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ORIGINAL ARTICLE

OVERVIEW OF VACCINATION STATUS AND COMORBIDITIES IN DEATHS DUE TO COVID-19 OMICRON VARIANT IN RIAU PROVINCE, 2022

Gambaran Status Vaksinasi dan Komorbiditas pada Pasien Meninggal Akibat COVID-19 Varian Omicron di Provinsi Riau, 2022

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ABSTRACT

Background: The Corona Virus Disease 2019 (COVID-19) pandemic is causing problems in public health. One of the prevention efforts is vaccination. Omicron, the new variant of COVID-19, is a variant that is spreading rapidly in Indonesia, including in Riau Province. **Purpose:** This study aims to describe the determinants of vaccination status in deaths of Omicron variant COVID-19 patients in Riau Province from February to April 2022. **Methods:** Cross-sectional research was conducted using secondary data. A total of 158 patients who died with confirmed COVID-19 and the Omicron variant via S-Gene Target Failure (SGTF) and sequencing test, and were treated at a referral hospital in Riau Province within two months (8 February – 4 April 2022) were included in the study. The distribution of patient deaths was analyzed univariately and bivariately. **Results:** Most of the death cases were unvaccinated (67.09%). As many as 48.73% of the 158 deaths were elderly ≥61 years, and the majority (70.13%) of cases were unvaccinated. It was found that 64.56% of the 158 patient deaths occurred in mainland Riau, and the majority (67.65%) were unvaccinated. Diabetes mellitus (35.86%) and cardiovascular disease (28.97%) were the highest comorbidities. **Conclusion:** In preventing deaths due to COVID-19, it is necessary to accelerate and increase vaccination coverage, especially for children and the elderly in land and coastal areas. Vaccination can optimize

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protection against COVID-19. Apart from that, efforts are needed to prevent the severity of comorbidities.

ABSTRAK

Latar Belakang: *Pandemi Corona Virus Disease 2019 (COVID-19) menyebabkan adanya masalah dalam kesehatan masyarakat. Salah satu upaya pencegahan yanitu dengan dilakukan vaksinasi. Omicron, varian baru COVID-19, merupakan jenis varian yang cepat menyebar di Indonesia, termasuk di Provinsi Riau.* ***Tujuan:*** *Tujuan penelitian ini adalah mendeskripsikan determinan status vaksinasi pada kematian pasien COVID-19 varian Omicron di Provinsi Riau pada bulan Februari hingga April 2022.* ***Metode:*** *Penelitian cross-sectional dilakukan menggunakan data sekunder. Sebanyak 158 pasien yang meninggal dengan terkonfirmasi COVID-19 dan varian Omicron melalui S-Gene Target Failure (SGTF) dan atau sequencing test, serta dirawat di RS rujukan Provinsi Riau dalam dua bulan (8 Februari – 4 April 2022) dilibatkan dalam penelitian. Distribusi kematian pasien dianalisis secara univariat dan bivariat.* ***Hasil:*** *Sebagian besar kasus kematian terjadi pada pasien yang tidak vaksinasi (67,09%). Sebanyak 48,73% dari 158 kematian terjadi pada lansia ≥61 tahun, dan sebagian besarnya (70,13%) kasus tidak mendapatkan vaksinasi. Diketahui, 64,56% dari 158 kematian pasien terjadi di daratan Riau, dan sebagian besarnya (67,65%) tidak menerima vaksinasi. Diabetes melitus (35,86%) dan penyakit kardiovaskular (28,97%) merupakan penyakit penyerta tertinggi.* ***Simpulan:*** *Dalam mencegah kematian akibat COVID-19, percepatan dan peningkatan cakupan vaksinasi perlu dilakukan khususnya pada anak-anak dan lansia di wilayah daratan dan pesisir. Vaksinasi dapat mengoptimalkan perlindungan terhadap COVID-19. Selain itu, perlu upaya pencegahan keparahan akibat penyakit penyerta.*

INTRODUCTION

The Omicron variant of Corona Virus Disease 2019 (COVID-19) has caused global concern. The variant has rapidly spread across the globe of almost 57 countries and infected approximately 2,152 people since it was first detected in South Africa on 24 November, 2021 (1). The Southeast Asian countries are without exception. Cases were identified in some countries such as Singapore (885), Thailand (739), Cambodia (34), Philippines (2), and Malaysia (62) as of December 30, 2021 (2). The Omicron variant is three to six times more contagious than Delta, while the mortality rate of the Omicron patients is lower than the previous variants, e.g., Delta (3). In Indonesia, the Omicron variant was first detected in DKI Jakarta Province on December 15, 2021 (4). As of February 21, 2022, most (70.59% of 34) provinces in Indonesia have observed the variant with 6,257 cases of pain, one of which is in Riau Province (5).

