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Original Article

COVID-19 Pneumonia: Epidemiology, Clinical Characteristics and Outcomes from a Developing Country a Single Center Experience from Pakistan -

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ABSTRACT

Background: The first case of COVID-19 pneumonia was reported in Pakistan at the end of February 2020. In this single center study we report epidemiology, clinical, laboratory, and radiology findings, treatment and outcome of patients with COVID-19 pneumonia.

Methods: This retrospective study was undertaken between 21st March to 15th May 2020 where 6712 persons were screened for exposure and symptoms of COVID-19 and 2715 was test by RT-PCR. In all 317 patients with confirmed COVID-19 were admitted. Data were retrieved from hospital electronic health records and analysis performed using SPSSv.20.

Results: COVID-19 positivity rate in general public was 24·9% and 38.6% in in-patients. A total of 317 patients were admitted in corona wards. Their mean age was 47·1 ± 14·8 and 66·5% were males. Exposure or contact history was given by 43.2%. Median duration of symptoms was six days (IQR 3-8·7) with fever in 75·4%, cough in 59.0% and dyspnea in 59%. Co-morbids were hypertension in 27.1%, diabetes in 27.4%, ischemic heart disease in 6·0%, and 63 (19.9%) had ESRD. Disease was severe in 40.4% of patients with significantly increased inflammatory markers, CRP-H, ferritin, D-Dimer, NLR in 81-97%, bilateral infiltrates and ground glass opacity in 73.9% and complication ARDS in 71%, secondary infection in 24·3%, and multi-organ failure in 8·7%. The overall death rate was 16.1%, 30.4% in severe and 7.9% in non-severe disease.

Conclusion: The COVID-19 infected a quarter of the tested population where majority had non-severe disease. Severe disease was associated with old age, high co-morbids and mortality.

Keywords: COVID-19 infection; Clinical characteristics; Outcomes; Epidemiology; Developing country

INTRODUCTION

In December 2019, Wuhan city in China reported several cases of pneumonia of unknown origin [1]. This pathogen was identified as a novel enveloped RNA beta-coronavirus and was subsequently named Severe Acute Respiratory Syndrome Coronavirus (SARS-COV2) [2]. This was later designated by World Health Organization (WHO) as COVID-19 [3]. In Pakistan the first case of COVID-19 was identified on February 26, 2020 where majority of the initial positive cases were returning pilgrims from Iran [4]. Till 15th May 2020 Pakistan reported 38,799 confirmed cases, 834 deaths and 10,880 recoveries. The death and recovery rates at this stage were 2·1% and 28·0% respectively [5]. Karachi the largest city of Pakistan had 10,992 confirmed cases with 181 deaths [5]. Our institute is a Public Sector Dialysis and Transplant Center located in Karachi where all services and treatment is provided free of cost to all patients [6].

In view of the COVID-19 emergency and high risk of infections in our patient population, a dedicated COVID-19 outpatient and admission facilities were established on March 21, 2020. To help the government in this pandemic these free facilities were also offered to the general population. In this retrospective study on COVID-19 pneumonia we report epidemiology, clinical characteristics and outcomes from a low income country. We describe the screening and testing results of 6712 individuals and clinical characteristics and outcomes of 317 COVID-19 patients admitted in the institute from 21st March to 15th May 2020 with their follow-up upto 31st of May 2020.

MATERIALS AND METHODS

This single center retrospective study included 6712 individuals, 6391 screened for COVID-19 in clinic and 321 in wards and 317 patients were admitted between 21st March to 15 May 2020 with follow up till 31st May 2020. The records of admitted patients were retrieved from the Hospital Electronic Health Records (HER) database. The study was approved by the Ethical Review Committee of the institute, Ref No: SIUT-ERC 2020/A-217.

Criteria for Covid-19 test

All individuals attending the outpatient clinic were assessed by a team of doctors. The criteria to perform RT-PCR (Reverse Transcription Polymerase Chain Reaction) test for COVID-19 in clinic for general public were strictly based on exposure history and clinical symptoms. Exposure history included of foreign or local travel, attending large public gathering, public dealing and exposure to a COVID-19 positive individual. Symptoms included Fever >37.7^{0}C, Cough, Myalgia, Dyspnea, Oxygen saturation < 95% on room air. Exceptions to these criteria were health care workers and family members of positive patients who were tested irrespective of history or symptoms. The criteria to test for COVID-19 for regular inpatients with CKD, End Stage Renal Disease (ESRD), renal transplant recipient and malignancy were fever >37.7°C, Oxygen Saturation < 95% on room air and x-ray chest showing infiltrates.

Detection of COVID-19

All patients in the clinic were tested by a nasopharyngeal swab. Samples for in-patient included nasopharyngeal swabs, bronchoalveolar lavage and endotracheal aspirate. Sample was prepared using 800 µl of Viral Transport Medium (VTM) for Ribonucleic Acid (RNA) extraction on an automatic Abbott m2000 sample preparation system.

Real time RT-PCR was performed using Maccura RT-PCR kit (Maccura Biotechnology Company Ltd. China) according to kit instructions. Patients were retested two weeks after first positive, if negative retested after 24 hours. If positive after two weeks, they were tested at third week and if positive no further tests were undertaken.

Disease severity

Disease severity was assessed by National Guidelines of Government of Pakistan [7].

Asymptomatic: Patients who had no symptoms.

Mild disease: Patients who had any of the following symptoms, fever, fatigue, cough, anorexia, malaise, muscle pain, sore throat, nasal congestion or headache but vitally stable with oxygen saturation ≥ 95% on room air.

