

# COVID-19 Infection Associated with Psychosis in Hemodialysis Patient

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## ABSTRACT

Hemodialysis is a medical procedure to correct electrolyte imbalance and remove fluids and waste products from the blood of patients with end-stage renal disease. Dialysis patients are immunosuppressed and hence at risk of complications of coronavirus infection. In addition, dialysis for most patients is performed in-center, with therapy offered three times per week for 3.5 hours per session in sites highly exposed to virus contamination. A weak immune system and low cytokine storm explain why COVID-19 may be less severe in dialysis patients as death due to COVID-19 or effects on comorbidities in COVID-19 patients is due to overresponse against the virus by the immune system and cytokine storm. However, during the frequent trips between the dialysis center and home, the risk of coronavirus infection could be high. Moreover, hemodialysis patients constitute a distinct and high-risk group that is often associated with low immunity, decline or loss of the ability to work, substantial economic burden, the inability to fulfill family responsibilities and participate in an active social life, and suffer from various complications such as muscle weakness, pruritus, fatigue, diabetes, hypertension, and restless legs. These factors are associated with lower quality of life and poor clinical outcomes, leading to a higher risk of psychological problems than in the general population. We report a rare case of new-onset psychosis (mostly delirium) following COVID-19 infection in a middle-aged hemodialysis patient with rapid recovery.

The incidence and prevalence of end-stage kidney disease and dialysis are increasing worldwide. Patients on dialysis are immunosuppressed and suffer from various medical comorbidities such as diabetes, hypertension, and cardiovascular disease. Also, these patients tend not to react to infection in the same way as the general population due to their depressed immune system. In addition, researchers have shown a remarkable reduction in the numbers of T cells, T helper cells, killer T cells, and natural killer (NK) cells in peripheral blood mononuclear cells (PBMCs).<sup>1</sup> In addition, dialysis patients tend to have reduced inflammatory cytokines levels in their serum fluid compared to non-dialysis patients. More recent data, collected in the Italian region with the major SARS-CoV-2 spread<sup>2</sup> and in Zhongnan Hospital of Wuhan University,<sup>3</sup> explain why the effect of COVID-19 is less severe in hemodialysis patients.

Patients with end-stage kidney disease are particularly vulnerable to severe COVID-19 as they

tend to be older.<sup>4</sup> In one study, for example, nearly one-third of hospitalized dialysis patients with COVID-19 died; those who died were older (75 vs. 62 years) and had more comorbidities.<sup>5</sup> In the general population, specific and uncontrolled fears related to infection, pervasive anxiety, frustration and boredom, and loneliness have been hypothesized to impair subjective wellbeing and quality of life. Resilience and positive social support are protective factors against stress, which may help regarding lifestyle changes and re-adaptation mechanisms during the COVID-19 pandemic.<sup>6,7</sup>

People living with kidney disease are twice as likely to have a mental health problem in the UK. A new statement, "Kidney disease and Mental Health," highlights how vulnerable kidney patients already were before the coronavirus pandemic and shows their mental health could worsen even more.<sup>8</sup> Researchers have reported major fears about the effect on mental health amongst our population with chronic kidney disease (CKD) who are being

shielded in isolation, and hence could develop a protracted period of isolation and anxiety, with no apparent sign of a way out.<sup>8,9</sup> Psychological stress was inevitable among some dialysis patients, so it is important to identify high-risk individuals and provide psychological intervention for them in advance. Previous studies about SARS pointed out that the psychological implications of the epidemic should not be ignored in dialysis patients.<sup>10,11</sup>

### CASE REPORT

A 46-years-old single male with known hypertension complicated with end-stage CKD was started on hemodialysis in 2002. He underwent a kidney transplant a few months later. He was followed closely with a good kidney function, but chronic allograft nephropathy ensued progressively and in 2014 he returned to thrice-weekly dialysis sessions. He acquired hepatitis C virus infection and developed chronic gout arthritis. He was teetotal with no history of alcohol intake or smoking. He had no history of cardiac, pulmonary, or hepatic diseases. Also, there was no history of hyponatremia or hypocalcemia. He denied any history of narcotics or anticholinergic medications use.

He could not recall any exposure to people with COVID-19 infection, but he was tested at the dialysis center after complaining of lost smell and taste and was found to be COVID-19 positive. Ribonucleic acid-polymerase chain reaction (RNA PCR) COVID-19 obtained from nasopharyngeal swab was used to confirm COVID-19. He had mild to moderate symptoms with a productive cough, loss of smell and taste, and loss of appetite three days prior. On examination, he was afebrile, and had a pulse of 85 beats per minute and regular blood pressure range between 160/90 mmHg before the hemodialysis session and 140/80 mmHg post session. His respiratory rate was 22 breaths per minute, oxygen saturations of 95% on air, and a BMI of 32 Kg/m<sup>2</sup>. Chest examination revealed normal air entry, no adventitious sounds or murmur, abdominal examination revealed a central distribution of adiposity, but no organomegaly or masses, no audible bruits, and there was no pedal edema. He did not require admission to the hospital for further evaluation and treatment.

