

## Original Research Article

# Overview of 254 mild cases of COVID-19 in Bangladeshi cohort: a cross-sectional observation

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## ABSTRACT

**Background:** The first recognition of a cluster of COVID-19 patients in China in late 2019, has become a major concern due to its greater transmissibility and vulnerability of the patient to turn to fever, cough, breathlessness, pneumonia then eventually severe acute respiratory distress syndrome requiring intensive care unit (ICU) support. But most of the affected patients get cured following mild symptoms and very only a few of them get hospitalized. The objective of the study was to observe the demographic characteristics, clinical symptoms, comorbidities, and biomarkers (hematological, inflammatory, hepatic, renal, and metabolic) of mild cases of COVID-19 infected patients admitted to the hospital during the peak four months of the pandemic.

**Methods:** Age, sex, symptoms, comorbidities, and biomarkers (Hb%, WBC, lymphocyte, neutrophil, platelet count, HCT(hematocrit), NLR(neutrophil-lymphocyte ratio, d-NLR derived neutrophil-lymphocyte ratio, PLR(platelet-lymphocyte-ratio), d-Dimer, ferritin, CRP(C-reactive protein), PT(prothrombin time), INR(international normalized ratio), SGPT, S.creatinine, HbA<sub>1c</sub> of all rt-PCR positive mild cases were recorded in this retrospective observational study in a tertiary care hospital dedicated to COVID-19 at Dhaka, Bangladesh was done from 15th May to 9th September, 2020. Age, sex, symptoms, and comorbidities were compared by chi-square test and biomarkers were compared by one-way ANOVA.

**Results:** Out of 254 cases 44 were female and 210 were male with a ratio of 1:4.77. Average age was 39.04. Largest population belongs to the 30-39 years of age range. Among the symptoms, anorexia (18.5%), fever (17.71%), and anosmia (16.9%) were most prevalent symptoms among the mild cases. However, diabetes mellitus (DM) and hypertension (HTN) were predominant comorbidities. Mostly all the biomarkers were significant among groups (Hb%, Total WBC, neutrophil count, platelet count, HCT, NLR, d-NLR, d-Dimer, ferritin, CRP, PT, SGPT, creatinine, HbA<sub>1c</sub> except lymphocyte count, PLR, and INR. The severity of disease progression depends on the co-morbidity and hyper-responsiveness inflammatory or immunological biomarkers to predict.

**Conclusions:** In mild cases of COVID-19 male predominance was more and the most affected group was 30-39 years. They suffered more from anorexia and fever and DM and HTN were common comorbidities. Mostly all the biomarkers were significant. Moreover, further large-scale studies are needed to evaluate the number of mild cases and their prognostic features to develop and modify the treatment strategy and public health awareness time to time.

**Keywords:** COVID-19, Mild cases, Symptoms, Comorbidities, Biomarkers, Bangladesh

## INTRODUCTION

From late December 2019 to the end of February 2020, more than 116 million people have been affected globally with more than 2.6 million died due to the COVID-19 pandemic.<sup>1</sup> This large number of patients shows a case fatality ratio ranging from 0.1% to 25% in different countries, demonstrating that severe acute respiratory syndrome (SARS) corona virus is a virulent and highly contagious disease.<sup>2</sup> Total affected cases and death become exponential and the WHO declared COVID-19 as pandemic on 11th March, 2020. However, the first case was detected on 8th March 2020 in Bangladesh. From then up to 5th March 2021, Bangladesh deals with a total of 549,184 confirmed cases and a death rate of 8441.<sup>3</sup> There may be many more undiagnosed cases due to limited facilities. Bangladesh has the second-highest infected case after India in South-East Asia.<sup>4</sup>

The disease can present with the typical presentation of severe acute respiratory illness; fever and respiratory symptoms, cough, and shortness of breath. The virus also manifests severe unusual features like diarrhea, stroke, musculoskeletal or cardiac complications lead to hospitalizations or even death.<sup>5-7</sup> Therefore, symptoms of the variable region can reflect the consequences of the COVID patients along with mortality as the asymptomatic and mild cases are rising exponentially.<sup>8</sup> Besides the dissemination in public media and press, there is scarcity of published studies particularly focused on mild cases of COVID-19 around the globe and in Bangladesh till today.<sup>9-11</sup> Practically, the clinical syndromes have been categorized into four groups: mild, moderate, severe, and critical. Mild cases show influenza-like illness (ILI), moderate with pneumonia (CRB 65 score 0), severe patients with severe pneumonia, whereas severe pneumonia patients may show severe pneumonia, sepsis, or ARDS, the septic shock which may be regarded as critical.<sup>12</sup> Almost 80% of the infections are self-limiting and hospital admissions may not require them. Around 15% of the patients with comorbidities such as diabetes, heart problems, hypertension, and obesity are prone to develop severe pneumonia. The rest of the 5% reported developing respiratory failure, ARDS, end-organ failure and require ICU support for a long period.<sup>12</sup>