Moderate disease: Above symptoms of mild disease plus hypoxia. Oxygen saturation < 95% but ≥ 90% on room air or chest x-ray with infiltrates involving < 50% of lung fields.

Severe disease: Clinical signs of pneumonia i.e. fever or cough

plus any of the following, respiratory rate > 30/min, oxygen saturation on pulse oximetry < 90% on room air, PaO_2/FiO_2 < 300 mmHg, chest x-ray with infiltrates involving > 50% of lung fields, organ dysfunction, altered mental status, reduced urine output, low blood pressure, or septic shock i.e. persistent hypotension despite volume resuscitation, requiring vasopressors to maintain mean arterial pressure ≥ 65 mmHg.

Criteria for home isolation and hospital admission

COVID-19 patients who were asymptomatic or had mild symptoms were advised home isolation. Patients were contacted daily by telephone for changes in symptoms and asked to get admitted if symptoms aggravated. Those with inadequate facilities at home were shifted to the isolation ward. Patients with moderate and severe disease in clinic or regular wards were admitted.

Investigations on admission

Radiological investigations were limited to x-ray chest. Laboratory investigations included Complete Blood Count (CBC), Absolute Neutrophil and Lymphocyte Count, Platelet Count, Activated Partial Thromboplastin Time (APTT) and Prothrombin Time (PT). Blood chemistry included Urea, Creatinine, Electrolytes, Random Blood Glucose (RBS), Bilirubin, Aspartate Aminotransferase (AST), Alanine Transaminase (ALT), Creatine Phosphokinase (CPK), and Lactate Dehydrogenase (LDH). Inflammatory markers included Ferritin, High-sensitivity C-reactive Protein (CRP-H) and D-Dimer. Other laboratory and microbiology testing was undertaken as part of standard care at the discretion of the treating physician. They included Blood Gases, Lactate, Procalcitonin, Troponin I and Cultures for upper respiratory tract secondary infections.

Treatment protocol

Respiratory management: Patients with < 95% oxygen saturation were given supplemental oxygenation. Patients were placed in prone position when oxygen saturation was < 92%, those with bilateral infiltrates, respiratory rate >22 breaths/minute and intubated patients with PaO_2/FiO_2 < 200 mmHg.

Antibiotic therapy: Following antibiotics were used empirically. Intravenous (IV) Ceftriaxone 1 gm 12 hourly, Levofloxacin 500-750 mg once a day orally or IV Piperacillin Tazobactam (according to creatinine clearance). Antibiotic were later changed according to culture report.

Hydroxychloroquine: 400 mg stat then 200 mg eight hourly for ten days. Medication was discontinued if QT interval prolongation observed on Electrocardiogram (ECG) and arrhythmias.

Steroids: Methylprednisolone dose was 1 mg/kg in the divided dozes for 5-7 days.

Anticoagulation therapy: Enoxaparin subcutaneously 1 mg/Kg given 12 hourly and in renal failure patients Heparin 5000 units subcutaneously given once a day.

Regimen for intravenous human IgG (IvIgG) and IL-6 receptor antagonist: A single dose of 25 gram of IvIgG was administered over six hours followed by IL-6 receptor antagonist (Tocilizumab) 8 mg/kg. Doses repeated after 48 hours if no improvement. These medications were given if patient met three or more of the following criteria age > 60 years, co-morbidity anyone (Hypertension, Diabetes, IHD, COPD, CKD, ESRD, malignancy, renal transplant recipients), oxygen saturation < 90% on room air, PaO_2/FiO_2 < 300 mmHg, CRP-H >100 mg/L, Ferritin >1000 ng/ml, D-Dimer > 0.5 mg/L, Absolute Lymphocyte Count <1.0 x 10^9/L, Platelet Count < 150 x 10^9/L and Neutrophil / Lymphocyte Ratio (NLR) > 3.0.

Study end points: 1) Alive cured with two negative RT-PCR 24 hours apart, 2) Alive discharged after two weeks, asymptomatic and oxygen free for 72 hours with positive RT-PCR and 3) Death. Definitions of Fever, Acute Respiratory Syndrome (ARDS), Acute Cardiac Injury, Septic Shock, Acute Kidney Injury (AKI) and Secondary Infections are given in (Supplementary Appendix.)

Statistical analysis

All the data were entered and analyzed in IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp. Continuous measurements were expressed as mean and standard deviation or median and Interquartile Range (IQR). Categorical variables were presented as frequencies and percentages. Comparison between non-severe and severe Covid-19 patients for continuous variables was determined using sample t-test or Mann-Whitney U or Wilcoxon Signed Rank test as appropriate. For comparison of categorical variables between two groups were done by using Fisher exact test or chi-square test or McNemar test as appropriate. The *p*-value of < 0.05 was considered as significant.

RESULTS

Between 21st of March 2020 to 15th May 2020, 6391 individuals presented at the Corona clinic for COVID-19 pneumonia testing by RT-PCR. Of these 6391, 2394 (37.4%) fulfilled our criteria for testing among which 595 (24.9%) were positive (Figure 1). Individuals who were not tested or were negative were advised social distancing and wearing of face masks. Of the 595 positive, 119 (20%) were admitted and the rest (80%) were advised home isolation. Of the 476 in home isolation 74 (15.5%) returned with symptoms requiring admission. Of the 321 tested in hospital wards, 124 (38%) were positive (Figure 1).