He had various laboratory investigations, including c-reactive protein (CRP), which was

elevated (13.3 mg/dL) while ferritin, D dimer, and chest X-ray were normal.

Five days later, the patient presented to a primary health care clinic with his brother to evaluate insomnia. He had been referring to himself by the wrong name and exhibited isolation behaviors, staying in his room all day without interaction with his family. In addition, he developed an auditory hallucination, which prevented him from sleep, where he heard voices of people talking to him and a new onset belief of someone conspiring against him.

He was provided with medical support from the private clinic and started on quetiapine 25 mg twice daily plus sodium valproate (Depakene) 100 mg twice daily post dialysis.

Three days later, he showed no improvement, and his family took him to a specialized psychiatric hospital. Head computed tomography (CT) scan was performed (as the sensitivity of magnetic resonance imaging (MRI) is known to be higher than CT, but MRI is not available in this center) and revealed no brain abnormalities. His relatives refused lumbar puncture.

Psychiatric clinicians increased the dose of quetiapine to 25 mg in the morning and 100 mg at night and the Depakene to 400 mg at night and advised to take post dialysis.

Five days later, when the insomnia and hallucination were still present, the dose of quetiapine was increased to 50 mg twice daily and Depakene decreased to 200 mg twice daily and he was advised to take the medications post dialysis.

Ten days later, he showed a significant improvement in his general health status and physical condition. His psychiatric hallucination and insomnia improved, and the patients recognized himself by the correct name and shared his family in daily activities. Table 1 shows the various laboratory tests performed before, at time of diagnosis, and post-recovery from COVID-19 infection.

Dialysis while COVID-19 positive was continued the same as before infection and included intermittent hemodialysis sessions, thrice weekly for a minimum of four hours duration using a hemodiafiltration-machine with a high flux dialyzer, with a blood flow of 300–400 mL/minute via brachiocephalic arteriovenous fistula.

During the dialysis session, his vitals were stable. He had a blood pressure of 140/70–150/80 mmHg,

**Table 1:** Laboratory tests performed before, at time of diagnosis, and post recovery from COVID-19 infection.

Variables	Pre-COVID-19	At time of COVID-19	Post-COVID-19	Range
Blood glucose, mmol/L (random)	12.7	13.1	10.1	3.0–7.7
Serum creatinine, umol/L	1318	1245	995	62–106
Sodium, mmol/L	137	134	133	136–145
Potassium, mmol/L	5.2	4.4	6.7	3.5–5.1
Chloride, mmol/L	96	94	93	98–107
Total bilirubin, umol/L	10.0	10.5	10.1	0–21.0
ALT, u/L	25.4	30.6	29.2	0–41.0
Alkaline phosphatase, U/L	94	97	85	40–130
Albumin, g/L	41.0	38.5	39.2	39.7–49.5
Total protein, g/L	70.2	70.8	77.6	64.0–83.0
Globulin, g/L	29	32	38	24–35
Corr. calcium, mmol/L	2.3	2.2	2.4	1.9–2.7
Phosphorus, mmol/L	1.21	1.41	1.0	0.87–1.45
Urea, mmol/L	17.1	15.2	12.2	1.7–11.9
Uric acid, mmol/L	410	428	418	202–416
HCO <sub>3</sub> , mmol/L	20.1	20.6	21.7	21.0–31.0
WBCs, 10 <sup>3</sup> /uL	7.4	6.5	9.2	2.2–10
Neutrophils	5.7	5	7.7	1–5
Lymphocytes	1.1	0.9	1.0	1.2–4.0
Hgb, g/dL	11.0	11.1	9.6	11.5–15.5
Hct, %	37.6	37.8	32.3	35.0–45.0
Platelets, 10 <sup>3</sup> /UL	133	120	199	140–400
CRP, mg/L	1.4	13.3	-	< 10.0

ALT: alanine aminotransferase; HCO<sub>3</sub>: bicarbonate; WBCs: white blood cells; Hgb: hemoglobin; Hct: hematocrit; CRP: C-reactive protein.

pulse rate of 70–90 beats/minute, and respiratory rate of 15–16 breaths/minute.

## DISCUSSION

To the best of our knowledge, this is the first case of post-kidney graft with chronic allograft nephropathy that returned to hemodialysis as a renal replacement therapy who also developed psychotic symptoms that occurred secondary to COVID-19. He started with simple symptoms that deteriorated to loss in orientation in person and deterioration of social and family life. He was prescribed anticonvulsant drug Depakene (used in the therapy of schizoaffective and affective psychosis) in combination with antipsychotic medication quetiapine. Depakene, which is highly dialyzable, was given at a dose of 10–5 mg/kg/day PO initially, divided q6–q12 hr and increased by 5–10 mg/kg/day at weekly intervals and quetiapine, which is not dialyzable, at 150–750 mg/day q12 or q8 with no dosage adjustment for chronic renal failure.<sup>12</sup> The doses were increased after

a few days to achieve a good and rapid recovery and return to his usual normal life status.

