

- Genetics/ Virus

Genes Linked to Pneumonia Severity May Explain Covid-19 Death Variations: Study

Higher deaths in Maharashtra and areas with 'European ancestry' may be linked to the gene

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New Delhi: Higher Covid-19 deaths in Maharashtra and several other parts of India with 'European genetic ancestry' may be linked to the presence of a particular human gene variant which is also found in higher proportion among Europeans, Russians and Americans but in lower proportions in Africans and Asians, a latest study from CSIR- Institute of Genomics and Integrative Biology (IGIB) and associated institutes, has suggested.

The varied presence of the gene variant in India implies that it is 'an at risk nation' with 'genetic protection' limited to only certain regions, says the study titled 'Human genetic factors associated with pneumonia susceptibility, a cue for Covid-19 mortality'.

Among the lead authors of the soon to be published study is director, IGIB, Anurag Agarwal, who is also a member of INSACOG -- Indian SARSCoV-2 Genomic Consortia.

Agarwal told ET the study showed "intriguing correlations with Covid-19 mortality but more work needs to be done to examine the issue further".

"The investigators at IGIB were looking at genetic predisposition to community acquired pneumonia and found patterns that also correlated with the current mortality variability for Covid-19. This work is still preliminary but provides a genetic basis for different risks and outcomes in pneumonia and would need to be explained further to gain biological understanding," Agarwal, who co-authored the study with scientist Ritushree Kuktrete and others, told ET.

THE CRUCIAL CYP1A1 GENE

Central to this study is the CYP1A1 gene -- which is a critical regulator of inflammatory and immune responses in case of a pneumonia infection -- and its genetic variant or allele-rs2606345.

The 'striking difference of allele frequency of rs2606345 (CYP1A1) among Europeans, Africans and Asians' has been identified in this study as a possible link for variations in death due to Covid-19 linked pneumonia.

"Our study revealed that the alternate allele (A in plus-strand or T in minus-strand) of rs2606345 increased pneumonia susceptibility in the Russian population. We also observed that this allele to be the major allele in European (66.6%) and Russian (~80%) populations unlike in the other populations (African 5%, Asian 5-30%, American 39%). We observed a striking similarity in the trend for the recent outbreak of Covid-19," the study explains.

In India, its frequency varies from 9% in Madhya Pradesh to 60% in Maharashtra where higher Covid mortality has been observed, the study points out. The spatial analysis of the genetically heterogeneous Indian population confirmed a similar trend with regions that have 'European genetic ancestry being more affected', the study states.

The IGIB research points to 'a significant positive correlation for the risk allele (T or A) of rs2606345, with a higher Covid-19 mortality rate worldwide and within a genetically heterogeneous nation like India'.

"The highest number of Covid-19 deaths have been observed in Maharashtra, where allele frequency of A ranges from 30% to 60%," notes the study. It also points out that with a 'median risk allele frequency

of over 30%, India is an at-risk nation, with only some regions expected to have genetic protection'. Save the northeastern states, the allele frequency is significant across several Indian states. The same is seen borne out in both the first wave in 2020 and in the ongoing second surge, as per the study.

AIR POLLUTION FACTOR

An interesting linkage has been found with ambient air pollution. Since ambient air pollution is also linked with inducing higher CYP1A1 gene expression just like a 'protective' allele, the study points to gene-environment interactions at play.