



RESEARCH ARTICLE

Geographical barriers restricted SARS-CoV-2 variant distribution between East and West Malaysia until emergence of Variants of Concern

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ABSTRACT

The COVID-19 pandemic has driven unprecedented global efforts to track the evolution of SARS-CoV-2. Malaysia presents a distinctive setting for studying SARS-CoV-2 variant dynamics, as its population is divided between East and West Malaysia by the South China Sea. This study examines the distribution of SARS-CoV-2 variants across East and West Malaysia during the pandemic. Malaysia-specific lineages (B.1.524 and B.1.466.2) predominated during the early wave of the pandemic, and were associated with moderate infection rates and relatively stable hospitalisation. The B.1.466.2 lineage and its sublineage AU.2 established localised circulation in East Malaysia but failed to spread to West Malaysia, likely constrained by geographic isolation. The subsequent introduction of variants of concern (VOCs), particularly Beta, Delta, and Omicron, correlated with marked increases in infection rates and hospital admissions, reflecting their enhanced transmissibility and virulence. Notably, the case fatality ratio during the B.1.524/B.1.466.2-dominant period remained lower compared to peaks observed during Delta dominance, suggesting differences in clinical severity or healthcare burden. The spread of highly transmissible and immune-evasive VOCs clearly demonstrated the weakened effect of geographical barrier in variant distribution. Targeted, region-stratified genomic surveillance should be prioritised for timely variant detection and effective containment.

Keywords: SARS-CoV-2 variants; East Malaysia; West Malaysia; geographical barrier.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic had an unprecedented effect on global health, economies, and tested the cohesiveness of global response to the pandemic. First identified in Wuhan, China at the end of 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rapidly disseminated across the globe and infected millions of individuals (Hui *et al.*, 2020; World Health Organization, 2025b). As the virus continues to spread and evolve, it acquires traits such as enhanced transmissibility, immune escape properties, and variable clinical outcomes (World Health Organization, 2025a). The emergence of these variants has driven successive waves of infection worldwide, highlighting the critical role of genomic surveillance in monitoring viral evolution and linking genetic changes to patterns of transmission and disease impact (Tosta *et al.*, 2023).

Malaysia, like many countries, has faced multiple epidemic waves associated with different SARS-CoV-2 lineages (Azami *et al.*, 2022, Chong *et al.*, 2020, Sam *et al.*, 2022; Yu *et al.*, 2022). At the beginning of the pandemic, Malaysia was spared from the large outbreaks due to implementation of strict public health and social measures, and movement control orders (MCO) (Suleiman *et al.*, 2021). Experiences with previous outbreaks such as Nipah in 1998 (Chua, 2003) and H1N1 in 2009 (Sam & Abu Bakar, 2009) facilitated implementation and compliance with these preventive

measures. Earlier variants such as B.1.524 and B.1.466.2 were implicated in widespread community transmission, while later waves were dominated by Delta and subsequently Omicron sublineages (Azami *et al.*, 2022; Sam *et al.*, 2022). Although nationwide public health measures were implemented to mitigate viral spread, these strategies became less effective due to the emergence of highly transmissible variants of concern (VOC) with relatively high rates of severe illness which threatened to overwhelm healthcare systems (Md Asari *et al.*, 2025; Md Nadzri *et al.*, 2024).

Most countries report SARS-CoV-2 variant distribution at a national level, reflecting their contiguous geographical layout (Our World in Data, 2025). Malaysia, however, presents a unique case. The country has a population of approximately 32 million people, with about 75% residing in urban areas (Department of Statistics Malaysia, 2025b). The land is geographically divided into West Malaysia (Peninsular) and East Malaysia (Sabah and Sarawak) in the north of Borneo, separated by the South China Sea (Department of Information Malaysia, 2016). West Malaysia is more densely populated and economically developed, while East Malaysia is characterised by lower population density, a larger rural population, and comparatively limited infrastructure and economic opportunities (Department of Statistics Malaysia, 2025a). Despite this geographical segregation, publications describing SARS-CoV-2 lineages in Malaysia typically present data as a single national picture or focus on individual lineages linked to specific epidemiological

events, such as the spread of B.1.524 during large gatherings or B.1.466.2 through importation-related outbreaks (Suppiah *et al.*, 2021; Zainulabid *et al.*, 2022).

