

Distribution of SARS-CoV-2 Variants in West Java Based on Genomic Surveillance Data, 2021-2022

Cut Nur Cinthia Alamanda¹, Ida Parwati², Gusti Ayu Prani Pradani¹, Azzania Fibriani³

¹ West Java Health Laboratory, Bandung, West Java, Indonesia. E-mail: cut_alamanda@yahoo.co.id

² Department of Clinical Pathology and Laboratory Medicine, Faculty of Medicine, Padjadjaran University/Dr. Hasan Sadikin General Hospital, Bandung, Indonesia

³ Bandung Institute of Technology, Bandung, West Java, Indonesia

ABSTRACT

Coronavirus Disease 19 (COVID-19), the disease caused by SARS-CoV-2, was declared a pandemic in early 2020. With the emergence of different strains of SARS-CoV-2 mutations, efforts to reduce infection rates and help vulnerable populations remain in question. Genomic surveillance has been carried out on COVID-19 cases to detect new variants and monitor trends in circulating variants. Genomic surveillance is important because it can detect virus characteristics, estimate the prevalence of specific variants in the community, assess the extent to which medication can combat the variants, and analyze virus transmission in outbreaks. The purpose of this study was to investigate the prevalence of SARS-CoV-2 genomic variants in West Java and to inform policymakers in developing strategies to reduce the transmission rate of the SARS-CoV-2 virus. According to the inclusion criteria, variant sequence data were acquired from Global Initiative on Sharing All Influenza Data (GISAID) for the period January 1st, 2021–December 31st, 2022 and evaluated cross-sectional descriptively. This data were obtained from West Java. The majority of the samples came from Bandung Regency, where the Delta (AY), BA1 and BA5 variations predominated. The dynamic of the SARS-CoV-2 cases was influenced by government policies such as imposition of the restriction on community activities and public holiday. Because SARS-CoV-2 is subject to mutations, the various varieties must still be monitored to determine the influence on society. In the future, surveillance for any microorganisms with the potential to cause epidemics is urgently needed in order to mitigate the spread of the disease.

Keywords: SARS-CoV-2, mutation, variant, West Java

INTRODUCTION

The World Health Organization (WHO) received information in December 2019 regarding a pneumonia outbreak in Wuhan, Hubei Province, China, the cause of which is unknown. On January, 30th 2020, WHO declared the disease's causative agent as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) and designated it as a Public Health Emergency of International Concern (PHEIC), while on February 11th, 2020, WHO officially named the disease caused by SARS-CoV-2 as Coronavirus Disease-19 (COVID-19), after which the SARS CoV-2 outbreak was declared a pandemic by WHO on March 11th, 2020, and data on April 14th, 2020 reported the number of 1,844,653 confirmed cases and 117,021 death cases.¹⁻³

SARS-CoV-2 is a member of the Coronavirus genus and the Coronaviridae family. Coronavirus is a spherical, single-stranded RNA virus with a genome size of 26 - 32 kb. It is a member of the Coronaviridae subfamily, which includes four genera: Alphacoronavirus (CoV), Betacoronavirus (CoV),

Gammacoronavirus (CoV), and Deltacoronavirus (CoV). Human Coronaviruses such as SARS, MERS, and SARS-CoV-2 are included in the CoV. SARS-CoV-2 is composed of four structural proteins: membrane proteins (M), spike proteins (S), envelope proteins (E), and nucleocapsid proteins (N), as well as sixteen non-structural proteins (nsp 1-16).^{1,3-5}

Despite the fact that the epidemic has been ongoing for about two years, many cases of illness and death have been reported. As of January 31, 2023, WHO recorded 753,479,439 confirmed COVID-19 cases worldwide, with 6,812,798 deaths.⁶ Data in Indonesia as of January 31st, 2023, a total of 6,730,016 confirmed cases and 160,814 death cases, with West Java accounting for 1,113,278 confirmed cases and 13,767 death cases.^{7,8}

