Original Article

Clinical Characteristics and Risk Factors Analysis of COVID-19 Infections- A Single Center Observational Study

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Abstract

Introduction: COVID-19 emerged as a major public health outbreak in late 2019. Bangladesh reported its first case on 8th March 2020 and at Sylhet Div area, first case detected in April 2020, authority adopted a policy of extensive contact tracing, quarantine and initially hospitalizing of all cases. Clinical characteristics of COVID-19 cases have been described as per national and WHO guideline.

Objectives: To analyze clinical characteristics and the risk factors of COVID-19 infection.

Methods: Clinical records of all COVID-19 confirmed cases aged ≥12 years admitted to COVID Unit or treated at home isolation with complete outcomes at Sylhet area were included in the study. Duration of this study was 1st April to 27th December 2020. Epidemiological history, comorbidities, clinical features, investigations, management and complications of all cases were recorded in preform data sheet and analyzed. Variables were compared between mild and severe diseases.

Results: The sample comprised of 515 cases (mean age 30.98 years, male 81.55%). Majority were mild (92%) and 6.4% required intensive care, with 85% admitted within the first five days. Older age (≥51 years), underlying comorbidities, cough, breathlessness, reduced oxygen saturation and abnormal chest radiographs on admission were significant determinants for severity. The case fatality rate was 0.77% and the four commonest complications were ARDS (4.40%). liver injuries (4.07%), bacteraemia (2.33%) and kidney injuries (1.16%).

Conclusion: Lower case fatality rate was possibly contributed by young cases with mild diseases and early hospitalization. Abnormal chest radiographic, elderly and other comrbidities require frequent measurement of oxygen saturation with pulse oximetry and close monitoring within the first few days to detect early deterioration and to take appropriate measures. Ivermectin seems to be effective in the treatment of Covid-19 infection but need further large multi-center case control study.

Key words: Coronavirus Disease 2019 (COVID-19), Acute Respiratory Distress Syndrome (ARDS), Reverse-Transcriptase-Polymerase Chain Reaction (RT-PCR).

Introduction

The coronavirus disease 2019 (COVID-19) pandemic caused by the novel severe acute respiratory syndrome coronavirus-2 (SARS- CoV-2) has infected more than 30 million people with over 2,200,000 deaths worldwide[1]. Bangladesh reported its first case on 8th March 2020. Most of the initial reported cases were relatives of overseas workers specially who return from Italy. In April, May and June, Bangladesh had experiences highest number of case detection, hospital admission and case fatality. Sylhet Combined Military Hospital gives medical support to Armed Forces personnel, their families, parents and in-laws' of Sylhet area.

Initially Sylhet Covid-19 control cell escalated its preparedness response by implementing contact tracing, early identification of cases and compulsory hospital admission regardless of disease severity strategies, aiming to break the cycle of transmission but at one stage bound to allow mild cases to get treatment at home or unit isolation. As of 28th December 2020, COVID-19 cases in Sylhet area numbered 515 with 511 recoveries and 04 fatalities, giving CFR (case fatality rate) of 0.77%. Overall, 95% presented with a mild disease on admission and 3.5% subsequently progressed to severe disease[2]. Out of 4 dead cases, only one was serving soldier and rest were retired solders/parents of >51 years of age with multiple comorbidities. Mild cases treated symptomatically along with either hydroxyl-chloroquin/Ivermectin with or without antiviral. Sever and critical cases got treatment in HDU (High Dependency Unit) / ICU (Intensive Care Unit) set up with extra medication like oxygen support, steroid, antibiotics with or without biologics. Reports on case fatality rate vary between geographical regions with studies reporting different outcomes and risk factors[3]. This disparity has raised a few postulations including the effectiveness of government policies, epidemic preparedness and response, and bias in reporting of the actual number of cases[4].

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Materials and Methods

This was a observational study, carried out among the Covid-19 patients treated in military establishment in Sylhet area during April 2020 to December 2020. The patients reporting with symptoms suggestive of Covid-19 infection to the fever clinic in Sylhet either physically or over Telephone were included for study. The Nasopharyngeal and/or oropharyngeal swab samples were used for reverse-transcriptase-polymerase chain reaction (RT-PCR) analysis was done either at civil or at CMH, Sylhet Covid-19 PCR Lab with other relevant investigations. RT-PCR for Covid-19 positive cases and/or HR-CT Scan of Chest positive evidence for Covid-19 infection were included for the study.

