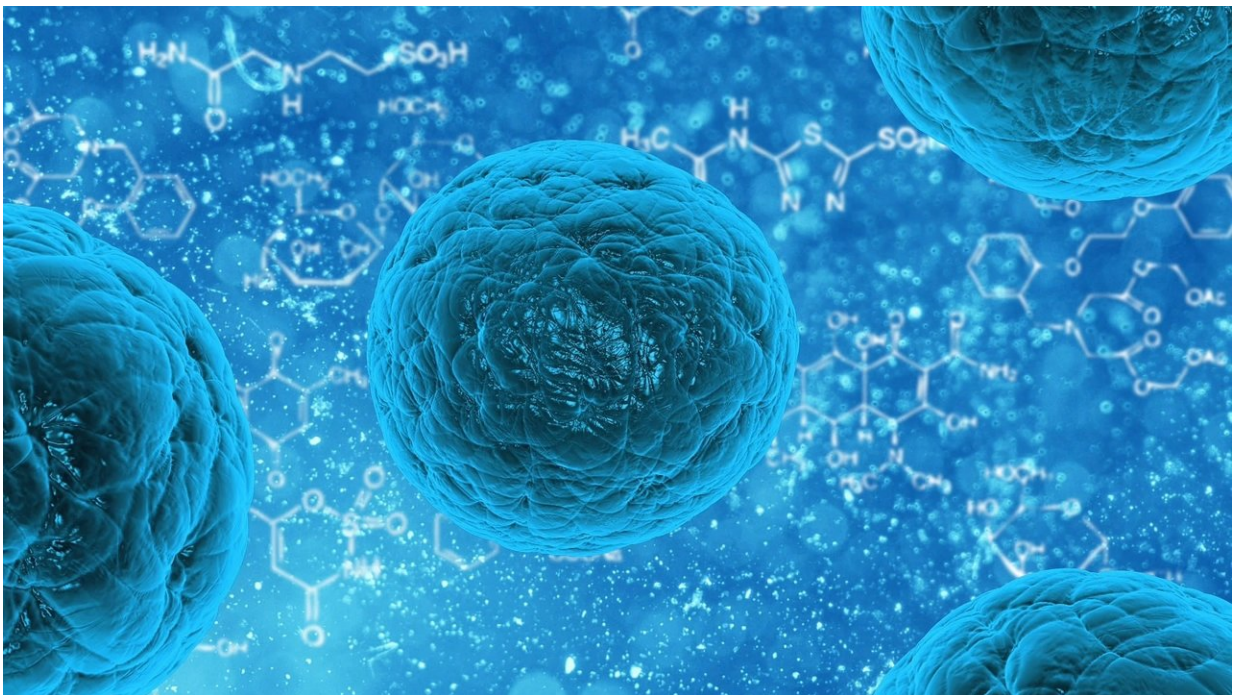


Higher COVID-19 mortality in men could be explained by differences in circulating proteins and immune system cells

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New research presented at the ESCMID Conference on Coronavirus Diseases (ECCVID, online 23-25 September) suggests that the higher risk of poor COVID-19 outcomes in men could be explained by differences in circulating proteins and immune system cells compared

with women. The study is by Gizem Kilic, Radboud University Medical Center, Nijmegen, Netherlands, and colleagues.

Although the disease symptoms of COVID-19 caused by SARS-CoV-2 are mild in most of the cases, [elderly people](#) and individuals with co-morbidities such as cardiovascular diseases and diabetes are more susceptible to COVID-19, especially in the case of males. However, why males are more susceptible to develop severe infections has not yet been fully understood.

In this study, the authors analysed the levels of circulating [inflammatory proteins](#) and whole blood cell populations related to COVID-19 infection severity in two healthy Western European cohorts and investigated whether these immune parameters vary between sexes.

They detected and quantified the levels of 96 circulating proteins, and also the white blood cell population. "Following the age adjustment of data by statistical modelling, we identified several circulating inflammatory proteins and cell populations which might be behind the higher susceptibility of males to develop severe infection and COVID-19 disease," explains senior co-author Professor Mihai Netea, also of Radboud University Medical Center, Nijmegen, Netherlands.

The team found that certain white blood [cells](#) in the [immune system](#), including total, naïve, memory T and naïve CD4+ T cell counts that are reported to decrease with COVID-19 severity were also lower in healthy males. However, levels of an important growth factor in T cell generation, interleukin-7, were similar in males and females.

Furthermore, they discovered that molecules involved in inflammation including monocyte chemoattractant protein-1 (MCP-1), interleukin-8, [hepatocyte growth factor](#) (HGF) that stimulates immune and epithelial cells, and S100 calcium binding protein A12 (S100A12 or EN-RAGE)

levels were high in healthy males of both cohorts and also in patients in the intensive care unit. This indicates that immune mediators that contribute to a more severe COVID-19 infection are already intrinsically higher in males.

The authors conclude: "Sex is one of the major factors which influence our immune system response. Our results suggest that differences between the sexes in the baseline characteristics of the immune system such as circulating proteins and immune cell populations might explain the predisposition of [males](#) over females to develop severe COVID-19 infection."

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