Original Article

COVID-19 Vaccination and Admission Severity: Clinician-Rated WHO Severity and AI-Classified Lung Involvement on Chest X-Ray in a 2022 Indonesian Hospital Cohort

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Abstract

Background: COVID-19 remains a global public health concern. Differences in disease severity and hospitalization have been observed between vaccinated and unvaccinated individuals. This study aimed to evaluate COVID-19 vaccination status and clinician-assessed clinical severity, as well as artificial intelligence (AI)-classified lung parenchymal involvement.

Methods: This retrospective cohort study included COVID-19 patients from January to December 2022. Clinical severity at admission was determined by World Health Organization criteria (mild, moderate, severe, critical). Lung parenchymal involvement was classified using a previously validated VGG16-based deep learning model applied to admission chest X-ray images. Vaccination status, verified through the national Satu Sehat registry, was categorized as unvaccinated, single-dose, or two-dose, without regard to time since last vaccination and vaccine type cause not consistently available.

Results: A total of 153 patients were included, 31 patients (20%) unvaccinated, 22 patients (15%) single-dose, and 100 patients (65%) two-dose recipients. Critical disease occurred in 12.9% of unvaccinated patients based on clinician assessment. No patients were classified as having severe lung parenchymal involvement by the AI model. Moderate lung involvement was more frequent in unvaccinated patients (29.0%) compared with single-dose (27.3%) and two-dose groups (7.0%). In multivariable ordinal logistic regression, two-dose vaccination was independently associated with lower odds of higher based on WHO clinical severity (adjusted odds ratio [aOR]=0.41; 95% confidence interval [CI]=0.19–0.86; *P*=0.018) and lower odds of more severe AI-classified lung involvement (aOR=0.32; 95% CI=0.14–0.71; *P*=0.005).

Conclusion: Two-dose vaccination was associated with lower clinician-assessed severity and reduced AI-classified lung parenchymal involvement at admission in this retrospective hospital-based cohort.

Keywords: artificial intelligence, chest X-ray, clinical severity, COVID-19, vaccination

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus and primarily affects the respiratory system. Viral entry occurs through binding of the spike protein to the angiotensin converting enzyme 2 (ACE2) receptor, followed by membrane fusion.[1] Although infection predominantly involves the lungs, ACE2 expression in multiple organs contributes to extrapulmonary manifestations affecting the cardiovascular, neurological, and gastrointestinal systems.[2] The most typical clinical symptoms include fatigue, fever, and dry cough. The disease may progress to respiratory distress, pneumonia, and systemic inflammation.[3]

Clinical severity is generally classified into four categories—mild, moderate, severe, and critical—according to established criteria.[4,5] Disease severity is also associated with long-term sequelae, including anxiety, chest pain, depression, dizziness, and hair loss.[6] Because pulmonary involvement is central to disease progression, objective assessment of lung

injury at hospital admission is clinically relevant for risk stratification and monitoring.

The COVID-19 vaccination program in Indonesia commenced in January 2021 as part of the government's efforts to reduce viral transmission. Although initially met with hesitancy, public acceptance increased by the end of 2021.[7] Evidence indicates that vaccination is effective in preventing infection and reducing disease severity. Vaccinated individuals have lower risks of hospitalization and death and tend to experience milder symptoms compared with unvaccinated individuals.[8,9] The ZOE Health Study in the United Kingdom reported significantly milder symptoms among vaccinated participants.[10]

In addition to clinical manifestations, vaccination has been associated with reduced radiological lung involvement and lower secondary transmission.[10] However, real-world data from Indonesian hospitalized cohorts in 2022—when vaccination coverage, circulating variants, and treatment practices were evolving—remain limited**,** particularly data on imaging-based lung involvement at admission.

A systematic review demonstrated that greater clinical severity is associated with more extensive radiological sequelae, including inflammation and fibrosis.[11] Previous studies assessing vaccination status and radiological severity have relied on manual interpretation by radiologists, which may be affected by subjectivity and inter-observer variability.[11] To address these limitations, artificial intelligence–based diagnostic approaches using chest X-ray images have been developed. In healthcare, AI tools are increasingly applied in medical imaging to assist in identifying complex patterns and improving reproducibility.[12] Given that chest radiography is widely available in Indonesian hospitals, AI-assisted admission chest X-ray assessment represents a pragmatic biomarker of lung involvement.