The baseline characteristics on admission of the 317 patients are given in table 1. The mean age of the patients was 47.1 ± 14.8 years. The peak age was 31-60 years and 211 (66.6%) were males. There were three children; two boys aged 11, 12 years and one girl 15 years with ESRD. Exposure history was given by 137 (43.2%), 12.3% were health care workers and the 44.5% could not give any exposure or contact history. The median duration of symptoms on admission was six days (IQR 3-8.7 days). Of the 317, 311 (98.1%) had one or more symptoms. Common symptoms were fever in 75.4%, cough in 59% and dyspnea in 44.5%. On admission 96 (30.3%) had severe disease and 19 others progressed to severe disease after admission. Comparison of patients with non-severe and severe disease in terms of clinical characteristics, laboratory parameters, treatment and outcome is given in table 2. Patients with severe disease were seven years older than non-severe patients and had significantly higher frequency of symptoms. Of the 317 patients, 182 (57.4%) had co-morbids, while excluding 63 ESRD patients, 119 (37.5%) had co-morbids. Hypertension found in 41 (35.7%) in severe vs 45 (22.3%) in the non-severe group ($p = 0.010$). X-ray chest abnormalities were found in 207 (65.3%) of the patients. Normal x-rays were found in 49.5% of non-severe cases while bilateral infiltrates and ground glass opacity were more prevalent in severe disease. Comparison of laboratory investigation showed that in severe disease, haemoglobin was low, high neutrophil counts, low lymphocyte counts and increased median APTT and PT, blood urea and creatinine were increased higher in severe group. RBS was

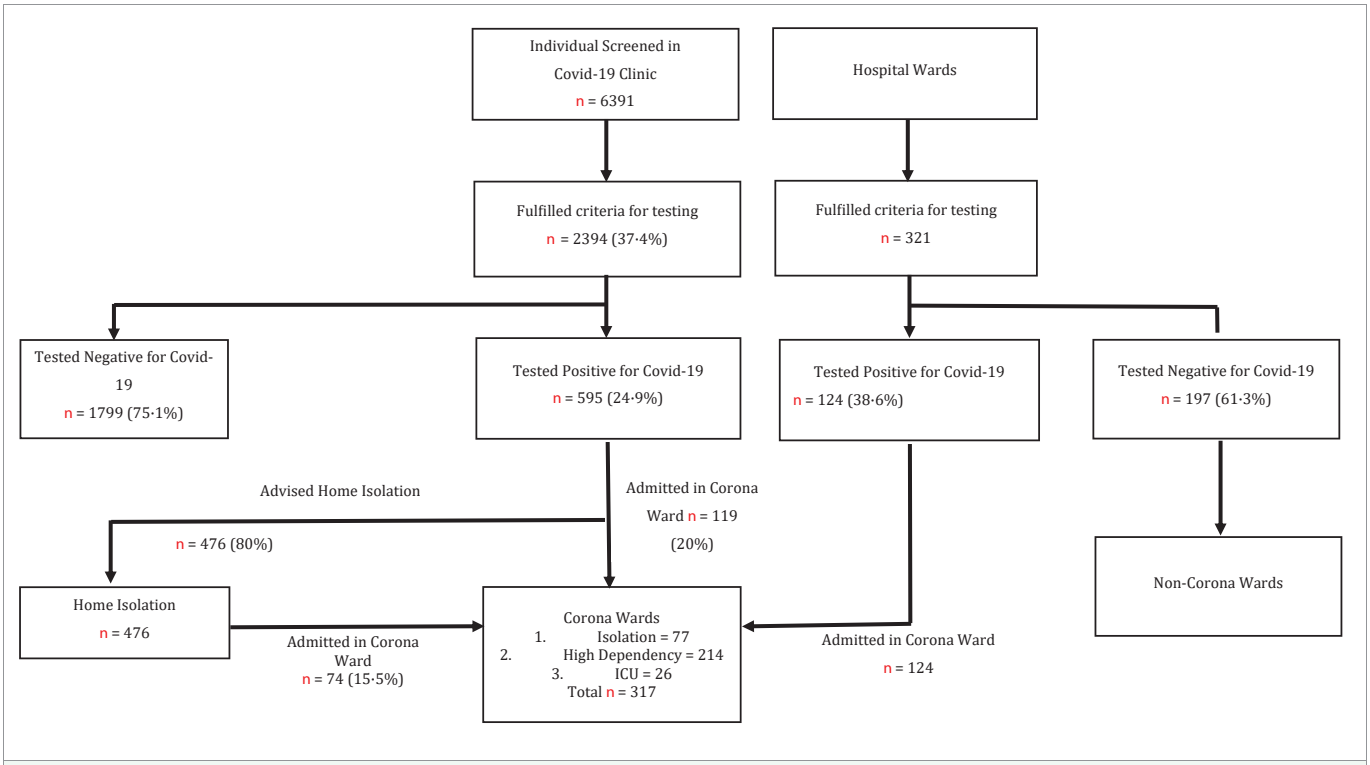

Figure 1: Patient enrollment for screening and assignment for testing and admission. (Period 21st March-15th May 2020)

tested in diabetic patients, median 10.9 (IQR 7.8-15.1) and increased in 59.1%. Enzymes LDH, CPK, ALT and AST were significantly increased in severe group. Inflammatory markers, NLR, D-Dimer, Ferritin and CRP-H were significantly higher in severe group.

Treatment

During admission, antibiotic therapy was given to 102 (32.2%), 63 (54.8%) in the severe group. Initially hydroxychloroquine was administered to 74 (23.3%), later withdrawn from protocol due to prolonged QT interval and arrhythmias in 33 (44.6%). Glucocorticoids were given later in the study period to134 (42.3%), mostly in severe disease. IvIgG and IL-6 receptor antagonist were given to 40 (12.6%) patients, 31 (27%) in severe vs. nine (4.5%) in non-severe group. Dialysis therapy was required in 77 (24.3%) of the patients 63 of these were ESRD patients. Oxygen therapy was given to all patients in severe group 100% *vs.* 36% in non-severe. To improve oxygenation 60% of the patients in severe group were placed in prone position.