What remains lacking is an in-depth analysis of lineage distribution and its clinical implications across the two geographically isolated regions in Malaysia. Understanding whether SARS-CoV-2 variant distribution differs between East and West Malaysia is particularly relevant, as the country geography could act as a natural barrier limiting viral flow and influencing local epidemic dynamics. This study addresses this gap by comparing SARS-CoV-2 variant distribution across East and West Malaysia, and offers insights into how geography shapes epidemic patterns. Such evidence can strengthen genomic surveillance frameworks, and inform travel and border control strategies not only for Malaysia but also for other countries with similarly segregated geographies.

MATERIALS AND METHODS

Information on COVID-19 infection cases, hospitalisations, and deaths in Malaysia was obtained from the Ministry of Health (MOH) GitHub database, covering the period from 26 January 2020 to 31 July 2024 (Ministry of Health Malaysia, 2025). This dataset provides daily updates and served as the primary source for epidemiological analysis. Additionally, 41,732 complete SARS-CoV-2 genome sequences from Malaysia during the same timeframe were retrieved from Global Initiative on Sharing All Influenza Data (GISAID) EpiCov database (www.gisaid.org). These genomic data were used to identify dominant non-VOCs and VOCs for each pandemic wave. To ensure consistency in analysis, the GISAID submission periods for each wave were aligned with the MOH clinical data (infections, hospitalisations, and deaths), which were grouped into corresponding time intervals. Lineage information from GISAID metadata was then compared with the clinical data to assess the impact of VOCs on disease severity and outcomes. All downloaded GISAID sequences were uploaded into Nextclade tool (<https://clades.nextstrain.org/>) for clade classification.

For infection rate analysis, daily confirmed cases from the MOH dataset were divided by the total Malaysian population for that year (32.7 million in 2020; 32.6 million in 2021; 32.7 million in 2022; 32.8 million in 2023; and 32.9 million in 2024) (Department of Statistics Malaysia, 2024). Hospitalisation rates were calculated by dividing total hospitalisations by confirmed infections for specific time periods. Similarly, the case fatality rate (CFR) was determined by dividing total deaths due to COVID-19 by confirmed infections during each interval of the pandemic waves.

RESULTS AND DISCUSSION

Temporal dynamics of early SARS-CoV-2 lineages and clinical impact in Malaysia pre-VOC period

The earliest phase of the COVID-19 pandemic in Malaysia was characterised by limited transmission, with initial cases primarily

imported from Singapore (The Borneo Post, 2020). COVID-19 cases, hospitalisations, and deaths fluctuated across different variant periods, demonstrating the distinct impact of each dominant variant. Variant dominance intervals were identified using Malaysian sequence metadata from GISAID to compare clinical outcomes across pandemic waves (Table 1).

During the early phase of the pandemic, the B lineage was dominant from 24 January 2020 to 18 August 2020, and was linked to a religious mass gathering (Chong *et al.*, 2020). This period saw an increase in infections and hospitalisations, but there were no reported deaths. While the implementation of Movement Control Order (MCO), a total lockdown across the country, successfully reduced transmission, the Sabah state election in East Malaysia in September 2020 triggered a widespread transmission of SARS-CoV-2 nationwide. The B.1.524 lineage was the dominant variant driving this third wave of infection, accounting for a significant proportion of sequenced cases (Sam *et al.*, 2022; Tan *et al.*, 2021). Despite this significant rise in cases, the CFR remained relatively low at 0.34%. This suggests that while B.1.524 was associated with increased transmissibility, its clinical severity was moderate, leading to manageable hospitalisations and deaths.

