IN HOSPITAL OUTCOME OF SARS COV-2 INFECTION AMONG SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS ON DISEASE MODIFYING DRUGS

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Abstract

Background: *COVID-19 is associated with hyperinflammatory syndrome causing worsening of disease severity. SLE is a rare autoimmune disease. Concomitant presence of both diseases may worsen COVID-19.*

Objective: *To characterize patients with Systemic Lupus Erythematosus (SLE) affected by COVID-19 and to observe medications on COVID-19 outcomes.*

Methodology: *SLE with confirmed COVID-19 patients on Hydroxychloroquine admitted in COVID dedicated hospital in Dhaka was included. Data were prospectively collected via a structured questionnaire form and review of medical records. Only hospital outcomes were observed.*

Results: *Total 17 patients were included, 11 of them had only SLE, 5 had lupus nephritis and only 1 had CNS lupus. All of them had confirmed COVID-19 detected by RT-PCR. 17 (100%) were taking immunomodulator (Hydroxychloro-quine), 7 (41.2%) steroids, 5 (29.4%) taking Mycophenolate mofetil before having COVID-19. Eleven (64.7%) of them had mild to moderate severity where 4 (23.5%) had severe & 2 (11.8%) had critical conditions. Of those 17 patients, 11 required supplemental oxygen (64.7%) during hospitalization, 2 (11.8%) admitted into ICU and required mechanical ventilation. Fifteen of them were discharged after 11 days (minimum 9, maximum 21) where 2 (11.8%) died due to hypoxic respiratory failure. Seven patients out of eleven who required supplemental oxygen were on prednisolone before illness only suffered mild to moderate illness.*

Conclusion: *Previous intake of immunosuppressants like Hydroxychloroquine & Mycophenolate mofetil before admission to hospital did not seem to influence the severity of infection.*

Key word: *SLE, COVID-19, Hydroxychloroquine, Outcome*

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Introduction

Bangladesh is among the top 30 countries and accounts for 0.49% of the COVID-19 cases of the world. Between 8 March 2020 and 27 June 2021, there are eight hundred eighty-eight thousand, four hundred six (888 406) COVID-19 cases confirmed by RT-PCR, GeneXpert, and Rapid Antigen tests including fourteen thousand, one hundred seventy-two (14 172) related deaths (CFR 1.6%).[1] Abnormalities of the immune system including lymphopenia have been related to morbidity in COVID-19 patients, and a hyperinflammatory syndrome has been associated with acute worsening of

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disease manifestations.[2] Immunosuppressant medications have also been proposed as treatment in an attempt to forestall the potential cytokine storm associated with poor outcomes.[3] Systemic lupus erythematosus (SLE) is an autoimmune disease characterised by autoantibodies, inflammation, and lymphopenia. The condition is frequently treated with hydroxychloroquine or chloroquine, both of which are being tested in the treatment of COVID-19.[4] It remains unclear whether patients with SLE are at increased risk of COVID-19 or if there is a paradoxical protective effect due to, in part, hydroxychloroquine use. However, several recent studies have failed to demonstrate significant clinical effectiveness of HCQ in COVID-19.[5] Although two series, reported that patients with chronic arthritis receiving immunosuppressants had low rates of severe disease from COVID-19 (0–2%), another series by Mathian and colleagues[7] described 17 patients with SLE, of whom 7 (35%) required mechanical methods of ventilation or extracorporeal membrane oxygenation.[6,7] To our knowledge, this is the first case series to report the characteristics and clinical course of COVID-19 in patients with SLE who were on Hydroxychloroquine since diagnosis in Bangladesh. Seventeen patients diagnosed with SLE on the basis of the revised classification criteria by the American College of Rheumatology[8] with confirmed COVID-19 infection has been included from May 2020 to May 2021 for the study.