Riau is situated in the central part of the east coast of the island of Sumatra, Indonesia, with the coastal area bordering the Strait of Malacca. In Riau Province, the Omicron variant was first discovered on 31st January, 2022. A previous study in Riau Province 2020 – 2021 showed that the proportion of deaths pre-Omicron was 3.25%, and more than half (51.59%) of death cases were the male sex (6). Nonetheless, the WHO reported that the Omicron variant could potentially increase the mortality rate similar to other COVID-19 variants (2). The rollout of vaccinations in Riau started with the inactivated vaccine on 13th January, 2021 (2,7). The coverage of the first vaccination dose on 9th February, 2022, was 89%, the second dose was 59%, and the third dose was 3% (8).

The mortality in the Omicron patients is influenced by various factors, one of which is the characteristics of the patients. A study in Prof. Dr. R. D. Kandou General Hospital, Manado, Indonesia found that most (73% of 79) deaths of COVID-19

patients during the dominant period of the Omicron wave were unvaccinated (9). The mortality risk factors of patients with the Omicron variant may be different. In South Africa, the majority (90.61% of 1,225) of deaths of patients by age during the Omicron wave was more than 60 years old (10). However, a study in England found that the majority (84.38% of 160) who died with the Omicron variant were aged above 70 years old (11).

A cohort study in the United Kingdom revealed that the risk of death from the Omicron variant was 67% lower than that of Delta, and the reduction in the risk of death in the Omicron group was more significant in the male group than in the female group. One of the supporting factors was that males have higher ACE2 receptor levels (Angiotensin Converting Enzyme 2) than females, which play a role in the occurrence of lung disorders in patients with COVID-19 (12).

A low Ct value indicates an increase in the concentration of genetic material usually correlated with a high risk of infection (13). A previous study in Italy reported that the severity of COVID-19 was significantly worse at the Ct value ≤20 compared to the Ct value >20 to ≤28 or Ct value >28 (14). The result of a case-control study in unvaccinated individuals in Qatar found that the protection of previous infections against inpatients or deaths caused by Omicron reinfection remained strong (15). A previous study also showed that Omicron has the ability to reinfect a patient even though he has received a second dose of COVID-19 vaccination (4).

Comorbidities are a risk factor influencing disease severity due to the Omicron variant of COVID-19. A previous study in Southern Sweden showed that an increased risk of more severe COVID-19 was associated with vaccinated cases of over 65 years old in male patients with one comorbidity or women with two comorbidities (16). Although the risk of death from the Omicron infection was lower than the Delta, the average Ct value was not different, which was 18.10. In coastal countries in Southwest Europe, such as Portugal, the majority (88.10% of 6,581) of cases of the Omicron had been vaccinated against COVID-19, and no deaths were found (17).

The COVID-19 patients' average length of stay in the hospital was four days (2 - 9 days) (10). A similar study in Northeastern Brazil discovered that the average length of hospitalization of patients dying from COVID-19 during the Omicron wave was four days, with most deaths occurring in the elderly and individuals who were not vaccinated or only received the first dose of vaccination (18). A systematic review study revealed that there was a difference between the length of treatment and discharge status, namely in patients who were discharged with a life status that had a longer length of stay (LoS) than patients who died (19).

Based on several studies above, mortality among the unvaccinated was significantly more than that of the vaccinated. Comorbidities are also one of many factors that influence the deaths due to the Omicron variant in COVID-19 patients. There have not been many similar studies in Indonesia, especially in Riau Province. In addition, Riau Province experienced a high increase in death cases due to the Omicron variant of COVID-19. This study aims to describe the overview based on vaccination status and comorbidities among Omicron variant COVID-19 patient deaths in Riau Province, Indonesia, from February to April 2022.