Globally, B.1.524 was first detected in Nepal on 31 July 2020, while Malaysia reported its first case on 1 September 2020 (GISAID EpiCoV Database, 2025). Of the 741 sequences attributed to this lineage in GISAID, 76.2% were reported from Malaysia. In contrast, neighbouring countries such as Singapore (12.8%), Thailand (5.0%), and the Philippines (1.5%) reported lower proportions. This overwhelming presence of B.1.524 in Malaysia highlights its local expansion, likely driven by the increased mobility associated with election-related travel.

The B.1.524 lineage carried the D614G mutation, a well-documented signature for increased infectivity (Zhou *et al.*, 2021), alongside the A701V mutation in the S2 subunit of the S protein. While A701V had been observed in Alpha, Beta and Gamma VOCs (Khetran & Mustafa, 2023), its functional significance remained unclear. These findings suggest that increased transmission of the B.1.524 lineage could be attributed to the D614G mutation or due to epidemiological factors, as reflected in the observed rise in infections and hospitalisations without a concomitant increase in CFR compared to earlier B lineage variants.

Geographical clustering and inter-region transmission barriers

A closer examination revealed distinct regional distribution of variants between East and West Malaysia. In East Malaysia, the B.1.466.2 lineage and its sub-lineages (B.1.466.2.2 [AU.2] and B.1.466.2.3 [AU.3]) accounted for a significant proportion of SARS-CoV-2 variant detected. The B.1.466.2 was first detected in Indonesia on 6 August 2020, and introduced into Malaysia in early 2021 (GISAID EpiCoV Database, 2025). During this period, 45.2% (643/1,324) of sequences submitted to GISAID were classified as B.1.466.2 (n=190), AU.2 (n=451), and AU.3 (n=2). Of these, 79.2% (509/643) were reported in East Malaysia, highlighting the lineage

Table 1. Overview of infections, hospitalisations, deaths and case fatality rates when each variant was dominant

Variant	Variant dominant period	Total infections	Infection rate (per 100,000 people)	Total hospitalisations	Hospitalisation rate (per 100,000 people)	Deaths (COVID-19)	Case fatality rate (%)
B	Jan 2020–Aug 2020	9,219	29	5,900	18	0	0
B.1.524	Sep 2020–Jan 2021	121,768	374	41,611	128	410	0.34
B.1.524/ B.1.466.2/ Beta/Delta	Jan 2021–Jun 2021	490,978	1,506	113,248	348	2,923	0.60
Delta	Jun 2021–Dec 2021	2,180,177	6,667	266,935	816	28,302	1.30
Omicron	Jan 2022–Jul 2024	2,500,624	7,487	193,408	579	5,547	0.22

Data obtained as of 31 July 2024.

dominance and expansion in this region. Despite its widespread presence, B.1.466.2 did not appear to cause any significant increase in cases, hospitalisations, or deaths compared to West Malaysia that saw a heterogenous circulation of B.1.466.2, Alpha, Beta, and Delta variants (Figure 2). This suggests that while the B.1.466.2 possessed key spike mutations (N439K, D614G, and P681R) associated with increased transmission and partial escape from neutralising antibodies (Thomson *et al.*, 2021; Liu *et al.*, 2022), external factors such as public health interventions, movement restriction, and geographical barrier may have prevented its spread. Unlike the B.1.524, which spread from East to West Malaysia during the election period when travel restrictions were relaxed, the confinement of the B.1.466.2 lineage to East Malaysia can be largely attributed to the MCO implemented in January 2021, which resulted in minimal movement between the two regions (Zamri *et al.*, 2021).