Case History

11 out of 17 patients were identified in the largest COVID unit of Bangladesh, which is Dhaka Medical College Hospital. Rest of them were identified from Mugda Medical College and Shaheed Suhrawardy Medical College, both of these centre are COVID dedicated hospital. All of them had COVID-19 infection confirmed by nasopharyngeal swab RT-PCR for COVID-19. All of them 17 (100%) of patients were young women mean age 35 years [SD 9]. 17 (100%) were taking immunomodulator (Hydroxychloroquine), 7 (41.2%) were taking steroids, 5 (29.4%) taking Mycophenolate mofetil. 5 (29.4%) had lupus nephritis & 1 had CNS lupus while rest of them had only SLE. Common co morbid conditions among them were HTN 5 (29.4%), Asthma 5 (29.4%), DM 2 (11.8%), and Pregnancy 1 (5.8%). SLE DAI was calculated in 13 patient's at least 1 month back before hospital admission and found 4.2 (SD 1.3). Most common presentation were coughing 17(100%), fever 15 (88.2%), sore throat 14 (82.4%), breathing difficulty 13 (76.5%). Of those 17 patients, 11 required supplemental oxygen (64.7%) during hospitalization, 2 (11.8%) required admission to the ICU, required intubation and mechanical ventilation. Fifteen of them were discharged after 11 days (minimum 9, maximum 21) where 2 (11.8%) died due to hypoxic respiratory failure. Eleven (64.7%) of them had mild to moderate severity where 4 (23.5%) had severe & 2 (11.8%) had critical conditions. Regarding laboratory findings, C-reactive protein concentration (median 43 mg/dl [IQR 13–123]), erythrocyte sedimentation rate (59 mm/h [42–113]), ferritin concentration (392 ng/mL [153–2151]), D-dimer (0.98 ng/L [0.4-5.3] were elevated in 15 (88.2%) of the hospitalised patients. The patients' mean absolute lymphocyte count appeared lower at the time of COVID-19 diagnosis 0.87 K/iL [SD 0.38]. Chest-X ray of admitted patients showed bilateral opacity in 12 (70.5%) & unilateral 5 (29.4%). All patients who were moderate to severely or critically ill were on Hydroxychloroquine (300 mg per day [IQR 200-400]). All patients received empirical antibiotics, 10 mg dexamethasone for 10 days and prophylactic enoxaparin. Two patients with severe hypoxaemia (required non-invasive ventilation followed by invasive mechanical intubation) also received moderate-dose intravenous methylprednisolone (250 mg loading dose followed by 6 mg Dexamthasone daily). However, both of them died due to hypoxic respiratory failure. Both of them were on Hydroxychloroquine since diagnosis but not on steroid before hospital admission. However, seven patients out of eleven who required supplemental oxygen were on prednisolone before illness only suffered mild to moderate illness.

Table-I

Clinical characteristics and laboratory findings of 17 SLE patients with COVID-19

Trait	Mean ± SD, frequency N (%)
Age	35±9
Sex	
Female	17 (100)
History of Contact	12 (70.5)
Co-morbidities	
HTN	5 (29.4)
DM	2 (11.8)
Asthma	5 (29.4)
Pregnancy	1 (5.8)
Clinical characteristics	
Duration of symptoms	7 ± 2 days
Duration of Recovery	17 ± 4 days
Signs & Symptoms	
Fever	15 (88.2)
Cough	17 (100)
Sore Throat	14 (82.3)
Sputum production	3 (17.6)
Shortness of breath	11(64.7)
Chest pain	3 (17.6)
Myalgia	10 (58.8)
Anosmia	9 (52.9)
Tachypnea	11 (64.7)
Hypotension	2 (11.7)
Hypoxia	11 (64.7)
Convulsion	1 (5.8)
SpO2 during adm. on air	90.9 ± 7.9
Clinical type	
Mild to Moderate	11 (64.7)
Severe	4 (23.5)
Critical	2 (11.7)
Laboratory findings	
Neutrophil count	11.7 K/iL [SD 7.2]
Lymphocyte Count	0.87 K/iL [SD 0.38]
Platelet Count	218 K/iL [SD 93]
CRP (N= 0-10 ng/ml)	43 mg/L [IQR 13–123]
ESR (N= 10- 20 mm/h)	59 mm/h [IQR 22–113]
Ferritin (N= 0-120 ng/ml)	392 ng/mL [IQR 153–2151]
D-dimer (N= < 500ng/ml)	0.98 ng/L [IQR 0.2-5.3]
APTT (N= 30-40 sec)	45.53 [SD 8.34]
RT-PCR for COVID-19 (Positive)	17 (100%)
Chest X-ray	
Bilateral Opacity	12 (70.6)
Unilateral Opacity	5 (29.4)

