COVID-19 among patients with pre-existing renal impairment: experience in a tertiary care hospital of Bangladesh

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ABSTRACT

Background: Patients with chronic kidney disease (CKD) are at increased risk for infection because of immunosuppressed state. CKD is an independent risk factor for poor outcome in coronavirus disease 2019 (COVID-19). This study was designed to describe clinical and laboratory parameters of COVID-19 patients with preexisting CKD.

Methods: This cross-sectional study was conducted in the Department of Nephrology, BIRDEM General Hospital from July to December 2020. Hospitalized adult patients with CKD not yet on dialysis, who tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by reverse transcriptase polymerase chain reaction (RT-PCR), irrespective of symptoms were included in this study. RT-PCR negative cases were excluded.

Results: Total patients were 40 (mean age 58.3 years, 52.5% male). Common comorbidities were diabetes mellitus (92.5%), hypertension (67.5%) and ischaemic heart disease (27.5%). Fever, cough, shortness of breath, headache and fatigue were common presenting features. Nearly one-fifth had no COVID-related symptoms. Lymphopenia and high inflammatory markers (ESR, CRP) were common. Sixteen patients were complicated by acute kidney injury, four patients required haemodialysis and 23 had electrolyte imbalance. Most cases were mild to moderate; most were transferred to COVID-dedicated hospitals or discharged with home isolation protocols. Three patients required intensive care unit shifting and two patients died.

Conclusion: Most CKD patients had comorbid conditions. Clinical presentation was typical in most cases. Case fatality rate was higher than Bangladeshi statistics.

Key words: chronic kidney disease, clinical characteristics, COVID-19, epidemiology.

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INTRODUCTION
After beginning as “atypical pneumonia” in Wuhan, the capital city of Hubei province of China in December 2019, the identified aetiological agent, the 2019 novel coronavirus (2019-nCoV), which was later renamed as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has rapidly spread all over the world and the world health organization (WHO) declared the resultant coronavirus disease 2019 (COVID-19) as pandemic in March 2020. As the name indicates, SARS-CoV-2 was initially thought to invade the respiratory system but it is now better understood that COVID-19 is a multi-system disease. Angiotensin converting enzyme 2 (ACE-2) receptors are widely distributed in human body, to which SARS-CoV-2 binds and thus almost every bodily systems are susceptible to be involved; renal tubular cells are not an exception.

Initial reports from China and later from other parts of the world showed that elderly people and those with obesity, diabetes mellitus, hypertension, cardiovascular diseases, chronic obstructive pulmonary disease and other co-morbidities are at increased risk for poor outcome in COVID-19.1,2 Patients with renal impairment and specially those receiving renal replacement therapy and kidney transplant recipients are at increased risk of infection by SARS-CoV-2 and likely to have poorer outcomes.3-6 Till date, in the ocean of scholarly publications on COVID-19, only a limited numbers focused on COVID-19 patients with a background co-morbidity of chronic kidney disease7 and we did not find any published report on COVID-19 among patients with chronic kidney disease, not yet on dialysis, in or from Bangladesh. In this context, we aimed to evaluate clinical and laboratory parameters of COVID-19 among patients with chronic kidney disease, not yet started on renal replacement therapy.

METHODS
This cross-sectional study was done in the Department of Nephrology of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh from 1st July to 10th December, 2020. Hospitalized, adult (≥18 years) patients, with a diagnosis of chronic kidney disease not yet on maintenance haemodialysis, who were confirmed as having SARS-CoV-2 infection by reverse transcriptase polymerase chain reaction (RT-PCR), irrespective of symptom or purpose of current admission were included in this study. Patients with a clinical diagnosis of COVID-19, who were not confirmed by RT-PCR for SARS-CoV-2 infections, were excluded. Data were collected in preformed case record forms from patients and hospital records at the time of discharge, referral to other centers or death, if were any.

