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MAIN PATHWAYS AND HOTSPOTS OF THE SPREAD OF THE SARS-COV-2 XFG ("STRATUS") STRAIN

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Abstract. The aim of this work is to describe the probable transmission routes and typical foci of the SARS-CoV-2 Omicron subvariant XFG ("Stratus"), based on data regarding its antigenic and virological properties and in comparison with other variants (Alpha, Delta, Omicron). It is shown that XFG, which exhibits pronounced immune evasion with a slightly reduced affinity for ACE2, relies on the same dominant transmission mechanisms as other Omicron subvariants: airborne and aerosol pathways in conditions of close indoor contact [1,3,4,13]. Key foci include households, work and educational collectives, places of mass gatherings, and nosocomial outbreaks in hospitals, where "healthcare worker-healthcare worker" and "patient-healthcare worker" transmission is significant [9,14,20,27]. An analysis of global and local COVID-19 clusters reveals the leading role of superspreading events and

international/interregional mobility in the early phase of the spread of new variants [3,5,7,13,14,22]. Implications for non-pharmacological interventions and the organization of genomic surveillance in relation to XFG are discussed.

Keywords: SARS-CoV-2; XFG ("Stratus"); Omicron; transmission routes; aerosol transmission; superspreading; nosocomial foci; genomic epidemiology.

Introduction

The emergence of SARS-CoV-2 variants with increased transmissibility and immune evasion (Alpha, Delta, Omicron) radically changed the course of the pandemic [2,15]. These variants, becoming "variants of concern" (VOCs), displaced preceding lineages due to a combination of higher fitness, altered antigenicity, and the ability to bypass established population immunity [1,4,21].
The XFG strain ("Stratus") is an Omicron subvariant [2] that demonstrates pronounced immune evasion due to the A475V and N487D mutations in its S-protein, which reduces the efficacy of a number of monoclonal antibodies and post-vaccination sera [18]. At the same time, XFG has shown reduced ACE2 binding efficiency compared to some competing variants, which requires compensatory adaptations for sustained spread [17].
Direct data on the actual epidemiological characteristics of XFG are currently limited; therefore, the analysis of its main routes and foci of transmission relies on comparison with other Omicron subvariants and the general patterns of SARS-CoV-2 circulation [1,3,4,5,13,14,22,23].

The purpose of this article is to systematize the available data on the biology of XFG and the transmission of SARS-CoV-2, and on this basis, to identify the most likely routes and foci of spread for the XFG ("Stratus") strain.

Biological Prerequisites for XFG Transmission

Current reviews show that the success of a VOC is determined by a complex interplay between altered antigenicity, transmissibility, and virulence [1,4,8,15,16,21].

Omicron subvariants are generally characterized by:

- numerous mutations in the S-protein that enhance immune evasion [2];

- an altered tropism profile with increased replication in the upper respiratory tract, which facilitates aerosol transmission [1,4].

For XFG, the following have been shown:

- pronounced immune evasion associated with the A475V and N487D mutations, which provide resistance to a broad spectrum of neutralizing antibodies [8,15,18];
- decreased affinity for ACE2 and less effective receptor interaction compared to some competing variants, which may limit its baseline infectivity and require compensatory evolutionary changes to increase fitness [11].

Studies of within-host variability and the transmission bottleneck demonstrate that most within-host variants are not fixed: during transmission from donor to recipient, a very narrow set of virions is transmitted on average, and only a few mutations become epidemiologically significant [20,23]. Therefore, the sustained spread of XFG is likely in conditions where its immune evasion provides an advantage and social contacts ensure a sufficient number of transmission events [15].

Main routes of transmission:

Airborne-droplet and aerosol route

A review of the evolution and transmission pathways of SARS-CoV-2 highlights the dominant role of the airborne and aerosol mechanisms: infection occurs through the inhalation of aerosols and large droplets containing the virus, especially in enclosed, poorly ventilated spaces [4,21,23].
A systematic review of COVID-19 clusters showed that the vast majority of recorded outbreaks occurred indoors - in households, workplaces, food service establishments, religious institutions, and leisure centers; relatively few clusters were associated with schools, whereas hospitals and nursing homes were significant contributors [27].
Given that XFG is an Omicron subvariant with predominant replication in the upper respiratory tract and pronounced immune evasion [1,4,25], it can be reasonably assumed that, as with other VOCs, the aerosol/airborne route remains its primary pathway:

- close-range conversation;
- sharing spaces in offices, classrooms, and on public transport;

- prolonged gatherings in enclosed spaces without adequate ventilation.

