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Battling the JN.1 Surge: Unveiling strategies to shield against the next wave of COVID with homoeopathy

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Abstract
This article delves into the emergence of the JN.1 sub-variant of the Omicron strain, labelled a "variant of interest" by the World Health Organization. Originating from BA.2.86, JN.1 carries the spike protein L455S mutation, raising concerns about its potential to evade vaccine immunity. With a global prevalence of 27.1%, impacting nations like India, Canada, France, Singapore, Sweden, and the UK, JN.1's increased transmissibility and immune evasion potential are highlighted. In India, JN.1 contributes to a surge in cases, notably with lower hospitalization rates. The article explores JN.1's pathophysiology, emphasizing the ACE2 receptor binding impact of the S: L455S mutation. Clinical features from mild to severe cases are detailed, and investigative methods, including genomic sequencing and serological assays, are crucial for understanding and managing JN.1. Despite vaccine resistance, current immunization remains effective against severe outcomes. The article concludes by discussing homoeopathic management, stressing a holistic symptom relief approach, and underscores the importance of collaborative efforts, transparency, and ongoing research to mitigate JN.1's impact and protect global public health.

Keywords: COVID variant, JN.1, vaccine, immunity, homoeopathy

Introduction
A sub-variant of the Omicron strain of coronavirus has been classified as a "variant of interest" by the World Health Organization, because of "its rapidly increasing spread." It is called as JN. 1. [1] JN.1 is a descendent lineage of BA.2.86 (informally referred to as “Pirola”), with the earliest sample collected on 25 August 2023 [2]. In comparison with the parent lineage BA.2.86, there is an additional L455S mutation in the spike protein in JN.1 [3]. It is anticipated that, cases amid a surge of infections of other viral and bacterial infections, JN.1 may cause an increase in Sars-Cov-2 [coronavirus], especially in countries entering the winter season [4]. There is limited evidence on how capable JN.1 is of getting around the immunity offered by vaccines.

Epidemiology
WHO mentioned that JN.1 is now responsible for global prevalence at 27.1% and as of 16 December 2023, there were 7344 JN.1 sequences submitted to GISAID (1) from 41 countries. Among these, India, Canada, France, Singapore, Sweden, the UK are affected the most. JN.1's continued growth suggests that it is either better at evading our immune systems or more transmissible than other circulating variants. In India, the new cases have pushed the active caseload to more than 4,565 with more than 260 cases of JN.1 and 5 deaths due to the virus, with fatalities in Kerala, Karnataka, Haryana and Bihar,. India has an incidence of 841 cases according to the Union Health Ministry and has climbed to the 9th position globally among the countries with COVID-19 cases. Kerala has maximum number of COVID-19 cases (2,522), followed by Karnataka (568), Maharashtra (369) and Tamil Nadu (156).
The Ministry of Health says the cases have gone up since the first week of December, after the emergence of JN.1 sub variant and cold weather conditions. Unlike Covid-19's earlier mutated versions, the number of hospitalisations and other complications is lower in the JN.1 sub variant. India's SARS-COV-2 Genomics Consortium (INSACOG) mentions that there is no need for panic.
However, it is found that JN.1 can evade immunity and spread fast, unlike earlier variants like XBB and previous versions of COVID-19. This causes infections in cold conditions, especially among those who had COVID-19 earlier and were vaccinated.

Table 1: Global proportions of SARS-CoV-2 variants, week 44 to week 48 of 2023

Lineage	Countries[§]	Sequences[§]	2023-44	2023-45	2023-46	2023-47	2023-48
VOIs							
XBB.1.5*	128	316 888	8.2	7.9	8.6	7.4	7.3
XBB.1.16*	119	103 516	9.6	9.0	6.6	5.6	4.2
EG.5*	93	143 675	53.7	54.1	51.7	46.5	36.3
BA.2.86*	49	5 972	4.4	4.8	5.8	7.1	5.9
JN.1*	41	7 344	3.3	5.3	10.1	16.7	27.1
VUMs							
DV.7*	40	4 635	1.2	0.9	0.9	1.0	0.6
XBB*	143	90 441	2.3	2.0	1.8	1.2	1.0
XBB.1.9.1*	118	85 640	6.7	5.4	5.5	4.3	3.3
XBB.1.9.2*	95	37 764	1.7	1.1	0.7	0.5	0.2
XBB.2.3*	107	34 573	3.5	3.4	2.5	2.3	1.6
Unassigned	95	155 778	3.4	4.2	4.2	6.4	11.9

Number of countries and sequences are since the emergence of the variants.
Includes descendant lineages, except those specified on the table. For example, XBB* does not include XBB.1.5 XBB.1.16 EG.5. XBB.1.9.1 XBB.1.9.2. and XBB.2.3

Pathophysiology

The pathophysiology of COVID-19, arising from the SARS-cov-2 virus, entails an intricate interplay between the virus and the human organism. Despite its heightened transmissibility, there appears to be no substantial increase in virulence concerning symptom severity.

