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RESEARCH ARTICLE

XBB.2.3, Prevalence, Structural, Genomic, and Pathogenic Properties.

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ABSTRACT

Background: The World Health Organization -WHO- declares the end of COVID-19 pandemic on May 5, 2023, and the contagious and pathogenic XBB.2.3 "Acrux" begins to spread worldwide. XBB.2.3 has a higher transmission rate and greater evasive capacity of immune-generated antibodies and vaccines than the XBB.1.16 strain, the potential to evade all forms of immunity, including those conferred by current booster vaccination or by previous infections, besides that current virus vaccines and their boosters may provide little or no protection against XBB.2.3*. Those infected with XBB.2.3*, are expected to acquire more opportunistic secondary infections that contribute to the severity of the disease and more long-term problems (Post-COVID Syndrome) and a possible increase in the mortality rate. **Aim:** The purpose of the manuscript is to present a systematic review on the prevalence, structural, genomic, and pathogenic characteristics of XBB.2.3 and its descendants as of May 31, 2023, emphasizing the symptoms generated in children, adults, and the elderly.

Material and methods: Original scientific articles published in Medline, Pubmed, Science Direct, Web of Science, Scopus, EBSCO and BioMed Central databases, official health organizations (WHO, CDC, ECDEC, DOH Philippines) electronic publications, and specialized media in the subject, were electronically searched to accomplish the aim of the study. Articles published in any language were included from 2020 to present using a variety of keywords in combination. The studies relevant to our review were analysed and compared. **Results and discussion:** XBB.2.3 probably originated in India, but is expanding, being detected as early as Europe in mid-January 2023 and as of May 31, 2023, in more than 47 countries, including the United States, India, Philippines and Thailand. XBB.2.3* has five defining mutations; S:D253G (previously found in Lambda and Iota variants), S:P521S (new since XBB family), S:S486P and the unprecedented ORF1a:G2091S, and ORF7a:A13V. S:S486P is probably the responsible of the superior transmissibility of XBB.2.3*, appears to have a 37% rate of infection and hospitalisation, which is 3-8% higher than other sub-variants. **Conclusions:** XBB.2.3* SARS-CoV-2 strain has a higher transmission rate than XBB.1.16*, exhibits a greater evasive capacity of immune-generated antibodies and vaccines than XBB.1.16*, and even has the potential to evade all forms of immunity, including those conferred by current booster vaccination or by previous infections. Those infected with XBB.2.3*, are expected to acquire more opportunistic secondary infections that contribute to the severity of the disease and more long-term problems (Post-COVID Syndrome) and a possible increase in the mortality rate. Preliminary data from the study suggest that current virus vaccines and their current boosters may provide little or no protection against XBB.2.3*. The potential consequences of XBB.2.3* underscore the importance of coordinated, proactive and productive efforts to contain its spread.

Introduction:

As the COVID-19 pandemic continues to evolve, new variants of the SARS-CoV-2 virus are emerging.

These new strains have the potential to trigger off significant changes in the transmissibility, severity, and immune evasion capacity of the virus.

While XBB.1.16 currently get the attention of health experts and mainstream media around the world, the new and lesser-studied XBB.2.3 is emerging as a more worrisome threat to global health.

XBB.2.3 probably originated in India, but is expanding, being detected as early as Europe in mid-January 2023 and to date in more than 47 countries, including the United States and Thailand.

XBB.1.16 is for now the "center of attention", becoming the predominant variant in many countries around the world¹.

Discussion

In a study published in *medRxiv* on April 26, 2023, Rajesh Karyakarte and colleagues from Department of Microbiology, Medical College and Sassoon General Hospitals in Maharashtra, India, found that from a total of 2,944 sequences downloaded from the GISAID database, of which 2,856 were included in the study following data curation, the sequences from India were dominated by the XBB.1.16* lineage (36.17%) followed by XBB.2.3* (12.11%) and XBB.1.5* (10.36%)².

Currently in India, was detected six XBB.2.3 sublineages, of which XBB.2.3.2 is on the upswing right now³.

XBB.2.3* has four defining mutations; S:D253G (previously found in Lambda and Iota variants), S:P521S (new since XBB family), and the unprecedented ORF1a:G2091S, and ORF7a:A13V.

Recently, several fast-growing XBB lineages, such as XBB.1.16 (K478R), XBB.2.3.5 (K478N), and XBB.2.3.4 (K478Q), have acquired RBD mutations on K478⁴.

However, the K478 mutation did not emerge in our prediction of evolutionary trends for XBB.1.5 RBD.

This contradiction may be attributed to the mutational prediction model applied, primarily relies on the cohorts recruited, and haven't captured the immune background that introduced K478 mutation.

One possible background that may give rise to K478 is repeated BA.5/BQ.1.1/XBB exposure, as F486 could mask the immunogenicity of K478.