As maximum patients suffer from mild symptoms, they do not require to get hospitalized. The rest of them get admitted to the hospital for proper management. Thus, the maximum of the cases remain undiagnosed and the disease progression is unnoticed. As COVID-19 has no specific treatment, in Bangladesh care was taken to treat the mild symptoms (cough, pyrexia), whereas several medications were initially tried according to National guideline and O<sub>2</sub> therapy, high flow nasal cannula (HFNC), non-invasive ventilation (NIV) and ventilator support along with different pharmacotherapy have been given to the critically ill patients.<sup>12</sup> A study on 99 ICU patients reported that instrumental oxygen therapy through HFNC had a

better outcome in critical patients than NIV or MV, but never reported in mild cases.<sup>13</sup>

There is no notable pharmacotherapy for mild cases but few cases may turn into moderate cases. The hospital admitted COVID-19 patients who were diagnosed as mild cases, themselves took some self-medications before getting hospitalized (vitamin D, zinc, low molecular weight heparin, azithromycin, ivermectin) that may act as immune-modulators. Though these drugs are prescription-only, they are easily available in Bangladesh due to lack of monitoring and pharmacovigilance.<sup>14</sup> Mild cases have been hospitalized with the reason not to progress to the worst one. Besides having no specific antiviral therapy against SARS-CoV2, the patients whose disease severity progressed towards critical were treated with re-purposeful drugs like favipiravir or remdesivir around the world and to some extent in Bangladesh. In a study, out of 473 patients, 80 moderate cases out of 82 and 27 critical cases out of 99 got favipiravir; and 85 critical cases out of 99 got remdesivir in tertiary care hospital in Bangladesh.<sup>15,16</sup>

In this retrospective cross-sectional study, the place and population were considered as COVID-dedicated hospitals in Dhaka, Bangladesh; conducted from May 2020 to September 2020 which was the pick of pandemic in our country. The objective of the descriptive study was to overview the demographic characteristics, symptoms, comorbidities, and significant biomarkers (hematological, inflammatory, hepatic, renal, and metabolic) with different age groups and sex during the four months.

## METHODS

This cross-sectional retrospective descriptive study was done in mild cases of COVID-19 admitted in Holy Family Red Crescent Medical College Hospital (HFRMCH), from May 17 to September 9, 2020. The HFRMCH was a 720 bed foremost non-government hospital with 9 bed ICU selected as 'COVID-dedicated' by the Government of Bangladesh for four months.

Total 254 mild cases of COVID-19 patients (confirmed by rt-PCR from the nasopharyngeal swab) who were admitted to the Holy Family Red Crescent Medical College Hospital, Dhaka during the study period of the peak of pandemic in Bangladesh were included in the study and moderate, severe, and critical COVID-19 patients were excluded according to national guidelines.<sup>12</sup>

The study was approved by the designated hospital authority and institutional ethics board. The mild cases were categorized into five age groups. Demographic characteristics, symptoms, comorbidities, and biomarkers associated with clinical progression of the disease were recorded in a pre-formed data sheet. Chi-square and one-way ANOVA test was done by using SPSS version 26.0. All p values were two-tailed, with p<0.05 considered statistically significant with a 95% confidence interval.

## RESULTS

### Demographic characteristics

Out of 254 cases, 210 were male and 44 were female with 1:4.77 with the age range of 18 to 76 years. Average age was 39.04 years. The highest percentage of patients belonged to 30-39 years of age (Table 1). The male: female was significant ( $p=0.000941$ ).

### Clinical characteristics and co-morbidities

Regarding respiratory symptoms, fever (17.71%), cough (14.96%), and breathlessness (14.17%) topped the list (Table 2). Fever and cough were more prominent in the 30-39-years age group, breathlessness was more frequently reported among the 50-59-years age group. Whereas, anorexia (18.5%) and anosmia (16.9%) were the two most important neurological symptoms; myalgia (5.12%) and weakness (2.36%) was less (Table 2). Anorexia was more prevalent in the 30-39-years group and anosmia was more in the 40-49-years group. Another symptom was diarrhea (4.3%) not shown in the table. Respiratory and neurological symptoms among the different age group were not statistically significant ( $p=0.713$ ).

