Chapter 1- Introduction

COVID-19 pandemic, also known as the coronavirus pandemic is a global epidemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS CoV-2). The virus was confirmed to have spread to Bangladesh in March 2020 with the first three identified cases being reported on 8th March 2020 (DGHS, 2021). Since then, the disease has continued to spread day by day across the nation affecting people at large. Currently, over 476 million cases have been confirmed worldwide with over 6 million deaths (Worldometer, 2021). The highest number of cases were reported from U.S.A followed by India, Brazil, France and the U.K. In case of death, highest number of deaths were reported from U.S.A followed by Brazil, India, Russia and Mexico. In Bangladesh, almost two million cases have been diagnosed so far, with Dhaka division reporting the highest number of cases followed by Chattogram, Rajshahi, Khulna, Sylhet, Rangpur, Barisal and Mymensingh (DGHS, 2021). The number of deaths reported is around 29,000 and the case fatality rate is 1.49. Death was reported in people of all age groups with a slight male predominance, and the highest number of deaths were reported among individuals above 60 years of age (DGHS, 2021).

The spread of COVID-19 is rapid, with transmission occurring from close contacts and from droplets. The mean incubation period is about 3-9 days with a range of between 0-24 days, however, transmission can occur before any symptoms arise in about 44% of the cases(Siordia Jr, 2020). The disease can be classified in to asymptomatic, mild, moderate and severe cases. Asymptomatic cases are RT-PCR positive, but show no other signs and symptoms. Mild cases have an influenza like illness whereas moderate and severe cases show clinical signs of pneumonia(DGHS, 2021).Although all patients are susceptible to developing COVID-19 infections, certain cohorts have an increased risk for development of severe disease. These include patients with comorbidities like diabetes mellitus, hypertension, asthma, chronic kidney disease, chronic liver disease, ischemic heart disease etc. Pregnancy is also a factor that can lead to severe conditions. Hence, in case of pregnant women, a saturation level below 94% is categorized as a severe case. Immunocompromised situations such as patients with malignancies, on steroids and on chemotherapy are also at higher risks of developing COVID-19.

The most common symptoms for COVID-19 are fever, cough, shortness of breath and loss of taste and smell. Other common symptoms include, myalgia, headache, fatigue, anorexia, diarrhea, vomiting, abdominal pain, etc.

The treatment modalities for COVID 19 varies based on case severity. For mild cases, symptomatic management is given. Thromboprophylaxis is only indicated in patients with uncontrolled co-morbidities and prothrombic conditions. Monitoring of oxygen saturation at rest and on exertion and looking for danger signs is essential for mild cases. Danger signs include a drop of O_2 saturation to 93% or below, shortness of breath, chest pain, lightheadedness, disorientation, extreme weakness etc. For moderate cases, apart from symptomatic treatment, O_2 is given at a maximum of 5L/min if required to maintain a saturation level of 94% or more. Additionally, thromboprophylaxis, antiviral treatment, steroid therapy and antibiotics can be given based on the patient's condition. Investigations like CBC, CRP, D-dimer, S. LDH, S. ferritin, S. creatinine, ALT, CXR PA view/HRCT of chest or other markers can be done according to the clinician's decision. For critical illness, the treatment involves along with symptomatic treatment, oxygen therapy, anticoagulation, maintenance of euvolemia, steroid, antiviral and antibiotics; specific therapy using Tocilizumab, Baricinib are given based on patient's need. Some therapies like convalescent plasma therapy, use of ivermectin and Bevacizumab can also be given as clinical trials.

Prevention of COVID-19 is of utmost importance since the disease can be life threatening. Simple preventive measures such as handwashing techniques, social distancing and isolating oneself when afflicted by symptoms of the disease or becoming an asymptomatic case are the major methods of prevention. With the introduction of vaccination, the incidences of the disease are expected to fall. Nevertheless, COVID-19 cases have also been reported among the vaccinated population thus suggesting that vaccination alone is not enough to control this pandemic. Additionally, emergence of new strains of the virus could limit the efficacy of vaccination. Hence, as long as the disease continues to exist within our community, it is necessary to focus on the clinical features of patients presenting with COVID-19 so that treatment can be modified from time to time and improve patient outcome.

Rationale

This study was designed to provide a clear concept on the diagnosis, treatment, control and prevention; and management of COVID-19 transmission. Results from this study can be used to make proper policies for public health concerns.

Aims of the study

1. To better understand the comprehensive clinical characteristics of COVID-19 patients among the Bangladeshi population.
2. To analyze the clinical features, clinical course of disease and immediate outcome at hospital settings for COVID-19 patients

Objectives

General

To analyze the clinical features, clinical course and immediate outcome at hospitalized COVID-19 patients

Specific

- To explain the demography of the COVID-19 patients admitted to selected hospital
- To elaborate each clinical feature of COVID-19 positive patients
- To explain any systemic involvement during COVID-19 infections
- To identify the various co-morbidities, present in COVID-19 patients
- To evaluate the immediate possible outcome for selected patients

Chapter 2- Literature Review

2.1 Background

Coronavirus is a type of RNA viruses that belongs to the subfamily Coronavirinae in the family of Coronaviridae. Other four genera of the subfamily are Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus (Brian and Baric, 2005).The betacoronavirus can be additionally split in to four lineages: A, B, C and D. SARS-CoV-2 that has recently been identified has been classified as subgenus Sarbecovirus of the lineage B genus of betacoronavirus (Letko, et al., 2020). While α- and β- CoV are able to infect mammals, γ-, and δ- CoV tend to infect birds. Owing to its widespread availability, large genetic diversity and frequent recombination of the different coronavirus species, along with the increased time humans spend with animals, coronaviruses can occasionally mutate to infect human hosts (Zhu, et al., 2020). Humans have been infected by corona viruses for a long time since it is one of the viruses responsible for the common cold(Boopathi, et al., 2021). So far at least six species were identified that can infect human hosts (also called HCoV). Among them, α-CoVs HCoV-229E and HCoV-NL63; and β-CoVs HCoV-HKU1 and HCoV-OC43 have resulted in mild respiratory symptoms with mild pathogenicity. Depending on the lineage of the coronavirus species as well as the immunocompromised nature of the infected human host, the symptoms can vary from mild illness to severe respiratory distress or even death (Fung and Liu, 2019). Although the new coronavirus SARS-CoV-2 was first discovered in a cluster of patients in Wuhan, China, the original source of this virus is yet unclear (Yan, et al., 2020).