Contact and fomite transmission

Studies on global transmission and nosocomial clusters indicate that although viral RNA is detected on surfaces, the epidemiological contribution of fomites is significantly less than that of aerosol transmission [4,9,23].

In most nosocomial outbreaks, the key factors were close contact during patient care, shared staff facilities, and non-compliance with mask-wearing policies, rather than contact with environmental surfaces [9,14,20]. Consequently, for XFG, the contact route remains secondary and is mainly significant in conditions of high contamination and poor hand hygiene.

Outbreak epicenters

Main types of epicenters and transmission routes (extrapolated to XFG)

Key epicenters and transmission channels of SARS-CoV-2

Epicenter type / Route	Characteristics for highly contagious variants	Citations
Household and family clusters	High secondary attack rate, local transmission chains	[5,14,27]
Work/school groups	Clusters of various sizes, often a source of interregional spread	[3,7,14,27]
Nosocomial outbreaks	Predominantly transmission between HCWs and patients, role of mask-wearing policies	[9,20]
Mass gatherings (superspreading events)	A small number of events form large clusters and international introductions	[3,5,13,22,27]
International and interregional travel	Multiple independent introductions, large-scale early spread	[5,7,13,22]

Households and local clusters

Genomic-epidemiological analysis of large cities has shown that local clusters form around households and nearby communities; most introductions create small

transmission chains, while only a few become large clusters [5,7]. In Brazil, the spread of Omicron subvariants BA.4, BA.5, BQ.1, and XBB was characterized primarily by local geographical distribution, with episodes of rapid intercity expansion associated with travel or lapses in control measures [14]. For XFG, which is capable of infecting people with pre-existing immunity, the following can be expected:

- high secondary attack rates in households;
- an increase in the proportion of intra-family outbreaks as restrictions in public spaces are tightened;
- the formation of neighborhood clusters through a combination of household and nearby social transmission.

Work, educational, and social spaces

A systematic review of SARS-CoV-2 clusters revealed that numerous outbreaks are linked to workplaces (meat processing plants, offices, factories), leisure facilities, religious gatherings, public transport, and bars/restaurants [27]. Genomic studies of local epidemics (e.g., in the Houston metropolitan area) have revealed more than a thousand independent introductions leading to clusters of various sizes; many large clusters are associated with work and social contacts, as well as high population mobility[5]. Similarly, for XFG, the key venues for outbreak formation are:

- open-plan offices and industrial facilities;
- universities, high schools, dormitories;
- indoor religious and cultural events;
- nightclubs, bars, restaurants.

These settings are particularly dangerous when combining high population density, loud speech/singing, and inadequate ventilation [4,27].

Nosocomial outbreaks

Studies on nosocomial outbreaks demonstrate the complex structure of in-hospital transmission:

- many presumed epidemiological links are not confirmed by sequencing, reflecting a significant proportion of community-acquired cases among patients and staff [9,10,14,24].
- among confirmed in-hospital transmissions, "HCW-HCW" (shared break rooms, meetings, shifts) and "patient-HCW" scenarios are predominant, whereas "HCW-patient" transmission is less common, likely due to the use of PPE [9,24].
- analysis of two major hospital outbreaks in South Africa showed that intra-host diversity and bottleneck estimates make it possible to trace transmitted minor variants, confirming transmission within the hospital [20].

Considering XFG's immune evasion [17] and the high level of contact in healthcare facilities, this subvariant can potentially cause nosocomial outbreaks, especially:

- in departments with high staff workloads and long hospital stays;
- in geriatric and intensive care units;
- with relaxed mask-wearing policies and inadequate ventilation.

Effective control includes: regular screening of healthcare workers (HCWs), limiting staff rotation between departments, a strict mask policy, rapid isolation, and using whole-genome sequencing (WGS) to clarify transmission pathways [9,10,14,19,24].

Long-term care facilities and socially vulnerable groups

Systematic reviews of COVID-19 clusters highlight the particular vulnerability of nursing homes and long-term care facilities, which combine a high proportion of at-risk individuals, crowded living conditions, and constant staff presence [27]. With the emergence of immune-evasive variants like XFG, these institutions can become key epicenters for severe outcomes, even if overall morbidity is relatively controlled.