A specific type of AI, known as deep learning, is particularly effective in processing and analyzing complex data such as medical images. Deep Convolutional Neural Networks (CNNs), a subtype of deep learning models, are widely used for image recognition and classification tasks in medical imaging. These architectures enable automated categorization of lung radiographic involvement based on learned imaging features rather than subjective visual scoring.[13]

In our previous research, we developed G-COV, an artificial intelligence–based software platform operating with deep convolutional neural networks (CNNs) integrating patients' demographic data, comorbidities, clinical complaints, vital signs, and chest X-ray images.[13,14] The model achieved 97.20% accuracy for COVID-19 detection and severity classification in prior validation datasets.[13]

The development dataset did not overlap with the present cohort, and in this study, the imaging branch was applied without retraining to admission chest X-rays to classify lung parenchymal involvement. Clinician-assessed clinical severity and AI-derived radiological categories were analyzed as distinct outcome variables to avoid conceptual overlap. Associations between vaccination status and these outcomes were evaluated using bivariate and multivariable analyses, adjusting for key confounders. These findings may provide clinically relevant evidence for hospital-based risk assessment in Indonesian settings.

While our previous studies focused on model development and validation, the present study represents a distinct clinical application. Specifically, we investigate the association between COVID-19 vaccination status and clinician-assessed clinical severity, as well as AI-derived lung radiological involvement, at admission in an Indonesian hospital-based cohort in 2022. To our knowledge, this is among the first Indonesian hospital-based studies combining government-verified vaccination data from the Satu Sehat registry with AI-assisted admission chest X-ray assessment while maintaining clear separation between clinician-derived and algorithm-derived outcomes. The study aimed to address the gap in evidence linking vaccination status to clinical and imaging severity at hospital admission.

METHODS

This retrospective study used medical records data from COVID-19 patients admitted to Dr. Zainoel

Abidin Hospital, Banda Aceh, Indonesia, from January to December 2022. Ethical approval was obtained prior to study initiation from the Health Research Ethics Committee of Dr. Zainoel Abidin Banda Aceh Hospital (No. 095/ETIK-RSUDZA/2023).

The study included patients with confirmed SARS-CoV-2 infection by RT-PCR or rapid antigen tests and verifiable vaccination status through Satu Sehat (a nationally integrated health database by the Indonesian government). Patients diagnosed solely based on antibody testing were excluded. The study employed a non-probability sampling approach by recruiting all patients fulfilling the inclusion and exclusion criteria. Because the cohort was restricted to hospitalized patients, the estimated associations reflect relationships conditional on hospitalization and may be affected by selection (collider) bias.

Demographic characteristics that are included are age and sex. Information on comorbidities and duration of hospitalization was also retrieved. Comorbidities were identified through a structured review based on physician-documented diagnoses at admission and during hospitalization, supported by diagnostic codes in the medical records. Each comorbidity was coded as a binary variable (present/absent), and patients could have more than one comorbid condition. All documented comorbidities were analyzed without assigning a dominant category.

Clinical symptoms at presentation (fever, cough, dyspnea, anosmia, sore throat, chest pain, headache, generalized weakness, loss of consciousness, and gastrointestinal symptoms) were assessed by the attending physician at admission and documented in the medical records. Vital signs (blood pressure, heart rate, respiratory rate, and peripheral oxygen saturation) were obtained during the initial clinical examination.

Clinician-assessed clinical severity at admission was categorized according to the WHO COVID-19 severity classification (mild, moderate, severe, and critical) and used as the clinical reference variable. Clinicians were not blinded to vaccination status in routine care, and severity categorization relied on standard clinical documentation, formal inter-rater reliability assessment was not performed in this retrospective design. In addition, an AI-derived severity output generated by the G-COV model using structured clinical parameters and imaging data was analyzed as a secondary variable separately from clinician-assessed WHO severity.