Previously, coronaviruses have led to many other epidemics such as the severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV). It is through the knowledge and experience of these outbreaks that SARS-CoV-2 could be better understood.

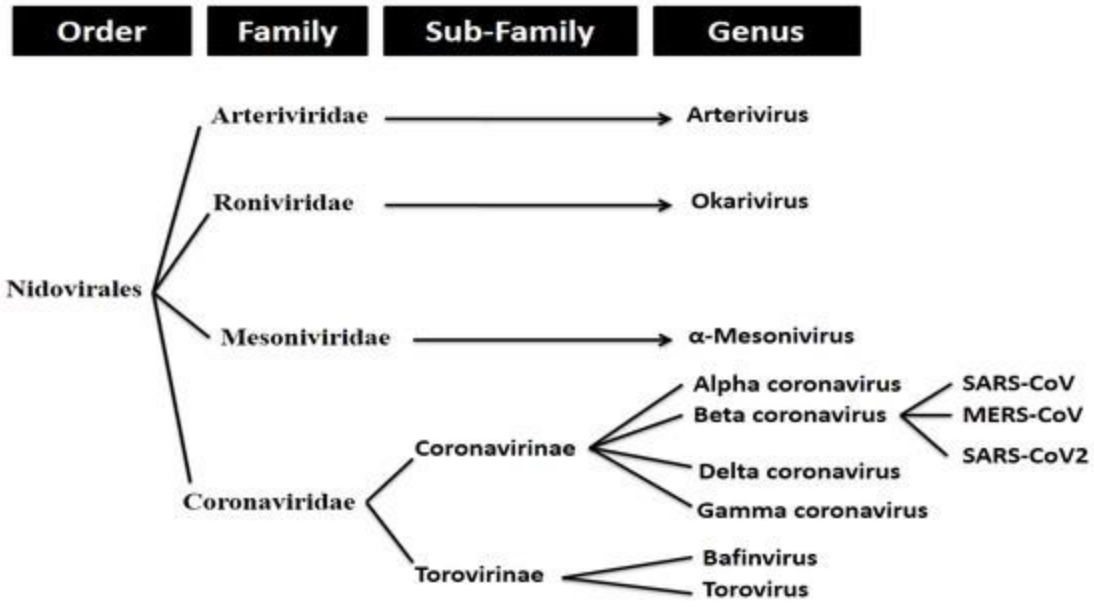

Figure 2.1: Classification of coronaviruses
(Source: Rehman et al, 2020)

2.2 Origin and evolution of coronavirus

Coronavirus (CoV) was probably present for ages before its discovery. It was first discovered in 1965 by isolation from a child's nasal washings (Tyrrell and Bynoe, 1965). Following this discovery, many other strains of coronaviruses were identified that were considered to be harmless causing mild upper respiratory tract infections or the common cold (Yin and Wunderink, 2018). The first pandemic to be caused by CoV was SARS. An outbreak of atypical community acquired pneumonia was first reported in 2002 at Guangdong province, China(Anand, et al., 2020). Upon further investigations, it was found that the infecting pathogen was never identified previously and the disorder was named severe acute respiratory syndrome (SARS)(Peiris, et al., 2003). The incubation period was usually 4-6 days after which patients developed flu like symptoms and pneumonia. The pandemic had spread to 29 other countries and by June 2003, SARS led to over 8000 cases worldwide and had a mortality rate of about 9.6%. In an attempt to identify the source of this new virus, samples were taken from animals at live-animal markets in Guangdong province and it was found that masked palm civets and two other species were already

infected with SARS-CoV. Since the disease was zoonotic, large-scale culling of masked palm civets were carried out. However, further studies showed that only civets sold at the market had the overt clinical symptoms of SARS-CoV and no wild or domestic civets were infected. This suggested that civets were not likely the primary hosts or natural reservoirs of the virus (Li, 2005; Wang, et al., 2006). On the contrary, studies revealed the ability of bats to host several zoonotic viruses while rarely displaying any signs and symptoms(Li, 2005). Furthermore, the increased consumption of bats or bat-based products in southern China raised the suspicion that bats could be the primary hosts for SARS-CoV. Upon collecting serum samples from over 400 bats from nine different species, six genera and three families, it was found that only different species of horseshoe bats from the Rhinolophus genus tested positive for SARS-CoV. Thus, it was concluded that horseshoe bats were the primary hosts of the virus while civets were intermediate hosts and the virus eventually made its way to human hosts (Fung and Liu, 2019).

On emergence of cluster of pneumonia cases in Wuhan, China in 2019, suspicion of yet another outbreak was revealed. All confirmed cases of SARS-CoV-2 from 1st to 20th January 2020 that were admitted to Wuhan Jinyintan Hospital were studied and 49% of the subjects had some form of previous exposure to Hunan Seafood Wholesale Market which had live-animals on sale(Chen, et al., 2020). Further study of the viral genome showed that this species of coronavirus was 96.2% identical to a bat coronavirus. Other studies done on genome sequencing of SARS-CoV- 2 also showed similar results suggesting bats to be the primary reservoirs for the virus. However, the intermediate host in passing the virus to human's hosts still remains unclear since several animal species were present at the Wholesale Market(Jiang, et al., 2020).

2.3 Transmission

Human to human transmission can easily occur between close contacts and multiple routes of transmission has been identified. Although the disease primarily spreads by respiratory droplets, respiratory secretions and direct contact, studies have reported the presence of this virus in fecal swabs as well as blood, suggesting that infection could spread in this way also(Zhang, et al., 2020). Since ACE 2 receptors are present in abundance in the lung

alveoli as well as the enterocytes of the small intestine(Hamming, et al., 2004), routes of infection as well as disease manifestation can be understood from this.