Entry and Attachment: Replication kinetics of BA.2.86.1 (parent lineage of JN.1) on primary nasal epithelial cells (hNEC) mirror those of other XBB-derived variants. The virus predominantly infiltrates the body through respiratory droplets emitted during coughing, sneezing, or talking. Its spike (S) protein binds to angiotensin-converting enzyme 2 (ACE2) receptors on host cell surfaces, especially in the respiratory tract. An ACE2 binding assay revealed a significantly higher dissociation constant (KD) value for the JN.1 receptor-binding domain (RBD) compared to the BA.2.86 RBD (Figure 1D), suggesting that the S: L455S mutation reduces binding affinity to the human ACE2 receptor. Conversely, a pseudo-virus assay indicated significantly higher infectivity of JN.1 compared to BA.2.86 [5, 6].

Cellular Invasion: Post-attachment, the virus enters host cells, particularly those in the respiratory epithelium, utilizing cellular machinery for self-replication.

ACE2 and Cardiovascular Effects: Epithelial cells, alveolar macrophages, and dendritic cells (DCS) constitute the main components of innate immunity in the airway. DCS and macrophages phagocytize apoptotic cells infected by the virus. Additionally, SARS-COV can bind to dendritic-cell-specific intercellular adhesion molecule-3-grabbing non-integrin (DC-SIGN) and DC-SIGN-related protein (DC-SIGNR, L-SIGN), besides ACE2. Cardiovascular complications, including myocarditis and blood vessel inflammation, have been documented.

Inflammatory Response: The virus stimulates an immune response, resulting in the release of cytokines and other signalling molecules. In certain cases, particularly with co-morbid conditions, an exaggerated immune response may lead to a cytokine storm, causing widespread inflammation and tissue damage. Patients with severe diseases exhibit elevated plasma concentrations of proinflammatory cytokines, including interleukin (IL)-6, IL-10, granulocyte-colony-stimulating factor (G-CSF), monocyte chemoattractant protein 1 (MCP1), macrophage inflammatory protein (MIP) 1α, and tumour necrosis factor (TNF)-α. T cell exhaustion could contribute to disease progression. Endothelial cells also express ACE2. Microvascular permeability resulting from endothelial injury can facilitate viral invasion, leading to thrombosis and pulmonary embolism [5, 6].

Immune Response and Resolution: JN.1 exhibits a higher immune evasion property. The immune system strives to eliminate the virus, and in most cases, patients recover.

Nevertheless, uncertainties persist regarding antibody escape and the severity of BA.2.86 and JN.1, particularly due to the additional spike mutation L455S [5, 6].

However, there are uncertainties relating to antibody escape and severity of BA.2.86 and JN.1 particularly due to additional spike mutation L455S.

Clinical features

1. **Mild cases**
   - Fever
   - Runny nose
   - Sore throat
   - Headache
   - Fatigue
   - Body ache

2. **Gastrointestinal issues**
   - Mild stomach cramps
   - Loose stools
   - Loss of Appetite
   - Persistent Nausea.

3. **Severe cases**
   - Breathing difficulties
   - Chest pain or pale
   - Grey or blue skin, lips or nail beds

Investigations for JN.1

Several pivotal tests play a vital role in evaluating the characteristics and consequences of these variants.

Genomic Sequencing: Genomic sequencing is indispensable for recognizing and characterizing new COVID variants. While RT-PCR can confirm the virus's presence, it lacks information about specific mutations. Genomic sequencing enables scientists to scrutinize the entire genetic code of the virus, facilitating the identification of mutations that might affect transmissibility, severity, or vaccine effectiveness. Regular sequencing efforts are crucial for monitoring the virus's evolution and guiding public health strategies.