Another potential source of K478 is Delta-imprinted convalescents who experienced BA.5/BQ.1.1/XBB infections, which could result in abundant K478X-sensitive mAbs.

This may explain why K478X is mostly observed in India^{2,5}.

Recent studies have shown that subsequently exposed to Omicron twice after two doses of WT-based mRNA vaccines still produce significantly low levels of Omicron-specific antibodies, despite the enhanced neutralization breadth against BQ.1.1 and XBB variants^{6,7}.

Additionally, individuals who have received two doses of mRNA vaccines and experienced

two rounds of Omicron infection also have low levels of Omicron-specific antibodies.

This implies mRNA vaccines may generate a stronger immune imprinting effect compared to inactivated vaccines, potentially due to its stronger primary humoral immune response.

However, a head-to-head comparison is needed for validation^{8,9}.

XBB.2.3 is defined by S:P521S and S:S486P mutations in the S-protein, and in the proteins of its Open Reading Frames -ORFs⁻¹⁰.

Other XBB.2.3 mutations are:

1. S:D253G (observed in Lambda and Iota variants).
2. S:P521S (observed only in XBB sublineages).
3. ORF1a-G2091S and ORF7a-A13V.

In XBB.2.3 the "Reference Mutation Reversion" (T) is detected; 16342:C->T (ORF1b:959S), which defined BA.2.10¹¹.

Concerns about XBB.2.3*

Current infections generated by XBB.1.16 appear to be triggering more problems in vulnerable groups (elderly, obese, immunocompromised and those with existing comorbidities or who possess certain genetic markers) regardless of immunity generated by vaccination.

A study published in *medRxiv*, reports that XBB.1.16 produces a greater severity of COVID-19 than currently circulating variants, since "approximately 25.7% of all infected require hospitalization, of which 33.8% will require supplemental oxygen"¹².

XBB.2.3* are showing several concerning properties such as:

1. Increased transmissibility.

XBB.2.3 has a higher transmission rate than the XBB.1.16 strain, allowing it to spread more rapidly between humans and populations.

This increased transmissibility is due to a greater binding capacity with ACE2 since its S-protein mutations.

2. Increased antibody evasion capacity.

XBB.2.3 exhibits a greater evasive capacity of immune-generated antibodies and vaccines than XBB.1.16, and even has the potential to evade all forms of immunity, including those conferred by current booster vaccination or by previous infections¹³.

3. Greater potential to generate severe disease: XBB.2.3 may lead to more severe cases of COVID-19, as it is able to evade the last defense immunity conferred by T cells in the human host.

Along, it is speculated that XBB.2.3 mRNA may cause damage to T cells, even to a greater extent than those generated by HIV infections¹⁴.

Those infected with XBB.2.3, are expected to acquire more opportunistic secondary infections that contribute to the severity of the disease, more long-term problems (Post-COVID Syndrome) and a possible increase in the mortality rate.

4. Uncertainty surrounding vaccine efficacy.

Preliminary data from the study suggest that current virus vaccines and their boosters may provide little or no protection against XBB.2.3.

While manufacturers of mRNA-type vaccines (primarily Pfizer and Moderna) are working to adapt their formulations, it is unclear how long it will take for updated XBB.2.3 vaccines to become available.

XBB.2.3 is currently the most evolutionarily capable recombinant variant, which appears to be evolving aggressively, able to evade all forms of immunity, develop antiviral resistance to therapeutic molecules, and generate greater virulence and pathogenicity.

XBB.2.3 is rapidly evolving and generating more concerning sublineages such as XBB.2.3.2, XBB.2.3.4, XBB.2.3.5 and XBB.2.3.6.

In these sublineages, worrisome mutations have been detected in the S, N and ORF proteins, responsible for immune suppression and weakening of several host cellular functions¹⁵⁻¹⁹.

To date, more XBB.2.3 sublineages are emerging and closely monitored²⁰⁻²⁴.

Some of the descendants such as XBB.2.3.6 show interesting mutations²⁵.

For example, XBB.2.3.6+N:T165I and XBB.2.3.6+N:T166I, in addition to XBB.2.3.6: T22843C, C7105T, C1063T, T8164C, and C28767T(N:T165I).

5. Addressing the threat posed by XBB.2.3

Recommended actions include:

1. Better genomic surveillance: Health authorities should intensify genomic sequencing efforts to detect and monitor XBB.2.3, as well as any other emerging strains.

2. Rapid adaptation of vaccines: Vaccine manufacturers should prioritize the development of updated vaccines that effectively target XBB.2.3.

3. Strengthening public health measures: Wearing masks, social distancing, and hand hygiene, remain crucial to mitigate the spread of COVID-19, including that produced by XBB.2.3.