Efforts are currently underway to minimize transmission rates, preserve vulnerable populations, and prevent further socioeconomic damage. The development of diagnostic instruments, treatments, and vaccinations to combat the pandemic continues, but there are still challenges caused by alterations in the SARS-CoV-2 virus. These alterations, known as

mutations, occur as the virus replicates. Variants are viruses that have one or more novel mutations.⁹

COVID-19 cases were subjected to genomic surveillance to detect new variants and monitor trends in circulating variants. Genomic surveillance is significant because it can detect virus characteristics, estimate the prevalence of specific variants in the community, assess the extent to which medication can combat the variants, and analyze virus transmission in outbreaks.^{9,10}

Indonesia is the world's largest archipelagic country and the fourth most populous country. Indonesia has been one of the ASEAN countries with very high COVID-19 incidence since mid-October 2020, and as of June 6th, 2021, only 5.51% of the population had received full vaccination, therefore it was formerly regarded as the new pandemic center after India, under this case-based surveillance. The use of genomics at the global, national, and regional levels is essential for developing an effective intervention approach. Since 2020, several teams and institutions (including the Yogyakarta COVID-19 Study Group in Central Java and the West Java Health Laboratory) have performed Whole Genome Sequencing (WGS) of strains circulating in Indonesian territory and have shared genetic data and metadata via the Global Initiative platform. SARS-CoV-2 lineage B.1466.2, one of the variants defined by WHO in Variant Under Monitoring (VUM), was first reported in Indonesia in November 2020. This variant was projected to arrive in Java in mid-June 2020 and evolve into a new clade by the end of August 2021.^{11,12}

Based on this context, the purpose of this study was to investigate the distribution of the SARS-CoV-2 genomic variation in West Java. This study is expected to provide information to the government or policymakers about the distribution of the SARS-CoV-2 genome variant, particularly in West Java, to be used in mapping and studying the flow of COVID-19 transmission so that they can design strategies to reduce the SARS-CoV-2 virus's transmission rate.

METHODS

Data collection of COVID-19 sequences retrieved from the Global Initiative on Sharing All Influenza Data (GISAID) database (<https://gisaid.org/>) (accessed on February 1st, 2023) with the inclusion criteria: keywords: Asia/Indonesia/West Java; Asia/Indonesia/Jawa Barat; Asia/Indonesia/JaBar; using the following time frame: from January 1st, 2021 to December 31st, 2022. The inclusion criteria were complete genome size (> 29,000 bp) and low coverage (NS> 5%), while the exclusion criteria were high coverage (1% NS; 0.05 unique amino

acid mutation).¹³ The study used descriptive and cross-sectional design. The approach examined metadata such as collection date, location, gender, age, and lineage (variant).

Demographic data were evaluated by age and gender categories, sample distribution in West Java, and sample proportions for all West Java regencies and cities. Data on the distribution of variants in West Java were evaluated based on shifts in variance over time as well as patterns of various variants circulating in each district and city in West Java from January 1st, 2021 to December 31st, 2022. SARS-CoV-2 was classified using Pango nomenclature or the Phylogenetic Assignment of Named Global Outbreak Lineages (PANGOLIN).

The Ethics Committee of Hasan Sadikin Hospital, Bandung approved this study protocol with letter no. LB.02.01/X.6.5/438/2023.

RESULTS AND DISCUSSIONS

In this study, 4612 West Java WGS Sequence Data that met the inclusion criteria and keywords were acquired. Six (6) samples were acquired from Asia/Indonesia/JaBar, 32 samples from Asia/Indonesia/Jawa Barat, and 4,577 samples from Asia/Indonesia/West Java.

Not all of the COVID-19 patient sequences gathered from January 1st, 2021 to December 31st, 2022 had complete age and gender data, hence not all of them could be shown. According to the statistics, the number of female patients was 53.8% and male patients 44.4% while 1.8% had no information, as indicated in Table 1.

