

LETTER TO THE EDITOR

## Presentation and outcomes of SARS-CoV-2 Omicron variant infection in haemodialysis patients

Alice Chimon<sup>1,\*</sup>, Elsa Ferrière<sup>1,\*</sup>, Mohamed Ali Lammouchi<sup>2,\*</sup>, Narindra Jouan<sup>3,\*</sup>, Pierre-Antoine Michel<sup>2</sup>, Kenda Saloum<sup>4</sup>, Laurence Morand-Joubert<sup>4</sup>, Aurélie Schnuriger<sup>4</sup>, Marianne Leruez-Ville<sup>5</sup>, Jacques Fourgeaud<sup>5</sup>, Djamel Dahmane<sup>3</sup>, Boutheina Bentaarit<sup>3</sup>, Bruno Guéry<sup>1</sup>, Hamed Fessi<sup>2</sup>, Hajer Kazdaghi<sup>2</sup>, Farah Sounni<sup>2</sup>, Timothée Fearon<sup>2</sup>, Idris Boudhabhay<sup>1</sup>, Jean-Michel Pawlotsky<sup>6</sup>, Khalil El Karoui<sup>2,†</sup>, Slim Fourati<sup>6,†</sup> and Hamza Sakhi<sup>3,†</sup>

<sup>1</sup>Nephrology Department, Necker Hospital, APHP, University of Paris, Paris, France, <sup>2</sup>Nephrology Department, Tenon Hospital, APHP, Sorbonne University, Paris, France, <sup>3</sup>Nephrology Department, Mondor Hospital, APHP, University Paris Est, Créteil, France, <sup>4</sup>Virology Department, Trousseau Hospital, APHP, Sorbonne University, Paris, France, <sup>5</sup>Virology Department, Necker Hospital, APHP, University of Paris, Paris, France and <sup>6</sup>Virology Department, Mondor Hospital, APHP, University Paris Est, Créteil, France

\*These authors are co-first authors.

†These authors are joint senior authors.

Correspondence to: Khalil El Karoui; E-mail: [khalil.el-karoui@aphp.fr](mailto:khalil.el-karoui@aphp.fr)

Haemodialysis patients have a high risk of severe forms of infection after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [1, 2] and present defective humoral and cellular responses to vaccination [3].

The Omicron (B.1.1.529) variant of concern (VOC) of SARS-CoV-2 was first detected in November 2021 [4] and has spread rapidly in Europe, even in countries with high levels of vaccination [5]. In the general population, clinical outcomes after Omicron infection appear reassuring. These findings in the non-dialysis population could be explained by both a lesser viral intrinsic pathogenicity but also and mainly specific host properties at the population level [6], including residual immunity acquired during previous waves and vaccination campaigns.

To date, SARS-CoV-2 Omicron infection remains poorly described in the dialysis population. In this specific population, up to 28% of the dialysis patients have low neutralizing antibody titers against Omicron despite three mRNA vaccine doses

[7]. In this retrospective study, we sought to evaluate the clinical presentation, virological outcomes and humoral response after SARS-CoV-2 Omicron infection in a multicentric cohort of in-centre haemodialysis patients.

Detailed methods appear in the Supplementary data.

Among 198 in-centre patients regularly followed in the three participating centres in the Paris area, 55 patients (27%) followed the inclusion criteria.

### PATIENTS' CHARACTERISTICS

Clinical and biological characteristics are described in Table 1. SARS-CoV-2 variant assessment was available in 85.5% (eight patients had a low viral load, not allowing for determination of SARS-CoV-2 variant). Omicron VOC was detected in 100% of identified cases.

Received: 2.5.2022; Editorial decision: 6.5.2022

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Table 1. Patients' characteristics according to SARS-CoV-2 infection severity