2.4 Clinical features

The clinical features of SARS-CoV-2 is highly variable from person to person with asymptomatic cases to acute respiratory distress syndrome and multi-organ failure. From various studies of laboratory confirmed cases, the common clinical manifestations included fever, cough, fatigue, production of sputum, shortness of breath and sore throat. Additionally, some patients may present with gastrointestinal symptoms like diarrhea and vomiting. Some studies have noted that the clinical manifestations differ with age. One study suggests patients over 60 have a higher level of inflammatory indicators and a greater chance of respiratory failure(Liu, et al., 2020). Other studies have reported the case fatality rates to be increased in patients with comorbidities such as diabetes, hypertension, COPD, cardiovascular diseases, etc. Such patients rapidly develop acute respiratory distress syndrome, shock, metabolic acidosis and coagulation dysfunction leading to death(Huang, et al., 2020).

2.4.1 Antibody response

In the early stages of infection, antibodies to SARS-CoV-2 are not detectable. One study by Liu et al (2020) reported that IgM antibodies against SARS-CoV-2 were detectable from the 4^{th} day of illness onset which increased over time and peaked at 20 days after which it gradually declined and was markedly reduced after 28 days. Anti-SARS-CoV-2 specific IgG antibodies were detectable from day 7 of illness onset and peaked at approximately 25 days of illness onset and the levels were still maintained high 4 weeks later. In the early stages of infection, no significant difference was observed in serum IgG levels between mild and severe cases, but after 15 days of disease onset, both IgM and IgG levels were vigorously raised in cases of severe illness. Furthermore, the timing in developing IgM and IgG antibodies varied greatly among patients and this could be associated with age and comorbidities of the patient.

2.4.2 Cytokine response

The immune system has an attractive mechanism capable of responding to a variety of pathogens. For any normal antiviral immune response, activation of the inflammatory pathways of the immune system is necessary, however, exaggeration of the host's immune system can lead to severe disease if this remains uncontrolled (Braciale and Hahn, 2013). Cytokines are produced by numerous immune cells including the macrophages, dendritic cells, natural killer cells and the T and B lymphocytes.During an innate immune response to any viral infection, there are pattern recognition receptors (PRRs) that recognize the different molecular structures distinctive to the invading virus. These structures are referred to as pathogen associated molecular patterns (PAMPs). When PAMPs bind to PRRs an inflammatory response is triggered against the invading virus. This results in activation of various signaling pathways and later transcription factors which induce gene expression responsible for production of several products involved in the host's immune response to the virus. Among these are the genes encoding several pro-inflammatory cytokines. The major transcription factors activated by PRRs are activation protein 1, nuclear factor kB and interferon response factors three and seven. These transcription factors induce the expression of genes that encode the inflammatory cytokines, chemokines and adhesion molecules. This sequence of events results in the recruitment of leukocytes and plasma proteins to the site of infection where they perform many effector functions that help to combat the triggering infection (Thompson, et al., 2011).

Three important pro-inflammatory cytokines of the innate immune response are IL-1, TNF-α, and IL-6. These cytokines are produced by mast cells, tissue macrophages, endothelial cells, and epithelial cells during an innate immune response. When there is an acute increase in circulating levels of different pro-inflammatory cytokines such as IL-6, IL-1, TNF- α, and interferon, it causes a sudden influx of various immune cells such as macrophages, neutrophils, and T cells in to the infection site. This is called "cytokine storm" and it has a destructive effect on human tissue due to damage of vascular barrier, capillary damage, diffuse alveolar damage, multiorgan failure and finally death. Lung injury is one consequence of the cytokine storm that can easily progress into acute

respiratory distress syndrome (ARDS)(Shimizu, 2019). This leads to low oxygen saturation level and hence is a major cause of death in COVID-19 patients.

Multiple studies suggest that some patients with COVID-19 suffer from a cytokine storm (CS). One study analyzed the cytokine levels of 41 COVID-19 confirmed cases with pneumonia and found elevated levels of IL-1β, IL-7, IL-8, IL-9, IL-10, FGF, G-CSF, GM-CSF, IFN-γ, IP-10, MCP-1, MIP-1A, MIP1-B, PDGF, TNF-α, and VEGF in these patients as compared to healthy adults (Huang, et al., 2020).One specific marker that was significantly raised in severe cases of COVID-19 was IL-6. Multiples studies showed this specific finding where raised IL-6 levels were significantly higher in cases who died (Ruan, et al., 2020) or when comparing between mild and severe cases (Chen, et al., 2020). CS has been reported in many viral infections including the previous two coronavirus infections-SARS and MERS. Both proinflammatory and anti-inflammatory cytokines are raised in the serum of patients with CS. Hence in COVID-19 patients, along with antiviral therapy, anti-inflammatory therapies that reduce cytokine responses are necessary (Ragab, et al., 2020).

2.4.3 Cellular response

Cellular response of COVID-19 varies from patient to patient. In patients with mild symptoms and patients with severe disease who have recovered exhibit a normal immune response to eliminate the virus. However, patients with fatal severe COVID-19 went through three stages: normal or hypofunction, hyperactivation and then anergy. Ultimately, these patients are unable to resist the viral infection and they die (Zhou and Ye, 2021).

In the early stages of COVID-19, the total number of white blood cells in peripheral blood is either normal or decreased(National Health Commission of the People's Republic of China, 2020). T and B lymphocytes are cells that are important indicators for detecting immune function. These T lymphocytes are further classified into two important subsets: CD3+ CD4+ Tlymphocytes and CD3+ CD8+ T lymphocytes. CD4+ T cellscan differentiate into a range of helper and effector cell types, as well as have the ability to indicate B cells, assist CD8+ T cells, have direct antiviral activity, recruit innate cells and promote tissuerepair. On the other hand, CD8+ T cells can kill infected cells and affect the

activation of the immune response. As another important component, B lymphocytes play a rolein humoral immunity by secreting antibodies. In normal viral infections, the lymphocyte counts increase in response to the infection. However, contrary to this, in Covid-19 infections, the lymphocyte counts decrease with increasing severity of the disease (Schulte-Schrepping, et al., 2020). The number of T lymphocytes in sever patients were lower than in mild patients, and much lower in deceased patients. Even the B lymphocytes are decreased with patients with severe illness having lower counts than those with mild illness. Nevertheless, B lymphocyte counts were within the normal range (Zhou and Ye, 2021).