Figure 1 depicts the results of an analysis of the number of WGS samples versus the number of COVID-19 cases in West Java by age and gender

Table 1. Subject characteristics based on age and gender

Characteristics	Amount	Percentage (%)
Gender		
Female	2484	53.8
Male	2048	44.4
No data	80	1.8
Age (years)		
< 5	133	3.5
6 – 19	410	10.9
20–29	831	22.0
30 – 39	727	19.3
40 – 49	616	16.3
50 – 59	538	14.3
60 – 69	320	8.5
70–79	134	3.5
> 80	66	1.7

group. The number of WGS samples in each age category is comparable to the number of COVID-19 cases. Females (20-29 years old) and males (30-39 years old) made up the majority of the population. This demonstrates that the WGS examination in West Java accurately represented the sample population infected with COVID-19.

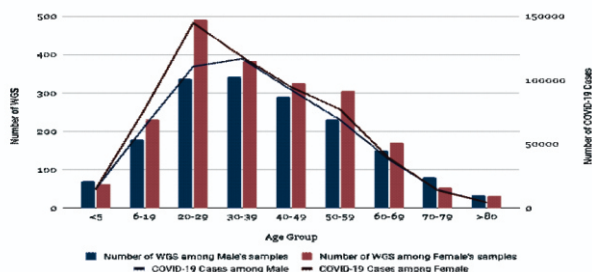


Figure 1. Comparison of the number of WGS COVID-19 samples with the number of COVID-19 cases in West Java for the 2021-2022 period

This statement can also be supported by examining the number of sequenced samples and COVID-19 instances over time. The graph in Figure 1 depicts an increase in COVID-19 cases, which is always followed by an increase in WGS implementation, and vice versa. The suitability of this data was achieved because of a Ministry of Health policy for "Tracking and monitoring (surveillance) of the SARS-COV-2 virus genome" in January 2021, which was then issued as a target for carrying out COVID-19 surveillance for each region for a specific period in the form of a ministerial instruction in the country.

In Figure 2, information can also be obtained about the influence of the Imposition of the Restriction on Community Activities (IRCA)

implementation policy on the number of COVID-19 cases. There was a decrease in cases during the Large-Scale Social Restriction (LSSR) stage 2 extension, which began in January-February 2021 and lasted with IRCA until May 2021. After the Eid al-Fitr vacation in May 2021, there was an upsurge in COVID-19 cases, which peaked in July 2021, when the government adopted IRCA level 4.

COVID-19 cases decreased from August to December 2021, but then surged during the Christmas 2021 and New Year 2022 holidays, therefore the government prolonged IRCA. According to Haning and Mita's research, the trend of growing COVID-19 instances rose over Christmas and New Year 2021, reaching a peak on January 30, 2021 (14,518 confirmed COVID-19). Despite a decrease in COVID-19 instances in February 2021, it increased dramatically following the Eid Al-Fitr 1442H holiday in June 2021 and peaked in July 2021.¹⁴

Figure 3 depicts the distribution of cities/regencies as sources of isolation for the COVID-19 sample in West Java, with Bandung

