Global Influenza Hospital Surveillance Network

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GIHSN report of activity prior to the WHO Consultation on the Composition of Influenza Virus Vaccines for use in the 2025-2026 Northern Hemisphere Influenza Season.

Report prepared the 7th of February 2025

1 - Description of the network

GIHSN is collecting clinical and virological information from hospitalized cases through a network of sites located in different regions of the world (figure1). This combined clinical and virological surveillance allows the identification of viruses responsible for severe influenza. This severity is assessed by the oxygen requirement of cases registered by the sites. In this report, viruses detected and sequenced from cases requiring oxygen supplementation are identified in the phylogenetic trees provided, to determine if specific lineages or clades are associated with more frequent severe presentation.

For the 2024-2025 surveillance in GIHSN, influenza activity was detected from September, with a co-circulation of A/H1N1, A/H3N2 and B viruses in different relative proportions.

This report collates the sequencing data of hospitalized patients from 5 sites reporting 100 sequences available in the GISAID database on 2025/02/06: *Cote d'Ivoire (10), USA (9), Pakistan (55), Senegal (2), Ukraine (24).* Samples were collected between W37-2024 and W4-2025. Additional sequences from Spain and Romania are under analysis but could not be integrated in the report as deposited in the GISAID database after 2025/02/06.

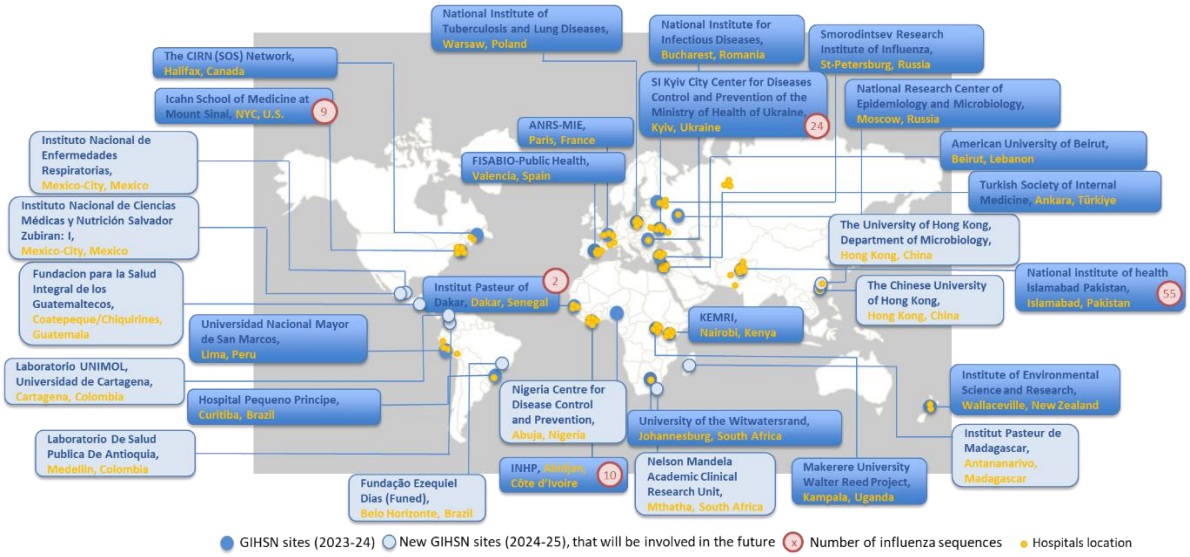

Fig. 1 Map showing the repartition of the participating countries, between September 2024 and January 2025, , with the number of influenza sequences shared by sites. Eleven new sites (in pale blue) have joined the GIHSN for the 2024-2025 season but just started implementation.

2 - Description of the virus sequenced in the GIHSN

2.1 - Influenza A viruses

A(H1N1)pdm09 viruses

A(H1N1)pdm09 viruses were detected in most part of the world and predominated in Asia. A(H1N1)pdm09 viruses sequenced from the GIHSN network (n=54) were collected between W37-2024 and W4-2025, and were collected mainly from Pakistan (32/54, 60%).

Sequencing results indicated that 22% of these viruses (12/54) belonged to 6B.1A.5a.2a.1 clade close to reference strain A/Victoria/4897/2022, while 70% (42/54) belonged to 6B.1A.5a.2a clade (Fig. 2).

Most 5a.2a.1 viruses were detected in Pakistan (11/12), while the diversity of origin of 5a.2a viruses was larger (21/42 from Pakistan, 15/42 from Ukraine, 4/42 from USA, 2/42 from Cote d'Ivoire).

Among 5a.2a clade, most viruses (27/42, 64%) belonged to C.1.9.3 subclade characterized by HA1: S83P substitution. In addition, 12/42 (29%) viruses belonged to C.1.9 subclade.