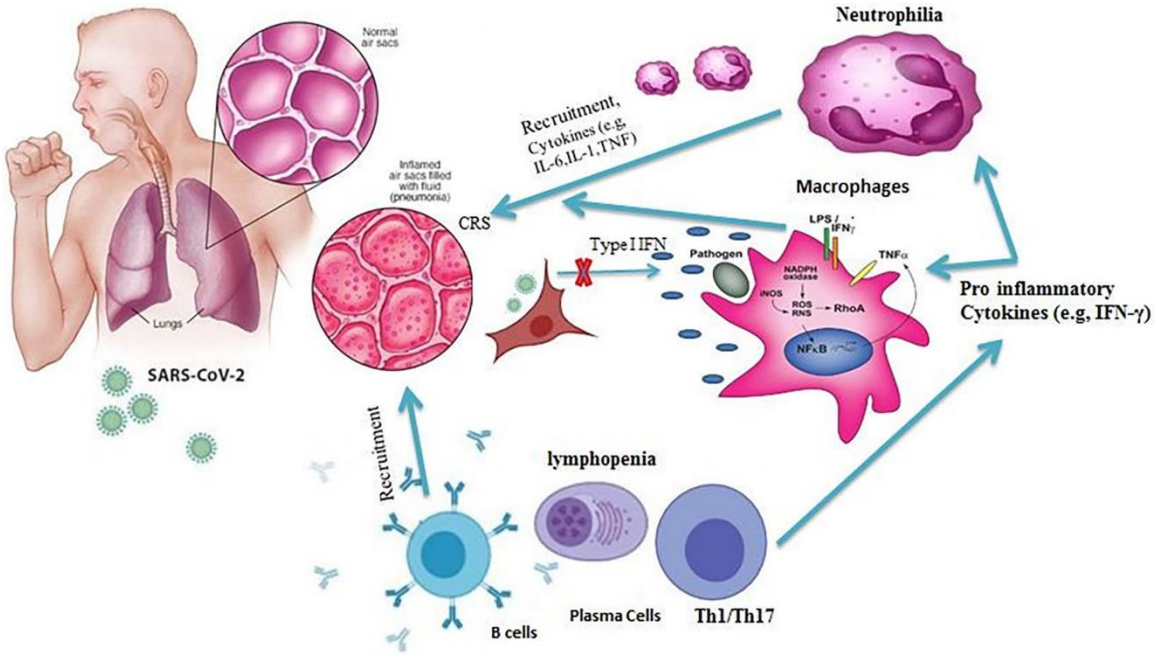

Figure2.2: Cellular immune response to SARS-CoV-2
(Source- Rokni, et al., 2020)

Due to the initial local respiratory SARS-CoV-2infection, the circulating innate immune cells in the blood, including natural killer cells, monocytes, neutrophils and dendritic cells changes. The neutrophils are increased in circulation of severe COVID-19 patients, while

the dendritic cells the body's most potent full-timeantigen-presenting cells (APCs), decreases with severity of disease.

2.5 Association of hematological and biochemical markers with COVID-19 infections

While the clinical characteristics of COVID-19 are diverse, recent studies have also shown alterations in laboratory parameters among these patients. As such, these can be used as biomarkers to evaluate disease progression and categorize presenting patients as mild, severe or fatal in clinical conditions. Many laboratory parameters make it possible to assess the severity of the disease and predict the risk of evolving towards more serious afflictions such as respiratory distress syndrome, disseminated intravascular coagulation and multiple organ failure (Lippi and Plebani, 2020). Some of these are thrombocytopenia, neutrophilia, elevated liver enzymes, hypoalbuminemia, creatinine and inflammatory markers like interleukin-6 and C-reactive protein (Ramírez-Truque and Herrera-Morice, 2020). However, the main progression predictors were identified as lymphopenia, elevated D-dimers and ferritin levels while also considering LDH, troponin and CPK in the marker panel.

In the case of inflammatory response markers, COVID-19 causes an exacerbated immune reaction which provokes an inflammatory response called 'cytokine storm.' Lymphopenia and elevated proinflammatory cytokines were reported to be frequent in severe cases of COVID-19 as compared to mild cases(Liu, et al., 2020). One study by Huang et al (2020) showed plasma concentrations of IL2, IL7, IL10, GCSF, MCP1, IP10, MIP1A, and TNF-α to be higher in Intensive Care Unit (ICU) patients rather than patients not in ICU. Another study by Qin et al (2020) showed infection related biomarkers like procalcitonin, CRP and serum ferritin to be elevated along with the inflammatory cytokines. CRP was reported to be present in higher levels in patients with disease progression as compared to people who are stable or recovering(Liu, et al., 2020). The same study also showed albumin to be significantly diminished in the disease progression group. LDH that is used as a marker for lung tissue damage, is frequently abnormal in COVID-19 patients (Lippi and Plebani, 2020). However, the abnormalities are more common in patients with severe disease as compared to mild ones.

In case of cardiac markers, one meta-analysis of 28 studies found seriously ill COVID-19 patients to have increased levels of creatinine kinase-MB, troponin, myoglobin and NT-proBNP. Furthermore, another study by Deng et al (2020) recognized that most patients had normal levels of troponin on admission, but in about 37.5% cases levels increased during hospital stay, especially in those that died.

For hepatic markers, one study found more than 90% of patients with abnormal hepatic tests to have mild symptoms on admission. However, patients with abnormal hepatocellular or a mixed type of hepatic tests on admission were more prone to develop serious illness. Nevertheless, damage of liver due to use of medications could not be ruled out in this study(Cai, et al., 2020).

Renal disease among patients with COVID-19 can present in the form of proteinuria, hematuria, or acute renal injury thus contributing to a greater mortality risk. Upon post-mortem renal histopathological examinations of patients who died from COVID-19, one study found that SARS-CoV-2 infection induced severe acute tubular necrosis and lymphocyte infiltration. The viral antigen was found in the tubules of all renal tissue samples(Diao, et al., 2020). Another study showed abnormal renal parameters such as proteinuria, hematuria and leukocyturia on a routine urine test on admission among COVID-19 patients without any previous history of kidney disease(Zhou, et al., 2020).

Infection with COVID-19 can cause damage to pancreatic islet cells resulting in acute diabetes. This is why amylase and lipase levels are useful for follow up purposes(Wang, et al., 2020). One study reported 17% of patients with pneumonia due to COVID-19 also showed higher values of amylase or lipase(Wang, et al., 2020).