METHODS

This cross-sectional study used secondary data from the electronic National All Record (e-NAR), Primary Care vaccine (e-PCare), and routine reports of COVID-19 surveillance in Riau province from 8th February to 4th April 2022. The total sampling technique was employed. The study's inclusion criteria covered all patients who died with COVID-19, confirmed by laboratory tests of Polymerase Chain Reaction (PCR), and diagnosed with the Omicron variant through positive S-Gene Target Failure (SGTF) tests and/or Whole Genome Sequencing (WGS). The patients included in the study were those treated at the referral hospital of Riau province. The SGTF test was utilized due to its high sensitivity of 98.90% and a specificity of 99.90% in detecting the Omicron variant (14). On the other hand, the study's exclusion criteria encompassed patients who died without undergoing variant examinations at the referral hospital, those diagnosed with a different variant at the referral hospital, and individuals who passed away outside the referral hospital. This study was approved by the Health Research Ethics Committee of STIKES Payung Negeri Pekanbaru (Approval Number: No.0021/STIKES PN/KEPK/V/2022).

The conceptual framework of this study aimed to assess the factors of vaccination status contributing to mortality among patients with the Omicron variant. The factors considered in the analysis included age, sex, Ct value (cycle threshold), previous infection, number of comorbidities, location of residence, and length of

stay in the hospital. Additionally, the study also delved into the timing of death and type of comorbidities observed among patients with Omicron variant COVID-19.

The term "vaccination status" was defined as the COVID-19 vaccine status of deceased patients with SGTF test and/or WGS results confirmed Omicron variant, as reported in e-NAR. This categorization encompassed individuals into two groups: those who were unvaccinated and those vaccinated against COVID-19. The term "age" was defined as the age in years at the time of initial diagnosis, consisting of ≤20 years, 21–40 years, 41–60 years, and ≥61 years. The categories of sex, was male and female. The cycle threshold value (Ct value), defined as a number from PCR results when diagnosed with COVID-19, consists of ≤20, more than 20 to ≤28, and more than 28 (20). Previous infection was reinfection with two results of PCR tests confirmed positive of COVID-19 in the same individual in more than 90 days (21). The categories of number comorbidity, are no comorbidities, one comorbidity, and two and more comorbidities.

The location of residence was defined as the patient's permanent domicile, considering whether the regency capital is affected by tides or not. The categories encompass coastal, mainland, and areas outside of Riau. The capital district with coastal areas was Dumai, Rokan Hilir, Bengkalis, Siak, and Meranti Islands. The capital district with mainland areas was Pekanbaru, Kampar, Kuantan Singingi, Indragiri Hulu, Indragiri Hilir, Pelalawan, and Rokan Hulu. The length of stay was defined as the duration of a patient's admission until death in the Riau Province hospital, categorized into three groups: 1–7 days, 8–14 days, and ≥15 days. The time of death was defined as the count of COVID-19 fatalities in Riau Province hospitals within one week, as per the epidemiological surveillance calendar through routine reports of COVID-19 surveillance. The type of comorbidity is defined as comorbidities diagnosed by the doctor when patients are admitted at a referral hospital and reported by the routine report of COVID-19 surveillance.

Figure 1 shows the flow chart of subject selection for mortality patients with the Omicron variant COVID-19. The total source population was 288 cases in the COVID-19 report from the Riau Provincial Health Office, 158 cases met the inclusion and exclusion criteria: 136 cases with positive SGTF tests and 22 cases with WGS-confirmed Omicron variant.

STATA version 15.1 was used for data analysis. Descriptive statistics were applied for categorical and continuous variables. Univariate analysis was done by frequency and percentage distributions. Bivariate analysis used the Chi-square test at a significance limit (α) of 5% and prevalence ratio (PR) with 95% confidence interval.