The composition of the patients was male and female of all ages above 12 years and from all socioeconomic status but maximum are of young servicemen. The clinical course of each patient was monitored continuously by clinical history, monitoring the severity of respiratory and other symptoms, oxygen saturation and serial investigations daily or as frequently on the basis of severity of the disease. Symptoms, physical signs and laboratory data were documented on pre-design questioners. The cases were classified according to WHO guideline.

Cases admitted at designated hospitals were managed according to COVID-19 Management Guideline of CMH, Dhaka based on the national guideline of Bangladesh and WHO[5]. Each case was staged according to clinical severity; stage-I: asymptomatic case, stage-II: symptomatic without pneumonia, stage-III: pneumonia without hypoxia, stage-IV: pneumonia with hypoxia requiring oxygen supplementation therapy and stage-V: critically ill. Close monitoring for signs of early deterioration and appropriate aggressive interventions were instituted. All cases were admitted at hospital or isolated at home/mess for 14 days, or until free of SARS-CoV-2 carriage by repeat RT-PCR. We classified stages-I to III diseases as mild diseases, whilst stages-IV and V as severe diseases. We defined disease complication according to ISARIC (International Severe Acute Respiratory and Emerging Infection Consortium)-WHO Case Report Form[6].

Results

The total number of 515 Covid-19 patients was studied. Out of which 420(81.55%) were male and 95(18.45%) were female. Male female ratio was 4.42:1. Age range was 12 to71 years (mean age: 30.98 years) with more than half of the severe cases aged ≥51 years (Table-I). A significant number of cases (62.7%) had a history of contact with known COVID-19 cases within the past 14 days of diagnosis and/or symptoms onset.

Table-I: Distribution of patients according to age, contact history and sex (n=515)

Variable		n	%
Age range (years)	12-30	285	55.34
	31-50	198	38.45
	>51	32	6.21
Contact history with COVID-19 cases	Contacted	323	62.7
	Not contacted	192	37.3
Sex	Male	420	81.55
	Female	95	18.45

Male:Female= 4.42:1; Mean age 30.98 Years

Table-II shows that almost 54.5% remained afebrile up to admission. Similar out of 515 COVID-19 cases, 153(32.5%) had cough and/or sputum. Other symptoms included sore throat (80, 15.3%) and rhinorrhoea (53, 10.3%). Only less than 2.8% of cases presented with anosmia, 18(3.5%) of cases reported diarrhoea, the median of illness onset to admission was 3 days. Those who had severe COVID-19 were admitted later at day 6 as compared to those with mild disease. About 25% of admitted cases had at least one comorbidity and some have multiple comorbidities. Hypertension was the most common comorbidity (46, 8.93%) followed by diabetes mellitus (25, 4.85%) and asthma (13, 2.52%). About 48(9.32%) active smokers while 26(5.0%) had severe COVID-19 disease. Table–II also shows out of 515 COVID-19 studied cases 258(50.2%) presented with stage-I and 162(31.6) with stage–II and maximum in stage-I and II (81.8%), followed by 70(13.6%) at stage-III, 90(3.6%) at stage-IV while 6(1.1%) presented at stage-V.

Table-II: Clinical History, comorbidities and disease staging of COVID-19 cases upon admission

Variable		n	%
Presence of symptoms	**Cough**	153	32.5
	Fever	234	45.5
	Sore throat	80	15.3
	Running nose	53	10.3
	Shortness of breath	27	5.3
	Diarrhoea	18	3.5
	Anosmia	14	2.8
	Nausia & vomiting	7	1.8
	Ageusia	4	0.77
Presence of comorbidity	Hypertension	46	8.93
	Diabetes mellitus	25	4.85
	Asthma	13	2.52
	Chronic pulmonary disease	10	1.94
	Chronic heart disease	8	1.55
	Obesity	6	1.16
	Chronic kidney disease	4	0.78
	Active smoking	48	9.32
Severity of Cases	Stage-I	258	50.2
	Stage-II	162	31.6
	Stage-III	70	13.6
	Stage-IV	90	3.6
	Stage-V	6	1.1