Viral Culture: Viral culture entails isolating and cultivating live virus samples from patient specimens. This test is valuable for studying the behaviour of new variants, evaluating their replication capabilities, and understanding their impact on cell cultures. Moreover, viral culture is essential for assessing the efficacy of antiviral drugs and vaccines. Although more resource-intensive than PCR, the insights gained from viral culture are invaluable for shaping targeted interventions.

Serological assays: Serological assays, such as antibody tests, offer insights into an individual's immune response to the virus. Monitoring antibody levels over time helps researchers understand the durability of immunity, particularly concerning new variants. Additionally, serological tests can identify previous infections, aiding in estimating the virus's prevalence within a population. Combining serological data with genomic sequencing enhances our understanding of immune responses and informs vaccination strategies [7].

Antigen testing: Antigen tests detect specific proteins on the virus's surface. While less sensitive than RT-PCR, they provide rapid results, making them valuable for mass screening and surveillance efforts. Monitoring antigen test results alongside genomic sequencing offers a broader perspective on the prevalence and distribution of new variants. Swift identification of potential hotspots allows for prompt public health interventions to curb variant spread.

T-cell response assays: Assessing T-cell responses to the virus complements information from antibody tests. T-cell response assays measure the activation of specific immune cells responsible for recognizing and eliminating infected cells. Understanding T-cell responses is crucial for evaluating the breadth and longevity of immunity, especially in the context of new variants. Combining T-cell data with genomic information provides a comprehensive view of the adaptive immune response.

Drug susceptibility testing: As new variants emerge, evaluating their susceptibility to antiviral drugs becomes critical. Drug susceptibility testing is done to assess their effectiveness by exposing virus samples to different antiviral agents. This information guides treatment strategies and identifies potential challenges in managing infections caused by specific variants. Continuous monitoring of drug susceptibility ensures that therapeutic interventions remain effective against evolving strains [8].

Preventive measures

Promoting Regular Handwashing

It is essential to underscore the importance of proper hygiene practices, particularly by encouraging children to engage in frequent handwashing with soap and water for at least 20 seconds. Parents and guardians play a crucial role in educating their children about avoiding touching their face, especially the eyes, nose, and mouth, to minimize the risk of infection.

Embracing a Wholesome Lifestyle

Adopting home-based healthy food choices to support children's overall well-being is paramount. A balanced diet is crucial, complemented by incorporating a brief morning physical exercise, even a two-minute activity like jumping, which can positively impact immunity by releasing endorphins.

Ensuring Proper Face Mask Usage

Consistent and correct use of face masks, especially in crowded or enclosed spaces, is imperative. Parents are advised to ensure that children wear well-fitted masks over their noses and mouths, teaching them the proper way to put on and remove masks to prevent contamination.

Prioritizing Social Distancing

Social distancing continues to be a pivotal preventive measure, especially for individuals with high-risk comorbidities, such as those undergoing cancer chemotherapy, the elderly, people with diabetes, and those with uncontrolled hypertension.

Vaccination

The World Health Organization (WHO) has stated that current vaccines will persist in providing protection against severe disease and death from JN.1 and other circulating variants of the COVID-19 virus. JN.1 has shown 2.9-to-4.3-fold resistance to sera from individuals vaccinated with an XBB.1.5 mRNA vaccine booster.

Protection offered by XBB.1.5 monovalent vaccines is likely to be effective against JN.1.

Homoeopathic management of jn1 variant Covid

Mild Cases

Aconite

- Acute, sudden, and violent invasion, with fever
- Most valuable febrifuge with mental anguish & restlessness
- Chilly if uncovered or touched.
- Dry heat, red face.
- Coryza much sneezing
- Mucous membrane dry, nose stopped up; dry or with but scanty watery coryza.
- Throbbing in nostrils
- Oppressed breathing < least motion
- Cough, dry, short, hacking; < at night and after midnight

1. Arsenic Album

- Great anguish and restlessness.
- Fear of death.
- Great prostration, with rapid sinking of the vital forces.
- Sneezing without relief. Thin, watery, excoriating discharge.
- Suffocative catarrh. Nose feels stopped up.
- Swollen, burning throat.
- Cough worse after midnight.
- Pain in upper 1/3rd of right lung.
- High grade fever.
- Great heat about 3 am.

