Determinants of Life-Threatening COVID-19

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1. Introduction
Since the early days of the COVID-19 pandemic, it has been well known that certain comorbidities, such as diabetes, obesity, and being of old age, increase the likelihood of contracting life-threatening COVID-19. However, reports of young, healthy people being hospitalized and dying were unexpected and terrifying. Thus, the focus of this project is to determine what leads to this outcome for people who do not seem to be high-risk, as well as propose potential screening methods for identifying these individuals.

2. Research Topic
The main idea of this research: The genetic and environmental factors that influence the severity of COVID-19
The question to be answered: How do the genetic and environmental factors interact and affect the immune system’s response to SARS-CoV-2?
The significance of this research: Information on what causes severe COVID-19 can be used to determine who is more vulnerable and assess the risk of a patient contracting severe COVID-19.

3. Research Method
My research method has been to gather relevant sources on this topic and analyze their findings. Most of these sources are either clinical studies or literature reviews that analyze trends. In order to better understand these sources, I have also gathered background information on cellular signaling in the immune system.

4. Discussion of Findings

![Diagram of intracellular signaling pathway](image)

Figure 1. Graphic showing the intracellular signaling pathway in a normal immune response to SARS-CoV-2 (left) and how it is inhibited by auto-antibodies (right). Adapted from “Autoantibodies against type I IFNs in patients with life-threatening COVID-19,” by Bastard et al., 2020.

- Genetic Factors
  - Some patients have auto-antibodies (auto-Abs) against type-1 interferons (IFNs ), which are crucial for fighting SARS-CoV-2 (Bastard et al., 2020)
  - Auto-Abs also limit the expression of interferon-stimulated genes (ISGs), which are essential for mobilizing immune cells (Combes et al., 2021)

- Environmental Factors
  - Higher COVID mortality rates and lower vitamin D levels in people living in higher latitudes (Rhodes et al., 2020)
  - Higher exposure to SARS-CoV-2 increases the strength of the immune response and the chance of dangerous inflammatory responses (Wang et al., 2020)
  - Vaccine hesitancy varies by community due to beliefs, income, past experiences, etc., and the chance of contracting severe COVID-19 increases in areas with more hesitancy (Khubchandani et al., 2021)

Figure 2. Graph plotting the COVID-19 mortality rates of several countries versus their latitudes. Mortality rate tends to increase with latitude. Adapted from “Vitamin D deficiency and COVID-19 severity – plausibly linked by latitude; ethnicity, impact on cytokines, ACE2 and thrombosis,” Rhodes et al., 2020.

5. Recommendations for Assessing Risks
Some limitations include not being able to conduct lab research and work with a team. Since there is also an abundant amount of information, as well as new information being released at a fast pace, it was difficult to narrow this topic down and focus on specific factors. Despite this, being able to conduct research on COVID-19 has helped me expand on prior knowledge from my coursework and educate myself and others about the pandemic. I have also become more interested in conducting lab research, which I hope to be able to do with other people to expand this project and develop a functional risk assessment.

6. Limitations and Future Work

![Diagram of screening methods](image)

Figure 3. Flowchart illustrating the potential screening methods for identifying individuals with life-threatening COVID-19 severity.

- Develop models for quantitatively assessing the risk of contracting severe COVID-19 from gathered data
- Measure IFN levels and test for auto-Ab presence in COVID patient blood samples
- Measure vitamin D levels and survey patient on their job occupation, locations they frequently visit, residence, etc.

References

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