Vaccination status was verified using the national Satu Sehat vaccination registry. Vaccination status was reflected by the registry-recorded dose count prior to admission. Vaccine product, booster doses, and time since the last dose were not consistently available, which may introduce exposure misclassification and limit causal interpretation.

Missing data were handled using a complete-case approach. Variables with incomplete documentation were excluded from specific analyses, and no imputation was performed due to the retrospective design. The number of excluded records and variable-level missingness rates are reported in the Results/flow diagram. Patients with incomplete medical records for key variables or unclear COVID-19 severity classification were excluded.

To assess lung parenchymal damage, admission chest X-rays were analyzed using a deep convolutional neural network (CNN)–based artificial intelligence model (G-COV). For each patient, the admission chest X-ray closest in time to the initial clinical severity assessment was used to align imaging with the admission timepoint. Deep learning, particularly CNNs, has become a dominant approach for classification tasks in medical imaging and is effective in detecting complex patterns in multidimensional data such as chest radiographs.

The CNN architecture used in this study was VGG16, a widely recognized deep learning model used in medical imaging applications. The model was pre-trained on an independent dataset with ground-truth labels assigned by expert radiologists (as described in the original G-COV development and validation studies) and was applied to the current cohort without retraining**,** minimizing circularity. The VGG16 model employs sequential convolutional and pooling layers; convolutional layers use small receptive fields (3×3) to detect image patterns, while

pooling layers reduce dimensionality to improve robustness.

For radiological assessment in this study, the imaging branch was used to produce an AI-derived lung damage category from admission chest X-ray images. Any AI-derived severity output from the multimodal (late-fusion) framework was analyzed separately from clinician-assessed WHO severity. One admission chest X-ray per patient (n = 153) was analyzed and classified into four categories of lung parenchymal involvement: normal, mild, moderate, and severe damage. The AI-derived lung damage classification was treated as an objective radiological biomarker and used as the primary radiological outcome variable. The final classification was generated using fully connected layers with softmax activation. The model's performance characteristics, including reported accuracy, are based on prior development/validation work and are not re-estimated in the current retrospective cohort.

Pre-trained models such as VGG16 are known for transfer learning capabilities and can be adapted to new tasks such as lung parenchymal damage estimation. The architecture includes several convolutional layers followed by max-pooling, enabling efficient down-sampling while preserving discriminative features. The final layers enable classification based on extracted features.[13] In this study, the model was used to generate standardized radiological categories from admission images for statistical association testing, rather than as a standalone clinical decision tool.

Associations between vaccination status and categorical outcomes were first assessed using bivariate tests (chi-square or Fisher's exact test when expected cell counts were <5). To address potential confounding, multivariable regression models were planned with adjustment for age, sex, and comorbidities (e.g., hypertension and diabetes) and other clinically relevant covariates available in the dataset. Because both outcomes are ordinal, ordinal logistic regression was used when proportional odds assumptions were met; otherwise, multinomial logistic regression was applied. Results are reported as adjusted odds ratios (aOR) with 95% confidence intervals (CI), with statistical significance set at $P<0.05$. All statistical analyses were performed using SPSS version 27.0.

RESULTS

Distribution of patients by vaccination status is presented in the STROBE flow diagram (Figure 1). Among 153 hospitalized COVID-19 patients, 100 (65%) had received a two-dose vaccination regimen, 31 (20%) were unvaccinated, and 22 (15%) had received a single vaccine dose. There was no missing data for vaccination status.

