Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Treatment impact on COVID-19 evolution in hemodialysis patients

To the editor: We retrospectively studied 248 patients on maintenance hemodialysis affected by coronavirus disease 2019 (COVID-19)[1] in 19 private and academic maintenance hemodialysis centers in the Paris, France, area.

The mean follow-up period was 40 ± 19 days. The hospitalization rate was 58%. The overall mortality was 18.1% (30% in hospitalized patients) (Supplementary Tables S1 and S2). Ninety-six patients (39%) were previously treated with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. By multivariate analysis (Table 1), the main risk factors associated with mortality were age, facility living, dyspnea, and previous immunosuppressive treatment. Average treatment effects were further analyzed by propensity score analysis (Supplementary Methods and Supplementary Table S3). Hydroxychloroquine (odds ratio [OR], 1.02; 95% confidence interval [CI], 0.6–1.71; $P = 0.95$), macrolides (OR, 1.64; 95% CI, 0.94–2.84; $P = 0.079$), and third-generation cephalosporins (OR, 1.35; 95% CI, 0.8–2.29; $P = 0.265$) had no significant effect on mortality. Conversely, previous immunosuppressive treatment was associated with increased mortality (OR, 2.67; 95% CI, 1.43–5.01; $P = 0.002$), and previous treatment with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers was associated with reduced mortality (OR, 0.51; 95% CI, 0.31–0.85; $P = 0.01$).

In this large cohort of patients on maintenance hemodialysis, we highlight the deleterious role of previous immunosuppressive therapy in coronavirus disease 2019 outcome. These data are in line with those observed in patients who had undergone kidney transplantation, who demonstrate a high mortality rate (~20%–30%).[2]

Moreover, since angiotensin-converting enzyme 2 is the receptor for viral cellular entry, a role for angiotensin-converting enzyme inhibitors and angiotensin receptor blockers has been suggested in coronavirus disease 2019 pathophysiology. In our cohort, these treatments were associated with a significant reduction in mortality risk after propensity score weighting. However, large retrospective studies have not confirmed the impact of these treatments on severity of coronavirus disease 2019[3,4] in the general population. Further studies of cellular angiotensin-converting enzyme 2 expression in patients on maintenance hemodialysis could explain this effect since decreased angiotensin-converting enzyme 2 activity has been reported in this population.[5–7]

Table 1 | Multivariate analysis of the risk of death (outcome)

Variable	OR (95% CI)	*P*
Characteristics		
Age	1.04 (1.01–1.09)	**0.029**
Facility living	17.29 (3.95–75.6)	**<0.001**
Comorbidities		
Chronic respiratory failure	7.47 (1.18–47.39)	**0.03**
Immunosuppressive therapy	8.32 (2.19–31.55)	**0.002**
Symptoms at diagnosis		
Dyspnea	3.14 (1.24–7.96)	**0.015**
Blood tests		
Procalcitonin	1.005 (0.99–1.0107)	0.065

CI, confidence interval; OR, odds ratio.
P values in bold are considered as statistically significant.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Demographics, comorbidities and presentation of the cohort.

Table S2. Treatment and outcome.

Table S3. Variable used for propensity score analysis.

Supplementary Methods.

Supplementary References.

1. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054–1062.
2. Akalin E, Azzi Y, Bartash R, et al. Covid-19 and kidney transplantation. *N Engl J Med*. 2020;382:2475–2477.
3. Mancia G, Rea F, Ludergnani M, et al. Renin-angiotensin-aldosterone system blockers and the risk of Covid-19. *N Engl J Med*. 2020;382:2431–2440.
4. Reynolds HR, Adhikari S, Pulgarin C, et al. Renin-angiotensin-aldosterone system inhibitors and risk of Covid-19. *N Engl J Med*. 2020;382:2441–2448.
5. Yang C-W, Lu L-C, Chang C-C, et al. Imbalanced plasma ACE and ACE2 level in the uremic patients with cardiovascular diseases and its change during a single hemodialysis session. *Ren Fail*. 2017;39:719–728.
6. Roberts MA, Velkoska E, Ierino FL, Burrell LM. Angiotensin-converting enzyme 2 activity in patients with chronic kidney disease. *Nephrol Dial Transplant*. 2013;28:2287–2294.
7. Malik U, Raizada V. Some aspects of the renin-angiotensin-system in hemodialysis patients. *Kidney Blood Press Res*. 2015;40:614–622.

Sylvain Chawki[1], Albert Buchard[2,20], Hamza Sakhi[3,20], Karim Dardim[4,20], Karim El Sakhawi[3], Mokhtar Chawki[5], Henri Boulanger[6], Tomek Kofman[7], Djamal Dahmane[3], Philippe Rieu[8], David Attaf[9], Salima Ahriz-Saksi[6], Frederic Besson[10], Remy Boula[10], Ali Hafi[10], Afshin Massoumi[7], Ali Zineddine Diddaoui[5], Luc Fromentin[5], Patrick Michaut[11], Rachida Nebbad[12], Jean-François Desassis[13], Laurence Nicolet[13], Abderrahmane Ghazali[14], Julie Sohier-Attias[15], Larbi Lamriben[16], Arezki Adem[16], Emmanuel Dupuis[17], Mohamad-Khair Rifard[18], Dominique Joly[19], Khalil El Karoui[3,21] and Philippe Attias[8,21]; on behalf of the HD-CovIDF Study Group