	All (n = 55)	Mild or asymptomatic (n = 47)	Severe (n = 8)	P-value
Age (years)	59.00 (43.50, 75.00)	58.00 (45.00, 74.50)	69.00 (42.25, 77.75)	.390
Male	36 (65.5)	30 (63.8)	6 (75.0)	.700
BMI (kg/m <sup>2</sup> )	23.06 (20.20, 26.90)	23.29 (20.02, 26.84)	22.58 (21.96, 25.72)	.658
ESRD characteristics				
Haemodialysis duration (years)	1.68 (0.44, 4.24)	2.06 (0.44, 4.17)	1.50 (0.59, 4.80)	.981
Primary kidney disease				.787
Diabetic/vascular	26 (47.3)	23 (48.9)	3 (37.5)	
Other glomerular disease	10 (18.2)	8 (17.0)	2 (25.0)	
Non-glomerular kidney disease <sup>a</sup>	19 (34.5)	16 (34.0)	3 (37.5)	
Comorbidities				
Hypertension	47 (85.5)	40 (85.1)	7 (87.5)	1.000
Diabetes	26 (47.3)	22 (46.8)	4 (50.0)	1.000
Cardiovascular comorbidities <sup>b</sup>	14 (25.5)	12 (25.5)	2 (25.0)	1.000
Immunocompromised <sup>c</sup>	16 (29.1)	11 (23.4)	5 (62.5)	<b>.038</b>
COVID-19 characteristics				
Prior SARS-CoV-2 infection	13 (23.6)	11 (23.4)	2 (25.0)	1.000
Time (days) from previous SARS-CoV-2 infection to diagnosis	268.00 (201.50, 464.75)	238.50 (188.50, 319.75)	542.50 (488.25, 596.75)	.116
Number of vaccine injections	3.00 (2.00, 3.00)	3.00 (2.00, 3.00)	2.50 (2.00, 3.00)	.540
Time (days) from last vaccination to diagnosis	39.00 (17.00, 176.00)	41.00 (17.00, 198.00)	29.00 (19.50, 41.50)	.534
Deaths	3 (5.6)	0 (0)	3 (37.5)	<b>.002</b>
Serological characteristics				
Anti-S: level (BAU/mL) before Omicron infection	242.00 (36.00, 845.00)	300.00 (92.00, 1047.00)	1.75 (0.00, 24.75)	<b>.003</b>
Anti-S: time (days) from previous serology to Omicron infection	24.50 (33.00, 3.50)	26.00 (33.00, 12.00)	0.00 (6.00, 0.50)	<b>.020</b>
Anti-S: highest level (BAU/mL) after Omicron infection	5680.00 (2130.00, 5680.00)	5680.00 (3242.00, 5680.00)	33.80 (28.35, 2856.90)	.171
Anti-S: time (days) from Omicron infection to serology	26.50 (14.00, 30.25)	26.50 (14.00, 30.50)	16.50 (2.75, 30.25)	.368
Virological characteristics				
Viral load (Ct) at diagnosis	22.35 (18.86, 30.86)	22.49 (19.50, 33.50)	16.70 (15.03, 20.05)	<b>.011</b>
Time (days) from diagnosis to negative qRT-PCR	14.00 (12.00, 19.25)	14.00 (12.00, 17.00)	21.00 (19.00, 22.00)	<b>.008</b>
Negative qRT-PCR at day 14	28 (53.8)	28 (59.6)	0 (0.0)	<b>.016</b>

Note: quantitative data are expressed as median (Q1, Q3) and qualitative data as n (%).

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; BMI, body mass index; ESRD, end-stage renal disease; COVID-19, coronavirus disease 2019; anti-S, anti-spike protein; Ct, cycle threshold; qRT-PCR, quantitative reverse transcription polymerase chain reaction; Q1, quartile 1; Q3, quartile 3.

Bold value correspond to *p* value < .05.

<sup>a</sup> There were six cases of thrombotic microangiopathy, three cases of cast nephropathy or amyloidosis, three cases of uropathy, one case of antiphospholipid syndrome, one case of autosomal dominant polycystic kidney disease, one case of autosomal recessive polycystic kidney disease and four cases of nephropathy of unknown origin.

<sup>b</sup> Ischaemic cardiopathy, stroke or peripheral artery disease.

<sup>c</sup> Immunosuppressive therapy or chemotherapy, including prednisone (*n* = 9 patients, with 5 patients receiving only prednisone as immunosuppressive agent), calcineurin inhibitor (*n* = 3), mycophenolate mofetil (*n* = 2), belatacept (*n* = 1), eculizumab (*n* = 3), lenalinomide (*n* = 1), pomalidomide (*n* = 1) and rituximab (*n* = 1).

A total of 19 (34%) patients were female, the median age was 59 years and the median duration of dialysis was 22 months. In all, 26 patients (47.3%) had diabetes, 14 (25.5%) had cardiovascular disease and 16 (29.1%) were immunocompromised. Two patients (3.6%) received one vaccine dose, 16 (29.1%) received two doses, 27 (49.1%) three doses and 3 (5.4%) four doses; 7 (12.7%) patients were not vaccinated. A total of 13 patients (23.6%) had a history of previous SARS-CoV-2 infection in a median of 268 days before the current infection. The median number of total immunizing events (vaccination or infection) was three. The median delay between the last immunizing event and Omicron infection was 38 days. Before Omicron infection, 45 patients (84.5%) had detectable anti-S IgG (median

of sampling 24 before infection); median anti-S IgG level was 242 BAU/mL, 26 (47%) patients had IgG anti-S level >264 BAU/mL and 13 (23.6%) patients >1000 BAU/mL.