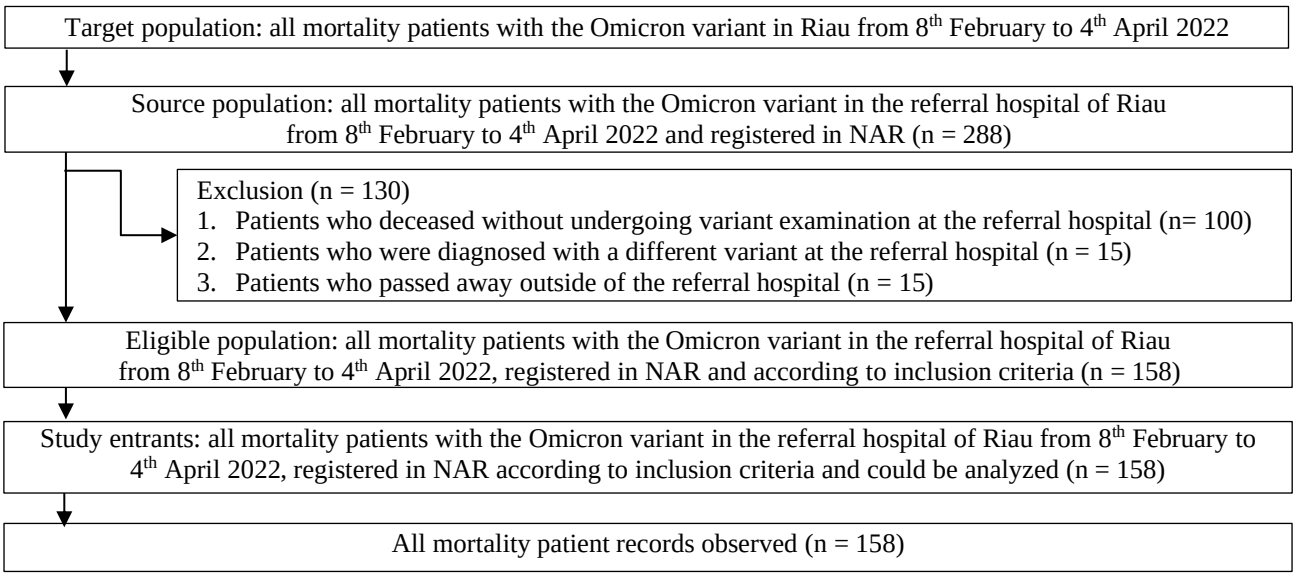

Figure 1. Flow Chart of Subjects Selection for Mortality Patients with Omicron Variant COVID-19

RESULTS

Table 1 shows the comparison of mortality of patients with Omicron variant with and without vaccination for COVID-19. As many as 106 (67.09%) of cases were unvaccinated for COVID-19. As many as 6.96% of the 158 patient deaths were aged ≤20 years, and the majority (81.82%) of cases were unvaccinated. As many as 48.73% of the 158 mortality patients were elderly ≥61 years, and the majority (70.13%) of cases were unvaccinated. Of the 158 patient deaths, 54.43% were male, and the majority (63.95%) of cases were unvaccinated. Based on the Ct value, 36.08% of the 158 patient deaths with a Ct value of ≤20 and more (61.40%) cases were unvaccinated; 46.20% of the 158 patient deaths with a Ct value of more than 20 to 28, and most (72.60%) were unvaccinated. Only 6.33% of the 158 deaths were of COVID-19 patients with reinfection, and the majority (70%) were unvaccinated. As many as 49.37% of the 158 deaths of COVID-19 patients were with ≥2 comorbidities and more (66.67%) cases were unvaccinated.

Table 1
Comparison Of Patient Mortality from Omicron Variant with And Without COVID-19 Vaccination

Category	Unvaccinated		Vaccinated		PR	95% CI	p-value
	n= 106	%	n= 52	%			
Age group, years							
≤20	9	81.82	2	18.18	2.25	0.98 – 5.15	0.03
21 – 40	4	36.36	7	63.64	1.00		
41 – 60	39	66.10	20	33.90	1.81	0.81 - 4.05	0.06
≥ 61	54	70.13	23	29.87	1.92	0.87 – 4.27	0.03
Sex							
Male	55	63.95	31	36.05	0.87	0.65 - 1.16	0.36
Female	51	70.83	21	29.17	1.00		
Ct value							
≤20	35	61.40	22	38.60	0.95	0.67 – 1.34	0.79
20 < Ct ≤28	53	72.60	20	27.40	1.12	0.82 – 1.53	0.41
>28	18	64.29	10	35.71	1.00		
Previous infection							
Reinfection	7	70	3	30	1.14	0.30 – 4.24	0.84
First time	99	66.89	49	33.11	1.00		
Number of Comorbidity							
≥2 comorbidity	52	66.67	26	33.33	0.86	0.61 – 1.21	0.46
1 comorbidity	44	65.67	23	34.33	0.85	0.60 – 1.20	0.42
No comorbidity	10	76.92	3	23.08	1.00		
Location of residence							
Coastal	35	74.47	12	25.53	3.35	0.97 – 11.50	0.01
Mainland	69	67.65	33	32.35	3.04	0.89 – 10.40	0.01
Outside of Riau	2	22.22	7	77.78	1.00		
Length of stay, days							
1 – 7 days	87	66.92	43	33.08	1.00		
8 – 14 days	14	63.64	8	36.36	0.82	0.85 – 1.13	0.82
≥15 days	5	83.33	1	16.67	1.24	0.85 – 1.81	0.40