Complications

During admission, 119 (37.5%) developed ARDS, 37 (18.3%) in non-severe and 82 (71.3%) in the severe group. Secondary upper respiratory tract infections were more frequent in the severe group 28 (24.3%). Common bacterial organisms were *Coagulase negative staphlococcus* in 24 (32%), *Klebsiella* in 17 (22.7%) and *Acinetobacter* in 11 (14.1%), Fungal organisms were isolated in three (4%), *Candida Tropicalis* in two and *Aspergillus flavus* in one.

Characteristics and outcome of patients given IvIgG and IL-6 receptor antagonist therapy

IvIgG followed by IL-6 receptor antagonist was given to 40 patients, 31 with severe disease and nine with non-severe. Co-morbids were diabetes in 16 (40%), hypertension in 11 (27.5%), COPD in three (7.5%), and six (15%) had ESRD. X-ray chest showed ground glass opacity in 18 (45.2%) and bilateral infiltrates in ten (25%). Complications included ARDS in 32 (80%), secondary infection 19 (47.5%), acute cardiac injury in six (15%) and AKI in three (7.5%). Laboratory parameters before and 48-72 hours after therapy were available in 36 patients as four died before repeat markers (Table 3). No change was observed in neutrophil and lymphocyte counts, while NLR improved. PT remained elevated and APTT decreased. LDH reduced from median 542 to 424 U/L. Inflammatory marker D-Dimer remained elevated and marked reduction was observed in CRP-H from 176 (IQR 80-229) mg/L to 20.4 (IQR 9.8-36.7) mg/L. In all 16 (40%) patients died, four of these had ESRD, seven (17.5%) were alive cured and 17 (42.5%) were alive discharged when asymptomatic.

Outcomes

The overall mortality in 719 COVID-19 positive patients, tested in clinic and wards was 51 (7.1%). Considering 317 admitted patients, the median length of hospital stay of all alive patients was four (IQR 1-7) days and seven (IQR 4-9) days in severe group. The end point were 70 (22.1%) were alive cured (RT-PCR negative), 196 (61.8%) were alive discharged who were asymptomatic and oxygen free for four days but RT-PCR positive and 51 (16.1%) died (Table 2). The number of deaths in 254 non-ESRD admitted patients was 30 (11.8%) and among 63 ESRD patients 21 (33.3%). Of the 51 patients who died 21 (41.2%) had ESRD, ten (62.5%) in non-severe group and 11 (31.4%) in severe group. The mean age of the patients who died was 51.2 ± 17.1 years and 30 (58.8%) were males. At admission LDH was increased n 95.7%, ferritin > 1000 ng/ml in 66·7%, CRP-H >100 mg/L in 66.7% and D-Dimer > 0.5 in 90.5% (Table 4).

Table 1: Demographics and clinical signs and symptoms at admission of COVID-19 infected patients (*n* = 317).

	Results
Age (years)	47·1 ± 14·8 (11-80)
Age range in years	
≤ 30	56 (17.7%)
31-60	208 (65.6%)
> 60	53 (16.7%)
Gender	
Male	211 (66.6%)
Exposure history	
Local and international travel	31 (9.8%)
Attending large public gathering and public dealing	58 (18.3%)
Contact with Covid-19 positive patient	48 (15.1%)
Health care worker	39 (12.3%)
No exposure history	141 (44.5%)
Clinical signs and symptoms	
Duration of symptoms (days)	6 (3-8.7)
Fever	239 (75.4%)
Cough	187 (59.0%)
Dyspnea	141 (44.5%)
Myalgia	21 (6.6%)
Headache	17 (5.4%)
Nausea / Vomiting	14 (4.4%)
Sore Throat	13 (4.1%)
Abdominal pain	11 (3.5%)
Diarrhea	4 (1.3%)
Temperature (°C)	36·9 (36.8-37.2)
≤37·7°C	58 (18.3%)
>37·7°C	259 (81.7%)
Pulse (b/m)	92·5 (84-105)
Respiratory rate (br/min)	24 (20-31.5)
Systolic blood pressure (mmHg)	128 (116-140)
Systolic blood pressure > 140 mmHg	75 (23.7%)
Systolic blood pressure < 90 mmHg	9 (2.9%)
Diastolic blood pressure (mmHg)	79 (70-89)
Diastolic blood pressure > 90 mmHg	57 (17.9%)
Blood oxygen saturation levels (SPO_2 %)	96 (91-98)
Disease severity	
Non-severe	221 (69.7%)
Severe	96 (30.3%)

All the data are n (%), mean ± SD (range), median (IQR).

DISCUSSION

In the study period, COVID-19 positivity rate was 24·9% in the outpatient clinic and 38.6% in the wards. In all 317 admitted patients, 40.4% with severe and 59.6% with non-severe disease. The mean age was 47.1 ± 14.8 year and 66·5% were males. Exposure or contact history was given by 43.2%. Median duration of symptoms was six days (IQR 3-8.7) with fever in 75.4%, cough in 59.0% and myalgia in 44.5%. Main co-morbids were hypertension in 27.1%, diabetes in 27.4% and ischemic heart disease in 6.0%. Of the 317, 63 (19.9%) had ESRD and 16 (5%) were renal transplant recipients. Inflammatory markers ferritin, CRP-H, D-dimer and NLR were increased in > 80% of the patients with severe disease. Antibiotics were given to 32.2%, Glucocorticoids were given to 42.3%, 78.3% in the severe group. IvIgG and IL-6 receptor antagonist were given to 40 patients. Most complications were encountered in severe group, ARDS in 71.3%, secondary infections in 24.3%, acute cardiac injury 12.2%, and multi-organ failure in 8.7%. Of the 317, 83.9% were alive discharged/cured and 16.1% died. Death rate in non-severe was 7.9% and 30.4% in severe group. Death rate in non ESRD patient was 11.8% and 31.4% in ESRD patients. COVID-19 infection in our country spread through individuals who returned from pilgrimage in Iran and thereafter by person to person transmission.

