, causing changes in peripheral white blood cells and immune cells such as lymphocytes [12].

The CRP level in older patients is significantly higher than that in young and middle-aged group, similar to MERS-CoV [7]. Ample studies have reported a chronic condition of cytokine homeostasis dysregulation in aged subjects known as "inflame-aging" phenomenon associated with increased levels of systemic pro-inflammatory cytokines (e.g. CRP). This age-related pathophysiologic process plays a critical role in the risk of developing cytokine storm and subsequently acute respiratory distress syndrome (ARDS) in COVID-19 older patients with severe infection [16]. In our study, we reported that among older patients, development of ARDS and septic shock was significantly higher than in young and middle-aged ones. In convenience with many preceding studies [17].

Regarding imaging, chest imaging is the cornerstone for detecting lung abnormalities during viral infection, and CT examination represents the most direct and rapid examination that confirms diagnosis and detects changes in patient's condition to guide the treatment plan. We found that the incidence of severe lung affection in older patients is significantly higher than in young and middle-aged ones. Typical features of COVID-19 CT presentation include bilateral ground-glass opacification (GGO) multi-lobar with a peripheral or posterior distribution, mainly in the lower lobes, and presentation of superimposed consolidative opacities found mainly in the older population. The multi-lobar involvement was more common in older patients group than in young and middle-aged one [18].

Regarding outcome and mortality rate, we found that the average number of hospital stay days was almost the same between both groups; however, the death rate among older patients was significantly higher, consistent with several preceding reports [7,13,16].

Our study reported that ARDS and septic shock occurrence was an extremely strong predictor of fatal outcomes among older patients. This agrees with the study, which stated that once ARDS occurred, the 28-day mortality would be nearly 50% [19].

Regarding various treatment lines, antiviral is particularly important in treating COVID-19, but until now, no specific drugs targeting new coronaviruses were found. In this study, hydroxychloroquine was the main drug used in both groups based on early studies that suggest its potential anti-viral activity along with anti-inflammatory effects [20]. The older patients group also received

favipiravir antiviral due to its mechanism of action to inhibit virus RNA-dependent RNA polymerase and safety data [21]. Tocilizumab is a recombinant humanised monoclonal antibody used as an immune modulator in life-threatening cytokine release syndrome. In severe COVID-19 cases, they develop a cytokine that produces long-term damage and lung tissue fibrosis, resulting in using tocilizumab to treat severe COVID-19 patients [22]. From this clinical point of view, our older patients received tocilizumab, with significantly higher proportion than in young and middle-aged group.

Respiratory support is an essential treatment for patients with severe viral infections. The present study revealed that older COVID-19 patients significantly required respiratory support over young and middle-aged ones, as well as nasal cannula oxygen administration and mechanical ventilation. The older patients group was significantly more likely to receive higher respiratory support levels matched with the results of Liu W., *et al*. study [23].

The major limitations of the present work were the small sample size included. In addition to different medications regimen patients received, different clinical outcomes may result.

Conclusion

The older population remains the most vulnerable group with major morbidity and mortality in COVID-19 pandemic.

Declaration of Competing Interest

The authors have no conflicts of interest to disclose.

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