5. Other emerging sublineages of XBB.

Other XBB sublineages are rapidly emerging and are also of concern such as XBB.2.3.2, XBB.2.3.4, and XBB.2.3.8 which have yet to demonstrate sustained growth and prevalence potential.

To date, constant COVID-19 attacks are still expected worldwide triggered from XBB.1.16*, XBB.1.9* and XBB.2.3*, so the pandemic is far from over.

We must be careful with the narrative that the new sublineages are becoming less worrisome, generate mild disease, we must now enter an endemic phase by eliminating health precautions and that we have to learn to live with the virus.

Tomokazu Tamura and colleagues from Department of Microbiology and Immunology, Faculty of Medicine, Hokkaido University, Sapporo, Japan, published in Nature Communications the article "Virological characteristics of the SARS-CoV-2 XBB variant derived from recombination of two Omicron subvariants"²⁶.

The phylogenetic analyses suggested XBB emerged through the recombination of two cocirculating BA.2 lineages, BJ.1 and BM.1.1.1 (a

progeny of BA.2.75), during the summer of 2022.

Point out that XBB.1 is most strongly resistant to BA.2/5 breakthrough infection sera to date and more fusogenic than BA.2.75.

The recombination breakpoint is in S-RBD and each spike region, confers immune evasion and increased fusogenicity.

They provide the structural basis for the interaction between XBB.1 spike and human ACE2.

The authors conclude this multiscale investigation provides evidence suggesting that XBB is the first observed SARS-CoV-2 variant to increase its fitness through recombination rather than amino acid substitutions.

Although various “local variants” including XBB have simultaneously and convergently

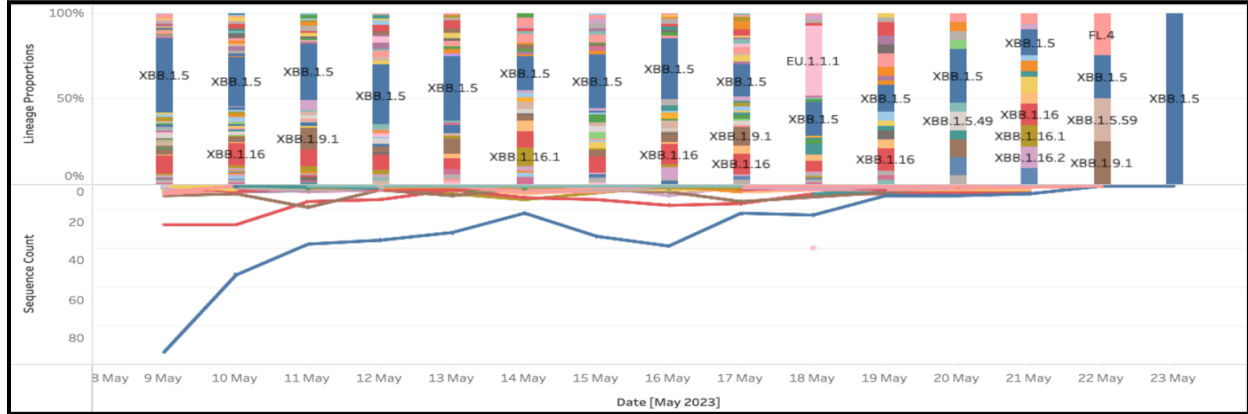
emerged in late 2022, local variants showing a higher fitness will eventually spread to the whole world, like XBB.

Therefore, continued in-depth viral genomic surveillance and real-time risk evaluation of newly emerging SARS-CoV-2 variants, even though considered local variants at the time of emergence, should be crucial.

According to Raj Rajnarayanan in his “Global SARSCoV2 Variant Landscape At a Glance! Tracking Circulating SARSCoV2 Lineages #Global #20Day Trends NYITCOM Research Report and Circulating Variants in the US States: All-Specimen Collected in the last 15 days, Updated on 31/05/2023”, published the prevalence of SARS-CoV-2 Lineages Over Time, 20 Day Trends as of 28/05/2023 (World) and 31/05/2023 (United States of America)²⁷:

Pango Lineage	% of Total World	% of Total United States of America
XBB.1.5	19.8%	30.63%
XBB.1.16	9.9%	10.00%
XBB.1.9.1	7.1%	4.73%
EG.1	3.5%	1.61%
FL.4	3.3%	2.54%
XBB.1.9.2	3.3%	1.88%
XBB.1.16.1	3.3%	2.14%
FL.2	2.9%	0.80%
XBB.2.3	1.7%	0.98%
XBB.2.3.2	1.5%	1.07%
XBB.1.16.2	1.2%	1.70%
XBB.1.5.37	1.2%	1.07%
FU.1	1.1%	0.71%
FD.1.1	1.0%	0.18%
XBB.1.5.24	1.0%	0.89%
FL.5	0.9%	0.54%
XBB.1.5.1	0.4%	0.80%

Rajnarayanan in the report “Circulating SARS-CoV-2 lineages prevalence Variants in the following US States: All Specimen Collected in the last 15 days”, shows the SARS-CoV-2 lineages prevalence over time in USA as of 31/05/2023.



