Risk factors associated with severe disease and death in COVID-19 patients

Introduction

COVID-19 can affect anyone, and the disease can cause symptoms ranging from mild to very severe. However, some people may be more likely to have severe illness than others because they have characteristics or medical conditions that increase their risk. Given that the burden to the health system due to COVID-19 is a consequence of the disease severity, it is important to identify these risk factors in order to find at-risk individuals and develop prevention and treatment measures appropriate to these groups. Once identified, information on the proportion of high-risk individuals will also inform government responses in managing healthcare resources according to the burden of disease. This information can also inform plans to identify and protect the vulnerable in the society especially when countries are loosening initial restrictions.

Key Messages

- While everyone is at risk of SARS-CoV-2 infection, some people may be more likely to progress to severe illness than others because they have characteristics or medical conditions that increase their risk.
- The major risk factors associated with severe disease and death include older age (>65 years), male gender and the presence of comorbidities.
- Comorbidities such as heart disease, hypertension, diabetes and chronic obstructive respiratory disease are the most common in COVID-19 deaths but HIV-1 and TB infection are also associated with increased risk of death from COVID-19 in Africa.
- It is important to ensure that all persons at high risk of developing severe disease and mortality are identified to facilitate prompt access to health facilities and appropriate supportive care and to inform prevention strategies.

Evidence from China, Italy, France and the UK identified several risk factors such as older age (>65 years), male gender, the presence of co-morbidities and certain clinical manifestations (e.g. shortness of breath and fever) as some of the key risk factors associated with severe illness or death[1-4]. Table 1 summarizes findings from systematic reviews and meta-analyses conducted to synthesize evidence on COVID-19 risk factors.

Table 1: Summary of meta-analyses of risk factors associated with severe COVID-19 and mortality

Risk Factor	Study	Odds/Risk ratio (95% CI)	What it means
Age	Zheng et al.	OR = 6.06 (3.98 - 9.22), P < 0.00001	Disease progression (to critical state and death) was 6.06 times more likely in older individuals (>65 years) compared to younger ones
	Parohan et al.	OR= 4.59 (2.61 – 8.04), p<.001	Individuals older than 65 years were 4.59 times more likely to die from COVID-19 compared to those younger than 65
Male gender	Martins-Filho et al.	RR=1.3 (1.1 - 1.4), p < 0.001	Being male increased the risk of mortality 1.3 times compared to being female
	Zheng et al.	OR = 1.76 (1.41 - 2.18), P < 0.0 0 0 01	Disease progression (to critical state and death) was 1.76 times more likely in men compared to women
	Abate et al.	RR=1.63(1.33-1.99, p=0.000	Being male increased the risk of mortality 1.63 times compared to being female
Co-morbidities	Espinosa et al.	OR=2.4, (1.7-3.3) p=0.0001	The risk of death for a patient with a comorbidity compared to one with no comorbidity was 2.4 higher
	Abate et al.	RR= 2.20(1.75 - 2.77)	Mortality among hospitalized patients with COVID-19 was two times more likely in patients with any co-morbidity as compared to those who didn't have co-morbidities
	Martins-Filho et al.	RR= 1.6, 95%CI 1.4 - 2.0	The risk of in-hospital death for patients with co-morbidities was 1.6 times higher
Clinical manifestation	Zheng et al.	shortness of breath: OR=4.16, (3.13-5.53), P < 0.00001	Patients with fever are 4.16 times more likely to progress to severe disease
	Shi et al.	Shortness of breath: OR = 4.34 (2.68–7.05), P < 0.001	The risk of mortality in patients with shortness of breath was 4.34 times higher
	Martins-Filho et al.	Shortness of breath: RR=1.8, (1.4 - 2.2)	The risk of in-hospital death for patients with shortness of breath was 1.8 times higher

Age

Increasing evidence has shown that older patients are more likely to develop severe illness and have a higher risk of in-hospital death[1-5]. For example, over 95 per cent of fatalities due to COVID-19 in Europe have been of people aged 60 years or older. In the United States, 80% of deaths were among adults aged 65 years and older.

Gender

Men were found to be more likely to develop critical illness and succumb to COVID-19 compared to women[6,7]. Mortality data from China, Italy and the USA show that majority of deaths recorded were in men[2,5,8].