Infection with certain coronaviruses is associated with recent-onset psychotic symptoms; however, new-onset psychosis in otherwise asymptomatic patients infected with COVID-19 has not been described.<sup>13</sup> CRP, which was elevated in this case report, was considered a potential peripheral marker of immune activation, which has a causal or triggering role in schizophreniform psychosis.<sup>14</sup> Generally, CRP is increased in bacterial infection than in viral infection. Interestingly, CRP has been suggested as a serum marker of disease aggravation in COVID-19 patients.<sup>14</sup> Others found that even after accounting for identified inflammatory conditions, demographic factors influenced the reference limits of CRP; therefore, demographic characteristics, including age, sex, and race, had been suggested to be used to adjust the upper reference limit for CRP.

CRP is an acute-phase protein that operates as an initial sign of infection, such as a viral infection or inflammatory conditions. It is a protein manufactured

in the hepatic cells and is usually observed at a range of < 10 mg/L in the plasma body fluids. During infectious or inflammatory disease states, CRP levels rise rapidly within the first six to eight hours and peak at levels of up to 350–400 mg/L after 48 hours.<sup>15–16</sup> The effect of this drug combination was sedation after increasing both doses.

Elevated baseline D-dimer had been reported in COVID-19 patients, and it is associated with inflammation and CRP level, but there was no association with the venous thromboembolism score in these patients. Interestingly, D-dimer level decreased with the drop in the CRP levels. In our patient, with the exception of CRP, all tests were normal including brain CT. One report documented a brief psychotic reaction among three patients who were negative for COVID-19.<sup>17</sup> One case was attributed to fear of COVID-19 infection. Another described a case of COVID-19–related delusions in a COVID-19–negative patient who had an underlying diagnosis of schizophrenia.<sup>18</sup> Patients infected with SARS-CoV-2 were reported to develop changed mental condition, which is defined as an acute alteration in personality, behavior, cognition, or consciousness.<sup>19</sup> Individuals who acquired COVID-19 infection may develop hematological disorders such as thrombosis or clotting abnormalities. These blood clots may consequently render the patients with a thromboembolic phenomenon, including cerebrovascular accidents and multiple organ systems attacks and failures, while also attacking the brain with headaches, dizziness, and loss of taste and smell. In our case, a brain CT was done to exclude stroke and other pathology.

The American College of Radiology Appropriateness Criteria favors head/brain radiological-imaging for assessing patients with altered mental status in most clinical scenarios. Hence, we propose that if there is a clinical warning for head radiological-imaging of COVID-19 patients with a changed mental status, the radiologist must contemplate studying the health information system (HIS) electronic record in more detail or converse the pros and cons with the main primary clinicians to safeguard all concerned, and hence the paybacks of such investigation offset the dangers and risks in the setting of a viral outbreak.<sup>20</sup>

The immune response in SARS-CoV-2 infection is of interest, and there might be a hyperinflammatory response, but in our case,

all these were normal or just slightly high as for CRP.

The neuropsychiatric consequences (mental disorders that are the sequelae of brain damage or disease) can arise either through direct effects of central nervous system infection or indirectly via an immune response or medical therapy. Our case mainly had mild symptoms with a normal CT scan of the brain, and there were no neurological abnormalities. However, systemic review stated that the etiology of the psychiatric consequences of infection with coronavirus is likely to be multifactorial and might include the direct effects of viral infection in the brain.

## CONCLUSION

This is a case of acute psychosis that included auditory hallucination and persecutory delusion (suspiciousness) with confusion as the patient was not aware of himself. It seems that he also had reduced awareness of the surroundings and was hypoactive with social isolation and less verbal communication.

These symptoms are suggestive of delirium. The patient had multiple risk factors in developing delirium, given his medical background. With high CRP and a confused patient, lumbar puncture must be done to rule out encephalitis. This was not done in our case, and we suspect COVID-19 infection was the cause of the psychosis (delirium).

It is clear that once his medical problem causing the delirium improved (suspected COVID-19), his psychotic symptoms and confusion improved. Both medications quetiapine and Depakene work only as a sedative.

The unusual or rarity in this case is the hypoactive state of delirium, as most delirium cases had hyperactive state. COVID-19 may affect mental health in different ways. In general, small numbers of people had psychiatric disorder post COVID-19 infection. Dialysis patients are already overwhelmed with various medical comorbidities and psychiatric problems, and hence quality data, and ongoing surveillance is essential in every dialysis center. Nephrologists must be aware of the possibility of various psychiatric disorders such as depression, anxiety, fatigue, post-traumatic stress disorder, and rarer neuropsychiatric syndromes in dialysis patients with COVID-19 infection.

### Disclosure

The authors declared no conflicts of interest. Consent and ethical approval for this publication were obtained with reference number SRC#CR11/2021.

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