Note: The blue line represents XBB.1.5, and the red line XBB.1.16.

From April 22 to May 27, 2023, an increase of XBB.2.3 increase with subsequent decrease XBB.1.16 (+1.75%), and XBB.1.9.1 (+1.68%) (+0.90%, -0.91%) is shown²⁷ prevalence, an increase of and a slight

Table. Variations of Recombinant Variants Prevalence in the United States of America (April 22, 2023 to May 27, 2023)

Variant	(April/22) Difference	(April/29) Difference	(May/06) Difference	(May/13) Difference	(May/20) Difference	(May/27) Difference
XBB.1.5	52.82%	51.36% (-1.46%)	51.93% (-0.89%)	43.01% (-9.81%)	42.01% (-10.81%)	28.10% (-24.72%)
XBB.1.16	9.54%	8.37% (-1.17%)	7.73% (-1.81%)	7.26% (-2.28%)	6.16% (-0.89%)	11.29% (+1.75%)
XBB.1.9.1	4.66%	6.69% (+2.03%)	4.83% (+0.17%)	3.76% (-0.90%)	3.77% (-0.89%)	6.34% (+1.68%)
XBB.1.16.1	2.60%	2.51% (-0.09%)	1.93% (-0.67%)	1.08% (-1.52%)	1.76% (-0.84%)	2.75% (+0.15%)
XBB.1.9.2	2.28%	1.99% (-0.29%)	2.21% (-0.07%)	4.03% (+1.75%)	2.64% (+0.36%)	1.38% (-0.90%)
XBB.2.3	1.19%	2.09% (+0.90%)	2.90% (+1.71%)	1.61% (+0.42%)	0.63% (-0.56%)	0.28% (-0.91%)
XBB.1.5.15	1.19%	1.05% (-0.14%)	1.38% (+0.19%)	-	0.63% (-0.56%)	1.10% (-0.09%)
XBB.1.5.1	0.98%	1.99% (+1.01%)	1.80% (+1.82%)	0.54% (-0.89%)	1.38% (+0.40%)	0.83% (-0.15%)
XBB.1.5.17	0.87%	1.05% (+0.18%)	0.55% (-0.32%)	1.08% (-0.44%)	1.01% (+0.14%)	-

Note. The differences are calculated related to April 22, 2023. Source: Authors.

XBB.2.3* prevalence in United States of America as of May 27, 2023, is XBB.2.3.3 (0.75%), XBB.2.3.2 (0.38%), XBB.2.3.7 (0.25%) and XBB.2.3.11 (0.13%)²⁷.

CDC data of SARS-CoV-2 variants prevalence in the United States during the weeks ending April 22 to May 27, 2023 is²⁸

Variant	(April/22)	(April/29) Difference	(May/6) Difference	(May/13) Difference	(May/27)* Difference
Variant	78.2%	73.2% (-5.0%)	66.9% (-11.3%)	64.0% (-14.2%)	53.8% (-24.4%)
XBB.1.5	6.6%	8.0% (+1.4%)	9.4% (+2.8%)	9.2% (+2.6%)	11.8% (+5.2%)
XBB.1.9.1	5.6%	8.4% (+2.8%)	12.5% (+6.9%)	14.3% (+8.7%)	15.1% (+9.5%)
XBB.1.16	2.4%	2.4% (0.0%)	2.4% (0.0%)	2.4% (0.0%)	2.2% (-0.2%)
XBB.1.5.1	2.4%	3.0% (+0.6%)	3.7% (+1.3%)	4.0% (+1.6%)	6.1% (+3.7%)
XBB.1.9.2	1.6%	2.1% (+0.5%)	2.7% (+1.1%)	3.5% (+1.9%)	4.8% (+3.2%)
XBB.2.3	1.6%	1.6% (0.0%)	1.6% (0.0%)	1.8% (+0.2%)	1.5% (-0.1%)
FD.2	0.7%	0.5% (-0.2%)	0.3% (-0.4%)	0.3% (-0.4%)	0.1% (-0.6%)
BQ.1.1	0.4%	0.3% (-0.1%)	0.2% (-0.2%)	0.2% (-0.2%)	0.2% (-0.2%)

*Beginning May 11, 2023, Genomic Vigilance data will be reported biweekly, based on the availability of positive test samples. The archived genomic surveillance data is available at data.cdc.gov

Notes. The differences are calculated related to April 22, 2023. Source: Authors. XBB.1.16.; 3.9% prevalence on 27 My, 2023.