Table-II

Hospital outcome 17 SLE Patients with COVID-19

Outcome	Frequency, N (%)
Improved & Discharged	15 (88.2)
†Dexamethasone 6 mg	11(64.7)
ICU admission	2 (11.8)
Dexamethasone 6 mg	
††Methylprednisolone 250 mg	
Death	2 (11.8)

† 11 patients had hypoxia, Dexamethasone 6 mg given once daily for 10 days.
††2 patients need ICU support - Methylprednisolone 250 mg as loading dose, followed by Dexamethasone 6 mg daily till death (5 days)

Discussion

To our knowledge, our study represents first case series of SLE patients with COVID-19 from Dhaka, Bangladesh. Here, we described clinical characteristics and hospital outcome of 17 SLE patients who had confirmed COVID-19 pneumonia, admitted in COVID dedicated unit of Dhaka, Suhrawardy and Mugda Medical College Hospital. As SLE is relatively rare, studies that focus on this subset of patients consist mostly of small case series. In a French study of 17 SLE patients with COVID-19, all of whom were on long term HCQ, 82% were admitted to the hospital, 41% required admission to the ICU, and 14% of patients died from COVID-19-related complications[9], similar to our study observation. The largest publication to date from the GRA's physician-reported registry described 85 patients with SLE, with a significantly higher percentage of SLE in hospitalized COVID-19 patients (17%) compared to those not requiring hospitalization (11%).[10] Gartshteyn Y et al, described that use of immunosuppressants like Hydroxychloroquine on admission did not alter the severity of COVID-19.[11] Similarly, we did not observe any association between the use of Hydroxychloroquine and decreased risk for hospitalization due to COVID-19. However, interestingly 4 SLE patients who were on steroid (prednisolone) as an adjunct to hydroxychloroquine for variable duration (minmum 1 month before hospital admission) did not suffer

severe or critical COVID-19 though they required supplemental oxygen. RECOVERY trial has proved that patients hospitalized with COVID-19, the use of dexamethasone resulted in lower 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone than who are not requiring oxygen at all.[12] However, 2 of our patients died had been admitted with lupus with CNS involvement with severe COVID pneumonia and SLE with 21 weeks pregnancy with severe COVID pneumonia were not on steroid at least 4 months before diagnosed as COVID-19. Both of them died due to hypoxic respiratory failure although tocilizumab, remdisivir were not given due to unavailability of medications and pregnancy issue. Clinical and laboratory characteristics of our SLE patients with COVID-19 were similar to COVID-19 patients without rheumatic diseases.[10,13] Our study has some limitations. Firstly, this is only case series comprising of very small number of SLE patients, only hospital outcome was measured, has not powered to show association between COVID-19 with Hydoxychloroquine or Steroid (prednisolone) and to measure probability of COVID-19 infection among SLE patients. Nevertheless, we do have some strength. SLE patients with confirmed COVID-19 were included, so it is unlikely sign & symptoms related to SLE. Patients who are on Hydroxychloroquine, Mycophenolate mofetil and Prednisolone since there initial diagnosis are also being reported here with outcome. Further large scale study is needed to evaluate immunosuppressant effect on COVID-19 infection & mortality among them.

In summary, our data suggest that patients with SLE with COVID-19 have a high rate of hospitalization but a higher mortality rate to the general population in Dhaka. Previous intake of immunosuppressants like Hydroxychloroquine & Mycophenolate mofetil before admission to hospital did not seem to influence the severity of infection. However, intake of steroid before COVID-19 infection might prevent transition to severe to critical COVID-19 among SLE patients.

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Competing interests

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