The common comorbidities among the mild cases of COVID-19 were diabetes mellitus (22.44%) and hypertension (16.92%). The other comorbidities were IHD (4.33%), bronchial asthma (3.15%), and CKD (1.96%). DM and HTN were more in the 40-49-years age group. On the other hand, IHD was prevalent in the >60-years age group (Table 3).

Regarding hematological parameters, Hb% was highly significant among different groups which were highest in the 30-39-years and lowest in the >60-years age group. Total WBC count was highest in >60-years whereas lowest in <30-years age group, that was significant among groups. Whereas, the neutrophil count was very significant among groups which was highest in >60- years and lowest in 30-39-years age group. Platelet count was highly significant among groups that was highest in the 50-59-years and lowest in the >60-years age group. On the other hand, HCT count was highest in the 30-39-years and lowest in the >60-years age group, HCT was significant among groups. NLR was very significant which was highest in >60-years and lowest in <30 years age group. d-NLR was also significant that was highest in the 50-59-years and lowest in the <30 years age group. Lymphocyte count and PLR was not significant (Table 4). Regarding inflammatory parameters, d-Dimer was >60 years group and lowest in the 50-59-years group, was significant among groups. Ferritin was significantly higher between the group that was highest in >60-years and lowest in <30-years group. CRP was very significant among the group that was highest in the >60-years and lowest in the <30-years group. Prothrombin time (PT) was significantly high among the 50-59-years and low in <30-years group. On the other hand, SGPT was significant among the group that was highest in 30-39 years and lowest in 40-49 years group. S.creatinine was significant among the group that was highest in the >60 years and lowest in the >60-years group. Whereas, HbA<sub>1c</sub> was significant among groups that was highest in 50-59 years and lowest in >60 years age group.

**Table 1: Age distribution of the mild cases of COVID patients (N=254).**

Age range (in years)	Total patients	Male		Female		Statistical value
		Numbers	Percentage (%)	Numbers	Percentage (%)	
<30	75	61	29.04	14	31.8	Chi-square 18.6014. P value=0.000941. The result is significant at $p<0.05$
30-39	120	110	52.38	10	22.72	
40-49	38	26	12.4	12	27.27	
50-59	5	3	1.42	2	4.13	
60 and above	16	10	4.76	6	13.63	
<b>Total</b>	<b>254</b>	<b>210</b>	<b>100</b>	<b>44</b>	<b>100</b>	

**Table 2: Common symptoms in different age range of mild group of COVID-19 patients.**

Symptoms	Total (N=254) (%)	<30 years (N=75) (%)	30-39 years (N=120) (%)	40-49 years (N=38) (%)	50-50 years (N=5) (%)	> 60 years (N=16) (%)	Statistical value
Sore throat		12 (4.72)	4	2	2	2	
Fever	45(17.71)	9(12)	14(11.67)	6(15.79)	2(40)	8(50)	Chi-square=8.8775, P=0.713359.
Cough	38(14.96)	7(7.33)	13(10.83)	7(18.42)	2(40)	5(31.25)	
Breathlessness	36(14.17)	5(6.67)	8(6.67)	6(15.79)	5(100)	12(75)	Result is not significant at $p<0.05$
Anorexia	47(18.50)	7(9.33)	18(15)	17(44.74)	1(20)	4(25)	Chi-square=20.1649, P=0.064029.
Anosmia	43 (16.9)	1(1.33)	12(10)	25(65.78)	3(60)	2(12.55)	
Myalgia	13 (5.12)	1(1.33)	5(4.17)	2(5.26)	3(60)	2(12.55)	Result is not significant at $p<0.05$
Weakness	6(2.36)	1(1.33)	2(1.67)	1(2.63)	1(20)	1(6.25)	