It was found that 64.56% of the 158 patient deaths occurred in mainland Riau, and the majority (67.65%) were unvaccinated. Only 5.70%of patients reside outside Riau and the majority (77.78%) were vaccinated against COVID-19. The majority (82.28%) of deaths were of patients with a length of hospitalization of 1-7 days and the majority (66.92%) were unvaccinated. The result of the Chi-square test found that the death of Omicron variant COVID-19 patients in the age group of ≤20 years, aged ≥61 years, and location residences in coastal and mainland against unvaccinated had a significant relationship (Table 1).

The first of deaths of patients with the Omicron variant were identified in the 6th week (February 8 - 12, 2022), totaling five patients. Death cases

continued to increase until the peak wave in the 10th week (March 6 - 12, 2022) with as many as 40 patients. Furthermore, the death of Omicron patients decreased in the 14th week (Figure 2).

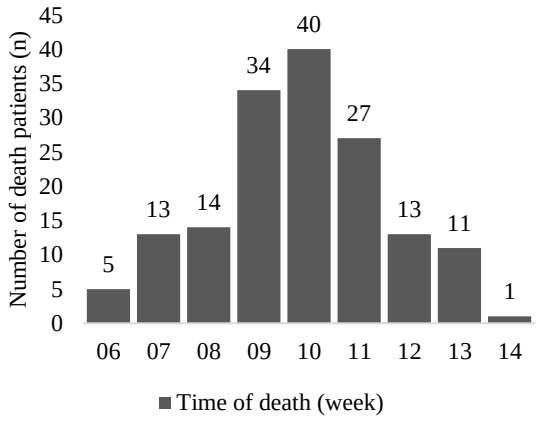

Figure 2. Number of Patient Deaths with Omicron Variant COVID-19 Per Week

Table 2 shows the distribution of frequency of comorbidity in mortality of 145 patients with the Omicron variant COVID-19 in Riau province, Indonesia. Diabetes mellitus was the most comorbidity in mortality patients with the COVID-19 Omicron variant (35.86%). We also found cardiovascular disease (28.97%), chronic kidney failure disease (25.52%), and hypertension (23.45%) among mortality patients with the Omicron variant. Other comorbidities among mortality patients with the Omicron variant were acute renal failure, sepsis, cancer, tuberculosis, pneumonia, liver disease, COPD, obesity, pulmonary edema, diaphragmatic hernia, toxoplasmosis, HIV, immune thrombocytopenic purpura, and eclampsia.

DISCUSSION

The resurgence of COVID-19 in Riau Province, Indonesia, was dominated by the Omicron variant evolved at a time when 59% were fully vaccinated, and an additional 3% had received at least three doses of COVID-19 vaccine as part of the national vaccine rollout program (8). Nevertheless, our survey showed more deaths of the Omicron variant of COVID-19 patients without vaccination than with vaccinations. Previous studies of the Omicron variant during the COVID-19 pandemic in Brazil, South Africa, and Germany also found mortality in unvaccinated populations averaged three to four times higher than in a fully vaccinated population (22).

Table 2
Distribution of Frequency Comorbidity in Mortality Patients with Omicron Variant COVID-19

Type of Comorbidities	Frequency of Death with Comorbidities	
	Total (n=145)	Rate (%)
Diabetes Mellitus	52	35.86
Cardiovascular diseases	42	28.97
Chronic kidney diseases	37	25.52
Hypertension	34	23.45
Acute kidney failure	22	15.17
Sepsis	15	10.34
Cancer	11	7.59
Tuberculosis	10	6.90
Pneumonia	4	2.76
Liver disease	4	2.76
Chronic Obstructive Pulmonary Disease (COPD)	2	1.38
Obesity	2	1.38
Others (Pulmonary edema, Diaphragmatic hernia, Toxoplasmosis, HIV, ITP, Eclampsia)	6	4.14

Deaths from the Omicron variant of COVID-19 patients occur in all age groups. We found that the deaths of Omicron variant COVID-19 patients with unvaccinated in the age group of ≤20 years had a significant association. The findings suggested that the mortality of patients with the Omicron variant aged ≤20 years infected was two times greater in unvaccinated compared to vaccinated cases against COVID-19 (PR = 2.25, 95% CI 0.98 - 5.15). In addition, the older you get, the less the reserve of homeostatic function, so a person's body is easily infected with COVID-19. This study shows that the mortality of elderly patients with the Omicron variant ≥61 years of age infected was two times greater in unvaccinated compared to vaccinated cases against COVID-19 (PR = 1.92, 95% CI 0.87 – 4.27).