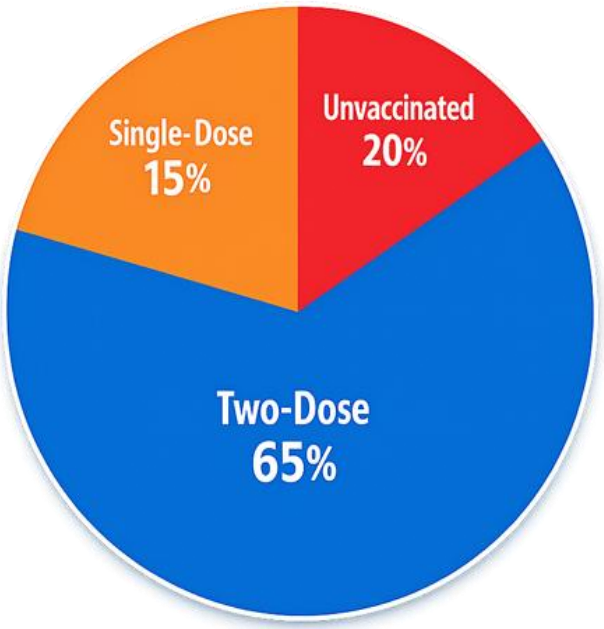

Figure 1. Proportion of Vaccination Status Among COVID-19 Patients (n = 153)

The mean age of patients was 57.77 years in the unvaccinated group, 60.32 years in the single-dose group, and 48.42 years in the two-dose group (with corresponding dispersion measures reported in Table 1). Age imbalance across vaccination groups was evident, with two-dose recipients being younger on average. Among unvaccinated patients, males constituted 54.8% of cases; the largest age group was 51–65 years (45.2%), followed by >65 years (38.7%). Most unvaccinated patients had at least one comorbidity, with hypertension (41.9%) and diabetes (35.5%) being the most common, while 19.4% had no comorbidities.

Table 1. Characteristics and Vaccination Status of the COVID-19 Patients

Characteristics	Unvaccinated (n=31)	Single-dose vaccination (n=22)	Two-dose vaccination (n=100)
Age, in years (mean)	57.77	60.32	48.42
>16–40	3 (9.7%)	3 (13.6%)	38 (38.0%)
41–50	2 (6.5%)	3 (13.6%)	9 (9.0%)
51–65	14 (45.2%)	5 (22.7%)	31 (31.0%)
>66	12 (38.7%)	11 (50.0%)	22 (22.0%)
Gender			
Male	17 (54.8%)	11 (50.0%)	63 (63.0%)
Female	14 (45.2%)	11 (50.0%)	37 (37.0%)
Comorbidities			
Diabetes	11 (35.5%)	7 (31.8%)	21 (21.0%)
Hypertension	13 (41.9%)	8 (36.4%)	23 (23.0%)
Lung disease	1 (3.2%)	1 (4.5%)	10 (10.0%)
Other	14 (45.2%)	7 (31.8%)	28 (28.0%)
None	6 (19.4%)	6 (27.3%)	43 (43.0%)
Hospitalization duration			
<6 days	17 (54.8%)	8 (36.4%)	63 (63.0%)
≥6 days	14 (45.2%)	14 (63.6%)	37 (37.0%)
Clinical symptom			
Fever	13 (41.9%)	8 (36.4%)	39 (39.0%)
Cough	20 (64.5%)	7 (31.8%)	44 (44.0%)
Dyspnea	15 (48.4%)	7 (31.8%)	39 (39.0%)
Anosmia	2 (6.5%)	0 (0.0%)	2 (2.0%)
Sore throat	1 (3.2%)	1 (4.5%)	6 (6.0%)
Chest pain	4 (12.9%)	2 (9.1%)	18 (18.0%)
Headache	2 (6.5%)	3 (13.6%)	21 (21.0%)
Body weakness	10 (32.3%)	7 (31.8%)	40 (40.0%)
Loss of consciousness	6 (19.4%)	4 (18.2%)	14 (14.0%)
Gastrointestinal symptoms	12 (38.7%)	9 (40.9%)	40 (40.0%)
Others	8 (25.8%)	5 (22.7%)	32 (32.0%)
Blood pressure			
Normal	17 (54.8%)	8 (36.4%)	57 (57.0%)
Hypertension	10 (32.3%)	14 (63.6%)	33 (33.0%)
Hypotension	4 (12.9%)	0 (0.0%)	10 (10.0%)
Pulse rate			
Normal	17 (54.8%)	15 (68.2%)	68 (68.0%)
Tachycardia	13 (41.9%)	6 (27.3%)	29 (29.0%)
Bradycardia	1 (3.2%)	1 (4.5%)	3 (3.0%)
Respiratory rate			
Normal	12 (38.7%)	10 (45.5%)	52 (52.0%)
Tachypnea	19 (61.3%)	12 (54.5%)	48 (48.0%)
Bradypnea	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oxygen saturation			
Normal	14 (45.2%)	15 (68.2%)	75 (75.0%)
Peripheral hypoxia	17 (54.8%)	7 (31.8%)	25 (25.0%)