Higher systolic blood pressure, pulse rate, respiratory rate and temperature were observed in those with severe diseases, many of whom were found very low oxygen saturation. Among 442(85.82%) cases underwent chest X-ray imaging, 322(72.85%) were reported normal and 120(27.15%)were abnormal in the form of peumonitis or Ground Glass Opacities (GGO). HR-CT- Chest done in 126(24.47%) cases out of whom 63(12.2%) were found ground-glass opacities followed by consolidation 32(6.2%), interstitial opacities 21(4.07%) and nodular opacities (10, 2.0%). Lymphopenia, coupled with raised inflammatory markers, were observed in the severe disease group, apart from increased liver transaminases levels and serum creatinine (Table-III).

Table-III: Imaging findings and laboratory parameters (n=442)

Variable		Number	Percentage
X-ray finding (n=442, 85.82 %)	Normal	322	72.85
	Abnormal	120	27.15
CT Scan of Chest (n=126, 24.47%)	Ground Glass Opacities	63	12.2
	Consolidation	32	6.2
	Interestitial Opacities	21	4.07
	Nodular Opacities	10	2.0
Laboratories Parameters (n=515, 100%)	ECG-Bardicardia	8	1.55
	Leucopenia	55	10.68
	Leucocytosis	76	14.75
	Lymphopenia	126	24.47
	Thrombocytopenia (<100000/cmm)	45	8.74
	ALT (>50U/L)	326	63.30
	LDH (<130 mg/dl)	197	38.25
	S. Creatinine (>1.17 mg/dl)	9	1.75
	CRP (>10 µgm/ml)	286	55.53
	D-Dimmer (>0.50 µgm/ml)	175	33.98

Table-IV shows the drugs used for the treatment of COVID-19 cases, their complications and outcome; In initial days; mild cases were treated with Hydroxychloroquine and Doxycycline but later on with Ivermectin and Doxycycline with other supportive medications including antithrombotic. Antiviral agents, especially Favipiravir or Remdasivir were initiated in 100% of severe disease but many of mild diseases either with or without comorbidities. Steroids and tocilizumab or Bevacizumab were prescribed sparingly. Acute liver and kidney injuries, and acute respiratory distress syndrome (ARDS) were the three most common complications seen in our COVID-19 cases. Among those severe cases, 7.7% developed secondary bacteraemia. Other complications developed in severe COVID-19 cases were cardiac arrhythmias and stroke. Duration of hospitalization was significantly longer among severe cases with a median of 14 days. This recorded 04 in hospital deaths with a case fatality rate (CFR) of 0.77%. All mortality occurred among the severe disease group, except one young soldier with mild disease, succumbed to sudden cardiac arrest in sleep.

Table-IV: Clinical use of medications, complications and clinical outcomes of COVID-19 cases

Variable		Number	Percentage
Clinical use of medications	Hydroxychloroquine	96	18.6
	Ivermectine	376	73.0
	Antibiotics	326	63.30
	Favipiravir	215	41.75
	Remdesivir	18	3.49
	Tosilizumab	15	2.91
	Bevacizumab	9	1.75
	Steroid	106	20.58
	Enoxaparin	64	12.42
	Rivaroxaban	198	38.44
Complications	Acute Respiratory Distress Syndrome	33	6.40
	Liver injury	21	4.07
	Acute renal injury	6	1.16
	Bacteraemia	12	2.33
	Arrhythmia	4	0.77
	Gastrointestinal haemorrhage	2	0.38
	Stroke	1	0.19
Clinical outcomes	Admission into Intensive Care Unit	33	6.40
	Death	4	0.77
	Duration of hospitalization (7-20 days, maximum 14 days)		