2.6 Disease burden

Worldwide, a total of 219 countries and territories have reported confirmed cases of Covid-19 with a death toll of over 3 million. The highest number of cases were found in the United States, followed by India and Brazil. In Bangladesh, with the rising number of cases and deaths from Covid-19 lies another fear of unemployment, and deepening poverty due to mandatory lockdowns and decline in national and international demands for manufactured goods such as the garments factories(Mohiuddin, 2020). Due to an overwhelming number

of cases, and lack of adequate ICUs, hospitals find it hard to meet patient demands and accommodate severely ill patients. Added to this is the attitude and practices of the general population regarding disease awareness and spread. Proper measures are not taken by many and over-crowding despite several warnings and strict regulations continue to exist. Hence, community transmission has become unavoidable. Again, infection of healthcare workers who are frontline fighters for this disease has worsened the situation to such an extent that there are not enough workers to deal with the excessive burden of diseases. One ray of hope that could stop this deadly disease is the emergence of effective vaccines (Fiske, et al., 2022).

2.7 Prevention

Coronavirus particles are rapidly inactivated – killed – by exposure to 70% ethanol or 90% isopropanol (rubbing alcohol), hydrogen peroxide solutions, hypochlorite bleach, soaps and detergents, as well as by UV light and the high temperatures of cooking (King, et al., 2020). Hence, preventive measures include physical distancing, use of masks to prevent droplet infections, constant washing of hands with soap and water to prevent transmission and use of personal protective equipment (PPE) by health care workers. Another method of prevention is the use of vaccinations to immunize people against the disease (Pradhan, et al., 2020).

2.8 Treatment

The treatment of COVID-19 is mostly symptom based with only few medications that deal with destroying the virus. For asymptomatic cases, isolation of the patient with supportive care is recommended. Regular hand washing, using paper towel or elbow to cough, and wearing a medical mask at all times is essential. In case of mild cases, symptomatic management and home isolation is enough. However, if patient has associated comorbidities that are controlled, they need to be carefully monitored at home using a finger pulse oximeter and danger signs should be watched out for. Mild cases with uncontrolled comorbidities require hospital admission. Such patients should receive thromboprophylaxis along with symptomatic management.

For moderate cases, symptomatic management and use of nasal cannula for O_2 therapy is given. Target SPO2 is 94% during initial resuscitation and 90% for stable patients. For pregnant patients and patients with other organ failure target SPO2 is 94%. Maintaining prone position for 4 -6 hours a day and use of thromboprophylaxis is necessary. Antiviral drug (Remdesivir) and steroid should be initiated. For severe cases, additionally, antibiotics need to be given. Oxygen flow needs to be escalated to maintain oxygen demand. Based on the requirement, the various devices for supply of oxygen can be used: Nasal cannula (up to 5 liter), Oxygen mask (6-10 liter) and non-Rebreather bag with reservoir bag (10-15 liter. Demand above that needs to be supplied using a High flow nasal cannula. Other drugs such as Tocilizumab and Baricitinib are used in severe or critical COVID-19 based on patient needs(MOHFW, 2020).

Chapter 3- Materials and Methods

3.1 Description of the study area

Chattogram city is a major seaport and the second largest city in Bangladesh after Dhaka. The city is located in the Chattogram district in the southeastern portion of the country near Myanmar. It is built on the banks of the Karnaphuli River that drains in to the Bay of Bengal. Having the largest sea port in the country, Chattogram is the main route for almost all of Bangladesh's import and export, and generates a huge amount of revenue each year, attracting many investors internationally.

The study was conducted at a tertiary care hospital in the heart of Chattogram city. This tertiary care hospital provides a variety of medical services including both inpatient and outpatient medical services. Since, the emergence of the pandemic, the hospital has arranged for accommodation of COVID-19 patients, including facilities at the intensive care units, and RT-PCR testing facilities.

3.2 Ethical consideration

Prior to the commencement of this study, the research protocol was approved by the ethical committee of Chattogram Veterinary and Animal Sciences University. A written informed consent was obtained from all study patients after explaining to them the aims and objectives of the study in easily understandable local language. No invasive procedure was conducted solely for the purpose of the study. All treatment was provided based on national protocol. Finally, confidentiality was maintained throughout the study by using case numbers rather than names to identify cases and keeping all case record forms stored in a locker.

3.3 Study Design

A prospective observational study was conducted in the above- mentioned hospital for a period of 6 months. All patients who were admitted to the COVID unit of the hospital with a confirmed diagnosis of COVID-19 through RT-PCR were included in this study.

3.4Study period

Data was collected between October 2020 and March 2021

3.5 Sample size

Sample size was determined according to (Thrusfield & Brown, 2017), using the estimated prevalence of 50%. The following formula was used

$$n = \frac{z^2 pq}{d^2}$$

Where n is the desired sample size, z is the standard normal deviate and d is the allowable margin of error.

According to a study by (Rana, et al., 2020), the prevalence of COVID-19 was found to be 36%. Hence, in this study,

Z= 1.96 which corresponds to a 95% confidence level,

p=0.36

q=1-0.36 =0.64

d= 0.05

Using this calculation, the final sample size was 354 patients.

However, due to time limitation of 6 months, as many as 306 patients could be included in this study.

3.6 Inclusion and exclusion criteria

Inclusion criteria

Patients over 18 years of age admitted to the hospital with symptoms of COVID-19 and having an RT-PCR positive for SARS CoV-2 during the study period.

Exclusion criteria

Patients who did not give consent

3.7 Admission criteria of patients

Based on the national guidelines on clinical management of COVID-19(DGHS, 2021), all suspected/ confirmed cases of COVID-19 with the following presentations were admitted to hospital.

- Patients with clinical or radiological evidence of pneumonia

- Patients having signs of severe pneumonia (RR > 30 /min or oxygen saturation<90%).
- Critically ill COVID-19 patients presenting with acute respiratory distress syndrome, sepsis, septic shock.
- Patients with hypoxia (SPO_2 ≤93%) even in the absence of any clinical signs
- Patient with multiple uncontrolled comorbidities or prothrombotic state such as high-risk pregnancy, active malignancy, etc.