Our positivity rate of 24.9% in general public was much higher than 13.3% in Iceland and 6.9% in Singapore [8,9]. This is most likely due to absence of preventative measures of social distancing and wearing of masks leading to person to person transmission. In agreement with other studies on COVID-19 pneumonia we also found male predominance. The mean age of our patients was 47.1 years while other studies reported a wide range from 47-70 years [10-17]. This is perhaps a reflection of life expectancy in a given population, 67.7 years in Pakistan, 79.1 year in USA and 77.4 years in China [18]. This age variation is also related to the presence of co-morbidities. The frequency of co-morbids in our cases excluding ESRD patients was 37.5%. Others with co-morbids in the range 23.7-32% had lower age ranges 47-51 years [10,11,15] while studies with higher co-morbids 48.4-86% had mean/median age from 55-70 years [12-14,16,17]. In our series patients with severe disease were seven years older and had higher co-morbids. Similar findings have been reported on patients with severe disease, critically ill or in ICU settings [14-16] where patients were older and had high co-morbids. Furthermore, major complications of ARDS, secondary infections, acute cardiac injury and multi-organ failure were more prevalent in older patients with severe disease. This in agreement with other COVID-19 pneumonia studies where these complications were associated with severity of disease and mortality [10-15,17,19].

Radiological investigations at admission were limited to x-ray chest where nearly half of the patients with non-severe disease had normal x-ray while bilateral infiltrates and ground glass opacity was found in 74% of the severe cases. These findings are in agreement with other studies where patient were classified by severity or were in ICU care [10,12,14,15,17]. Initial x-ray findings helped determine the severity of disease and treatment options. A number of laboratory biomarkers associated with COVID-19 disease were tested at admission [20]. In agreement with previous studies patient with severe disease and those in ICU or who died had low lymphocyte count < 1000, high levels of CPK, LDH, AST, ALT, D-Dimer > 1.5 ng/ml Ferritin > 1000 ng/ml, CRP-H >100 mg/L and NLR > 3.0. These findings are in agreement with previous studies on patients with severe disease, ICU admission or who died [10,13-15,19,21]. In fact a number of these markers have been shown to be predictors of severity of disease and mortality [19,21,22].

In absence of specific treatment for COVID-19 pneumonia we used medications that were reported to reverse cytokine storm, prevent secondary infections, benefit outcomes and were available in the country, HCQ [16,23] glucocorticoids [10-16,19,24] IL-6 receptor antagonist (Tocilizumab)[16,25] and IvIgG [1-13,15,19,26]. Initially

Table 2: Clinical characteristics, treatment and outcomes according to disease severity in COVID-19 infected patients (*n* = 317).