2. Belladonna

- Acute, sudden, and violent fever.
- Hot, red skin, flushed face, glaring eyes, throbbing carotids, excited mental state, hyperesthesia of all senses.
- Perspiration dry, only on head. Feet icy cold. No thirst with fever.

- Headache from suppressed catarrhal flow.
- Dry, as if glazed; angry-looking congestion
- Tickling, short, dry cough < at night.
- Stitches in chest while coughing.

3. Gelsemium
- Dizziness, dullness, drowsiness and trembling.
- Acute coryza with fever and dull headache.
- Watery and excoriating discharge.
- Sneezing; fullness at root of nose.
- Difficult swallowing with pain from throat to ear.
- Chilliness up and down back. Heat and sweat stages, long and exhausting.
- Muscular soreness with great prostration and violent headache.
- Chill, without thirst, along spine; wave-like, extending upward from sacrum to occiput.

4. Camphor
- First stages of a cold, with chill and sneezing.
- Fluent coryza due to sudden change of weather.
- Nose feels cold.
- Feeling of suffocation, difficult cold breathing.
- Violent, dry, hacking cough with palpitation.
- Great prostration.
- Icy coldness of the whole body.
- The patient will not be covered.

5. Bryonia
- Dryness of the mucus membranes
- Coryza with shooting and aching in the forehead.
- Swelling of tip of nose.
- Dryness, scraped and constricted feeling in the throat.
- Tough mucus in larynx and trachea which is loosened only after much hawking < worse coming into warm room.
- Dry, hacking cough from irritation in upper trachea.
- Cough, dry, worse at night.
- A person must sit up; worse after eating or drinking, with vomiting.
- Stitching pain in the chest.
- Difficult, quick breathing < every movement and must support chest.

6. Justicia adhatoda
- Acute catarrhal conditions of the respiratory tract.
- Coryza, profuse, fluent, with constant sneezing.
- Coryza with watery discharge from the eyes.
- Loss of smell and taste.
- Paroxysmal cough, with suffocation.
- Feeling of tightness in chest with difficult breathing.

Moderate to severe cases

1. Kali carbonicum
- Thick, fluent, yellow discharge from the nose.
- Post-nasal dropping
- Stitches in temples; aching in occiput, one-sided, with nausea.
- Cutting pain in chest; worse lying on right side.
- Dry, hard cough < 3 am, with stitching pains in the throat.
- Hoarseness and loss of voice.
- Sweat, backache, and weakness.
- Sensitive to every atmospheric change and intolerance of cold weather.
- Very irritable, full of fear and imaginations. Anxiety is felt in stomach.

2. Antimonium tartaricum
- Drowsiness, debility and sweat
- Great rattling of mucus in the chest but very little is expectorated.
- Velvety feeling in chest
- Rapid and difficult breathing with the feeling of suffocation, > sitting up
- Fever with intense chill and heat.
- Cold, clammy sweat, with great faintness
- Oedema and impending paralysis of the lungs.

3. Lachesis
- Icy coldness of the skin or of the limbs, or only of the feet
- Fever mostly night or in evening and accompanied by headache with rapid prostration of strength
- Coryza, preceded by headache
- Dry, intensely swollen, externally and internally
- Pajin in the throat on left side extending to ear < swallowing liquids.
- Sensation of suffocation and strangulation on lying down
- Feels he must take a deep breath
- Spasm of glottis
- Pain darting up the rectum every time be sneezes or coughs

4. Carbo vegetables
- Hectic fever, exhausting sweats.
- Coryza with ineffectual urging to sneeze.
- Tip of nose red and scabby, itching around nostrils.
- Patient is almost lifeless, coldness of extremities, cool breath, and imperceptible pulse.
- Oppressed and quickened respiration. Must be fanned hard, must have all the doors and windows open.
- Patient seems to be too weak to hold out.
- Cough, with burning in chest < in evening, in open air, after eating and talking.
- Coldness, with thirst. Chill begins in forearm.

Conclusion
There are only limited data on cross neutralization of JN.1. While RT-PCR remains the primary diagnostic tool for COVID-19, a multifaceted testing approach is indispensable for comprehending and managing the impact of new variants. Vaccination remains a cornerstone in the fight against JN.1, however, it evades immunity and can become the dominant variant across the globe. As the global community navigates the uncertainties surrounding JN.1, collaboration, transparency, and a commitment to scientific research will be paramount in mitigating the impact of this variant and safeguarding public health.

Conflict of Interest
Not available

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