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Short Communication

Admissions to a large tertiary care hospital and Omicron BA.1 and BA.2 SARS-CoV-2 polymerase chain reaction positivity: primary, contributing, or incidental COVID-19

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ABSTRACT

Objectives: SARS-CoV-2 Omicron variants BA.1 and BA.2 seem to show reduced clinical severity compared with earlier variants. Therefore, we aimed to assess and classify the cause of hospitalization for patients with COVID-19 identified with these Omicron variants in our hospital.
Methods: A retrospective analysis was performed on all patients identified with the SARS-CoV-2 Omicron variant between December 23, 2021, and February 27, 2022. Patients with a positive SARS-CoV-2 polymerase chain reaction (PCR) upon clinical admission or during clinical admission were classified into four categories: (1) primary COVID-19, (2) admission-contributing COVID-19, (3) incidental COVID-19, and (4) undetermined COVID-19.
Results: We classified 172 COVID-19 Omicron patient admissions, including 151 adult and 21 pediatric patients. Of the adult patients, 45% were primary COVID-19 cases, 21% were admission-contributing, 31% were incidental, and 3% were undetermined. Of the pediatric patients, 19% were primary COVID-19 cases, 29% were admission-contributing, 38% were incidental, and 14% were undetermined.
Conclusion: In the evolving landscape of COVID-19, the number of hospitalized patients with COVID-19 should be interpreted with caution. The different patient categories should be considered in public health policy decision-making and when informing the general public.
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Introduction

Monitoring national hospitalization rates for COVID-19 has been essential throughout the pandemic to guide public health decision-making and to evaluate vaccine efficacy. However, with the rapid worldwide spread of the SARS-CoV-2 Omicron variant of concern (associated with a decreased severity) and increasing immunity against SARS-CoV-2, interpreting the true impact of these hospitalization rates has been complicated (Viana et al., 2022; World Health Organization, 2021).

Due to the high SARS-CoV-2 incidence in the population with this variant, not all hospitalized SARS-CoV-2–positive patients were hospitalized solely because of COVID-19. We aimed to assess and classify the cause of hospitalization for patients with COVID-19 identified with the Omicron variant within our hospital to provide more insight into its burden on hospitalizations.

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Methods

This study was performed at the Erasmus MC University Medical Center in Rotterdam, The Netherlands (Erasmus MC), a large tertiary care hospital with 1125 beds, including 121 intensive care unit (ICU) beds. The majority of our adult clinic consists of single-occupancy rooms with private bathrooms, whereas our pediatric clinic mainly consists of multiple-occupancy rooms with shared bathrooms. A retrospective analysis was performed on all patients identified with the SARS-CoV-2 Omicron variant between December 23, 2021, and February 27, 2022. During this period, the SARS-CoV-2 testing strategy of the hospital was symptom-based with a low threshold and included a wide range of symptoms and clinical signs. Only for select patient groups, a PCR was performed regardless of symptoms. These groups were (1) patients who were admitted to a multiple-occupancy room in the adult oncology ward and pediatric ICU, (2) patients who had to undergo upper respiratory tract or major surgery, or (3) patients who had been in unprotected close contact with a proven COVID-19 case (usually a family member). Isolation measures were the same for all SARS-CoV-2 positive patients.

SARS-CoV-2 infection was identified by real-time transcription–mediated amplification with the Aptima® SARS-CoV-2 assay using the Panther system (Hologic, Marlborough, USA), or by the Xpert® Xpress SARS-CoV-2 assay on a GeneXpert® system (Cepheid®, Sunnyvale, USA). SARS-CoV-2 positive samples were further characterized by variant-specific PCR using VirSNiP (TIBmolbiol, Berlin, Germany) assays targeting S371-S373 and K417 as a proxy for the Omicron variant. While detection of K417N was considered indicative for the Omicron variant, S371L-S373P was considered indicative for BA.1 and S371F-S373P for BA.2.

SARS-CoV-2 Omicron variant positive patients at admission were divided into the following categories: (1) patients hospitalized >24 hours within 7 days of first positive SARS-CoV-2 PCR, (2) patients hospitalized <24 hours within 7 days of first positive SARS-CoV-2 PCR, and (3) patients with visits only to the Erasmus MC outpatient clinic within 7 days of first positive SARS-CoV-2 PCR. Data were collected from electronic health records (EHRs).

The main cause of hospitalization during the full length of stay of patients with a positive SARS-CoV-2 PCR upon or during clinical admission was classified. Classifications were defined by modified definitions developed by the National Intensive Care Evaluation Foundation (Table 1) (The National Intensive Care Evaluation Foundation, 2022). Classifications were performed by two epidemiologists through the evaluation of the patient's history in the EHR.

