



Risk factors for Covid-19 severity and fatality: a structured literature review

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Abstract

Purpose Covid-19 is a global threat that pushes health care to its limits. Since there is neither a vaccine nor a drug for Covid-19, people with an increased risk for severe and fatal courses of disease particularly need protection. Furthermore, factors increasing these risks are of interest in the search of potential treatments. A systematic literature review on the risk factors of severe and fatal Covid-19 courses is presented.

Methods The review is carried out on PubMed and a publicly available preprint dataset. For analysis, risk factors are categorized and information regarding the study such as study size and location are extracted. The results are compared to risk factors listed by four public authorities from different countries.

Results The 28 records included, eleven of which are preprints, indicate that conditions and comorbidities connected to a poor state of health such as high age, obesity, diabetes and hypertension are risk factors for severe and fatal disease courses. Furthermore, severe and fatal courses are associated with organ damages mainly affecting the heart, liver and kidneys. Coagulation dysfunctions could play a critical role in the organ damaging. Time to hospital admission, tuberculosis, inflammation disorders and coagulation dysfunctions are identified as risk factors found in the review but not mentioned by the public authorities.

Conclusion Factors associated with increased risk of severe or fatal disease courses were identified, which include conditions connected with a poor state of health as well as organ damages and coagulation dysfunctions. The results may facilitate upcoming Covid-19 research.

Keywords Covid-19 · SARS-CoV-2 · Review · Risk factors · Population at risk

Introduction

In the end of 2019, a novel respiratory disease, the coronavirus disease 2019 (Covid-19), occurred. The pathogen causing the disease was identified by next-generation sequencing as a novel coronavirus closely related to the SARS-coronavirus discovered in 2003 [1]. According to the WHO guidelines [2], this novel coronavirus was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). First cases of Covid-19 were reported from the Chinese city Wuhan located in the province Hubei in December 2019 [3]. The disease is spreading worldwide and was classified

as a pandemic by the WHO in March 2020 [4]. The virus is transmissible from human to human [5] and the number of infected people increases at an exponential rate, exceeding 1 mio. cases on 02.04.2020 and 1.5 mio. cases in 184 countries only a week later [6, 7]. At various disease hotspots such as New York, the health care system reaches its limits.

For diagnosis, the virus is mainly detected by real-time quantitative polymerase chain reaction (rt-PCR) in throat swabs [8, 9]. Due to limited test capacities, which require a special equipped laboratory, patients showing symptoms are tested only. On the onset of Covid-19 typical symptoms are fever, cough, myalgia and fatigue, while headache, sputum production, hemoptysis and diarrhea are less common. In the course of disease a subset of patients show pneumonia with abnormal findings on chest CT [10]. Severe cases are transferred to an intensive care unit (ICU) and frequently require artificial ventilation. The disease's case fatality rate is estimated between 3.4% and 11% [11].

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Table 4 Overview of risk factors reported by leading institutions

Robert Koch Institute [54]	U.S. CDC [55]	Johns Hopkins Medicine [56]	NHS UK [57]
Higher age (increase from 50–60 years)	Higher age (increase from 65 years)	Higher age (increase from 65 years)	Higher age (increase from 70 years)
Heart diseases	Living in a nursing home or long-term care facility	Diabetes	Organ transplant recipients
Diabetes	Chronic lung disease	Male gender	Lung diseases
Diseases of the respiratory system	Asthma	USA: obesity (BMI ≥ 30)	Blood or bone marrow cancer
Liver diseases	Heart diseases	USA: African American ethnicity	Heart diseases
Renal diseases	Immunosuppression	Comorbidities	Pregnancy
Obesity	Severe obesity (BMI ≥ 40)		Severe obesity (BMI ≥ 40)
Smoking	Diabetes		Chronic kidney diseases
Multimorbidity	Chronic kidney disease undergoing dialysis		Conditions affecting brain or nerves
Immunosuppression	Liver disease		Liver diseases

these could not be confirmed by the review, most of them seem to be very reasonable. Conditions resulting in a diminished immune system such as cancer, immunosuppression or being an organ transplant recipient weaken the body's own immune response to SARS-CoV-2. Another factor is expected to be the prevalent viral pressure, which is high in places where many partly immune-deficient people share little space such as nursing homes. Although studies from the USA were included, no justification for African American ethnicity being a risk factor was found in this review.

This review identified some risk factors not mentioned by public authorities. Mostly these are waiting time to hospital admission, tuberculosis, inflammation disorders and coagulation factors. It is possible that for these factors, especially coagulation factors, not enough evidence is present yet to be support by public authorities.

Conclusion

Most of the 28 records included in this review describe studies conducted in China. However, regarding the number of patients Italy is outstanding. **Conditions and comorbidities potentially connected to a poor state of health such as high age, obesity, diabetes and hypertension were identified as risk factors for severe and fatal disease courses.** It was found that severe and even more fatal courses of disease are associated with organ damages mainly affecting the heart, the liver and the kidneys. Further, inflammation and coagulation dysfunctionality were identified as risk factors. For coagulation factors, laboratory values were significantly different in Covid-19 patients but were mostly not mentioned as risk factors in the records' texts. A prospective study with 12 deceased Covid-19 patients supports this finding. Therefore, the influence of coagulation disorders developed during a SARS-CoV-2 infection should be further investigated.

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Data availability All data used is publicly available either by PubMed or CORD-19.

Code availability The python code used for preprocessing and search in CORD-19 will be made available upon request.

Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest.

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References

1. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*. 2020;395:565–74. [https://doi.org/10.1016/S0140-6736\(20\)30251-8](https://doi.org/10.1016/S0140-6736(20)30251-8).