	All (*n* = 317)	**Non-severe, *n* (%) 202 (59.6%)**	**Severe, *n* (%) 115 (40.4%)**	***p* - value**
Age (years)	47·1 ± 14·8	44.7 ± 14.6	51.4 ± 14.2	0.000092
Male	211 (66.6%)	130 (64.4%)	81 (70.4%)	0.270
Duration of symptoms (days)	6 (3-8.7)	5 (2-8)	6 (4-9.7)	0.308
Fever	239 (75.4%)	137 (67.8%)	102 (88.7%)	0.000033
Cough,	187 (59.0%)	104 (51.5%)	83 (72.2%)	0.000317
Dyspnea	143 (45.1%)	65 (32.2%)	78 (67.8%)	8.645E-10
Co-morbids	182 (57.4%)	107 (53.0%)	75 (65.2%)	0.034
Hypertension	86 (27.1%)	45 (22.3%)	41 (35.7%)	0.010
Diabetes	87 (27.4%)	49 (24.3%)	38 (33%)	0.092
Ischemic Heart Disease (IHD)	19 (6.0%)	12 (5.9%)	7 (6.1%)	0.958
Chronic Kidney Disease (CKD)	6 (1.7%)	3 (1.5%)	3 (2.6%)	0.672
Chronic Obstructive Pulmonary Disease (COPD)	11 (3.5%)	5 (2.0%)	6 (5.%2)	0.215
Chronic Liver Disease (CLD)	9 (2.8%)	7 (3.5%)	2 (1.7%)	0.496
Tuberculosis	8 (2.5%)	3 (1.5%)	5 (4.3%)	0.144
End Stage Renal Disease (ESRD)	63 (19.9%)	35 (17.3%)	28 (24.3%)	0.132
Renal Transplant Recipients	16 (5.0%)	14 (6.9%)	2 (1.7%)	0.059
Malignancy	9 (2.8%)	6 (3.0%)	3 (2.6%)	0.999
X-Ray Chest findings				
Normal	110 (34.7%)	100 (49.5%)	10 (8.7%)	2.1533E-13
Unilateral Infiltrates	66 (20.8%)	46 (22.8%)	20 (17.4%)	0.257
Bilateral Infiltrates	96 (30.3%)	51 (25.2%)	45 (39.1%)	0.010
Ground Glass Opacity	45 (14.2%)	5 (2.5%)	40 (34.8%)	2.293E-15
Laboratory Findings				
Hemoglobin (Hb) G/L (NR; M: 130-160.5, F: 110.5-50·4)	119·7 ± 27.2	124.6 ± 23.9	111.5 ± 30.0	0.000035
Decreased	140/307 (45.6%)	69/192 (35.9%)	71/115 (61.7%)	0.000011
Absolute neutrophil count (x 10^9/L) (NR; 2·0-7·0)	5.5 (3.3-8.1)	4.5 (2.9-6.9)	7.2 (4.7-10.1)	1.7626E-7
Increased	98/287 (34.1%)	42/179 (23.5%)	56/108 (51.9%)	8.9559E-7
Absolute lymphocyte count (x 10^9/L) (NR; 1.0-3.0)	1.3 (0.9-1.9)	1.5 (1.0-2.1)	1.1 (0·8-1.5)	0·000011
Decrease	93/302 (30.8%)	45/188 (23.9%)	48/114 (42.1%)	0·001
Platelets (x 10^9/L) (NR; 150-400)	230 (171-311)	223.5 (170·0-297.5)	243.5 (173.3 – 338.8)	0·140
Decreased	50/306 (16.3%)	33/192 (17.2%)	17/114 (14.9%)	0·603
Activated partial thromboplastin time (APTT) (sec) (NR; 25.8-32.8)	24·2 (22.0-26.8)	23.8 (21.9-26.2)	25·4 (22.3-28.4)	0·005
Increased	19/287 (6.6%)	8/180 (4.4%)	11/107 (10.3%)	0·055
Prothrombin Time (PT) (sec) (NR; 10.5-13.5)	10.9 (10.4-11.6)	10.8 (10.3-11.4)	11.2 (10.8-11.9)	0.000027
Increased	18/287 (6.2%)	12/180 (6.6%)	6/107 (5.6%)	0.720
Serum creatinine (µmol/L) (NR; 44.2-132.6)	85.7 (67.2-173.7)	78.7 (62.8-116.7)	99·5 (72.5-372.4)	0.000135
Increased	82/300 (27.3%)	41/188 (21.8%)	41/112 (36.6%)	0.005
Urea (µmol/L) (NR; 2.49-6.49)	5.6 (3.8-10·8)	8.6 (4.9-16.2)	4.6 (3·5-7.4)	5.3393E-10
Increased	135/300 (45.0%)	63/188 (33.5%)	72/112 (64.3%)	2.1894E-7
Random blood glucose (RBS) (mmol/L) (NR; < 9.911)	10·9 (7.8-15.1)	4.9 (7.2-14.9)	11.2 (7·9-16.5)	0.653
Increased	39/66 (59.1%)	22/39 (56.4%)	17/27 (63.0%)	0.594

Lactate Dehydrogenase (U/L) (NR; 140-271)	306.5 (207.3-491.8)	249.5 (191-403)	443.5 (312.5-719.5)	2.2597E-14
Increased	173/296 (58.4%)	78/186 (41.9%)	95/110 (86.4%)	6.6214E-14
Creatine phosphokinase (CPK) (U/L) (NR; M: 38-174, F: 26-140)	103 (62-230)	100 (62-186·7)	116 (64-329.5)	0.138
Increased	94/283 (33.2%)	53/182 (29.1%)	41/101 (40.6%)	0.050
Total Bilirubin (µmol/L) (NR; 3.42-17.10)	9.2 (6·7-13.5)	8.7 (5.9-12.3)	10.1 (7.5-13.4)	0.034
Alanine Aminotransferase (ALT) (U/L) (NR; 10-40)	30 (18-48.8)	27 (17-43.5)	37 (21-62)	0.005
Increased	87/280 (31.1%)	47/177 (26.6%)	40/103 (38.8%)	0.032
Aspartate Aminotransferase (AST) (U/L) (NR; 10-42)	40.5 (28-62.8)	35 (25-54)	52 (36-82)	0.000001
Increased	130/280 (46.4%)	63/177 (35.6%)	67/103 (65.0%)	0.000002
Troponin-I (pg/mL) (M: Upto 34.2, F: Upto 15.6)	21.6 (4.3-95.9)	30.3 (20.4-65.8)	12.5 (3.7-102.0)	0.141
Increased	20/48 (41.7%)	6/10 (60%)	14/38 (36.8%)	0.282
Neutrophil Lymphocyte Ratio (NLR) (NR; 1·0-3.0)	4.4 (2.1-8.1)	3.2 (1.6-5.5)	6.3 (4.1-10.2)	1.0846E-10
Increased	193/303 (63.7%)	96/189 (50.8%)	97/114 (85.1%)	1.8123E-9
D-dimer (mg/L) (NR; < 0.5)	0.69 (0·34-2.63)	0.430 (0.27-1.15)	1.94 (0.66-4.83)	7.1938E-11
Increased	167/277 (60.3%)	81/171 (47.4%)	86/106 (81.1%)	2.3784E-8
≥ 1.5	90/277 (32.5%)	34/171 (19.9%)	56/106 (52.8%)	1.2651E-8
Ferritin (ng/ml) (NR; M: 21.81-274.66, F: 4.63-204.0)	391.6 (126.8-1043.2)	255.71 (69.64 - 547.89)	833 (407.95 - 2133.9)	2.1333E-13
Increased	177/290 (61.0%)	87/183 (47.5%)	90/107 (84.1%)	7.1782E-10
> 1000	75/290 (25.9%)	30/183 (16.4%)	45/107 (42.1%)	0.000001
High Sensitivity C Reactive protein (CRP-H) (mg/L) (NR; <7.44)	55.3 (8.2-170)	19.9 (3.4-71.9)	154.9 (86.4-249.6)	3.1592E-20
Increased	225/287 (78.4%)	121/180 (67.2%)	104/107 (97.2%)	2.4224E-9
>100	105/287 (36.6%)	37/180 (20.6%)	68/107 (63.6%)	2.6224E-13
Treatment				
Antibiotics	102 (32.2%)	39 (19.3%)	63 (54.8%)	7.9903E-11
Hydroxychloroquine (HCQ)	74 (23.3%)	31 (15.3%)	43 (37.4%)	0.000008
Anticoagulants	70 (22.1%)	11 (5.4%)	59 (51.3%)	2.9609E-21
Glucocorticoids	134 (42.3%)	44 (21.8%)	90 (78.3%)	1.2772E-22
IL-6 receptor antagonists	40 (12.6%)	9 (4.5%)	31 (27.0%)	6.6001E-9
IVIgG	40 (12.6%)	9 (4.5%)	31 (27.0%)	6.6001E-9
Dialysis	77 (24.3%)	43 (21.3%)	34 (29.6%)	0.098
Oxygen Therapy	187 (59.0%)	72 (36.0%)	115 (100%)	4.0352E-29
Mechanical Ventilation	31 (9.8%)	··	31 (27.0%)	NA
High Flow Nasal Cannula	14 (4.4%)	··	14 (12.2%)	NA
Prone Position	108 (34.1%)	37 (18.3%)	71 (61.7%)	4.3992E-15
ICU Admission	72 (22.7%)	··	72 (62.6%)	NA
Complications				
Acute Respiratory Syndrome	119 (37.5%)	37 (18.3%)	82 (71.3%)	7.4301E-21
Secondary Infections	45 (14.2%)	17 (8.4%)	28 (24.3%)	0.000093
Acute Cardiac Injury	20 (6.3%)	6 (5.2%)	14 (12·2%)	0.186
Acute Kidney Injury	14 (4.4%)	8 (4.0%)	6 (5.2%)	0.600
Multi Organ Failure	10 (3.2%)	··	10 (8.7%)	NA
Shock	4 (1.3%)	··	4 (3.5%)	NA
Outcome				
Alive Discharge	196 (61.8%)	130 (64.4%)	66 (57.4%)	0.220
Alive Cured	70 (22.1%)	56 (27.7%)	14 (12.2%)	0.001
Death	51 (16.1%)	16 (7.9%)	35 (30.4%)	0.005
Length of hospital stay of alive patients (days)	4 (1-7)	3 (1-9)	7 (4-9)	0.000075