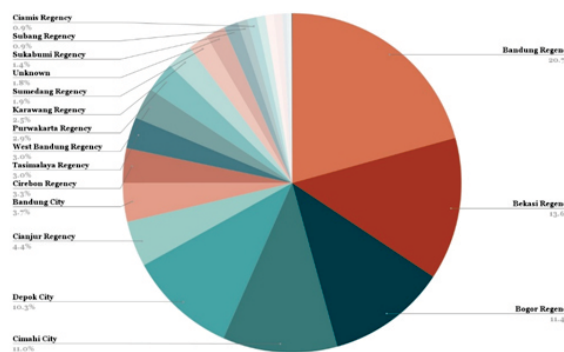


Figure 3. The proportion of samples of SARS-CoV-2 in West Java districts/cities

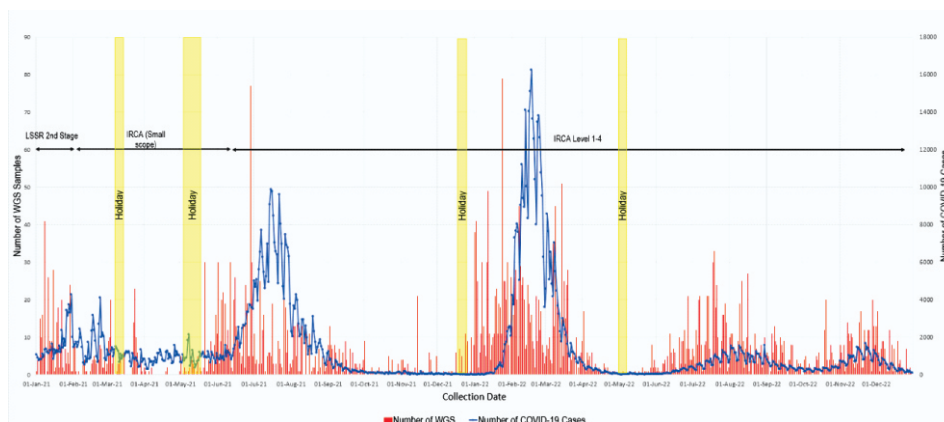


Figure 2. Relation to the number of COVID-19 cases, the number of cases at WGS in the January 2021–December 2022 period

Regency (27.4%), Bekasi Regency/city (14.1%), and Bogor Regency (11.4%) dominating the sample sources.

This dominance was driven by the great number of COVID-19 cases in the area because all three were in an agglomeration area, which was a single area made up of numerous city or district centers that were connected either by land or by water. Internal and exterior population migration were also linked to an increase in COVID-19 incidence.¹⁵

As shown in Figure 4, the distribution of the Delta variant (AY) (22.6%), the BA1 variant (21.4%), and the BA5 variant (20.5%) was dominated by the results of the WGS in the West Java sample population from January 1, 2021-December 31, 2022. These three variants were included in the WHO Variance of Concern (VOC).¹⁶

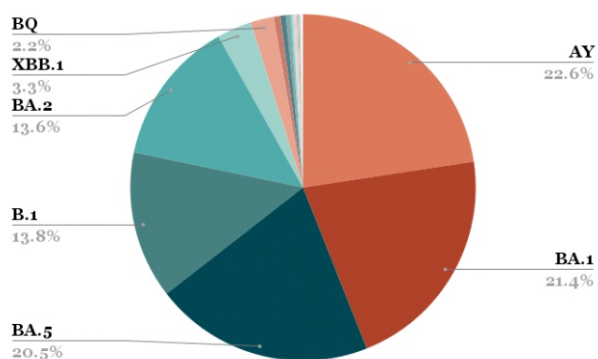


Figure 4. Proportion of variants

The proportion of the diversity of WGS results in each region in West Java is shown in Figure 5. The size of the pie chart in Figure 5 is precisely equal to the number of samples sequenced in that area.

Bandung Regency had the most variant diversity, with 18 variants (dominated by AY, BA1, and BA5 variants), Depok City had 15 variants (BA1, BA5, and AY), Bandung City had 13 variants (BA5, BQ, and XBB), Bogor Regency had 12 variants (B1, BA5 and AY), and Bekasi Regency had 12 variants (B1, BA1 and BA5). Various variants were only found in specific regions, such as the C variant, which was only found in Bandung district, CR, which was only found in Bandung Regency, Cimahi City, Tasikmalaya Regency, and Bandung City, CH, which was only found in Bogor Regency and Depok City, and DQ, which was only found in Bandung City.

The greater diversity of variations discovered in Bandung Regency compared to West Bandung Regency and Bandung City is most likely owing to the greater number of WGS samples from Bandung Regency compared to West Bandung Regency and Bandung City. Changes in the infection of the SARS-CoV-2 variant can be traced in the results of the analysis in Figure 6.