Note: 'Other' comorbidity includes Coronary Artery Disease, chronic hepatitis B, ischemic stroke, stroke (3 cases), CKD stage V (2 cases), epilepsy (2 cases), aplastic anemia, hypercholesterolemia, dyspepsia syndrome (4 cases), acute kidney injury (2 cases), dementia, congestive heart failure (2 cases), brain tumor, HIV infection, psoriatic arthritis, liver cirrhosis, systemic lupus erythematosus (SLE), and dyslipidemia (2 cases); 'None' indicates absence of any documented comorbidity

Slightly more than half of unvaccinated patients were hospitalized for <6 days (54.8%). In the single-dose group, patients aged >65 years accounted for 50% of cases, and most required hospitalization for ≥6 days (63.6%). Among two-dose recipients, males accounted for 63% of cases; the most common comorbidity category was absence of comorbidities (43%), and most were hospitalized for <6 days (63.0%). Between-group differences are quantified using standardized mean differences

(SMDs) in Table 1 to describe baseline imbalance. Hospitalization duration is reported descriptively and was not included as an adjustment variable in regression models.

In the unvaccinated group, cough (64.5%), dyspnea (48.4%), and fever (41.9%) were most frequently reported. Gastrointestinal symptoms (40.9%) and fever (36.4%) were most prevalent among single-dose recipients. Meanwhile, among two-dose recipients, cough (44.0%) was most frequent, followed by gastrointestinal symptoms (40.0%), body weakness (40.0%), fever (39.0%), and dyspnea (39.0%).

Peripheral hypoxia was more frequent in the unvaccinated group (54.8%) than in the single-dose (31.8%) or two-dose groups (25.0%). Similarly, tachycardia was more frequent in the unvaccinated group (41.9%) than in the single-dose (27.3%) or two-dose groups (29.0%). Exact denominators for each comparison are provided in the table, and no missingness was observed for vital sign measurements included in the analysis.

Clinical severity was determined by attending clinicians according to the WHO COVID-19 severity classification (mild, moderate, severe, and critical), based on clinical presentation and oxygen requirement. In contrast, lung parenchymal damage was quantified independently using an AI-based analysis of admission chest X-ray images. Radiological lung parenchymal damage was independently assessed using a VGG16-based deep learning model applied to chest X-ray images and categorized into normal, mild, moderate, and severe.

A previously developed G-COV artificial intelligence model was used to generate AI-derived outputs from admission data. Clinician-assessed WHO clinical severity is reported separately and is not interchangeable with AI-derived categories. The AI-derived lung parenchymal damage classifications are presented in Table 2.

No patients were classified as having severe lung parenchymal damage by the AI model at admission (0.0%), and this zero-frequency category was handled in sensitivity analyses by collapsing the outcome into three levels (normal/mild/moderate). Moderate lung parenchymal damage was more frequent in the unvaccinated group (29.0%) than in the single-dose (27.3%) and two-dose groups (7.0%). Clinical severity also differed significantly across groups (P=0.015), with unvaccinated individuals demonstrating higher proportions of severe (35.5%) and critical (12.9%) disease compared with vaccinated groups.

Effect sizes for bivariate associations (Cramer's V) are reported in Table 2. There is a significant association between vaccination status and the degree of lung parenchymal damage (P=0.002). Vaccination status was also significantly associated with clinician-assessed WHO clinical severity (P=0.015).

Multivariable regression analyses adjusting for key confounders are presented to quantify effect sizes with 95% CI. This section presents multivariable ordinal logistic regression models assessing the independent relationship between COVID-19 vaccination status and two ordered outcomes: clinician-assessed WHO clinical severity and AI-derived lung parenchymal damage.

