JIM Research Letter

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Detailed characterization of hospitalized patients infected with the Omicron variant of SARS-CoV-2

Dear Editor,

As the SARS-COV-2 Omicron (B1.1.529) variant spread, many hospitals began to see the highest level of hospitalized COVID-19 patients since the onset of the pandemic (https://covid.cdc.gov/covid-data-tracker/#datatracker-home). To better understand the clinical consequences of the Omicron variant and compare it to our experience with patients infected with the Delta (B.1.617.2) variant, we started a detailed chart review at our academic medical center as the wave of cases related to Omicron began in Northern California.

Data were collected for all patients admitted with known SARS-CoV-2 infection on or after December 29, 2021, through January 21, 2022, including age, sex, ICU status, oxygen requirements, and vaccination status. Clinical determinations were made as to whether hospitalization was primarily due to symptoms of COVID-19 or not, which we refer to as "incidental" infection. Patients were also defined as being at high risk for more severe COVID-19 if they had underlying cancer, need for immunosuppressive therapy, significant pulmonary disease, or body mass index greater than 40. SARS-CoV-2-positive respiratory samples were genotyped to determine variant status [1].

Statistical analysis was conducted using the Mann–Whitney *U* test for two independent samples for age. All other variables were analyzed using Fisher's exact test. Prior to the onset of the study, we obtained approval to access covid patient data and conduct this research from Stanford's internal review board.

We identified 335 patients requiring isolation for SARS-CoV-2 during the study period, of which 309 patients were successfully genotyped (92.2%). Genotyping revealed 274 Omicron and 35 Delta cases. As summarized in Table 1, 128 of 274 (46.7%) Omicron patients were hospitalized primarily for COVID-19 compared to 26 of 35 (74.3%) Delta patients ($p = 0.0022$). Among patients hospitalized primarily for COVID-19, we found Omicron patients were significantly less likely to require oxygen during hospitalization (53.1% vs. 80.8%, $p = 0.0094$) and had less need for critical care support (14.1% vs. 38.5%, $p = 0.0044$) relative to Delta patients. Significant differences were also observed in rates of vaccination (75.8% of Omicron fully vaccinated vs. 26.9% of Delta, $p < 0.0001$) and those at high risk for severe COVID-19 (57.0% of Omicron vs. 23.1% of Delta, $p = 0.0022$). Mortality was not significantly different (0% vs. 5.5%, $p = 0.6027$).

Not surprisingly, Omicron accounted for most of the cases during the study period. Consistent with reports suggesting a blunting of Omicron's pathogenicity [2], a dedicated clinical review of each case showed a significantly high percentage of "incidental" COVID-19 cases among hospitalized patients with the Omicron variant compared to Delta. This also correlates well with Omicron patients being significantly less likely to be placed on supplemental oxygen or require critical care support. The lack of significant difference in mortality likely reflects the relatively small sample size of our Delta cohort.

While it is well documented that vaccines are effective against the Omicron variant [3], patients in our cohort hospitalized for Omicron were significantly more likely to be vaccinated. This likely reflects the overall high rate of vaccination in our surrounding area and the large number of patients we observed hospitalized with Omicron who were at high risk for more severe illness due to underlying immunosuppression, respiratory illness, or morbid obesity [4].

The typical phenotype of patients documented throughout the pandemic [5] and observed in our sample of Delta patients is largely unvaccinated with and without high-risk features. However, patients hospitalized for Omicron were more often vaccinated but at high risk for severe illness from COVID-19. While it is well accepted that COVID-19 carries greater risks for the immunocompromised [3], Omicron appeared to highlight this risk in our highly vaccinated community. These results

Table 1. *Comparisons of SARS-CoV-2 patients hospitalized with confirmed Delta versus Omicron from December 29, 2021 through January 21, 2022*