The B1 variant dominated the West Java region from January to early June 2021, then the Delta (AY) variant, which was originally detected on January 6, 2021, dominated the samples in June and reached its

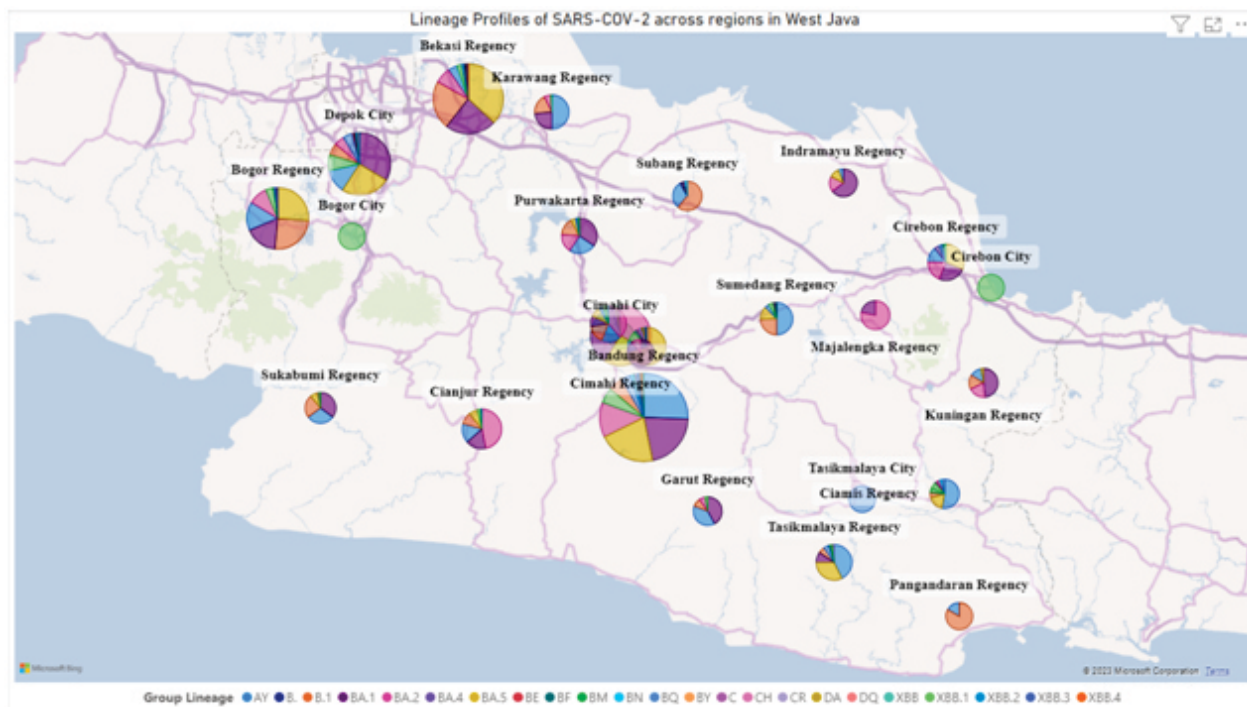


Figure 5. Map of the diversity of variants circulating in regencies and cities in West Java for the period January 2021-December 2022

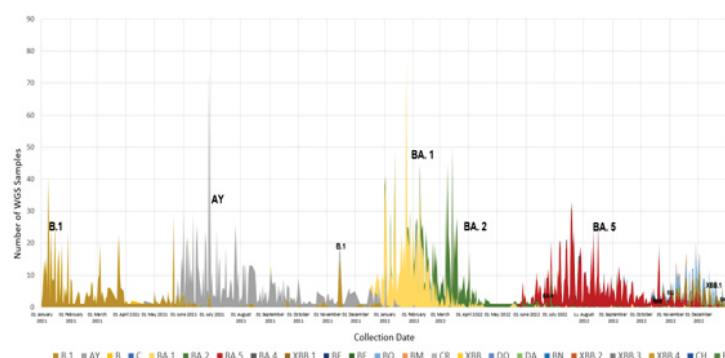


Figure 6. Variant SARS-CoV-2 time series from January 2021 to December 31, 2022

peak in July 2021. Delta will have received over 90% of all virus sequences submitted to GISAID by October 2021.⁶