In West Malaysia, early travel restrictions during MCO likely confined the B.1.1.354 lineage to that region before it was replaced by B.1.524 (Figure 1A). The B.1.524 was subsequently replaced by the co-circulation of B.1.466.2, Alpha, Beta, and Delta variants from early January to June 2021. The co-circulation of multiple SARS-CoV-2 lineages including B.1.524, B.1.466.2, Alpha, Beta, and Delta complicated the identification of the primary lineage driving the transmission during that period (Figure 1B). The infection rate and hospitalisation rate were notably increased (Figure 2B), indicating that VOCs like Alpha, Beta and Delta possessed higher transmissibility and pathogenic potential compared to non-VOCs. The sustained predominance of circulation of Beta over Alpha in Malaysia implies a selective advantage favouring Beta within the population. Beta carries key spike protein mutations (K417N, E484K, and N501Y) associated with enhanced transmission and immune

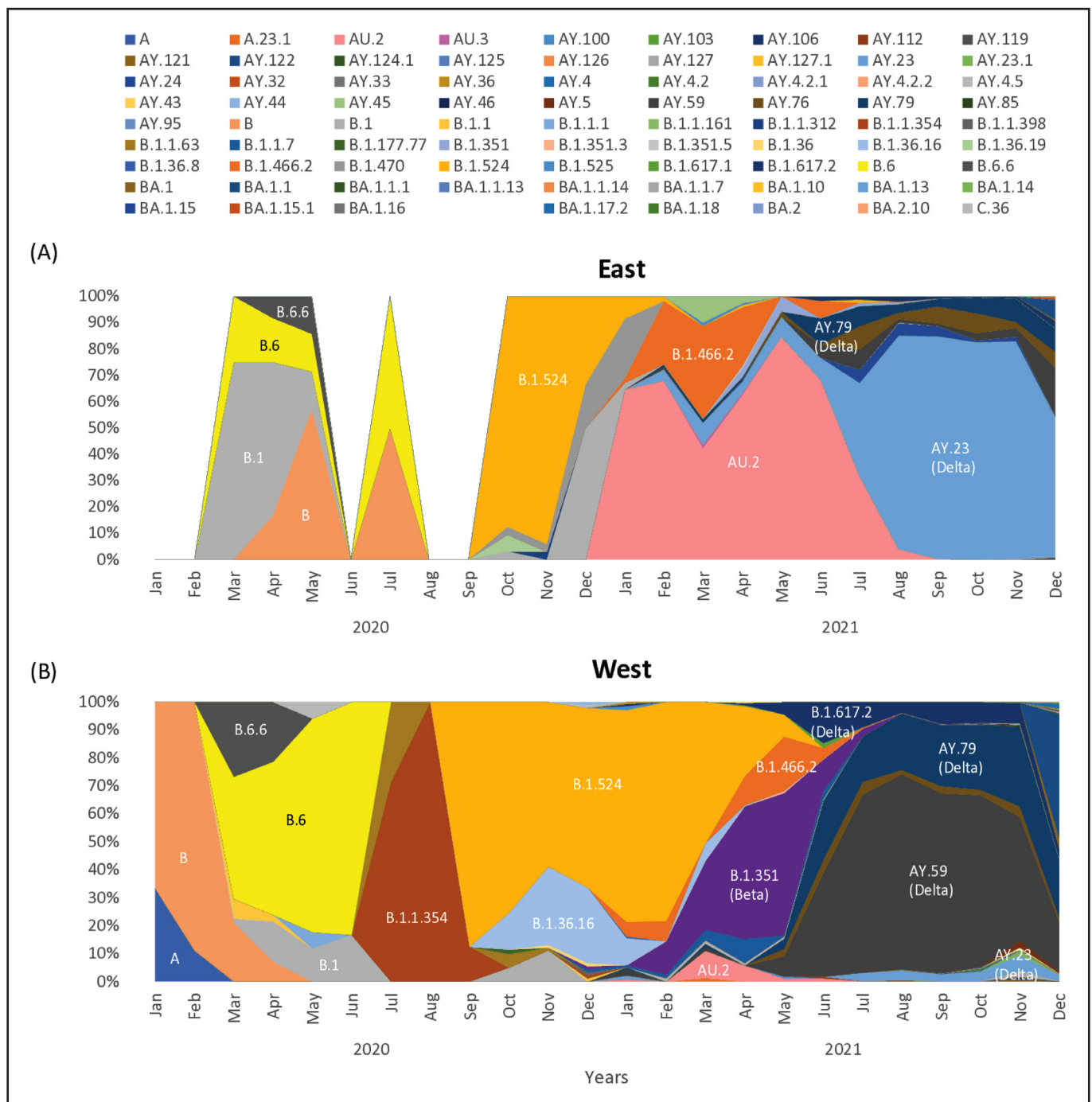


Figure 1. Distribution of non-variants of concern (non-VOC) and VOCs in (A) East Malaysia, and (B) West Malaysia, showing the transition from non-VOC lineages (B, B.1.524 and B.1.466.2) to VOCs (Alpha, Beta and Delta). The distribution was tabulated based on sequencing data obtained from GISAID from 1 January 2020 to 31 December 2021, highlighting the period of variants co-circulation.