All SARS-CoV-2 positive	Delta	Omicron	*p*-Value
Variant confirmed patients	35	274	
Hospitalized primarily for COVID-19			
Total (%)	26 (74.3)	128 (46.7)	0.0022
Age, median [IQR]	57.5 [54, 70]	67 [54, 80]	0.0507
Sex, female/male	13/13	57/71	0.6687
Requiring O_2 support (%)	21 (80.8)	68 (53.1)	0.0094
Critically Ill (%)	10 (38.5)	17 (14.1)	0.0044
Fully vaccinated[a] (%)	7 (26.9)	97 (75.8)	<0.0001
High risk for severe illness[b] (%)	6 (23.1)	73 (57.0)	0.0022
Mortality (%)	0 (0%)	7 (5.5%)	0.6027

[a]Fully vaccinated individuals were defined as being 2 weeks post two doses of BNT162b2 (Pfizer-BioNTech) or Mrna-1273 (Moderna) or 2 weeks post one dose of Ad26.COV2.S (Johnson/Janssen).
[b]High-risk patients include patients on immunosuppression (e.g., organ transplant, autoimmune disease); on long term higher than physiologic dosed steroids; with active cancer ± recently on chemotherapy; with clear underlying respiratory condition (e.g., asthma/chronic obstructive pulmonary disease); or with a BMI ≥ 40.

emphasize the need to continue to protect those at highest risk from COVID-19. It should be noted that our study was designed to look at the phenotype of patients admitted for COVID-19 and not to assess vaccine efficacy. It is very likely that our COVID-19 hospitalization rate and severity of illness would have been significantly worse with a lower vaccination rate in our community.

Our study has several similar findings to a recent study comparing patients with Omicron and Delta variants presenting to French emergency departments [6], including higher rates of vaccination, higher rates of "incidental" COVID-19, and lower need for critical care in Omicron patients who were hospitalized. However, there are important differences between this study and ours, including that our study focused only on patients who were hospitalized, and we were able to genotype the majority of potentially eligible patients for the study (92% vs. 46%).

For hospitals reporting COVID-19-related hospitalizations, critical illness, and deaths, we believe these data support the recommendation for detailed investigation with genotyping of cases—to separate incidental cases from patients hospitalized primarily for COVID-19 with different SARS-CoV-2 genotypes—to provide a more accurate picture of the impact of COVID-19.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

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References

1 Sibai M, Wang H, Yeung PS, Sahoo MK, Solis D, Mfuh KO, et al. Development and evaluation of an RT-qPCR for the identification of the SARS-CoV-2 Omicron variant. *J Clin Virol.*2022;**148**:105101.
2 Wolter N, Jassat W, Walaza S, Welch R, Moultrie H, Groome M, et al. Early assessment of the clinical severity of the

SARS-CoV-2 omicron variant in South Africa: a data linkage study. *Lancet*2022;**399**:437–46.
3 Collie S, Champion J, Moultrie H, Bekker LG, Gray G. Effectiveness of BNT162b2 vaccine against omicron variant in South Africa. *N Engl J Med.*2022;**386**:494–6.
4 Galmiche S, Luong Nguyen LB, Tartour E, deLamballerie X, Wittkop L, Loubet P, et al. Immunological and clinical efficacy of COVID-19 vaccines in immunocompromised populations: a systematic review. *Clin Microbiol Infect.*2022;**28**:163–77.
5 Tang P, Hasan MR, Chemaitelly H, Yassine HM, Benslimane FM, Al Khatib HA, et al. BNT162b2 and mRNA-1273 COVID-19 vaccine effectiveness against the SARS-CoV-2 Delta variant in Qatar. *Nat Med.*2021;**27**:2136–43.
6 Bouzid B, Visseaux B, Kassasseya C, Daoud A, Fémy F, Hermand C, et al. Comparison of patients infected with Delta versus Omicron COVID-19 variants presenting to Paris emergency departments. *Ann Intern Med.*2022. https://doi.org/10.7326/M22-0308

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