All data are n (%); n/N (%); mean ± SD; median (IQR); NR (Normal Range); NA (Not Applicable).

Table 3: Laboratory parameters in IvIgG / IL-6 receptor antagonist therapy (*n* = 36).

	Before	After	*p*-value
Absolute Neutrophil Count (x 10^9/L); (NR; 2.0-7.0)	7.90 (5.51-10.09)	7.97 (5.58-11.57)	0.555
Increase	22 (62.9%)	21 (58.3%)	0.229
Absolute Lymphocyte Count (x 10^9/L); (NR; 1.0-3.0)	0.98 (0.71-1.56)	1.10 (0.76-1.77)	0.315
Decrease	19 (52.8%)	16 (44.4%)	0.999
Neutrophil / Lymphocyte Ratio; (NR; 1.0-3.0)	7.1 (4.62-10.85)	9.5 (5.2-17.55)	0.016
Increased	33 (91.7%)	31 (86.1%)	0.000004
Platelets (x 10^9/L); (NR; 150-400) Median (IQR)	245.5 (199.25-310.75)	296.0 (217.0- 394·0)	0.009
Decrease	2 (5.6%)	2 (5.6%)	2.383E-7
Prothrombin Time (sec) (NR; 10.5-13.5)	10.9 (10.5- 11.4)	11.4 (10.9-12.4)	0.001
Activated Partial Prothrombin Time (sec) (NR; 25.8-32.8)	23.6 (21.8-27·6)	21.4 (20.5-24.1)	0.001
Serum Creatinine (µmol/L); (NR; 44.2-132.6)	91.5 (72.0-125.3)	77.8 (65.6-189.4)	0.044
Lactate Dehydrogenase (LDH) (U/L) (NR; 140-271)	524.0 (377.25-820.5)	424.0 (333.0-767.0)	0.050
Creatine Phosphokinase (CPK) (U/L) (NR; M: 38-174, F: 26-140)	173 (68.5-356.5)	132.5 (55.5-548.3)	0.574
Alanine Aminotransferase (ALT) (U/L) (NR; 10-40)	40.5 (25.0-54.75)	46.0 (31.0-78.0)	0.015
Aspartate Aminotransferase (AST) (U/L) (NR; 10-42)	59.5 (35.5-85.25)	51.0 (31.5-79.5)	0.969
D-Dimer (mg/L) (NR; < 0.5) Median (IQR)	1.04 (0.44-2.44)	3.29 (1.37-6.21)	0.001
Increased	24 (66.7%)	33 (91.7%)	0.002
High Sensitivity C Reactive Protein (H-CRP) (mg/L); (NR; < 7.44)	176 (80-229)	20.4 (9.8-36.7)	0.000002
Increased (> 100)	17 (47.2%)	3 (8·3%)	0·001
Ferritin (ng/ml); (NR; M: 21.81-274.66, F: 4.63-204.0)	1035.0 (464.0-2423·0)	761.0 (271.96-2336·0)	0.055
Increased (> 1000)	29 (80.6%)	27 (75.0%)	0.001

All data are n (%), median (IQR), NR (Normal Range).