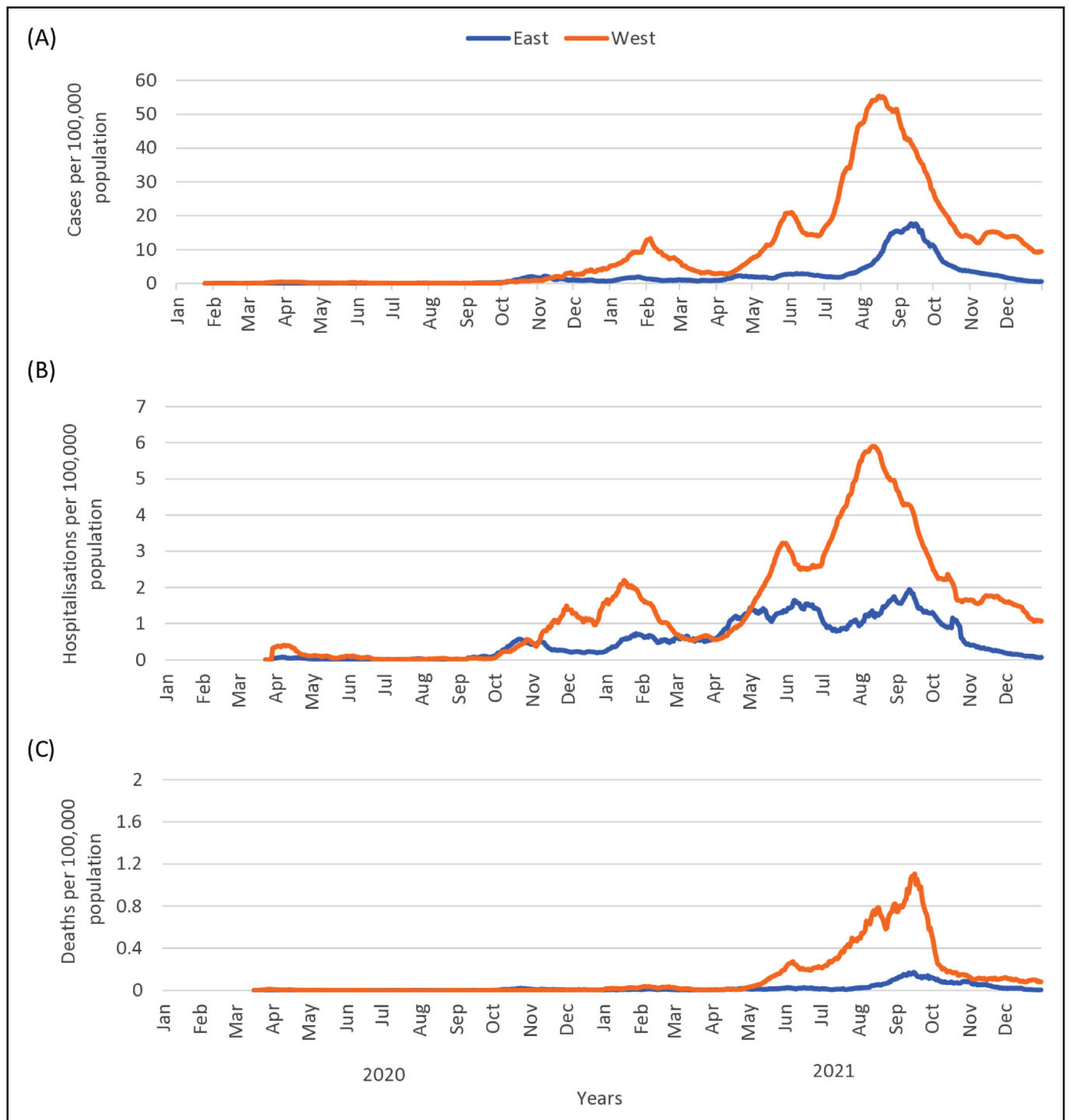


Figure 2. Distribution of (A) COVID-19 cases, (B) hospitalisations and (C) deaths in East and Malaysia from 1 January 2020 to 31 December 2021. A weekly moving average per 100,000 population for infections, hospitalisations and deaths were plotted to account for daily fluctuations. Data is obtained from MOH COVID-19 GitHub database (Ministry of Health Malaysia, 2025).

evasion, likely conferring greater competitive fitness that supported its persistence. This aligns with reports demonstrating that Beta exhibits increased resistance to neutralising antibodies, potentially facilitating extended community transmission in partially immune populations (Hoffmann *et al.*, 2021; Lucas *et al.*, 2021).

Reduced border restrictions and enhanced viral fitness on variant spread

Phylogenetic analyses indicate that Alpha and Beta emerged independently in the United Kingdom and South Africa, respectively, before disseminating globally (Tegally *et al.*, 2021; Rambaut *et al.*, 2020). Periods of co-circulation between the two variants were documented in several regions, with comparative analyses revealing

that Alpha generally outcompeted Beta in areas where both were introduced, with the exception of regions such as South Africa, Singapore and parts of Malaysia (West), where Beta established widespread local transmission (Kostaki *et al.