

JN.1: The new COVID-19 variant of concern?



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ABSTRACT

Emergence of new variants of COVID-19 is nothing new. Different variants evolved with additional mutations of the virus as part of the viral replication cycle have different infectious properties. JN.1 is the latest COVID-19 variant that seems to circulate the globe contributing to many infections and hospitalizations labeling it a variant of interest by the WHO. The scientific community has yet to understand its full lethal potential if any. In this mini-review, we summarized the facts known so far about this variant and its possible consequences if any for humanity.

Key words: JN.1; COVID-19; Spike proteins; BA.2.86; Transmissibility

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INTRODUCTION

Ever since the COVID-19 pandemic started back in 2019–2020, numerous variants and sub-variants of this virus emerged in different parts of the world.¹ While most of these variants emerged out of immune selection pressure from the host, few of them survived due to their advantageous mutations that enable them with enhanced transmissibility and capacity to evade immune surveillance.^{2,3}

Quite recently, we are witnessing one such wave of a new variant of concern (VoC), named JN.1.⁴ JN.1 also known as “Pirola” is the latest variant of SARS-CoV-2 creating concerns among researchers and health-care officials. JN.1 seems to have undergone mutations leading to changes in its transmissibility and resistance to vaccines.⁵ It is believed that JN.1 has arisen from the previous variant, BA.2.86

while the same has been derived from the “Omicron” variant - a highly transmissible strain of COVID-19 that peaked last year.⁶

JN.1 with genetic makeup as per the WHO is BA.2.86 + S:L455S and is first documented on August 25th, 2023.⁶ JN.1 as compared with parent BA.2.86 lineage carries an additional L455S mutation in its spike protein that could significantly provide JN.1 an additional immune evasion advantage in comparison with parent BA.2.86 lineage as observed in variants like HK.3 that carries the same L455F mutation.⁷ We need to however note that all these are low-confidence information as not much data is still available on these variants.

At present, there are 7344 JN.1 sequences available from 41 countries. This represents 27.1% of the total number of all sequences available, indicating a major JN.1 share.⁸

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The prevalence of JN.1 increased in the countries with the largest proportion of JN.1 reports from France (10.9%), US (2.1%), Singapore (1.0%), Canada (1.9%), UK (1.8%), and Sweden (1.8%) with the largest increases in Western Pacific region (1.1%), Europe (1.4%), and America (65.6%).^{9,10}

HOW JN.1 CAN BE A VoC

By random mutations in spike protein as part of the virus replication process, the virus can evolve into a virus of concern. These spike proteins are highly glycosylated and large type I transmembrane fusion proteins.¹¹ The 29 kb long RNA genome of coronaviruses is comprised 6–10 open reading frames that are responsible for encoding both the replicase and structural proteins for the virus.¹² Virus uses these spike proteins to hook to the target cells exploiting a host receptor, ACE2 in the case of COVID-19.¹³ In addition to its role in helping the virus to enter the cells, the S protein of the SARS-CoV-2 virus triggers the generation of neutralizing antibodies by the host, which is natural protective antibodies that are produced by our humoral immune system against the virus.¹⁴ As previously mentioned, JN.1 has mutations in the spike protein, which plays an important role in binding to human cells. If these mutations enhance the spike protein's affinity for the ACE2 receptor in human cells, it can make it easier for the virus to enter and infect host cells, thereby increasing its infection as well as transmissibility.¹⁵ Few variants also spike the viral load in the host making them an active reservoir for the virus by releasing larger number of virus particles into the environment.

CONCLUSION

It may be difficult, to predict the evolutionary trajectory of the coronavirus and its variants. The Centers for Disease Control and Prevention predicts that JN.1 cases may increase through the winter, making it a “variant of interest” if not a VoC. We need to remember the similar story for variant, HV.1, which in early December was the dominant strain in the United States but reduced <10% of cases in a few months. It might be too early to say the same for JN.1, however, it is imperative to take all necessary precautions and adopt COVID-19-appropriate behaviors to reduce the risk. We need to remember that even the mildest variants may pose significant risks to senior citizens and individuals with pre-existing comorbidity.

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