Among 5a.2a.1 clade, most viruses (11/12) belonged to D3 subclade characterized by the HA1:T216A substitution also found in A/Victoria/4897/2022 reference strain, and additional HA1: T120A substitution.

Although most cases requiring oxygen were infected with viruses of subclade C.1.9.3 (8/9 patients), the limited diversity of origin of these viruses (6/8 from Ukraine) and the small number of samples preclude analysis of any association between lineage or clade and oxygen supplementation. However, this signal will be further investigated during the surveillance this year (Fig. 2).

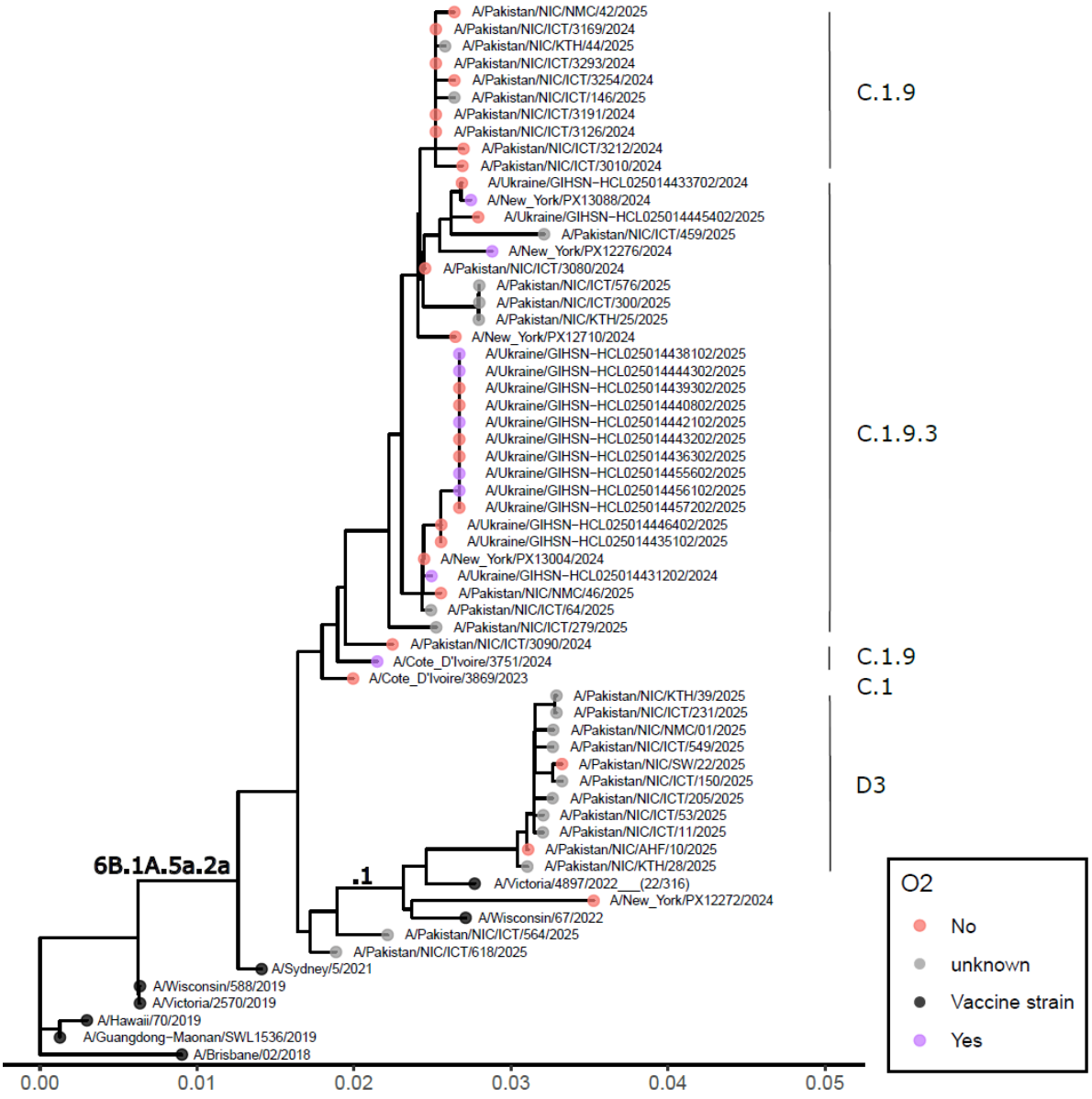

Fig 2: Phylogenetic tree of the A(H1N1pdm09) viruses analyzed between 1st of September 2024 and 1st of February 2025. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed using ggtree in R. Tips (samples) colors correspond to Oxygen supplementation (yes: purple; red:no) with vaccine reference strains displayed in black.