[1]Institut Universitaire d'hématologie, Hôpital Saint-Louis, Institut national de la santé et de la recherche médicale (INSERM), Unité U944, Paris, France; [2]BIOS Health, Cambridge, UK; [3]AP-HP, Department of Nephrology, Hôpital henri Mondor, Institut national de la santé et de la recherche médicale (INSERM) Unité U955, Créteil, France; [4]Association Limousine pour l'Utilisation

du Rein artificiel à domicile (ALURAD), Isle, France; [5]Department of Nephrology and Dialysis, Clinique Claude Bernard, Ermont, France; [6]Department of Nephrology and Dialysis, Clinique de l'Estrée, Stains, France; [7]ANDRA, Paris, France; [8]Department of Nephrology and Dialysis, Hôpital Privé Nord Parisien, Sarcelles, France; [9]FRESENIUS, Paris, France; [10]Clinique Lambert, Dialysis, La Garenne-Colombes, France; [11]Clinique Internationale du Parc Monceau, Nephrology and Dialysis, Paris, France; [12]Centre d'autodialyse le Figuier, Drancy, France; [13]Centre Edouard Rist, Nephrology and Dialysis, Paris, France; [14]Groupe Hospitalier Public Sud de l'Oise, Dialysis, Creil, France; [15]Centre de Néphrologie Suppléance à l'insuffisance rénale par des techniques autonomes (SIRTA), Argenteuil, France; [16]Clinique les Martinets, Dialysis, Rueil Malmaison, France; [17]American Hospital of Paris, Nephrology and Dialysis, Neuilly-sur-Seine, France; [18]Centre Hospitalier des Quatre Villes, Nephrology and dialysis, Saint Cloud, France; and [19]Assistance publique - hôpitaux de Paris, Hôpital Necker-Enfants Malades, Department of Adult Nephrology, Paris, France

Correspondence: *Khalil El Karoui, Assistance publique - hôpitaux de Paris, Hôpital henri Mondor, Department of Nephrology, Institut national de la santé et de la recherche médicale (INSERM) Unité U955, 51 av du Maréchal de Lattre de Tassigny, 94000 Créteil, France.E-mail: khalil.el-karoui@inserm.fr*

[20]These authors contributed equally to this work.

[21]These authors shared senior authorship.

Kidney International (2020) **98,** 1053–1054; https://doi.org/10.1016/j.kint.2020.07.010

Interleukin 6 levels after tocilizumab administration in transplant recipients with COVID-19

To the editor: It is with great interest that we read the article by Gautier-Vargas and colleagues that reported a favorable clinical response with tocilizumab in a kidney transplant recipient with severe coronavirus disease 2019 (COVID-19).[1] Our clinical experience has also been similar.[2] The authors reported a dramatic decrease of serum interleukin 6 (IL-6) levels from 430.8 pg/ml to 3.4 pg/ml within 2 days after the administration of tocilizumab. However, as previously published,[3,4] and in our own experience, IL-6 levels generally increase after the administration of tocilizumab. In our published case report,[2] the IL-6 level was 241 pg/ml before tocilizumab and increased to 1259 pg/ml after the administration of tocilizumab. Given that tocilizumab functions by acting as a competitive inhibitor of the IL-6 receptor (IL-6R), increased serum IL-6 levels after its administration are likely caused by inhibition of IL-6R–mediated clearance as well as the endogenous production of IL-6 with ongoing disease activity. Hence, we wonder if the rapid decline of serum IL-6 level after tocilizumab in the case reported by Gautier-Vargas and colleagues was due to spontaneous improvement of disease activity or factors not related to tocilizumab. Randomized controlled studies are necessary to confirm the benefit of tocilizumab in transplant recipients with COVID-19.

1. Gautier-Vargas G, Baldacini C, Benotmane I, et al. Rapid resolution of cytokine release syndrome and favorable clinical course of severe COVID-19 in a kidney transplant recipient treated with tocilizumab. *Kidney Int.* 2020;98:508–509.
2. Allam SR, Dao A, Madhrira MM, et al. Interleukin-6 receptor antagonist therapy to treat SARS-CoV-2 driven inflammatory syndrome in a kidney transplant recipient. *Transpl Infect Dis.* 2020;22:e13326.
3. Shimamoto K, Ito T, Ozaki Y, et al. Serum interleukin 6 before and after therapy with tocilizumab is a principal biomarker in patients with rheumatoid arthritis. *J Rheumatol.* 2013;40:1074–1081.
4. Nishimoto N, Terao K, Mima T, et al. Mechanisms and pathologic significances in increase in serum interleukin-6 (IL-6) and soluble IL-6 receptor after administration of an anti-IL-6 receptor antibody, tocilizumab, in patients with rheumatoid arthritis and Castleman disease. *Blood.* 2008;112:3959–3964.

Akhil R. Gade[1], Harshitha Alavala[2] and Sridhar R. Allam[2]

[1]Internal Medicine Residency Program, Department of Medicine, Medical City Fort Worth, Fort Worth, Texas, USA; and [2]Division of Transplant Nephrology, Tarrant Nephrology Associates/Premier Physicians Group Health, Fort Worth, Texas, USA

Correspondence: *Sridhar R. Allam, 1001 Pennsylvania Ave., Fort Worth, Texas 76104, USA. E-mail: sallam@tarrantnephrology.com*

Kidney International (2020) **98,** 1054; https://doi.org/10.1016/j.kint.2020.06.025