*, 2021). In neighbouring Southeast Asian countries, including Thailand, Vietnam, and Cambodia, Alpha remained the dominant circulating lineage until the emergence of Delta, which subsequently displaced all preceding variants (Our World in Data, 2025). The restricted circulation of Alpha and Beta in West Malaysia demonstrated the effect of spatial and mobility barriers on viral dissemination. This pattern mirrors observations in other geographically isolated regions such as Taiwan (Tsou *et al.*, 2024) and Western Australia (Costantino *et al.*, 2020),

where strict border controls and limited inter-regional movement delayed variant introductions and reduced epidemic intensity.

The Delta variant, first identified in India in October 2020, exhibited a delayed trajectory in Malaysia before achieving dominance (McCrone *et al.*, 2022). Although detected as early as January 2021, preceding Alpha (March 2021) and Beta (February 2021), Delta remained subdominant until June 2021. This contrasts sharply with rapid Delta-driven surges in the United Kingdom (Bolze *et al.*, 2022) and East Africa (Bbosa *et al.*, 2022). Multiple co-circulating lineages (B.1.524, B.1.466.2, Alpha, and Beta) and

stringent public health measures likely restricted Delta early establishment.

By July 2021, Delta had displaced all predecessor variants across East and West Malaysia, breaching the geographical barrier despite interstate travel bans (Figure 3). Sustained transmission occurred through manufacturing facilities and migrant worker dormitories that remained operational during the June 2021 full MCO, with workplace clusters comprising 50.7% of total clusters (Ministry of Finance, 2021; Yaakob, 2021). Delta clade distribution also differed regionally, with AY.23 in East Malaysia, and AY.59 and AY.79 in West

