Table 5: Theoretical factors that may influence the severity of H1N1 infection.

Factor	Description
Ethanol	Inhibits pulmonary CD8 T cell functions
Previous H1N1 exposure	Protective immunity
Viral load	May affect severity
Environmental toxins	Dioxin, arsenic, and cigarette smoke
Dust storms	Microbes, organic and inorganic materials

Ethanol: A study in mice showed that chronic ethanol consumption was associated with severity, mortality, and pulmonary virus titres compared to controls. Chronic consumption has been shown to inhibit pulmonary CD8 T cell responses, resulting in severe disease. [1] However, this has not been reported in humans.

Previous H1N1 exposure: Previous exposures to the H1N1 virus may be protective against the recent Pandemic H1N1 virus. This may explain why older patients were less severely affected by the recent H1N1 pandemic. [2]

Viral load: Increased viral load may be associated with increased risk of severity. [3, 4]

Environment factors: Environmental toxins such as dioxin, arsenic, and cigarette smoke may interfere with body antiviral response. A study in mice revealed that chronic low dose arsenic exposure significantly impaired the innate immune system, especially dendritic cell response to H1N1 influenza virus infections. The study also observed increases in viral titres and capillary leakage, as well as decrease in cytokine levels in the early course of infection. However, at a later stage, there was excessive inflammatory response in the lung and significant increase in the markers of lung injury. [5]

Dust storms: The outbreak of the pandemic H1N1 influenza in Mexico occurred in March/April, at the time when dust storms from the African desert usually pass over Mexico. Dust storms may contain pathogenic bacteria and viruses, as well as inorganic and organic materials. Dust storm inorganic and organic material exposure may cause pneumonia (Al Eskan disease, Persian Gulf syndrome, Persian Gulf War syndrome, Gulf War syndrome, or desert dust pneumonitis). In vitro studies have shown that dust storm material can inhibit alveolar macrophage defense function, increase reactive oxygen species, and cause DNA damage. In vivo studies in mice and rats have demonstrated that desert dust can cause increases in neutrophil, lymphocyte, and eosinophil counts, and increased level of interleukin-2 and -6, and tumour necrosis factor alpha, and that those responses are dose dependent. [6] Therefore, concomitant environmental factors may be important in causing severe and fatal cases.

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Note: Extra materials from the discussion included as supplementary text with agreement from the authors.