Table 2. Association between Vaccination Status, Degree of Lung Damage and Clinical Severity

Variables	Unvaccinated (n=31)		Single-dose vaccination (n=22)		Two-dose vaccination (n=100)		*P*
Degree of lung parenchymal damage							
Normal	8	(25.8%)	2	(9.1%)	15	(15.0%)	0.002**
Mild	14	(45.2%)	14	(63.6%)	78	(78.0%)	
Moderate	9	(29.0%)	6	(27.3%)	7	(7.0%)	
Severe	0	(0.0%)	0	(0.0%)	0	(0.0%)	
Clinical severity							
Mild	14	(45.2%)	15	(68.2%)	75	(75.0%)	0.015*
Moderate	2	(6.5%)	1	(4.5%)	8	(8.0%)	
Severe	11	(35.5%)	6	(27.3%)	11	(11.0%)	
Critical	4	(12.9%)	0	(0.0%)	6	(6.0%)	

Note: **Significant at P<0.05; **P<0.01

To address potential confounding, multivariable regression models were constructed with adjustment for age, sex, hypertension, and diabetes mellitus. Calendar period (month/quarter of admission) was additionally evaluated in sensitivity analyses to account for potential time-related confounding. Ordinal logistic regression (proportional odds model) was applied when the proportional odds assumption was satisfied. Sensitivity analyses using collapsed binary outcomes were conducted to assess robustness in the presence of sparse cells.

After adjustment for age, sex, hypertension, and diabetes mellitus, two-dose vaccination was independently associated with significantly lower odds of higher disease severity compared with unvaccinated patients (aOR=0.41; 95% CI=0.19–0.86; *P*=0.018). In this proportional odds model, the aOR represents the odds of being in a higher severity category versus all lower categories. Increasing age was significantly associated with greater severity (aOR=1.05 per year; 95% CI=1.02–1.08; *P*=0.002). Single-dose vaccination, male sex, hypertension, and diabetes were not statistically significant predictors in the adjusted model. The proportional odds assumption was satisfied, and the results are presented in Table 3.

Table 3. Multivariable Ordinal Logistic Regression for Clinician-Assessed WHO Clinical Severity

Vaccination Status	aOR	95% CI	*P*
Single-dose	0.74	0.34–1.64	0.459
Two-dose	0.41	0.19–0.86	0.018*
Age (per 1-year increase)	1.05	1.02–1.08	0.002*
Male sex (vs Female)	1.33	0.72–2.48	0.361
Hypertension	1.58	0.86–2.91	0.141
Diabetes Mellitus	1.67	0.89–3.12	0.109

Notes: Values are aOR with 95% CI; Model adjusted for age, sex, hypertension, and diabetes mellitus; *Statistically significant at *P*<0.05; Test of parallel lines: *P*=0.231 (assumption satisfied); Nagelkerke R^2=0.31

Table 4 shows the multivariable ordinal logistic regression results for AI-derived lung parenchymal damage severity. After adjustment for age, sex, hypertension, and diabetes mellitus, two-dose vaccination was independently associated with significantly lower odds of more severe lung damage compared with unvaccinated patients (aOR=0.32; 95% CI=0.14–0.71; *P*=0.005). Increasing age was also significantly associated with greater radiological severity (aOR=1.03 per year; 95% CI=1.00–1.06; *P*=0.037). Single-dose vaccination, male sex, hypertension, and diabetes were not statistically significant predictors in the adjusted model. Given the absence of an AI-classified severe category, sensitivity analyses using a three-level outcome yielded consistent direction and magnitude of association.