Discussion

This observational study in Sylhet area for all laboratory-confirmed COVID-19 cases representing a whole country's experience with definite outcome showing low mortality. We reported up to 95% having mild diseases with a low case fatality rate (CFR) of 0.77%. These findings were similar to other reports[1,7,8]. Older groups were mostly symptomatic and for those with comorbidities, the likelihood of progressing to poorer outcomes was high[9,10]. In this study, hypertension (8.93%), diabetes mellitus (4.85%), asthma (2.52%), cardiovascular disease (1.55%) and chronic kidney disease (0.78%) were the most prevalent comorbidities[11]. This distribution of comorbidities was much lower, as reported by Fu L et al in China[12]. In this cohort, underlying comorbidities such as Hypertension, Diabetes, chronic kidney disease and chronic pulmonary disease were associated with severe COVID-19 disease. The CFR for coronavirus disease in Bangladesh was low as compared to other coronavirus epidemics such as SARS-CoV (9.5%) and MERS- CoV (34.4%)[13]. In Sylhet area, the strategy of hospital isolation of all suspected and confirmed individuals contributed to the reduction of local transmission. This approach was similar to countries demonstrated lower CFR such as Singapore (0.05%) and Republic of Korea (2.10%) where "trace, test and treat" was practised[14-16]. In countries where selective hospitalization was implemented, the CFR was much higher in Italy (14.24%), Iran (5.47%), United States (3.44%) and United Kingdom (15.25%)[9,16]. This stringent hospital/ mandatory isolation containment has helped us in identifying individuals at risk of deterioration and allows for early intervention when they do deteriorate. The majority of affected individuals in our study were of younger age group, with a median age of this sample at 30.98 years with a male preponderance. In contrast, New York, China, Korea and Singapore reported a much older group of cases between 40 and 63 years. This skewed age distribution could be related to the more younger males were involved in Military service and living in close proximities in unit conception. As asymptomatic transmission and pre-symptomatic transmission of SARS-CoV-2 happens, clustering effects among young males can contribute to a higher transmission rate[17]. In addition, effective contact tracing, early confinement and stringent social distancing limited the spread of disease from younger, mobile population to the elderly, as compared to overseas study. We found that less than 35% of cases had a fever on admission, and this finding was similar to large cohort studies in China and New York[1,7]. In other coronavirus epidemics such as MERS and SARS, about 98–100% presented with fever on admission[13]. When clinical endpoints were considered, there were significant differences in severity of COVID-19 based on gender[18]. Majority of severe cases had non-specific radiographical changes like ground-glass opacity; bilateral lower zone involvements were consistent with computed tomography (CT) findings as described in other studies[19]. China utilized CT scan with an artificial intelligent solution and was found to be useful for early detection. CT Chest alone may be sufficient for COVID-19 detection and management specially suspected but negative RT-PCR cases[20]. Various risk factors have been associated with the worst prognosis throughout the illness[9,10,20.] In this sample, those with higher C-reactive protein, older age group, tachypnoea, abnormal CXR findings are also significantly associated with disease severity. These findings were similar to Chang et alin a sample of 211 cases[21,22]. Mild cases were treated with Ivermectin and/or antiviral with other supportive care but in patients with moderate to severe cases with comorbidities were also added antithrombotic and antibiotics. Steroid usage in our cohort (20.58%) was similar as compared to four studies from China, ranging from 7.6 to 44.9%[21-23]. Although one study indicated steroid may have a beneficial effect by reducing mortality in ARDS, it is not conclusive for routine use of steroid in COVID-19 treatment[23]. However, some studies showed a higher prevalence of ARDS (10–40%) presumably due to delay in hospitalisation[24]. The most common extra-pulmonary manifestations were deranged liver function (21,4.07%) and acute kidney injury (6, 1.16%). A review on liver injuries by Cha et al postulated that this complication could be due to direct viral attack on hepatocyte, cytokine storm or hypoxic injury secondary to severe acute respiratory syndrome[25]. First five days of hospitalization was vital in COVID-19 management as most of the ICU admission in the sample occurred at this period. Similarly, Gupta et al found in a study of 2215 ICU cases in the USA, the median time from onset to ICU admission was 7 days[26]. Cases with higher CRP level on admission had longer ICU stay, possibly due to its correlation with the level of inflammation reflecting severe COVID-19 disease in early stage[23].

Conclusion

In Armed Forces, this COVID-19 cohort was younger, with the majority having a mild disease and low mortality. Identification of factors associated with severe disease and early hospitalization allows risk stratification and monitoring of cases for timely interventions. Severe cases requiring ICU support are all those late reporters and having comorbidities; covid related complications and mortality are usually found in them.

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