## THE OUTCOME OF SARS-COV-2 INFECTION

The median follow-up was 57 days (49–59). A total of 47 (85%) patients were asymptomatic or paucisymptomatic (flu-like symptoms). Of these, eight (15%) patients were hospitalized presenting with severe forms of infection, including three (5.6%) deaths. The median hospitalization length was 8–31 days [4]. Treatment of hospitalized patients included

dexamethasone (five patients), tocilizumab (one patient), casirivimab/imdevimab (one patient) and tixagevimab/cilgavimab (one patient). Among hospitalized patients, eight (100%) needed oxygen therapy, but only one was transferred to the intensive care unit, without mechanical ventilation. No patient had confirmed pulmonary embolism. The three deaths occurred in 78-, 67- and 80-year-old patients (one patient being immunocompromised), at 4, 10 and 14 days after infection, with pre-infection anti-S IgG <27 BAU/mL despite two or three vaccine injections.

Factors associated with severe forms of infection (Table 1) included immunocompromised status (23.4% versus 62.5% in non-severe and severe forms,  $P = .04$ ) and low median anti-S IgG level before infection (300.00 versus 1.75 BAU/mL in non-severe and severe forms, respectively,  $P = .04$ ). Patients with severe forms have lower initial cycle threshold (Ct) suggesting higher viral load [mean Ct = 22.5 (19.5, 33.5) versus mean Ct = 16.7 (15.0, 20.0) in non-severe and severe forms respectively,  $P = .01$ ]. Age, sex, body mass index, diabetes or a history of cardiovascular disease were not associated with severe forms of infection, nor the number of vaccine doses, number of immunizing events or delay since the last dose.

Similar results were obtained when the eight patients infected with an undetermined variant were excluded (Supplementary data, Table S1).

## VIROLOGICAL AND HUMORAL OUTCOMES

Supplementary data, Fig. S1A illustrates the evolution of the viral load over time. The median Ct at diagnostic was 22.3 (18.9–30). A total of 14 patients had Ct >30 and 8 with Ct >35, suggestive of a very low viral load. The median delay before negative real-time reverse transcription-polymerase chain reaction (RT-PCR) was 14 days (12–19). This delay was significantly higher in severe versus non-severe forms (21 versus 14 days, respectively,  $P = .008$ ). In all, five patients presented with persistent positive RT-PCR after 21 days and only one after 28 days. Factors associated with positive RT-PCR after 14 days include lower initial Ct and severe form (Supplementary data, Table S2).

Repeat serological assays against S and N protein were available in 42 (76%) cases (Supplementary data, Fig. S1B). Anti-N IgG seroconversion occurred in 89% of patients, and a vast majority of patients showed anti-S elevation at the last follow-up (Supplementary data, Fig. S1B). The median last anti-S IgG level was 5680 (upper limit of the test) BAU/mL after a median of 27.50 (14.50–30.75) days post-infection. In all, 26 (60%) patients had anti-S IgG level >5680 BAU/mL at last follow-up. Factors associated with the highest anti-S levels (>2130 BAU/ml, e.g., first quartile) at last follow-up include a high number of vaccine doses, and high pre-Omicron anti-S titer (Supplementary data, Table S3).

In this study, we show that Omicron infection was frequent in in-centre haemodialysis patients during the fifth wave in Paris, France area despite large vaccine exposure.

Indeed, most patients received mRNA vaccination with booster injections leading to positive anti-S antibody levels before infection. The case fatality rate was 5%, and severe forms of infection were observed in 14%, suggesting that haemodialysis patients remain at high risk of severe complications after SARS-CoV-2 Omicron infection. Factors associated with severity included low previous humoral response and immunodepression, showing that host properties have a major role in Omicron severity [6]. Of note, our study highlights the risk of infec-

tion even in vaccinated patients with elevated anti-S IgG level, although outcome was favourable in most patients with these characteristics.

The median time to negative RT-PCR was 14 days. This delay was prolonged in patients with higher initial viral load and most severe clinical forms. Therefore, prolonged isolation measures could be proposed for patients with higher initial viral load to limit infection spread.

Importantly, we show that most patients had a strong elevation of anti-S IgG levels after infection. Consequently, although Omicron could lead to paucisymptomatic forms, humoral response post-infection remains frequent and intense in previously vaccinated haemodialysis patients. Determining whether this response is prolonged over time and associated with clinical protection against reinfection (as shown for previous variants [8, 9]) will require further studies.

Limitations of our study include the relatively low number of patients, the lack of SARS-CoV-2 variant assessment in eight patients due to a low viral load and the absence of evaluation of cellular response to Omicron infection.

In conclusion, although Omicron infection has been associated with a lower clinical severity than previous VOC in the non-dialysis population, haemodialysis patients remain at high risk of severe forms of infection and should benefit from continuous protection measures to limit SARS-CoV-2 infection.

## SUPPLEMENTARY DATA

Supplementary data are available at [ckj](#) online.

## ACKNOWLEDGEMENTS

We thank all the patients involved in this study.

## CONFLICT OF INTEREST STATEMENT

None declared.

## DATA AVAILABILITY STATEMENT

Anonymized data to produce figures and statistical analyses are available upon request.

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