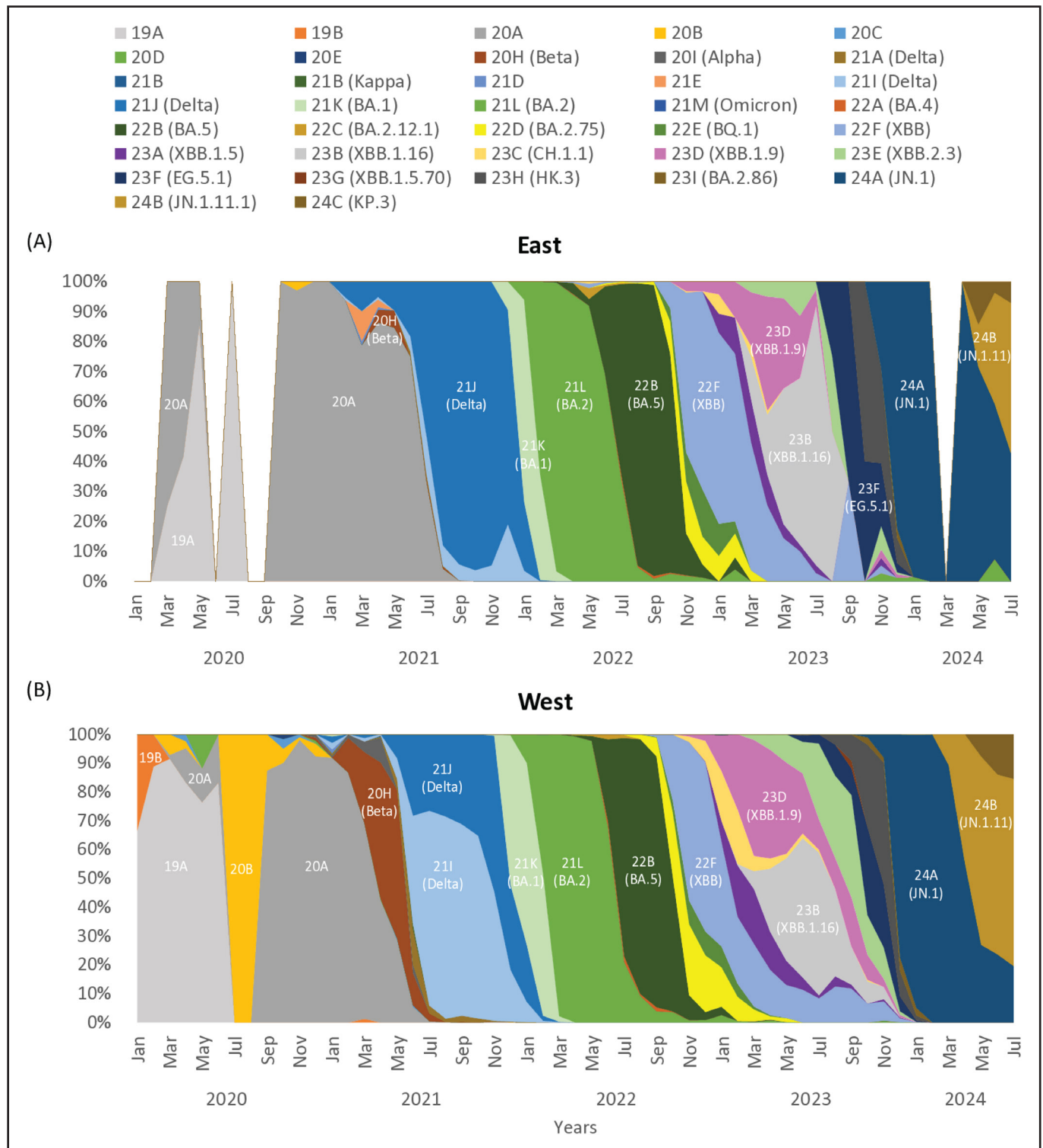


Figure 3. Clade distribution of non-variants of concern (non-VOC) and VOCs in (A) East Malaysia, and (B) West Malaysia, showing the transition from non-VOC clade to VOCs (Alpha, Beta and Delta). All clade following Delta are Omicrons. The distribution was tabulated based on sequencing data obtained from GISAID from 1 January 2020 to 31 July 2024.