3.8 Method of data collection

All patients that were admitted to the COVID unit, had an RT-PCR positive test and was above the age of 18, were considered for this study. After obtaining informed written consent, a direct face to face interview was conducted by the investigator. Following this, routine clinical and laboratory examinations were conducted and the patient was managed as deemed necessary. Data on laboratory results and patient management were obtained from patient's case record file and the condition of the patient was observed until discharge of the patient or death. All data was collected in a predetermined and approved case record form.

3.9 Variables used

- **Demographics:** Age, gender, occupation
- **Exposure history:** Contact history, travel history, number of affected family members, vaccination history
- **Risk factors:** Smoking, Chemotherapy, surgery, other comorbidities
- **Clinical features**
- **Biochemical parameters**
- **Patient outcome-** Died in hospital, recovered, referred to other hospitals or discharged on risk bond (DORB).

3.10 Statistical analysis

Collected data was then compiled on Microsoft Excel spreadsheet. Statistical analysis was done using windows-based software SPSS-22. Quantitative data was expressed as mean ± standard deviation and compared using student's t- test. Qualitative data was expressed as numbers and percentages and compared using chi-squared test. Univariate analysis was

done to compare the variables based on patient outcome. The results were presented in tables and charts. P- value of <0.05 was considered to be statistically significant.

Chapter 4- Results

4.1 Demographic characteristics of the patients

A total of 306 RT-PCR positive cases were enrolled in this study. Majority of respondents belonged to the 35 to 54 years age group. The male: female ratio was 7.5:1 and most patients were service holders (37.3%). Most patients had neither a history of contact with COVID patients (61.8%), nor a travel history (80.7%). In case of affected family members, majority (79.1%) did not have any family members that were affected. As for vaccination status, most of the patients were unvaccinated (98.4%).

To find out the variations in demographic characteristics between patients who survived and patients who expired from COVID-19, a univariate analysis was conducted for all the demographic variables using chi-square test. A p-value < 0.05 was considered as significant. The results are shown in **Table 4.1**.

Table 4.1: Univariate association with the demographic factors and adverse patient outcome

Variables	Categories	Total no of patients (%)	Patients who died (%)	95% Confidence interval	p value
Age					
	<35	17 (5.6)	0	-	***0.007***
	35 to 54	186 (60.9)	2 (1.1)	0.00-0.03	
	>55	103 (33.5)	8 (7.8)	0.03-0.13	
Gender					
	Male	271(88.6%)	8 (2.9)	0.01-0.05	0.320
	Female	35 (11.4%)	2 (5.7)	0.02-0.14	
Occupation					
	Job holder	114 (37.3)	2 (1.8)	0.01-0.04	0.449
	Business	84 (27.5)	2 (2.4)	0.01-0.06	
	Retired	69 (22.5)	4 (5.8)	0.00-0.11	
	Housewife	31 (10.1)	2 (6.5)	0.03-0.16	
	Student	8 (2.6)	0	-	

Contact history in past 14 days				
	Yes	117 (38.2)	2 (0.6)	0.01-0.04	0.327
	No	189 (61.8)	8 (2.5)	0.01-0.07	
Travel history to affected area in past 14 days				
	Yes	59 (19.3)	2 (0.6)	0.01-0.08	0.606
	No	247 (80.7)	8 (2.5)	0.01-0.05	
Number of affected family members				
	None	242 (79.1)	6 (2.5)	0.01-0.04	***0.046***
	One	43 (14.1)	4 (9.3)	0.00-0.18	
	Two or more	21 (6.8)	0	-	
Vaccinated				
	Yes	5 (1.6)	0	-	0.689
	No	301 (98.4)	10 (3.3)	0.01-0.05	

As observed, the variables age and number of affected family members had a significant association with patient death. In case of age, the elderly age group (>55 years) had a significantly (p=0.007) higher proportion of patients who died (7.8%) as compared to the younger age groups (01.1%). No deaths were reported under 35 years of age. For gender, majority of the patients who died were male patients with a male: female death ratio of 4:1. For occupation, patients who were retirees were more likely to expire. Although not so significant, patients with no history of travel or contact with infected individuals were more likely to have a worse outcome. As for affected family members, patients with a history of one affected family member had a significantly higher chance of death (p=0.046). In case of vaccination status, only 5 (1.6%) out of the 306 study subjects received at least one dose of vaccine. No deaths were observed among the vaccinated cases.

4.2 Risk factors among the patients

Among the various risk factors associated with COVID-19, hypertension was the most common (57.6%), followed by type 2 diabetes mellitus (47.2%); 33.5% of study subjects had a history of smoking, and 29.4% patients were obese. Other risk factors included bronchial asthma (15.2%), chronic kidney disease (10.4%), chronic heart disease (5.7%), cerebrovascular disease (5.4%), chronic obstructive pulmonary disease (3.8%),

immunosuppressive therapy (3.1%), chronic liver disease (1.6%), chemotherapy (0.6%) and surgery (0.6%). The various risk factors are shown in **Figure 4.1**.