A(H3N2) viruses

Circulation of A(H3N2) viruses was more limited in countries participating in the GIHSN network during the 2024-2025 season, with only 18 sequences generated. All but two viruses belonged to 3C.2a1b.2a.2a.3a.1 clade, with A/Massachusetts/18/2022, A/Thailand/8/2022, A/Croatia/10136RV/2023 and A/DistrictOfColumbia/27/2023 as reference viruses (Fig. 3).

The two viruses from the 2a.3a clade were from Cote d'Ivoire and classified as G.1.3.1 subclade.

Among 2a.3a.1 clade, most viruses (11/16) belonged to J2 subclade characterized by the HA1:K276E substitution also found in A/Croatia/10136RV/2023 and A/DistrictOfColumbia/27/2023 reference strains, and a variety of additional substitutions related to each cluster.

All three cases requiring oxygen supplementation were detected in the J2 subclade with HA1: D104N, which warrant further analysis on a larger cohort to investigate a potential association between severity and this subclade (Fig. 3).

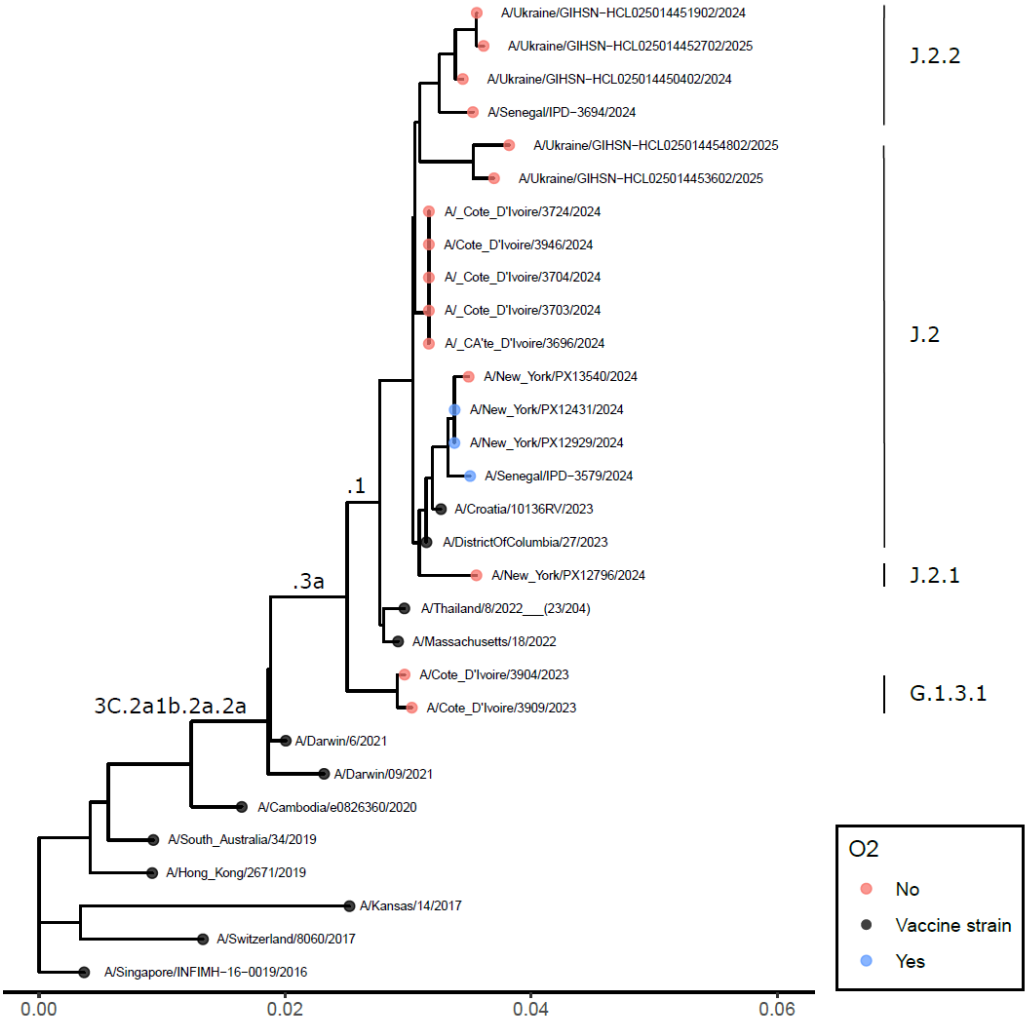

Fig 3: Phylogenetic tree of the A(H3N2) viruses analyzed between 1st of September 2024 and 1st of February 2025. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed using ggtree in R. Tips (samples) colors correspond to Oxygen supplementation (yes: blue; red:no) with vaccine reference strains displayed in black.