Table 4. Multivariable Ordinal Logistic Regression for AI-Derived Lung Parenchymal Damage

Vaccination Status	aOR	95% CI	*P*
Single dose	0.82	0.36–1.90	0.646
Two-dose	0.32	0.14–0.71	0.005*
Age (per 1-year increase)	1.03	1.00–1.06	0.037*
Male sex (vs Female)	1.21	0.64–2.30	0.552
Hypertension	1.52	0.80–2.89	0.198
Diabetes Mellitus	1.73	0.91–3.30	0.095

Notes: Values are aOR with 95% CI; Model adjusted for age, sex, hypertension, and diabetes mellitus; *Statistically significant at *P*<0.05; Test of parallel lines: *P*=0.187 (assumption satisfied); Nagelkerke R^2=0.34

DISCUSSION

A key strength of this study is the integration of real-world hospital data with national vaccination verification through the Satu Sehat system, combined with AI-assisted chest radiograph analysis to reduce inter-observer variability. The use of Satu Sehat enables objective verification of vaccination status based on government-certified records, minimizing recall bias and exposure misclassification commonly encountered in retrospective studies.

In addition, AI-assisted chest X-ray analysis is particularly relevant in the Indonesian healthcare setting, where variability in radiologist availability and workload may affect the consistency of radiological severity assessment**.** Importantly, clinician-assessed clinical severity and AI-derived radiological lung damage were analyzed as distinct outcomes, thereby avoiding conceptual overlap between clinical and algorithm-generated classifications. This integrated registry–electronic medical record–imaging framework illustrates a feasible learning health system model in a resource-constrained hospital environment.

Demographic profiles of the patients recruited in this study are generally consistent with previous

reports. A nationwide study indicated that the elderly population had the lowest vaccination rate in Indonesia as of March 2022.[15] In another study, male participants predominated (58.50%).[16] The predominance of men has been attributed to higher mobility and occupational exposure during lockdown periods.[17,18]

The proportion of individuals receiving a second dose in our cohort was comparable to previous findings reporting 77% completion of two-dose vaccination.[19] By mid-2022, second-dose coverage in Indonesia had increased substantially, particularly among healthcare workers and public officers.[15] However, engaging vulnerable populations such as the elderly remained challenging. Immunosenescence in older adults may contribute to exaggerated inflammatory responses and higher risks of severe outcomes.[17,20]

Given that age and comorbidity burden may confound the relationship between vaccination and severity, these factors were considered in the adjusted analyses to improve the robustness of the association estimates. Nevertheless, residual confounding related to age imbalance between vaccination strata and unmeasured factors such as calendar period or treatment protocol changes during 2022 cannot be fully excluded.

Among unvaccinated individuals, the most frequently reported symptoms were cough (64.5%), dyspnea (48.4%), and fever (41.9%). Gastrointestinal symptoms (40.9%) and fever (36.4%) were the most prevalent among patients receiving a single dose. In the two-dose group, cough (44.0%), gastrointestinal symptoms (40.0%), body weakness (40.0%), fever (39.0%), and dyspnea (39.0%) were commonly observed. Peripheral hypoxia was more frequent in the unvaccinated group (54.8%) compared with the single-dose (31.8%) and two-dose groups (25.0%). Tachycardia was also more frequent in unvaccinated patients (41.9%) than in single-dose (27.3%) or two-dose recipients (29.0%).

These descriptive differences support the observed association between vaccination status and clinician-assessed severity; however, because the cohort was restricted to hospitalized patients, the magnitude and direction of associations may be influenced by selection (collider) bias and should be interpreted cautiously.

Findings from the present study are consistent with previous literature. Cough, fever, dyspnea, and generalized weakness have been recognized as common clinical manifestations of COVID-19.[21] Although tachycardia has been reported as a potential post-vaccination event,[22,23] large cohort data suggest that tachycardic episodes are more strongly associated with SARS-CoV-2 infection itself than with vaccination.[24]

A review has summarized the effectiveness of vaccination in reducing disease progression across multiple populations.[25] Our adjusted findings further support the association between vaccination and reduced severity, with two-dose vaccination independently associated with lower odds of higher severity, based on WHO severity and greater AI-classified lung involvement, while acknowledging potential residual confounding.