Results

A total of 333 adult patients were identified with the Omicron variant, of which 287 patients were identified with BA.1 (86.1%), 28 patients with BA.2 (8.4%), and 18 patients with either BA.1 or BA.2 (5.4%). Of patients with BA.1 , 39.4% had a clinical admission of >24 hours, 9.8% had a clinical admission of <24 hours, and 50.9% had an outpatient visit only. For adult patients with BA.2, 50% were clinically admitted to the hospital and 50% had an outpatient visit. Ninety-six pediatric patients were identified with the Omicron variant. BA.1 was identified in 57 children (82.6%), BA.2 in 16 children (15.9%), and one child was identified with either BA.1 or BA.2 (1.4%). Of children identified with BA.1, 26.3% were clinically admitted >24 hours, whereas 1.8% had a clinical admission of <24 hours, and 71.9% had an outpatient visit only. For children with BA.2, 36.4% had a clinical admission of >24 hours and 63.6% only had an outpatient visit.

One hundred seventy-two patients were hospitalized for >24 hours and were identified with the Omicron variant of SARS-CoV-2 at admission or during admission (Table 2). Patients were classified (Table 1) and characterized (Table 2).

Table 1
Classifications for primary, admission-contributing, and incidental COVID-19.

Classification	Definition
Classification 1: Primary COVID-19	COVID-19 is the main cause of hospitalization: **(1A)** The patient is hospitalized because of COVID-19 symptoms and is receiving medical treatment for these symptoms. **(1B)** The patient is hospitalized because of COVID-19 symptoms, does not receive medical treatment, but is admitted for observation because of the underlying disease.
Classification 2: Admission-contributing COVID-19	COVID-19 is one of the causes of hospitalization: **(2A)** The patient is admitted for another medical cause but also has COVID-19 symptoms and is receiving medical treatment for these symptoms. **(2B)** Dysregulation of underlying disease owing to COVID-19 (e.g., sickle cell crisis provoked by SARS-CoV-2 without respiratory involvement).
Classification 3: Incidental COVID-19	COVID-19 is not the cause of hospitalization; the patient does not have any or only mild COVID-19 symptoms and does not receive any medical treatment for these symptoms.
Classification 4: Undetermined COVID-19	It is unknown whether the cause of hospitalization is related to COVID-19 symptoms.

Discussion

We identified that only 45% of our hospitalized adult patients with either BA.1 or BA.2, and 19% of pediatric patients, were primary COVID-19 cases. Patients with primary COVID-19 were significantly more often solid organ transplant recipients and showed significantly less BA.1 than patients with incidental COVID-19. They also seemed older and seemed to have a higher 28-day in-hospital mortality rate than patients with incidental COVID-19. They had, however, higher COVID-19 vaccination rates compared with patients with incidental COVID-19 (Sun et al., 2022).

Initial studies on patients with the Omicron variant mainly assessed the clinical severity of hospitalized patients with COVID-19. However, these studies did not differentiate between primary and incidental COVID-19, thereby providing a general conclusion for all patients, while inherent differences are to be expected (Maslo et al., 2022; Wolter et al., 2022). We suggest including our classification system when assessing the clinical severity of SARS-CoV-2 variants.

Although both primary and incidental COVID-19 hospitalizations have implications for workload and isolation capacity, patients with incidental COVID-19 generally interfere less with routine care. Our study population mainly consisted of patients with COVID-19 identified through our symptom-based testing strategy. Therefore, the number of patients with incidental COVID-19 may have been underestimated because asymptomatic COVID-19 cases may have gone unnoticed. Counting patients with incidental COVID-19 as primary COVID-19 admissions gives a skewed image of hospital workload and the COVID-19 burden. One should be careful to base health care and public health decisions solely on the total number of hospitalized COVID-19 patients. We recommend policy makers to consider the different groups of hospitalized COVID-19 patients in their decision-making.

Table 2
Characteristics of included hospitalized adults and pediatric patients with COVID-19 for each classification.