**Table 3: Comorbidities in different age range of mild group.**

Diseases	Total (N=254) (%)	<30 years (N=75) (%)	30-39 years (N=120) (%)	40-49 years (N=38) (%)	50-50 years (N=5) (%)	> 60 years (N=16) (%)	Statistical value
DM	57(22.44)	7(9.33)	10(8.33)	18(47.36)	3(60)	11(68.75)	Chi-square=10.2972, P=0.850656, Result is not significant at p<0.05
HTN	43(16.92)	2(2.67)	6(5)	15(39.47)	3(60)	10(62.5)	
IHD	11(4.33)	1(1.33)	1(0.83)	2(5.26)	1(20)	4(25)	
Bronchial-asthma	8(3.15)	2(2.67)	3(2.5)	1(2.63)	1(20)	1(6.25)	
CKD	5(1.96)	1(1.33)	1(0.83)	1(2.63)	1(20)	1(6.25)	

**Table 4: Changes of biomarkers in different age range of mild group.**

Diseases	<30 years (N=75) (%)	30-39 years (N=120) (%)	40-49 years (N=38) (%)	50-50 years (N=5) (%)	> 60 years (N=16) (%)	Significance test
Hb%	13.56±3.16	14.01±1.06	12.41±2.55	12.96±2.17	11.41±2.07	***
Total WBC	6093.33±2467.86	6537.5±1876.61	6755.26±2977.09	7380±1710.84	8106.25±3500.1	*
Lymphocyte	4758±3419.56	2296.31±818.24	2407.40±2548.55	3102.31±2135.41	1594.06±68.74	ns
Neutrophil	4212±992.77	3630.56±1827.96	4091.33±2342.82	3875.71±1315.57	5292.37±3402.3	**
Platelet count	234160±78393.84	255375±66336.68	252552.63±90523.4	287000±6613.22	215812.5±77471.04	***
HCT	42.02±9.22	43.13±3.16	38.85±7.88	40.22±6.13	35.78±6.33	***
NLR	1.55±1.15	1.7±0.9	2.13±1.3	1.66±0.79	4.65±4.41	***
d-NLR	0.01953±0.002	0.022±0.011	0.022±0.008	0.059±0.056	0.036±0.023	**
PLR	99.775±95.19	154.26±157.68	118.15±21.65	134.54±76.32	165.27±96.12	ns
d-Dimer	0.05±0.07	0.12±0.18	0.25±0.9	0.34±0.03		**
Ferritin	173.84±171.7	260.92±288.69	238.47±298.06	243±222.15	554.18±451.59	**
CRP	0.82±2.62	1.83±5.03	7.89±19.88	3±6	10.71±17.95	***
PT	10.61±5.95	11.44±5.34	10.2±7.51	13.36±0.58	12.2±6.29	**
INR	0.81±0.45	0.87±0.41	0.78±0.58	1.02±0.04	0.93±0.48	ns
SGPT	49.84±46.58	53.73±38.71	35.89±19.08	37±18.39	47.87±34.44	**
S. creatinine	0.95±0.34	0.99±0.33	1.08±0.45	1.41±0.76	1.7±1.87	*
HbA <sub>1c</sub>	3.04±2.9	3.27±3.17	2.67±3.44	5.68±0.46	2.55±3.19	**

Values are expressed as mean ±SD; Test: One-way ANOVA, \*\*\* highly significant at p≤0.001; \*\*significant at p≤0.01; \* significant at p<0.05, ns= not significant

## DISCUSSION

To our knowledge, not many studies have been conducted on mild cases of COVID-19 in Bangladesh. In this study cohort of 254 mild cases of COVID-19 (RT-PCR positive), female was 44 and male were 210 with 1:4.77 ratio, with the age range of 18 to 76 years and the difference was statistically significant (p<0.05). Most of patients belonged to 30-39 years with the mean age of 39.04 years. Similar findings were reported in other studies in Bangladesh where most of the patients were male (82.67%) and some previous studies showed male were more like 77% and 64%.<sup>6,13,16-17</sup> It was suggested that ACE2 is the target receptor for COVID-19 that is greatly stated in males than in females which is present.<sup>18,19</sup> Presence of X chromosome and sex hormones may play a

role for the less chance of getting infected with the virus in female.<sup>20</sup> Young people were more affected probably because they were unwilling to follow the movement restriction by the instruction of govt. in addition to necessary preventive measures as they believe proper hand washing is enough to protect them from the transmission.<sup>21</sup>

Fever (17.71%), cough (14.69%) and breathlessness (14.17%) were the predominant features and prevalent in the 30-39 years. Fever was experienced in 36.4% of cases and breathlessness was compatible with similar studies by Liu et al (11.5%) and Mutair et al (22.4%) respectively.<sup>22,23</sup> Regarding the neurological symptoms of anorexia (18.5%), anosmia (16.9%) was predominant followed by myalgia (5.12%) and weakness (2.36%) in descending order.<sup>24</sup> Anosmia was more in the 40-49 years age group.