The global prevalence of SARS-CoV-2 variants on 20/05/2023 and 28/05/2023 is²⁹:

Variant	(May 20)	(May 28)	Variant	(May 20)	(May 28)
XBB.1.5	24.5%	19.8%	XBB.2.3.2	1.5%	1.5%
XBB.1.16	7.6%	9.9%	XBB.2.3	1.4%	1.7%
XBB.1.9.1	6.4%	7.1%	FU.1	1.4%	1.1%
FL.4	3.1%	3.3%	XBB.1.16.2	1.2%	1.2%
XBB.1.9.2	3.0%	3.3%	FL.5	1.2%	0.9%
EG.1	2.8%	3.5%	XBB.1.5.1	1.1%	0.4%
XBB.1.16.1	2.3%	3.3%	XBB.1.5.37	1.0%	1.2%
FL2	2.1%	2.9%	XBB.1.5.24	1.0%	1.0%
FD.1.1	1.6%	1.0%			

Table. S-protein and NSP3 mutations in the XBB2.3 family.

National Library of Medicine. National Center for Biotechnology Information³⁰

XBB.2.3 FAMILY	S: V83A	S: H146Q	S: Q183E	S: D253G	S: F486L	S: F486S	S: P512S	S: D80Y	S: G184V	NSP3: R1341W	S: K182N	S: T478T	S: S98F	NSP3: P1076P
XBB.2.3	X	X	X	X	X	X	X							
XBB.2.3.1	X	X	X	X	X	X	X	X						
XBB.2.3.2	X	X	X	X	X	X	X		X	X				
XBB.2.3.3	X	X	X	X	X	X	X				X			
XBB.2.3.5	X	X	X	X	X	X	X					X		
XBB.2.3.9	X	X	X	X	X	X	X						X	
XBB.2.3.10	X	X	X	X	X	X	X							X

Data consulted on May 31, 2023.

XBB.2.3* has four defining mutations; S:D253G (previously found in Lambda and Iota variants), S:P521S (new since XBB family), XBB.2.3.2 is defined as (XBB.2.3+S:G184V).

Another XBB.2.3+S:G184V with ORF1a: P1786L was reported in 5 countries (81 sequences)³¹.

On March 16, 2023, WHO announced the "Statement on the Update of Working Definitions and Tracking System for SARS-CoV-2 Variants of Concern and Variants of Interest"³².

WHO updated its tracking system and working definitions for variants of SARS-CoV-2, to better correspond to the current global variant landscape, to independently evaluate Omicron circulating sublineages, and classify new variants more clearly when required.

Since the beginning of the COVID-19 pandemic, multiple Variants of Concern and Variants of Interest have been designated by WHO based on their assessed potential for expansion and replacement of prior variants, for causing new waves with increased circulation, and for the need for adjustments to public health actions.

There is consensus among experts in WHO's Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE) that compared to previous variants, Omicron represents the most divergent Variant of Concern seen to date.

Since its emergence, Omicron viruses have continued to evolve genetically and antigenically with an expanding range of sublineages, which so far have all been characterized by properties of evasion of existing population immunity and a preference to infect the upper respiratory tract (versus lower respiratory tract), as compared to pre-Omicron Variants of Concern.

The Omicron viruses account for over 98% of the publicly available sequences since February 2022 and constitute the genetic background from which new SARS-CoV-2 variants will likely emerge, although the emergence of variants derived from previously circulating Variants of Concern or of completely new variants remains possible.

The previous system classified all Omicron sublineages as part of the Omicron Variants of Concern and thus did not have the granularity needed to compare new descendent lineages

with altered phenotypes to the Omicron parent lineages (BA.1, BA.2, BA.4/BA.5).

WHO is also updating the working definitions for Variants of Concern and Variants of Interest.

The main update consists in making the Variants of Concern definition more specific, to include major SARS-CoV-2 evolutionary steps that require major public health interventions.

In addition, WHO will assign Greek labels for Variants of Concern, and will no longer for Variants of Interest.

WHO has now classified XBB.1.5 as a Variant of Interest and also continue to issue regular risk assessments for both Variants of Interest and Variants of Concern (see [latest risk assessment for XBB.1.5](#)).

For variant proportion projections (COVID Data Tracker Weekly Review of May 11, 2023), the CDC is shifting to every-other-week reporting³³.

That week's report shows that, over the past 2 weeks, XBB.1.5 makes up 64% of samples, down from 76.3% from the previous 2 weeks.

Levels of XBB.1.16 rose from 6.6% to 14.3% over the same period, with levels of XBB.1.9.1 rising from 6.5% to 9.2%.

Other subvariants shows increased proportions include XBB.1.9.2 and XBB.2.3.

On May 16, 2023, was detected the second case of XBB.2.3.2 in Italy as part of the surveillance in Milan³⁴.

The 143 WHO Weekly Epidemiological Update on COVID-19 published on May 18, 2023 (data as of May 14, 2023), reports that globally, from 17 April to 14 May 2023 (28 days), 24,884 SARS-CoV-2 sequences were shared through GISAID³⁵.