According to a study conducted by Chu *et al.*, during the SARS-CoV-2 pandemic, countries in Southeast Asia had three variants, namely Alpha (B1.1.1, Beta (B1.351), and Delta (B1.617.2), and between March and June 2021, Cambodia and Thailand recorded Alpha and Delta variants, while Beta variants were also found in Indonesia and Malaysia. Delta is a variety that requires attention due to its ability to infect beyond the previous alpha strain and has been detected in 135 countries, including Southeast Asia's Vietnam, Indonesia, Malaysia, and Thailand.¹⁷

In the late 2021 timeline, the AY variety predominated in the West Java region, and the BA.1 variant began to be found. The dominance of the variation shifted from AY to BA.1 in January 2022. On January 24, 2022, the most BA.1 samples were collected. In February, the BA variant 1 was still detected in considerable quantities and was identified as the BA variant for the first time. The BA.2 variant's supremacy began in March and continued until May 2023, albeit the numbers gradually fell. Not only were the BA.1 and BA.2 variations identified in mid-2023, around June 2023, but also the entry of BA.4, BA.5, XBB, and other BA derivative variants (BF, BE, CX, and Y).

This data was consistent with what researchers have found in South Africa, where they discovered a variety of variants ranging from the D614G variant, which was a derivative of Wuhan-Hu-1 in the first wave of infection (June/August 2020), to the Beta variant (November 2020-February 2021), which then evolved into the Delta variant (May-September 2021). Following the decline in Delta variant cases in mid-November 2021, a new Omicron variant with the B.1.1.529 lineage was reported. BA.1 (main clade), BA.2, and BA.3(18) are the three sub-lineages of the Omicron sequence.¹⁸

BA.5 variant dominance was recorded from June 2022 to the end of 2022. The BA.5 variant was recognized until the end of 2022, however, the XBB and BQ versions were discovered in November 2022. In October 2022, WHO stated that the XBB variant, a sub-lineage variant of BA.2.10.1 and BA.2.75 was found in 35 countries with a global prevalence of 1.3%, while the BQ variant, a sub-lineage variant of BA.5, was detected in 65 countries with a global prevalence of 6%.¹⁹

SARS-CoV-2, like most RNA viruses, is prone to genome alterations throughout each replication cycle. This is not surprising given the prevalence of mutations in SARS-CoV-2. The D614G mutation was discovered in mid-2020, and it was detected in more than 95% of sequencing data. This mutation transforms aspartic acid to glycine at position 614 of the Spike protein (D614G).²⁰⁻²²

Other mutations seen in the Beta and Gamma variants include E484K, which is a substitution of the amino acid glutamic acid(E) with Lysine(K) at the RBD484 position, and the K417 N/T mutation, which is found in the Beta, Gamma, and Omicron versions. Delta, BA.4, and BA.5 versions of L452R.²³

CONCLUSIONS AND SUGGESTIONS

The majority of the samples came from Bandung Regency, which has the most regencies and cities in West Java. The dynamic of the SARS-CoV-2 cases was influenced by government policies such as the imposition of the restriction on community activities and public holidays Bandung Regency has the most diversity of variations, with the Delta (AY), BA.1, and BA.5 varieties dominating. Because SARS-CoV-2 is subject to mutations, the various varieties must still be monitored to determine their influence on society.

In the future, surveillance for any microorganisms with the potential to cause an epidemic is urgently needed to mitigate the spread of the disease.

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