

LETTER TO THE EDITOR

Incidence of anti-glomerular basement membrane disease during the COVID-19 pandemic

KS Jansi Prema and Anila Kurien

Department of Pathology, Center for Renal and Urological Pathology, Chennai, India

Correspondence to: Anila Kurien; E-mail: anila_abraham08@yahoo.com

Since the emergence of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) there have been case reports of anti-glomerular basement membrane (GBM) disease in coronavirus disease 2019 (COVID-19) patients [1–3]. Predecki *et al.* [2] documented a significant increase in the incidence of anti-GBM disease during the COVID-19 pandemic. Winkler *et al.* [4] reported the recurrence of anti-GBM disease in a COVID-19 patient. Our data show that there is a 68% increase ($P = 0.026$) in anti-GBM disease among the biopsied patients with acute kidney injury (AKI)/rapidly progressive renal failure (RPRF) compared with the pre-COVID-19 cohort (Table 1).

Kidney biopsy revealed cellular crescents (Figure 1) with intense linear staining for immunoglobulin G (IgG) on the GBM (Figure 2) in all patients. The mean age of the 42 patients reported during the COVID-19 pandemic was 46.2 years (range 16–82 years). There were 15 male, 26 female and 1 transgender patient. The indication for kidney biopsy was RPRF in 33 patients and AKI in 9 patients. The mean serum creatinine was 8.9 mg/dL (range 2.2–28.1 mg/dL).

At the time of kidney biopsy, 39 patients were tested for SARS-CoV-2 infection by viral RNA testing; 4 patients were positive. Due to the limited availability of the test kits, circulating IgM and/or IgG antibodies to SARS-CoV-2 spike protein was tested in only nine patients and antibodies were detected in seven of them, suggesting recent infection. A negative test for viral RNA does not exclude SARS-CoV-2 infection as the possible triggering factor for the disease since the aberrant adaptive immune response to the virus targeting basement membrane becomes clinically apparent only after some days to weeks after

Table 1. Comparison of anti-GBM disease and biopsy numbers during the study periods

Study period	Patients with anti-GBM disease, n (%)	Biopsies with AKI/RPRF, n	P-value
1 March 2018 — 31 August 2019	38 (2.5)	1499	0.026
1 March 2020 — 31 August 2021	42 (4.2)	1004	

the acute infection. In the study of Predecki *et al.* [2], all eight cases studied were negative for viral RNA but four tested positive for antibodies. Follow-up details were available for 20 patients (Table 2).

The exact mechanism by which SARS-CoV-2 triggers anti-GBM disease is unclear. Pulmonary endothelial cells are infected by SARS-CoV-2 [5]. Subsequent inflammation and complement activation results in endothelial injury. This leads to unmasking of the previously sequestered epitopes on the alveolar basement membrane. Autoantigen may then stimulate plasma cells to secrete autoantibodies responsible for the development of anti-GBM disease. So anti-GBM disease becomes clinically apparent only days to weeks after the acute SARS-CoV-2 infection.

We present a temporal cluster of cases of anti-GBM disease related to the COVID-19 pandemic, thereby supporting the assumption of a possible role of SARS-CoV-2 infection in triggering anti-GBM disease.

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Table 2. Follow-up details

Age (years)	Gender	Serum creatinine at the time of biopsy (mg/dL)	Crescents (%)	Outcome
54	Male	22	100	Expired
42	Male	5.2	83.3	Improved
50	Female	6.8	100	Expired
30	Female	3.8	100	Improved
33	Female	4	75	Improved
52	Female	5.5	100	Expired
40	Male	28	100	On HD
40	Male	16.5	100	Expired
53	Male	11	100	Expired
28	Female	19.7	100	Expired
42	Female	4.2	70	Recovered
54	Male	9.3	100	On HD
30	Male	3.2	100	On HD
55	Female	5.6	100	Expired
32	Transgender	6.5	100	On HD
43	Male	17.4	100	On HD
58	Female	5.5	100	Improved
45	Male	20.5	100	On HD
54	Female	11.5	100	On HD
51	Female	2.4	80	Ongoing treatment

HD, hemodialysis.

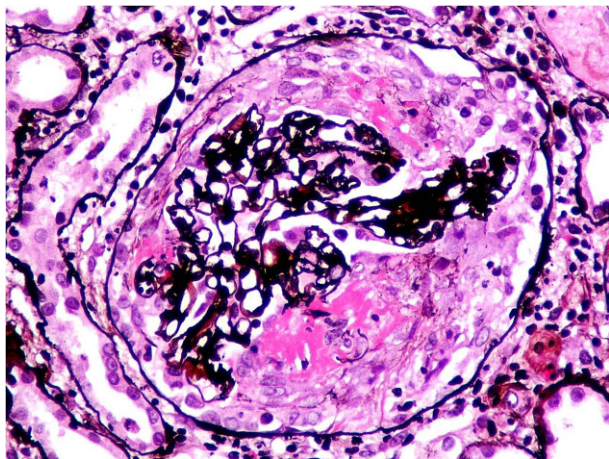


FIGURE 1: Jones silver stain shows fibrinoid necrosis of a segment of the capillary tuft with fragmented GBM and a cellular crescent.

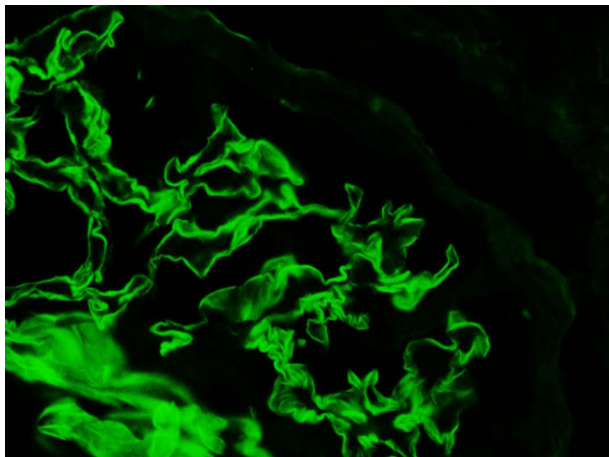


FIGURE 2: Linear staining of the GBM for IgG is the diagnostic immunofluorescence feature of anti-GBM disease.

CONFLICT OF INTEREST STATEMENT

None declared.

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