WHO is currently monitoring two Variants of Interest; XBB.1.5 and XBB.1.16, along with seven Variants Under Monitoring and their descendent lineages.

The Variants Under Monitoring are BA.2.75, CH.1.1, BQ.1, XBB, XBB.1.9.1, XBB.1.9.2, and XBB.2.3.

On 18 May 2023, XBB.2.3 was added to the list of Variants Under Monitoring.

The United Nation health agency has a "special observations" of two SARS-CoV-2 Variants of Interest; XBB.1.5 which, although still the most detected in the world (in 110 countries), has a downward trend for weeks and fell to 43.8% of total sequences in week 17 (from April 24 to 30, 2023) and XBB.1.16 which instead continues to grow and, in the same week, is at 11.6%, reported by 49 countries.

The available evidence explains the WHO, "does not show an increase in the severity of XBB-descendant lineages".

An epidemiological study conducted in Singapore to assess the severity of SARS-CoV-2 variants in 3,798 participants, found no significant difference in COVID-19 infection or hospitalization outcomes between XBB-descendant lineages, including XBB.1.16 and XBB.1.5³⁶.

In addition to XBB.2.3, increasing trends have been shown in recent weeks among the Variants Under Monitoring, which at week 17 XBB.1.9.1 weighs for 13.9% of the deposited sequences, XBB (9.85%) and XBB.1.9.2 (4.1%).

On May 22, 2023, The Nation of Thailand in the article "Covid-19 cases in the Thailand are continuing to surge with fatalities nearly doubling from the previous week" published that the weekly hospitalisation cases reached 2,632, with an average of 376 cases per day, an increase of 276 cases from the previous week³⁷.

The weekly deaths reached 64, with an average of 7 deaths per day, showing an increase of 42 deaths from the previous week.

There were 401 cases of pneumonia and 226 cases requiring respiratory support, according to Associate Professor Dr. Thira Woratanarat of Chulalongkorn University Faculty of Medicine.

Dr. Thira posted on Facebook, providing data on the severity rates of each sub-variant in Singapore, based on research conducted by Singapore's Ministry of Health, published in *medRxiv* on May 10 this year³⁸.

XBB.1.5, XBB.1.16, XBB.1.9, and XBB.2.3 sub-variants of COVID-19 comparison in the vaccinated population of Singapore, mostly with mRNA vaccines, the following findings were observed:

- Severe illness rate was approximately 6-8%.
- The rate of infection leading to hospitalisation was 29-37%.
- The rate of mild infection not requiring hospitalisation was around 55-63%.

- The XBB.2.3 subvariant, which is the latest sub-variant monitored by the World Health Organisation, appears to have a 37% rate of infection and hospitalisation, which is 3-8% higher than other sub-variants.

The online German newspaper Focus, Dienstag, on May 23, 2023, in the article "New coronavirus variant on the rise: What we know about Acrux, the fastest of the XBB clan" informs the WHO has classified the variant of the coronavirus XBB.2.3, also called Acrux, as a Variant Under Monitoring³⁹.

The new nickname system uses astronomical names to provide information about ancestry, explained T. Ryan Gregory, professor in the Department of Integrative Biology and at the Ontario Biodiversity Institute at the University of Guelph.

As a background to the new system, representatives of the "Global Health Network" explain: "The astronomian names are numerous and can be assigned in such a way that they give clues about variants that are not visible with Greek letters or PANGO aliases".

In the specific case of Acrux (XBB.2.3), this means:

- Start with A-H = descendant BA.2.
- The name contains an R in the name = a recombinant or a descendant of a recombinant.

According to the Robert Koch Institute, XBB.1.16 remains the most represented in Germany at 20%, followed by XBB.1.9.1 at 17%, with XBB.2.3 less than 3%³⁹.

Although the coronavirus also mutates continuously, the danger does not change at the same time.

So far, none of the XBB variants have indications of a more pathogenic capability compared to the previous lines.

The RKI, citing European health authority ECDC, also writes that the current dominant subline XBB.1.5 poses a low risk to the general population.

The online News Dept from New York, USA, on May 23, 2023, publish the article "COVID, why the XBB sub-variants worry China? What are the real risks?"⁴⁰.