Superspreading and the cluster structure of the epidemic

A national analysis of the outbreak in Austria showed that a limited number of "superstrains" and superspreading events (ski tourism, the hospitality industry) formed large clusters and led to international introductions; genomic sequencing made it possible to reconstruct transmission chains and estimate the average size of the transmission bottleneck (~10 virions) [3]. Other works on cluster analysis have revealed:

- the existence of several genetic "superspreader clusters" responsible for the majority of early outbreaks in various countries [22];
- a scale-free structure of the global transmission network, where a small number of variants and clusters constitute most potential transmission routes [13];
- significant heterogeneity in cluster size at the local level, with large clusters associated with highly mobile and socially active groups [5].

For XFG, which exhibits immune evasion, it can be assumed that:

- superspreading events (mass gatherings, conferences, religious meetings, tourism) will be critical for its early global spread;
- a limited number of large clusters may determine the overall transmission dynamics in individual countries.

International and Regional Spread

Phylogenetic and network analysis of the global spread of SARS-CoV-2 has shown that:

- the virus was introduced into most regions of the world through multiple independent introductions;
- the transmission network has a scale-free structure, with a few variants responsible for the vast majority of transmission pathways;
- the strong epidemiological connectivity between regions requires coordinated international measures [7,13].

Large Omicron outbreaks (e.g., in Shanghai in the spring of 2022) were initiated by imported cases that led to cryptic local transmission, which subsequently spread across almost the entire urban area, despite the phased intensification of non-pharmaceutical interventions [14].

Given this data, for XFG, it can be expected that:

- international air travel and tourism will be a key factor in its early spread;
- large agglomerations will function as source regions for surrounding areas [5];
- Timely genomic surveillance and testing of travelers are critical for early detection and slowing the spread [1,4,12,16,23].

The role of genomic surveillance and fitness assessment of XFG

Genomic surveillance has become a central element of tracking VOCs, allowing for:

- the prompt detection of new variants and their key mutations;
- the assessment of the relative fitness and growth rate of a variant's share;
- the reconstruction of introduction pathways and local clusters [1,4,5,10,12,16,24].

The following methods are used to assess the transmissibility and competitiveness of new variants (including XFG):

- classical population genetics models and epidemiological models (estimating the increase in the effective reproductive number relative to background lineages) [16];
- phylogenetic and phyloepidemiological methods (analysis of the dynamics of sequence proportions, clusters, and lineage growth) [1,4,5,12];
- experimental assessments of infectivity, affinity for ACE2, and immune evasion in pseudovirus and neutralization systems [1,17].

Initial data on XFG indicate strong immune evasion with reduced ACE2 affinity, which provides an advantage in conditions of high population immunity) [6] but may be inferior in baseline fitness to variants that combine immune evasion with high affinity (e.g., NB.1.8.1) [17]. This implies that the spread of XFG will be sensitive to the population's immunity structure and external factors (NPIs, mobility, vaccination).

Non-pharmacological interventions and evolutionary dynamics

Research on the impact of non-pharmacological interventions (NPIs) on the evolution of SARS-CoV-2 shows that:

- strict and consistent measures (mask mandates, social distancing, restrictions on mass gatherings) reduce the overall level of transmission [19] and limit the opportunity for new variants to emerge and become established;
- incomplete and inconsistent NPIs, especially in the context of partial immunity, can promote the selection of more contagious and immune-evasive variants [21,23].

Given the properties of XFG, the following measures are considered necessary upon its emergence:

- rapid adaptation of NPIs with a focus on indoor spaces, mass gatherings, and healthcare facilities;
- enhanced ventilation and stricter mask-wearing policies in public places [19];
- targeted strengthening of protection for vulnerable groups and long-term care facilities) [26].

Conclusion

The XFG ("Stratus") strain is an Omicron subvariant with pronounced immune evasion and the potential to cause new epidemic waves in populations with high levels of pre-existing immunity [6]. Based on comparisons with other VOCs, it can be concluded that its main transmission routes remain airborne droplets and aerosols, occurring primarily in enclosed spaces during close interpersonal contact. The primary sources of XFG spread will be households, workplaces and educational settings, mass gatherings, as well as nosocomial settings and nursing homes. A significant role is attributed to superspreading events and international travel, which create large clusters and multiple independent introductions. Containing the spread of XFG requires a combination of:

- robust genomic surveillance and the integration of sequencing with epidemiological data;
- targeted non-pharmacological interventions focusing on high-risk indoor environments;
- strengthening infection control in healthcare settings and long-term care facilities;
- adapting vaccine strategies to account for the immune evasion of Omicron subvariants.

This comprehensive approach helps to minimize the potential impact of XFG on morbidity and mortality, as well as on the resilience of healthcare systems.

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