Malaysia, likely reflecting founder effects from separate introduction events and limited inter-regional mixing during the restrictive period. This triggered the highest pandemic surge in hospitalisations and deaths, consistent with Delta increased transmissibility and pathogenicity globally (Dhawan *et al.*, 2022). With vaccination coverage at only 7% during this period, infections were driven primarily by enhanced transmissibility rather than immune evasion (Ministry of Health Malaysia, 2025).

In December 2021, Omicron was detected in Malaysia following its initial identification in South Africa and Botswana (Callaway, 2021). Unlike previous variants, Omicron rapidly displaced Delta, marking another significant shift in epidemic trajectory. Omicron clade distribution was uniform across East and West Malaysia, contrasting sharply with Delta regional divergence, thus reflecting lifted interstate travel restrictions, widespread vaccination-driven mobility resumption, and Omicron enhanced transmissibility that rendered geographical barriers ineffective (Cameroni *et al.*, 2022; Luo *et al.*, 2023). Despite increased infectivity, Omicron disease severity was notably lower than Delta. Hospitalisations and CFR did not rise proportionally with case surges, aligning with global observations of predominantly mild infections, particularly among vaccinated individuals (Lau *et al.*, 2023).

Overall, the emergence of Delta and Omicron demonstrated that geographical barriers, while effective against earlier SARS-CoV-2 lineages, became increasingly ineffective against highly transmissible VOCs. Island nations and geographically isolated regions that initially maintained stringent border controls and achieved near-elimination of COVID-19, such as New Zealand, Australia, and Taiwan, ultimately experienced substantial Delta and Omicron waves despite their natural barriers. New Zealand, which maintained COVID-19 elimination through strict border closures and quarantine protocols until mid-2021, recorded its first major outbreak with the Delta variant in August 2021, forcing abandonment of its zero-COVID strategy (Baker *et al.*, 2020; Jelley *et al.*, 2022). Similarly, Australia prolonged border restrictions and interstate travel limitations delayed but could not prevent Delta entry and subsequent nationwide spread by mid-2021 (Gupta *et al.*, 2024). Taiwan, which successfully contained transmission through geographical isolation and rigorous contact tracing for over a year, experienced its first major outbreak with Omicron in early 2022 despite maintaining strict entry requirements (Chen & Huang, 2024). These examples echo Malaysia experience, where the South China Sea barrier effectively segregated East and West Malaysia during the pre-VOC period but failed to contain Delta and Omicron due to their substantially higher reproduction numbers ($R_0 \sim 6-8$ for Delta, ~ 9.5 for Omicron) compared to ancestral lineages ($R_0 \sim 2.5$), overwhelming public health interventions even in geographically advantaged settings (Liu & Rocklöv, 2021; Nishiura *et al.*, 2021).

Implications for genomic sequencing in low- and middle-income countries (LMIC) setting

For LMICs, where genomic sequencing capacity and resources are limited, our findings emphasise the value of geographically informed genomic surveillance strategies. Early genomic surveillance coupled with rapid data sharing could have enabled earlier identification of region-specific circulation such as the confinement of B.1.466.2 to East Malaysia and the dominance of Beta in West Malaysia. Similar region-specific epidemiological heterogeneity has been also observed in other infectious diseases within Malaysia, where Japanese encephalitis demonstrated long-term endemicity in Sarawak (Montini Maluda *et al.*, 2020; Wong *et al.*, 2008), and Zika virus exposure was reported primarily among forest-fringe communities (Khoo *et al.*, 2022). These examples demonstrated that spatial and ecological factors continue to shape infectious disease dynamics in Malaysia, even beyond COVID-19.

In conclusion, our findings demonstrated that geographical or movement barriers can delay variant spread, but once a highly transmissible or immune-evasive variant arrives, and especially if controls are eased, these barrier effect become less effective. We propose that region-stratified sequencing is particularly important, as aggregated national analyses may mask localised transmission patterns and variant distribution. Sequencing efforts should prioritise border regions, high-transit areas, and regions with distinct epidemiological profiles in order to maximise the efficiency of variant detection and containment.

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Conflict of Interest Statement

The author declares that they have no conflict of interests.

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