Several studies show similar findings.<sup>16,25,26</sup> Almost 18.5% cases suffered from anorexia in the present study; and more in the 30-39-years age group; several studies show similar results.<sup>24,26</sup>

Among 254 patients, diabetes and hypertension were more predominant in the 40-49-years age, may be because these diseases are frequent in the middle-aged population. IHD was more in >60-years age group, as increased age predispose to IHD. Pre-existing diseases like cardiovascular disease, COPD, diabetes mellitus, hypertension, immunosuppression, obesity, and sickle cell disease prejudice patients to unfavorable conditions and increased the risk of death<sup>27</sup>. 22.44% of the mild cases was suffering from diabetes; several studies showed the similar result.<sup>17,19</sup> HTN (16.92%) was the 2nd most common comorbidities after DM which was consistent with several studies.<sup>17,23</sup> Only 1.9% patients were suffering from CKD that corresponds with other studies.<sup>19,22,23</sup>

Hb% was lowest in the elderly (>60 years) age group, maybe since Hb% decreases with aging. In a recent study it was found that hemoglobin level decreases in disease progression.<sup>28</sup> However, WBC count was more in elderly age group which was owing to the age and a study showed the similar findings and was significant.<sup>6</sup> The neutrophil is a key constituent of the leukocyte population and migrates from the venous system to the immune organ. Neutrophil releases a large amount of reactive O<sub>2</sub> species. Thus antibody-mediated cell-mediated cell may assassinate the virus directly expose virus antigen, and excite the cell-specific and humoral immunities.<sup>29</sup> Neutrophil count was highest in elderly age group that is comparable to another study and was significant.<sup>6</sup> The severity of COVID-19 is linked to lymphopenia.<sup>30</sup> Whereas lymphocyte count was highest in younger (30-39 years) age group and lowest in elderly age group and platelet count was highest in younger age group and was significant. In a similar study same result was found.<sup>6</sup> Hematocrit (HCT) was high in the 30-39 years and significantly less in the older patients. A high NLR was concomitant with a more severe outcome in a similar study.<sup>31</sup> NLR was significant among groups and highest in patients >60-years group and lowest in <30-years group that is similar to other study.<sup>32</sup>

The d-NLR was highest in the 50-59 years age group and lowest in the <30 years age group and statistically significant among groups. Yang et al show that d-NLR was 3.3 which was unlike the present study.<sup>32</sup> Elevated d-Dimer suggests extensive thrombin generation and fibrinolysis along with poor prognosis.<sup>33</sup> d-Dimer was highest in >60 years age group which corresponds to another study and lowest in the <30-years age group and was significant among groups.<sup>31</sup> Raised ferritin level has been regarded as an acute phase reaction parameter and may have an important role in inflammation regarding the development of a cytokine storm and it indicates the disease severity.<sup>34</sup> Ferritin was significant among groups and highest in >60-years age group and lowest in <30-years age group. It was suggested that the hospital death rate was

raised if the ferritin level >300 ng/mL.<sup>27</sup> CRP was highest in the >60 years and lowest in the <30-years group. Unlike the present study, a retrospective cohort study showed median CRP was 2.55 mg/L.<sup>35</sup> An elevated CRP is considered as pointer of ARDS as it represents the sign of intense inflammation.<sup>33</sup>

PT was highest in 50-59 years age group which corresponds to another study and was significant.<sup>36</sup> Elevated SGPT has more chance to develop in critical COVID-19 and end-organ damage.<sup>37</sup> SGPT was highest in 30-39-years age group; lowest in 40-49 years age group that corresponds to another study.<sup>35</sup> S. creatinine was highest in >60-years age group which corresponds to another study and lowest in <30-years age group and statistically significant among groups.<sup>35</sup> No remarkable findings was observed for INR and HbA<sub>1c</sub>.

## CONCLUSION

The novel SARS-CoV-2 virus is still posing challenges to the world and the mutating strains are causing exponential rise of morbidity and mortality. Males of middle-age group are predominantly affected and presents with mild symptoms and very few comorbidities. But the significant variations of few biomarkers among the elderly patients are crucial to predict the progression of disease. Therefore, epidemiological and demographic differences of clinical symptoms, comorbidities, and changes of biomarkers in mild cases are crucial to develop, review and modify the management strategy and public health awareness time to time.

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