A previously developed G-COV model was applied to generate AI-derived radiological lung damage categories, which were analyzed separately from clinician-assessed clinical severity. Critical (12.9%) and severe (35.5%) disease categories were more frequent among unvaccinated patients based on clinician assessment. Although the AI model includes a “severe” lung damage category, no patients were classified into this group. It’s likely reflecting the use of admission chest X-rays, when radiological abnormalities may not yet represent peak disease severity. Radiographic progression can occur after admission, and some clinically severe cases may initially demonstrate mild to moderate imaging findings.[13,14]

Alternative explanations should also be considered, including conservative model thresholds, domain shift related to imaging acquisition differences, or construct mismatch between algorithm-defined “parenchymal involvement” and clinically defined severity. The G-COV model employs a VGG16-based CNN architecture.[13,14]

While prior studies report high diagnostic performance for AI-assisted chest X-ray

classification, these metrics primarily relate to COVID-19 detection rather than severity grading. Therefore, in-cohort calibration and external validation remain important for clinical translation. In the present study, the model was applied without retraining to avoid overfitting and to maintain methodological separation between model development and clinical evaluation.

Lung parenchymal damage may contribute to persistent respiratory symptoms, reduced lung function, and pulmonary fibrosis. Findings from this study demonstrate an association between COVID-19 vaccination status and lower clinician-assessed severity as well as reduced AI-derived lung involvement at admission.[25]

The absence of AI-classified severe lung damage likely reflects both early imaging timing and evolving clinical patterns during the later pandemic phase. Prior studies similarly report milder disease among vaccinated individuals.[25] Vaccination-induced immunity has been associated with reduced viral load and less severe pulmonary injury.[10,26] Radiographic findings in vaccinated patients have shown greater radiolucency, suggesting improved lung aeration.[27]

LIMITATION

This study has several important limitations. First, its retrospective observational design precludes causal inference, and residual confounding cannot be excluded despite multivariable adjustment and sensitivity analyses. In particular, 2022 encompassed evolving SARS-CoV-2 variants, expanding vaccination coverage, and changing treatment protocols. Because variant-level data were unavailable at the individual level, time-period adjustment may not fully account for virologic and therapeutic heterogeneity. Second, the absence of detailed vaccination data—including vaccine product, booster status, and time since last dose—limits biological interpretation, prevents assessment of dose–response relationships or waning immunity, and may introduce exposure misclassification. Third, reliance on routine medical record documentation introduces potential outcome and covariate misclassification. Clinician-assessed WHO severity was based on standard care documentation without formal inter-rater reliability testing.

Fourth, the AI-derived lung involvement outcome, although generated using a previously validated VGG16-based model, was applied without in-cohort recalibration. Domain shift related to imaging acquisition protocols, projection differences, or population characteristics may affect calibration and generalizability. The absence of AI-classified severe cases at admission further constrains ordinal modeling assumptions, reduces precision at the upper severity range, and may reflect early imaging timing relative to peak radiographic progression. Finally, restriction to hospitalized patients introduces potential selection (collider) bias, as vaccination status influences hospitalization risk itself. Therefore, the observed associations apply to hospitalized populations and should not be extrapolated to community-level infection risk or overall vaccine effectiveness.

CONCLUSION

In this retrospective hospital-based cohort, two-dose COVID-19 vaccination was independently associated with lower odds of higher WHO-defined clinical severity and reduced AI-classified lung involvement on admission chest X-ray. The parallel evaluation of clinician-assessed and algorithm-derived outcomes strengthens the internal consistency of these findings while preserving conceptual separation between clinical and imaging metrics. Although the results support an association between vaccination and milder presentation at hospitalization, they should be interpreted as associative rather than causal, given potential residual confounding and selection bias. Prospective multicenter studies incorporating variant-period adjustment, longitudinal imaging trajectories, and formal external calibration of AI severity models are needed to strengthen generalizability and clinical applicability.

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CONFLICT OF INTEREST

All authors declare no financial or non-financial conflicts of interest in this research and manuscript preparation. The study was conducted independently without external intervention influencing data collection, analysis, interpretation, or publication decisions. The G-COV artificial intelligence tool was used objectively without commercial involvement that could introduce bias. No affiliations or personal interests affected the scientific objectivity and integrity of this manuscript.

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