RESULTS
Total patients were 40 with a mean age of 58.3 (range 27 – 75) years and there was slight male predominance (21, 52.5%). Most patients had multiple co-morbidities including diabetes mellitus (Table I). Most patients were symptomatic (Table II), while a small number of patients were picked-up as having SARS-CoV-2 infection when tested as prerequisite for surgery or other procedure(s).

| Table I Comorbidities of COVID-19 patients with pre-existing renal impairment (N=40) |
| Comorbidity                  | Frequency | Percentage |
| Diabietis mellitus          | 37        | 92.5       |
| Hypertension                | 27        | 67.5       |
| Ischaemic heart disease     | 11        | 27.5       |
| Hypothyroidism              | 4         | 10         |
| Benign prostatic enlargement| 7         | 17.5       |
| Polycystic kidney disease   | 2         | 5          |

| Table II Clinical manifestation of COVID-19 patients with pre-existing renal impairment (N=40) |
| Clinical presentation       | Frequency | Percentage |
| Fever                       | 33        | 82.5       |
| Cough                       | 9         | 22.5       |
| Shortness of breath         | 5         | 12.5       |
| Headache                    | 5         | 12.5       |
| Body ache                   | 3         | 7.5        |
| Fatigue                     | 7         | 17.5       |
| Loose motion                | 3         | 7.5        |
| Vomiting                    | 4         | 10         |
| Abdominal pain              | 2         | 5          |
| Asymptomatic                | 7         | 17.5       |

Most patients were anaemic, had low lymphocyte counts, high erythrocyte sedimentation rate, C-reactive protein (CRP), serum ferititin and D-dimer (Table III). Electrolyte imbalance was also common (Table III). Radiological findings included abnormal chest x-ray (Figure 1) and high resolution computed tomography (HRCT) scan findings (Figure 2).
### Table III
Laboratory parameters of COVID-19 patients with pre-existing renal impairment (N=40)

| Laboratory parameter                      | Value                        | Frequency | Percentage |
|-------------------------------------------|------------------------------|-----------|------------|
| Haemoglobin (gm/dl)                       | 9.4 ± 3.4 (6.1-12.9)         | -         | -          |
| Total white cells/cmm of blood            | 13121±5202(1200-46400)       | -         | -          |
| Lymphocytes (%)                           | 13.9 ± 6.4 (2.4-28.1)        | -         | -          |
| Lymphopaenia                              | -                            | 33        | 82.5       |
| Platelet count/cmm of blood               | 236666 ± 134312 (112000-367000) | -         | -          |
| Erythrocyte sedimentation rate/1st hour   | 55 ± 16 (26-100)             | -         | -          |
| C-reactive protein (mg/L)                 | 101.6 ± 37.8 (4.8-199)       | -         | -          |
| Serum ferittin (ng/ml)                    | 1375 ± 458 (292-4403)        | -         | -          |
| Procalcitonin (ng/ml)                     | 1.37 ± 0.52 (0.2-5.4)        | -         | -          |
| Lactate dehydrogenase U/L                 | 1380 ± 463 (384-3056)        | -         | -          |
| Positive D-dimer                           | -                            | 9/23      | 39.1       |
| Blood urea (mg/dl)                        | 111 ± 38 (34-248)            | -         | -          |
| Serum creatinine (mg/dl)                  | 4.3 ± 2.3 (1.6-10.1)         | -         | -          |
| Dyselectrolytaemia                        | -                            | 23        | 57.5       |
| Abnormal chest x-ray                      | -                            | 18        | 45         |
| Abnormal high resolution computed tomography scan of chest | - | 7/7 | 100 |
| Blood culture                             | -                            | No growth | -          |
| Urine culture                             | -                            | Significant growth | - |
| Emphysematous pyelonephritis              | -                            | 1         | 2.5        |
| Pyelonephritis                            | -                            | 3         | 7.5        |

**Figure 1** Chest x-ray postero-anterior view showing bilateral pulmonary involvement by SARS-CoV-2 infection

**Figure 2** High resolution computed tomography (HRCT) scan of chest showing bilateral ground glass opacity in COVID-19
**Table IV** Treatment and outcome of COVID-19 patients with pre-existing renal impairment (N=40)