Most of the patients who died were domiciled on the mainland, and most of them were unvaccinated against COVID-19. The same study into patient deaths in hospitals in northeastern Brazil found that, during the Omicron wave (January to February 2022), most of the deaths occurred in the elderly, and with 42.31% of the 26 deaths of patients unvaccinated or the first dose,

34.62% with the second dose of vaccination and 23.08% with the third dose (booster) (18,19). We found that the mortality of patients infected with the Omicron variant in coastal areas was three times greater in unvaccinated than in vaccinated cases against COVID-19 (PR = 3.35, 95% CI 0.97 – 11.50). In addition, we also found that the mortality of patients infected with the Omicron variant in mainland areas was three times greater in unvaccinated than vaccinated cases against COVID-19 (PR = 3.04, 95% CI 0.89 – 10.40). A similar study found in Hong Kong, located on China's southeast coastline, with the lowest coverage of vaccines in vulnerable populations (only 31.30% of 80-year-olds getting two doses of vaccination as of 6th March, 2022) caused 25.5 deaths per 1 million population throughout the Omicron wave In contrast, other coastal countries such as Singapore and the United Kingdom, with higher vaccine coverage (more than 90%) in the elderly group, had much lower mortality rates of 2.1 and four deaths per million people during the Omicron wave (23). These different factors may be influenced by vaccination coverage, ethnicity, and geography in a region.

Riau Province found a peak in deaths of Omicron variant COVID-19 patients from March 6–12, 2022. In a different situation in East Java Province, Indonesia, the forecasting results from February 2022 to December 2023 found the number of deaths beginning to show a significant decrease (24). Weak testing, tracing, and treatment interventions, as well as delays in transmission detection, referral, and treatment, are considered to have contributed to the increase in death cases (25).

In Riau Province, diabetes and cardiovascular disease are the most common comorbidities in the deaths of Omicron variant COVID-19 patients. In previous meta-analysis studies, it was obtained that the comorbidity of diabetes is estimated to 3-fold increase the risk of death from COVID-19 in hospitals (OR = 2.68, 95% CI 2.09-3.44) (26). Patients with COVID-19 with comorbid diabetes mellitus have an immune system that is hampered due to chronic hyperglycemia and impaired immune modulation (17). Previous research in Yogyakarta and Central Java, Indonesia, found that age ≥65 years, cardiovascular disease, and diabetes are substantial prognostic factors of COVID-19 mortality (27). Diabetes often appears alongside various comorbidities, such as hypertension, obesity, cardiovascular disease, and chronic kidney disease. Some comorbidities are associated with high ACE-2 receptor expression and the release of more proprotein convertases, making it easier for the virus to enter host cells (28).

Research Limitations

The limitation of this study was that a part of the diagnosis of Omicron variant was based on the results of Whole Genome Sequencing (WGS), which is the gold standard, while another used the S-Gene Target Failure (SGTF) test, but it is highly sensitive and specific. In addition, the comorbidity data analysis used the routine reports of COVID-19 surveillance which may be better if using data from patients' medical records.

CONCLUSION

Most of the death cases were unvaccinated, elderly, ≥61 years old, and occurred in mad Diabetes mellitus (35.86%), cardiovascular disease (28.97%), chronic kidney failure disease (25.52%), and hypertension (23.45%). Other comorbidities were acute renal failure, sepsis, cancer, tuberculosis, pneumonia, liver disease, COPD, obesity, pulmonary edema, diaphragmatic hernia, toxoplasmosis, HIV, immune thrombocytopenic purpura, and eclampsia. Our study indicates that accelerating complete vaccinations and increasing coverage by using any vaccines available, particularly among the elderly, is a vital strategy to optimize the protection against COVID-19. Improved comprehensive treatment of comorbidities in omicron patients is also urgently needed.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest in this study.

AUTHOR CONTRIBUTIONS

RR compiled and designed research, compiles manuscripts, collected data, and statistical analysis. IM and RM provided technical input for design, data analysis, and data interplay and critically revised the manuscript. FM, NE, MW, MUB, and EM contributed significantly to the interplay of results, compiling and critically revising the manuscript. All authors have read and approved the manuscript.

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