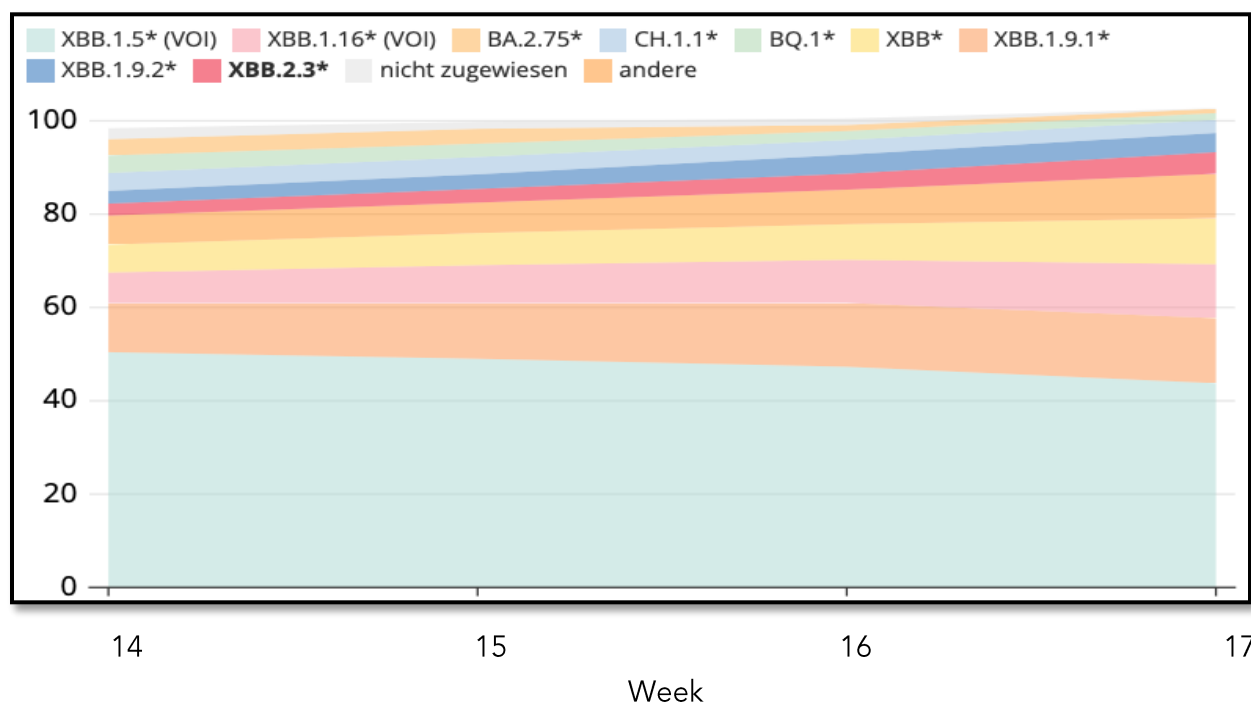
In China, the XBB subvariant was first detected in August 2022 and spawned a

series of "daughters", the last in chronological order XBB.2.3 included by the WHO on 18 May in the list of variants being monitored and also detected in Italy.

Today there are two concerning Variants of Interest; XBB.1.5 which, although still the most detected in the world (in 110 countries), has had a downward trend in previous weeks, and XBB.1.16 (reported in about fifty countries), which continues to grow and is considered to displace XBB.1.5⁴¹.

The available evidence, according to the WHO, does not show an increase in the severity of the disease caused by the descendants of XBB.

Figure. Global proportion of coronavirus variants according to WHO³⁹.



Notes. nicht zugewiesen: not assigned. andere: another.

For the listed sublines, as in previous weeks, no increase in disease severity is observed with increasing spread.

This is also the conclusion of the epidemiological study from Singapore, which failed to detect significant differences in the number of cases and hospitalizations between different XBB lines.

"I don't think there will be many serious courses through XBB.1.16 again", explained Ulf Dittmer, director of the Institute of Virology at the University Hospital of Essen.

Especially people who were first vaccinated and then mildly to moderately ill have very broad immunity, both through antibodies and T cells.

"This protects them very well from serious disease and no conceivable variant can prevent it completely"³⁹.

The epidemiological study conducted in Singapore to assess the severity of SARS-CoV-2 variants in 3,798 participants, found no significant differences in COVID-19 infection or hospitalization outcomes between XBB-descendant sublineages, including XBB.1.16 and XBB.1.5³⁸.

In addition, recent laboratory studies showed that XBB.1.16 and XBB.1.5 have similar immune evasion characteristics.

In addition to XBB.2.3, among the variants they are increasing and are being monitored are XBB.1.9.1, XBB and XBB.1.9.2.

In India as of May 22, 2023, according to Outbreak.info Location Tracker, India Variant Report⁴¹, the prevalence over last 60 days was XBB.1.16 (56%), XBB.1.16.1 (15%), XBB.2.3

(7%), XBB.1.16.2 (5%), XBB.2.3.2 (4%), XBB.2.3.3 (2%) and XBB.2.3.4 (2%)⁴⁰.

Now, five months later, with the WHO declaring the end of the pandemic emergency on May 5, the virus puts its hand in it and returns to the foreground with the emergency that threatens to overwhelm China⁴¹.