2.2 - Influenza B viruses

B/Victoria Lineage

Influenza B viruses co-circulated with Influenza A viruses in most part of the world during the 2024-2025 season. All 28 Influenza B viruses sequenced within the GIHSN network belonged to the V1A.3a.2 clade, with B/Austria/1359417/2021 as reference virus (Fig. 4).

Most of the sequences belonged to C.5.* subclades characterized by HA1:D197E substitution compared with B/Austria/1359417/2021 reference strain, with 4/28 viruses in C.5 subclade, 8/28 viruses in C.5.6 subclade, and 6/28 viruses in C.5.7 subclade.

Seven sequences belonged to the C.3 subclade characterized by HA1:S208P and originated from Pakistan.

Information on oxygen supplementation was available only for 7 patients, none of them requiring oxygen supplementation (Fig. 4).

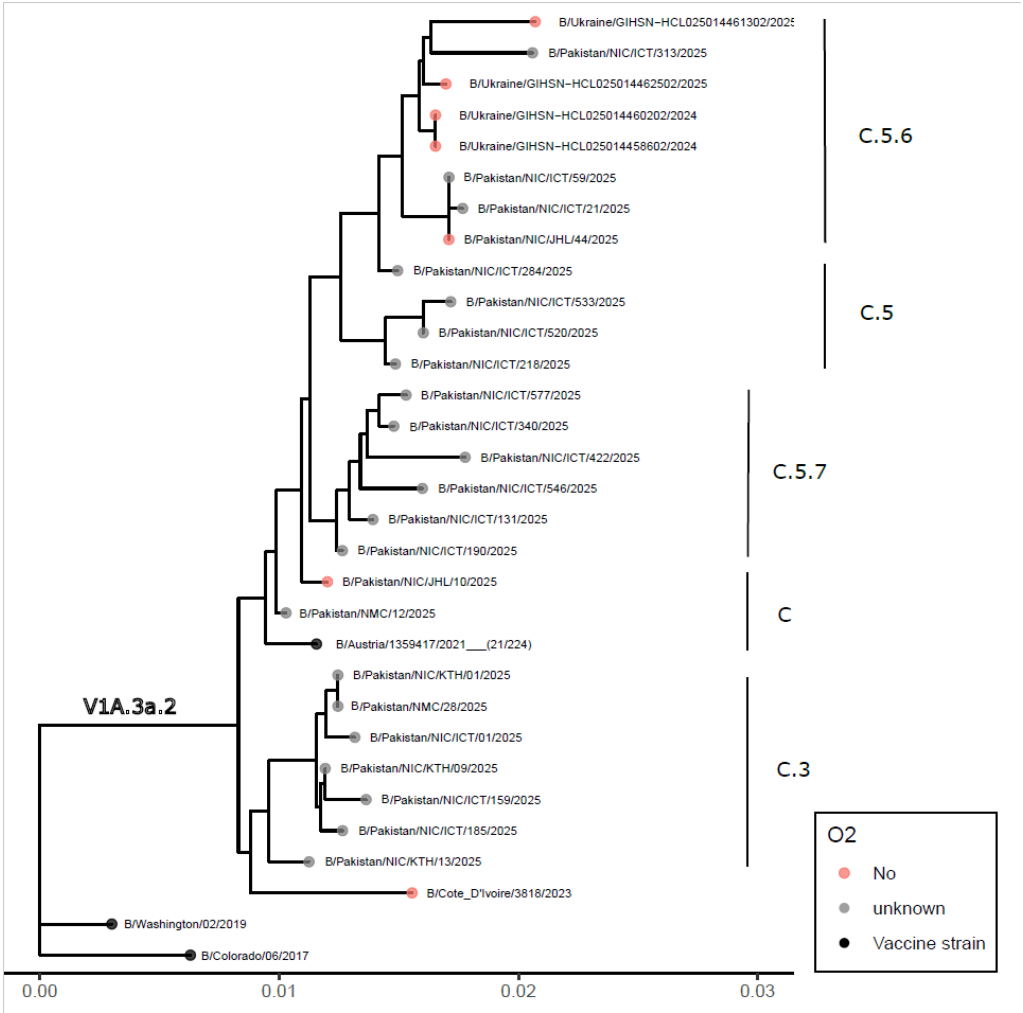

Fig 4: Phylogenetic tree of the B/Victoria viruses analyzed between 1st of September 2024 and 1st of February 2025. The phylogeny has been inferred using a Neighbor Joining approach (Seaview).

Visualization was displayed using ggtree in R. Tips (samples) colors correspond to Oxygen supplementation (yes: blue; red:no) with vaccine reference strains displayed in black.

B/Yamagata viruses

No B/Yamagata/16/88 viruses have been detected.

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