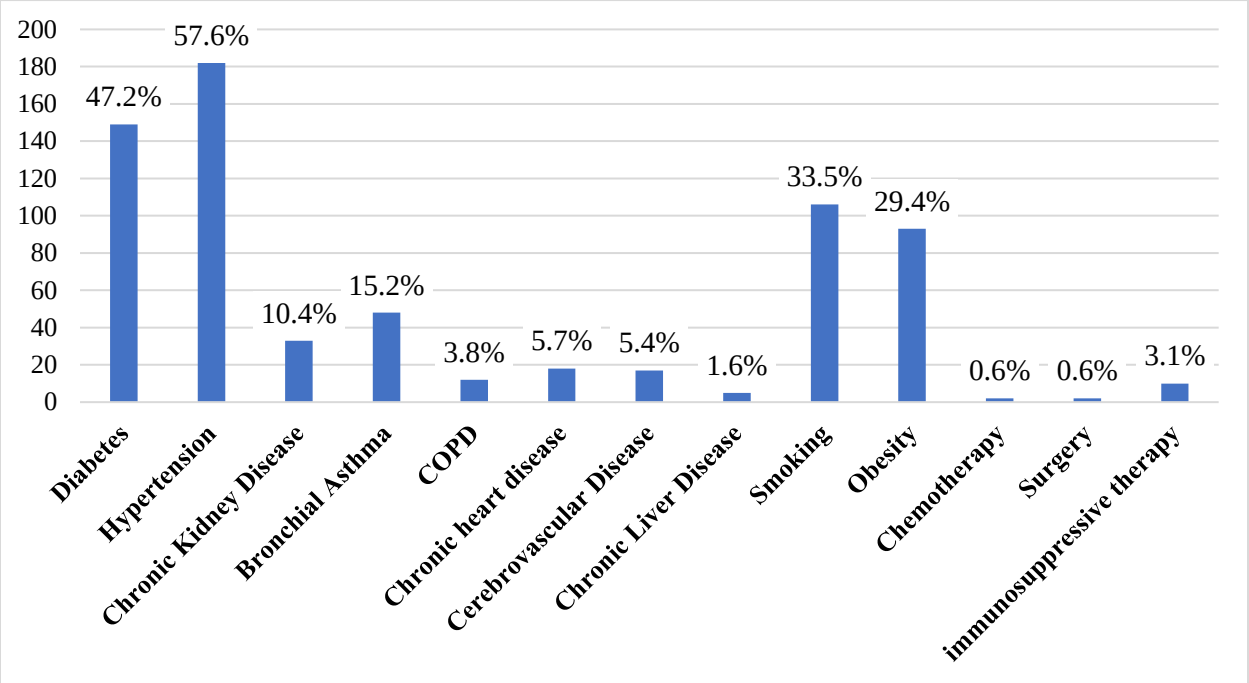

Figure 4.1: Risk factors among the study subjects (n=306)

To find out the different types of risk factors and their association with patient outcome, a univariate analysis was conducted for the different risk factors among the patients using chi-square test. A p-value < 0.05 was considered as significant. The results are shown in **Table 4.2**.

Table 4.2: Univariate analysis of risk factors associated with COVID-19 and patient outcome.

Risk factors	Categories	Total (%)	Died (%)	95% Confidence interval	P- value
Diabetes	no	167 (54.6)	0	-	***<0.001***
	yes	139 (45.4)	10 (7.2)	0.03-0.12	
Hypertension	no	134 (43.8)	0	-	***0.003***
	yes	172 (56.2)	10 (5.8)	0.02-0.09	
Chronic Kidney Disease	no	275 (89.9)	8 (2.9)	0.01-0.05	0.268
	yes	31 (10.1)	2 (6.5)	0.03-0.16	
Bronchial Asthma	no	262 (85.6)	6 (2.3)	0.00-0.04	***0.041***
	yes	44 (14.4)	4 (9.1)	0.00-0.18	
Chronic obstructive pulmonary disease	no	294 (96.1)	10 (3.4)	0.01-0.05	0.666
	yes	12 (3.9)	0	-	
Chronic heart disease	no	288 (94.1)	10 (3.5)	0.01-0.06	0.540
	yes	18 (5.9)	0	-	
Cerebrovascular Disease	no	291 (95.1)	8 (2.7)	0.01-0.05	0.080
	yes	15 (4.9)	2 (13.3)	0.06-0.33	
Chronic Liver Disease	no	301 (98.4)	10 (3.3)	0.01-0.05	0.846
	yes	5 (1.6)	0	-	
Smoking	no	204 (66.7)	6 (2.9)	0.01-0.05	0.441
	yes	102 (33.3)	4 (3.9)	0.00-0.08	
Obesity	no	217 (70.9)	6 (2.8)	0.01-0.05	0.324
	yes	89 (29.1)	4 (4.5)	0.00-0.09	
Chemotherapy	no	304 (99.3)	10 (3.3)	0.01-0.05	0.936
	yes	2 (0.7)	0	-	
Surgery	no	304 (99.3)	10 (3.3)	0.01-0.05	0.936
	yes	2 (0.7)	0	-	
Suppressive therapy	no	298 (97.4)	8 (2.7)	0.01-0.05	***0.024***
	yes	8 (2.6)	2 (25)	0.14-064	

The table above shows the various risk factors that were present among COVID-19 patients and their association with patient outcome. Patients with a history of diabetes ($p<0.001$), hypertension ($p= 0.003$), bronchial asthma ($p= 0.041$) and use of suppressive therapy ($p=0.024$) were significantly more likely to die from COVID-19.

4.3 Signs and symptoms among the study subjects

Common symptoms among study subjects included fever (99.3%), cough (91.8%), fatigue (81.7%), altered smell (81%), altered taste (71.6%), anorexia (56.5%), dyspnea (48.4%) and headache (48.4%). Other symptoms included generalized body ache (28.4%), sore throat (25.5%), conjunctivitis (23.5%), diarrhea (15%), nasal congestion (14.1%), vomiting (13.1%), dizziness (11.1%), chest pain (3.9%), confusion (3.3%) and skin rash (1.6%). **Figure 4.2** below shows the frequency of different symptoms that the patient has been admitted with.