Existing co-morbidities/underlying health conditions

The most commonly reported conditions that put patients at higher risk of severe disease and mortality were[7,9-12]:

1. Diabetes,
2. Hypertension,
3. Chronic lung disease, and
4. Cardiac disease

In the South African province of the Western Cape, **HIV-1 and TB infection are associated with 2-2.5 times higher risk of COVID-19 death**[13]. Additionally, presence of more than one co-morbidity was associated with poorer clinical outcomes[14].

Clinical manifestations

Symptoms of COVID-19 could also be predictors of severe disease and death. Patients with shortness of breath (dyspnea) were more likely to progress to critical illness or even die[6,15].

Conclusion

Older age, male gender, presence of co-morbidities and dyspnea are risk factors for severe disease and mortality. Identification of high-risk populations is important to reduce COVID-19 mortality. Firstly, it allows governments to make projections of the likely burden on the health system (e.g. capacity of critical care facilities) and implement necessary surge measures; and secondly, it informs the planning and implementation of strategies that can reduce transmission or poor outcomes in high-risk populations. Such strategies, known as shielding, involves minimizing interaction between high risk individuals such people over 65 years and those with comorbidities. However, this strategy is not feasible if a significant proportion of the population are shielded. In LMICs the feasibility of shielding should be addressed since rural areas are typically characterized by multigenerational households. Additionally, informal settlements, forced displacement camps (refugee, internally displaced), and low-income setting housing arrangements make it difficult to isolate vulnerable individuals because of the need to share amenities (such as toilets) and even sleeping rooms. It is therefore pertinent that a thorough assessment of the feasibility of shielding strategies is carried out. Information on high risk groups can also be used in the future when a vaccine is available in order to prioritize vaccination based on risk. Research on treatments should explore how to mitigate for the risk factors.

This brief was prepared by: Fatuma Guleid, Dr. Sam Akech, and Dr. Edwine Barasa

References

1. Wu, Z. & McGoogan, J. M. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. Jama 323, 1239-1242 (2020).
2. Di Lorenzo, G. & Di Trolio, R. Coronavirus Disease (COVID-19) in Italy: Analysis of Risk Factors and Proposed Remedial Measures. Front Med (Lausanne) 7, 140-140, doi:10.3389/fmed.2020.00140 (2020).
3. de Lusignan, S. et al. Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: a cross-sectional study. The Lancet Infectious Diseases (2020).
4. Kaeuffer, C. et al. Risk Factors Associated with Severe COVID-19 in Eastern France: Analysis of 1045 Cases. (2020).
5. Richardson, S. et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA 323, 2052-2059, doi:10.1001/jama.2020.6775 (2020).
6. Zheng, Z. et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. J Infect, doi:10.1016/j.jinf.2020.04.021 (2020).
7. Parohan, M. et al. Risk factors for mortality in patients with Coronavirus disease 2019 (COVID-19) infection: a systematic review and meta-analysis of observational studies. Aging Male, 1-9, doi:10.1080/13685538.2020.1774748 (2020).
8. Jin, J.-M. et al. Gender Differences in Patients With COVID-19: Focus on Severity and Mortality. Frontiers in Public Health 8, doi:10.3389/fpubh.2020.00152 (2020).
9. Yang, J. et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis 94, 91-95, doi:10.1016/j.ijid.2020.03.017 (2020).
10. Espinosa, O. A. et al. Prevalence of comorbidities in patients and mortality cases affected by SARS-CoV2: a systematic review and meta-analysis. Rev Inst Med Trop Sao Paulo 62, e43-e43, doi:10.1590/S1678-9946202062043 (2020).
11. Wang, B., Li, R., Lu, Z. & Huang, Y. Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. Aging (Albany NY) 12, 6049-6057, doi:10.18632/aging.103000 (2020).
12. Hu, Y. et al. Prevalence and severity of corona virus disease 2019 (COVID-19): A systematic review and meta-analysis. J Clin Virol 127, 104371, doi:10.1016/j.jcv.2020.104371 (2020).
13. Health, W. C. D. o. Western Cape: COVID-19 and HIV / Tuberculosis. Western Cape Department of Health (2020).
14. Guan, W.-J. et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Eur Respir J 55, 2000547, doi:10.1183/13993003.00547-2020 (2020).
15. Shi, L., Wang, Y., Wang, Y., Duan, G. & Yang, H. Dyspnea rather than fever is a risk factor for predicting mortality in patients with COVID-19. Journal of Infection (2020).

KEMRI | Wellcome Trust