| Characteristics                                      | Frequency | Percentage |
|------------------------------------------------------|-----------|------------|
| **Presentation**                                     |           |            |
| Symptomatic                                          | 33        | 82.5       |
| Asymptomatic                                         | 7         | 17.5       |
| **Classification of disease**                        |           |            |
| Mild to moderate                                     | 35        | 87.5       |
| Severe                                               | 2         | 5          |
| Critical                                             | 3         | 7.5        |
| **Where treated after confirmation of diagnosis**    |           |            |
| Remained hospitalized                                | 2         | 5          |
| Transferred to COVID-dedicated hospitals              | 17        | 42.5       |
| Discharged with advice for isolation protocol        | 18        | 45         |
| Shifted to intensive care unit (Critical)            | 3         | 7.5        |
| **Treatment given**                                  |           |            |
| Antibiotic                                           | 17        | 42.5       |
| Anticoagulant                                        | 10        | 25         |
| Steroids                                             | 6         | 15         |
| Antivirals                                           | -         | -          |
| **Outcome**                                          |           |            |
| Deterioration of kidney function (AKI on CKD)        | 16        | 40         |
| Deterioration of kidney function requiring haemodialysis | 4/16   | 25         |
| Death                                                | 2         | 5          |

Most patients were in chronic kidney stages 3-5 (not on haemodialysis), 16 were complicated by acute kidney injury (AKI) and 4 patients required haemodialysis initiation due to uraemic symptoms. After being detected as having SARS-CoV-2 infection, most of the patients were discharged with advice of isolation protocol or referred to COVID-dedicated hospitals, 3 patients required transfer to intensive care units (ICUs) and 2 patients died. Outcome of patients are shown in Table IV.

**DISCUSSION**

Globally, 13.5% patients are having chronic kidney disease with diverse aetiology; diabetes mellitus, hypertension and glomerulonephritis being the top three contributors. Chronic kidney disease is an immunosuppressive condition resulting from defective T and B lymphocyte functions and thus patients with chronic kidney disease are at increased risk for infections. Kidney transplant recipients are further at risk for infection due to immunosuppressive medication intake. Patients receiving in-center haemodialysis are at increased risk for SARS-CoV-2 infection, because of 12-hour exposure/week in confined places.

Demographic characteristics of chronic kidney disease patients reveal that most are elderly; have often other comorbidities including diabetes mellitus, hypertension, coronary artery disease, dyslipidaemia etc. The mean age of our chronic kidney disease cohort having SARS-CoV-2 infection was nearly 60 years, which was higher than COVID-19 patients from China, United States.
and Bangladesh. Male predominance is found in COVID-19 cohorts throughout the world, which was also evident in contemporary Bangladeshi cohort. Some hormones are said to be protective in females against severe COVID-19 disease. Fever and respiratory symptoms like cough and shortness of breath are typical presentation of COVID-19; our findings were not exception. But we found about one-fifth of our patients were picked up as having SARS-CoV-2 infection when tested as prerequisite for some interventions. Some unpublished reports found much higher rates of asymptomatic SARS-CoV-2 infections in general population (serological tests). Atypical clinical presentations are common in immunosuppressed conditions including chronic kidney disease. Most of our patients were anaemic, had low lymphocyte counts and high inflammatory markers; these findings are also universal for SARS-CoV-2 infections. Imaging and laboratory findings of our cohort were comparable to other reports from local and global perspectives.

Elderly population and patients with diabetes mellitus, hypertension, cardiovascular diseases, obesity and chronic pulmonary conditions are reported to have poor outcome in COVID-19. Patients with chronic kidney disease are also reported to have poor outcome; they may not present typically thus are late in presentation, they have often concomitant multiple comorbid conditions, all contribute to unfavorable outcomes.

**Limitation**

This study included only a limited number of patients of COVID-19 with background chronic kidney disease. We did not treat most patients at our facility, as most patients were referred to COVID-dedicated hospitals, so detail of treatment and real outcome data is not available.

**Conclusion**

From the observation of present study, it can be concluded that most patients with chronic kidney disease, who were infected by SARS-CoV-2, were elderly with diabetes mellitus and other co-morbidities. Their clinical presentation were comparable with contemporary other studies but many patients were asymptomatic regarding COVID-19. Laboratory markers may give clue for such cases. In absence of vaccines and recommended therapeutic options, maintaining isolation protocols, personal hygiene and social distancing are emphasized.

**Recommendation**

Multi-center studies, including larger study participants are warranted to have complete epidemiological and clinical aspects of COVID-19 in chronic kidney disease patients.

**Authors’ contribution:** MAR, TS planned the study, did literature search and drafted the manuscript. IJ, MMA, TSUH collected data. MAR, TS, MAA, TAC, SKS, WMMH, SI were involved in managing patients. All authors read and approved final manuscript for publication.

**Conflicts of interest:** Nothing to declare.

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