It is the group of XBB variants, including XBB.1.5, XBB.1.16 and the "latest arrival", XBB.2.3, that seriously threatens the Asian country.

On the horizon there are, as of June 2023, 65 million COVID-19 infections per week.

The XBB subvariant has generated a series of "daughters", the latest is XBB.2.3, called Acrux, was included on May 18 by the WHO in the list of Variants Under Monitoring.

A mutant of SARS-CoV-2, it is the "sister" of what was already a new mutation monitored in India, the United States, Spain, and some Asian regions.

To intercept it was the Sacco hospital in Milan, confirming that it was the second Italian case of XBB.2.3.2.

Today the "special observed" variants are XBB.1.5 which, although it is still the most detected in the world (110 countries), has a downward trend for weeks and XBB.1.16, which on the contrary continues to grow and is reported in about 50 countries⁴¹.

The Italian Positano News, on May 24, 2023, posted that the first appearance of the acronym XBB, to indicate a new SARS-CoV-2 variant "daughter" of Omicron, did it in August 2022⁴².

The Asia News Network on May 24, 2023, published that Thailand sees big jump in new Covid cases and fatalities⁴³.

Covid-19 cases in Thailand continue to rise, with almost twice as many deaths as the previous week.

Weekly hospitalization cases reached 2,632 with an average of 376 cases per day, an increase of 276 cases from the previous week.

Weekly deaths reached 64, with an average of 7 deaths per day, showing an increase of 42 deaths from the previous week⁴³.

There were 401 cases of pneumonia and 226 cases requiring respiratory support, according to associate professor Dr. Thira Woratanarat of Chulalongkorn University School of Medicine.

Dr. Thira provided data on the severity rates of each subvariant in Singapore, based on research conducted by Singapore's Ministry of Health, published on *medRxiv* on May 10 this year⁴³.

When comparing the XBB.1.5, XBB.1.16, XBB.1.9 and XBB.2.3 subvariants of COVID-19 in the vaccinated population of Singapore, mainly with mRNA vaccines, the following findings were observed:

- The rate of serious illness was approximately 6-8%.
- The infection rate leading to hospitalization was 29-37%.
- The rate of mild infection that did not require hospitalization was around 55-63%.

The XBB.2.3 subvariant, appears to have an infection and hospitalization rate of 37%,

which is 3-8% higher than other subvariants, Dr. Thira noted.

The CNN Philippines staff, published on May 25, 2023, the article "PH now has 28 cases of Omicron subvariant XBB.1.16", reporting that the country has detected 17 more cases, according to the Philippines Department of Health (DOH)⁴⁴.

Tagged as a variant of interest by the World Health Organization (WHO), the country recorded its first case of XBB.1.16 last April in Iloilo in Western Visayas.

The patient had no symptoms and has since recovered.

The DOH report also noted that a total of 199 infections in the country are XBB cases.

Of that, 182 were classified as XBB, including 25 XBB.1.5 cases, 101 XBB.1.9.1 cases, 17 XBB.1.9.2 and XBB.1.16 cases, and 10 XBB.2.3 cases, 1 case as XBC, and 4 as other omicron sublineages.

There were also 41 cases of the BA.2.3.20.

The DOH described the XBB.2.3 as an XBB sublineage that was added to the list of variants under monitoring by the World Health Organization on May 17.

The variant was initially flagged for its increasing global prevalence and has been detected in 53 countries or jurisdictions across 6 continents, according to sequence submissions in GISAID.

"Limited information is available for the variant and researchers are currently characterizing XBB.2.3 in terms of transmissibility, immune evasion, and ability to cause more severe disease" the DOH report read.

These report included results of the latest sequencing run conducted by the University of the Philippines-Philippine Genome Center from May 15 to 19⁴⁵.

Conclusions

XBB.1.16 for now is the "center of attention", becoming the predominant variant in many countries around the world.

While XBB.1.16 has attracted significant attention, it is XBB.2.3 that poses the most significant threat to global health.

XBB.2.3 has a higher transmission rate than the XBB.1.16 strain, allowing it to spread more rapidly between humans and spread between populations.

XBB.2.3 exhibits a greater evasive capacity of immune-generated antibodies and vaccines than XBB.1.16, and even has the potential to evade all forms of immunity, including those conferred by current booster vaccination or by previous infections.

Those infected with XBB.2.3, are expected to acquire more opportunistic secondary infections that contribute to the severity of the disease and more long-term problems (Post-COVID Syndrome) and a possible increase in the mortality rate.

Preliminary data from the study suggest that current virus vaccines and their current boosters may provide little or no protection against XBB.2.3.

The potential consequences of XBB.2.3 underscore the importance of coordinated, proactive and productive efforts to contain its spread.

As the pandemic continues to evolve, we must stay informed about emerging variants of the virus and respond with appropriate strategies to safeguard public health and ultimately end the COVID-19 crisis.

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