Table 4: Characteristics of expired patients (*n* = 51).

	Overall (*n* = 51)	Non-Severe, n (%) 16 (7.9%)	Severe, n (%) 35 (30.4%)	*p*-value
Age (years)	51.2 ± 17.1	50.9 ± 15.0	51.1 ± 18.1	0.968
< 30	9 (17.6%)	1 (6.3%)	8 (22.9%)	0.132
31-60	25 (49.0%)	11 (68.8%)	14 (40.0%)	
> 60	17 (33.3%)	4 (25.0%)	13 (37.1%)	
Gender				
Male	30 (58.8%)	12 (75.0%)	17 (48.6%)	0.137
Co-morbids				
Diabetes	22 (43.1%)	9 (56.3%)	13 (37.1%)	0.201
Hypertension	25 (49.0%)	11 (68.8%)	14 (40.0%)	0.057
End stage renal disease	21 (41.2%)	10 (62.5%)	11 (31.4%)	0.036
Ischemic heart disease	9 (17.6%)	4 (25.0%)	5 (14.3%)	0.436
COPD	2 (3.9%)	1 (6.3%)	1 (2.9%)	0.533
CKD	2 (3.9%)	0 (0.0%)	2 (5.7%)	0.999
Cancer	4 (7.8%)	1 (6.3%)	3 (8.6%)	0.999
CLD	3 (5.9%)	2 (12.5%)	1 (2.9%)	0.229
Acute kidney injury	3 (5.9%)	0	3 (8.6%)	0.540
Tuberculosis	3 (5.9%)	1 (6.3%)	2 (5.7%)	0.999
Renal transplant	1 (2.0%)	0	1 (2.9%)	0.999

X-Ray findings				
Normal	6 (11.8%)	3 (18.8%)	3 (8.6%)	0.111
Unilateral infiltrates	11 (21.6%)	6 (37.5%)	5 (14.3%)	
Bilateral infiltrates	15 (29.4%)	4 (25.0%)	11 (31.4%)	
Ground glass opacity	19 (37.3%)	3 (18.8%)	16 (45.7%)	
Inflammatory Markers				
LDH > 271	44/46 (95.7%)	12/13 (92.3%)	32/33 (97.0%)	0.490
Ferritin > 1000	28/42 (66.7%)	7/11 (63.6%)	21/31 (67.7%)	0.433
CRP-H > 100	28/42 (66.7%)	8/11 (72.7%)	20/31 (64.5%)	0.723
D-Dimer > 0.5	38/42 (90.5%)	11/12 (91.7%)	27/30 (90.0%)	0.999
PT > 13.5	11/44 (25.0%)	5/12 (41.7%)	6/32 (18.8%)	0.114
APTT > 32.8	15/43 (34.9%)	5/12 (41.7%)	10/31 (32.3%)	0.826
CPK (M > 174, F > 140)	19/44 (43.2%)	8/30 (26.7%)	11/14 (78.6%)	0.003
NLR > 3.0	45/49 (91.8%)	14/14 (100%)	31/35 (88.6%)	0.312
All data are mean ± SD, n (%), n/N (%).				

HCQ was used but later withdrawn due to adverse side effects and negative reports in literature [27].

The patients who received this regime had a combination of older age, severe disease, high inflammatory markers, and ARDS. Post therapy improvements were observed in lymphocyte counts, LDH, Ferritin, and CRP-H. Similar findings and improved outcomes were reported by others [25,26,28]. All the patients in severe group required oxygen therapy, mechanical ventilation in 27%, and high flow nasal cannula in 12%. We placed 60% of the patients in prone position to improve oxygen. Similar has been the experience of others in patients with ARDS and Covid-19 pneumonia [17,29].

The overall mortality in 719 COVID-19 positive patients in clinic and wards was 51 (7.1%). In the admitted patients the rate was 11.8% excluding ESRD patients and 33% in ESRD patients. The reported death rates vary from 1.4%-28% in [1,2,4-6] with high rates of 39-52% in critically ill patients and those with ARDS [10-11,16]. These variations most likely depend on co-morbids, severity of disease and treatment given in different situations. The death rate in ESRD patients was 33%, comparable to reported 31% by others [30]. This high death rate suggests that ESRD patients are at a higher risk of mortality.

This study has a number of strengths. Firstly, it reports COVID-19 pneumonia from a developing country where the disease spread by person to person transmission and majority had non-severe disease. Secondly, with limited treatment facilities our mortality rates were comparable to those reported from high income countries. Thirdly, our combination therapy of IvIgG/IL-6 receptor antagonist significantly reduced inflammatory markers resulting in low mortality and secondary infections in our severe cases. There are several limitations in our study. Firstly, due to paucity of testing and admitting facilities we could not test all persons from general public and also sent many positive patients in home isolation where 15% returned with severe symptoms. Secondly, we were not able to test for other virus infections nor did we give any antiviral therapy which may have contributed to our mortalities rates. Finally, our radiological investigations were limited to x-ray due to non-availability of Computerized Tomography where we may have missed early signs of COVID-19 infection.

CONCLUSION

This study provides experience of COVID-19 pneumonia from a developing country where the disease spread by person to person transmission. The positivity rate in general public was 24.9% and 38.6% in admitted patients. In the 317 hospitalized patients 40.4% had severe disease and 59.6% non-severe with mortality rates of 30.4% and 7.9% respectively. Severe disease was associated with older age, high inflammatory markers more frequent co-morbidities, complications and mortality rates. Awareness program for social distancing and wearing of masks is needed to prevent spread of COVID-19 infection.

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DECLARATION OF INTERESTS

We declare no competing interests.

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