	Total	Clas 1: primary COVID-19	Clas 2: admission-contributing COVID-19	Clas 3: incidental COVID-19	Clas 4: undetermined COVID-19
Adult patients, n (%)	151 (100)	68 (45.0)	32 (21.2)	46 (30.5)	5 (3.3)
Median age (range)	56 (18-90)	61 (18-90)	51 (18-82)	55 (22-90)	23 (22-49)
Male gender	82 (54.3)	35 (51.5)	20 (62.5)	25 (54.3)	2 (40)
Country of birth					
The Netherlands	90 (60.4)[2]	44 (65.7)[3]	18 (56.3)	26 (57.8)[3]	2 (40)
Other	59 (39.6)[2]	23 (34.3)[3]	14 (43.8)	19 (42.2)[3]	3 (60)
Solid organ recipient	23 (15.2)	16 (23.5)[a]	6 (18.8)	1 (2.2)	NA
Lung	9 (6.0)	8 (11.8)	1 (3.1)	0 (0)	NA
Kidney	13 (8.6)	8 (11.8)	4 (12.5)	1 (2.2)	NA
28-day in-hospital mortality	12 (7.9)	7 (10.3)	1 (3.1)	4 (8.7)	0 (0)
Vaccinated[1]	55 (53.9)[4]	37 (61.7)[5]	7 (30.4)[6,b]	11 (57.9)[11]	NA
Received booster vaccination	33 (34.7)[7]	25 (43.1)[8]	3 (14.3)[9]	5 (31.3)[12]	NA
BA.1 lineage	127 (84.1)	52 (76.5)[c]	27 (84.4)	43 (93.5)	5 (100)
BA.2 lineage	14 (9.3)	9 (13.2)	2 (6.3)	3 (6.5)	0 (0)
Oxygen therapy during admission	74 (50.7)[10]	56 (82.4)[d]	13 (40.6)[e]	5 (10.9)	NA
ICU during admission	13 (8.6)	6 (8.8)	1 (3.1)	6 (13.0)	0 (0)
ICU as admission department	10 (6.6)	5 (7.4)	0 (0)	5 (10.9)	0 (0)
SARS-CoV-2 PCR pos > 24 h after hospital admission	18 (11.9)	0 (0)	3 (9.4)	11 (23.9)	4 (80)
Pediatric patients, n (%)	21 (100)	4 (19.0)	6 (28.6)	8 (38.1)	3 (14.3)
Median age (range)	3 (0-17)	4 (0-8)	3 (0-13)	2 (0-7)	15 (12-17)
Male gender	12 (57.1)	2 (50)	5 (83.3)	4 (50)	1 (33.3)
Country of birth					
The Netherlands	19	4 (100)	5 (83.3)	7 (87.5)	3 (100)
Other	2	0 (0)	1 (16.7)	1 (12.5)	0 (0)
28-day in-hospital mortality	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
BA.1 lineage	16 (76.2)	2 (50)	5 (83.3)	7 (87.5)	2 (66.7)
BA.2 lineage	5 (23.8)	2 (50)	1 (16.7)	1 (12.5)	1 (33.3)
Oxygen therapy during admission	8 (38.1)	4 (100)	3 (50)	1 (12.5)	NA
ICU during admission	6 (28.6)	1 (25)	3 (50)	2 (25)	0 (0)
ICU as admission department	6 (28.6)	1 (25)	3 (50)	2 (25)	0 (0)

Clas, classification; ICU, intensive care unit; NA, not available; PCR, polymerase chain reaction; pos, positive.

[a] A significant difference was found between the number of solid organ recipients in the group of patients with primary COVID-19 versus patients with incidental COVID-19 ($P = 0.002$).

[b] A significant difference was found between the number of vaccinated patients in the group of patients with admission-contributing COVID-19 versus patients with incidental COVID-19 ($P = 0.073$).

[c] A significant difference was found between the number of vaccinated patients in the group of patients with primary COVID-19 versus patients with incidental COVID-19 ($P = 0.017$).

[d] A significant difference was found between the number of patients receiving oxygen therapy during admission in the group of patients with primary COVID-19 versus patients with incidental COVID-19 ($P < 0.001$).

[e] A significant difference was found between the number of patients receiving oxygen therapy during admission in the group of patients with admission-contributing COVID-19 versus patients with incidental COVID-19 ($P = 0.002$).

[1] Received two COVID-19 vaccinations (Pfizer/BioNTech, Moderna, or AstraZeneca) or one vaccination (Johnson & Johnson's Janssen).

[2] For two patients, this was unknown.

[3] For one patient, this was unknown.

[4] For 49 patients, this was unknown.

[5] For eight patients, this was unknown.

[6] For nine patients, this was unknown.

[7] For 56 patients, this was unknown.

[8] For 10 patients, this was unknown.

[9] For 11 patients, this was unknown.

[10] For 5 patients, this was unknown.

[11] For 27 patients, this was unknown.

[12] For 30 patients, this was unknown.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Conflict of interest

The authors declare no conflict of interest relevant to this article.

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Ethical approval statement

This study was approved by the medical ethical research committee of Erasmus MC (MEC-2021-0845-A-0002) and was not subject to the Medical Research Involving Human Subjects Act.

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None.

Authors' contributions

AV, CH, JR, RM, EN, LT, RP, AR, and JS conceptualized the study. AV and CH collected and analyzed the data. AV, CH, JR, RM, EN, LT, RP, AR, and JS interpreted the data. AV and CH drafted the work.

All authors read, reviewed, and approved the final manuscript, and all authors have read and agreed to the published version of the manuscript.

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