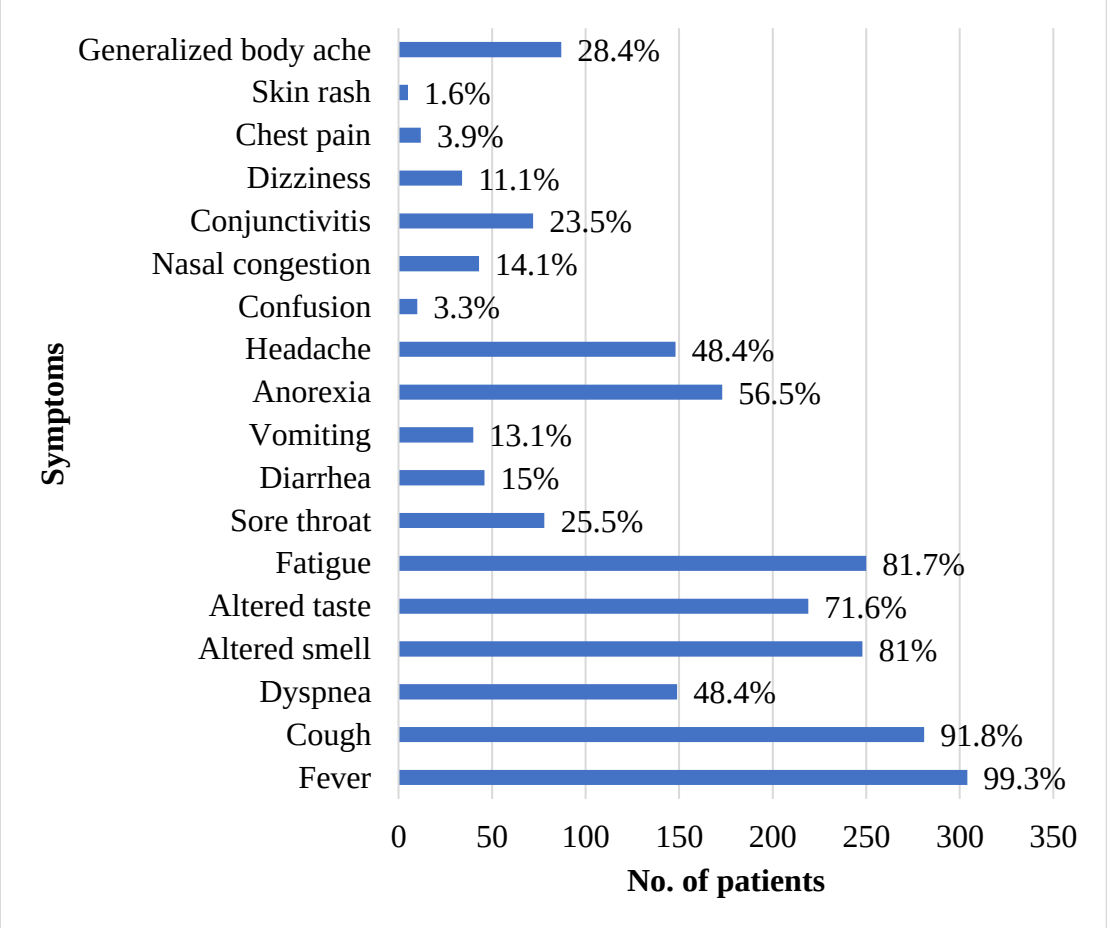

Figure 4.2: Presenting symptoms of study subjects

The signs observed on admission were wheezing (31.4%), crackles (21.9%), bronchial breath sounds (20.3%) and cyanosis (2%). **Figure 4.3** below displays the signs that the patients exhibited.

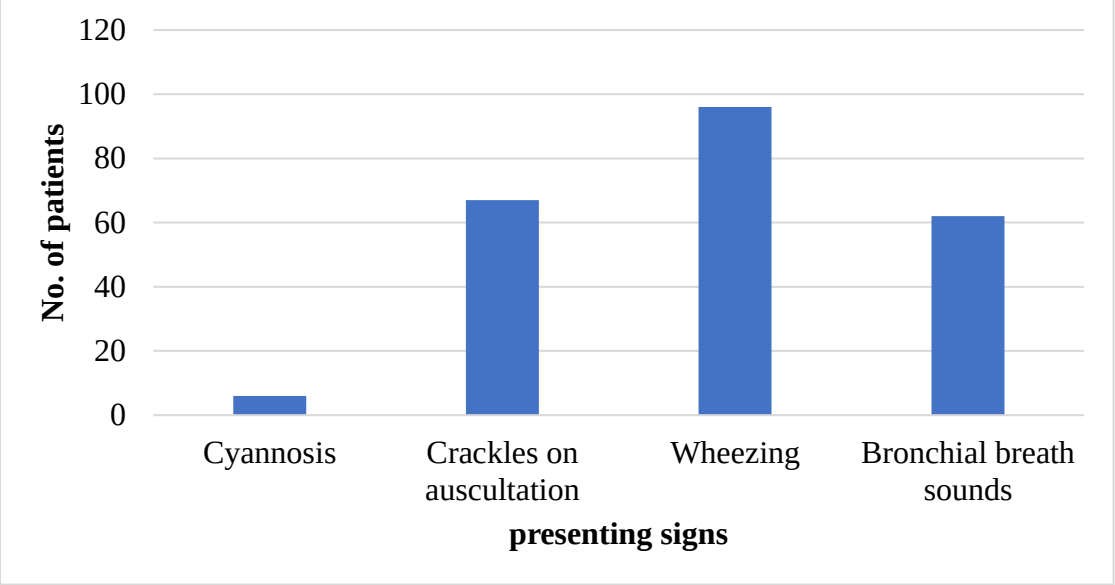

Figure 4.3: Presenting signs on admission among the study subjects.

To compare the differences in mean duration of signs and symptoms among patients who survived and patients who died, a univariate analysis was conducted keeping patient death as the dependent variable. Student's t-test was used for this and a p-value < 0.05 was considered as significant. The results are shown in **Table 4.3** and **Table 4.4.**

Table 4.3: Association of patient's signs and symptoms with patient outcome

Signs and symptoms	Patient Died	Mean duration (in days)	Std. Deviation	Std. Error of Mean	P- value
Fever	no	5.64	1.860	.108	***<0.001***
	yes	8.70	2.263	.716	
Cough	no	3.31	2.446	.142	***0.011***
	yes	7.20	3.824	1.209	
Dyspnea	no	0.62	.785	.046	***0.031***
	yes	2.60	2.459	.777	
Altered smell	no	1.65	1.426	.083	0.297
	yes	2.60	2.716	.859	
Altered taste	no	1.51	1.466	.085	***0.001***
	yes	5.20	2.348	.742	
Fatigue	no	1.75	1.484	.086	***0.009***
	yes	4.60	2.716	.859	
Sore throat	no	0.61	1.330	.077	0.611
	yes	0.40	.516	.163	
Diarrhea	no	0.18	.462	.027	0.133
	yes	0.40	.516	.163	
Vomiting	no	0.14	.420	.024	0.151
	yes	0.40	.516	.163	
Anorexia	no	1.18	1.458	.085	0.219
	yes	2.20	2.440	.772	
Headache	no	1.09	1.595	.093	0.568
	yes	0.80	1.229	.389	
Confusion	no	0.02	.141	.008	***0.045***
	yes	0.40	.516	.163	
Nasal congestion	no	0.39	1.180	.069	0.609
	yes	0.20	.422	.133	

Conjunctivitis	no	0.48	1.073	.062	0.407
	yes	0.20	.422	.133	
Dizziness	no	0.16	.583	.034	0.399
	yes	0.40	.843	.267	
Chest pain	no	0.04	.198	.011	0.518
	yes	0.00	0.000	0.000	
Skin rash	no	0.05	.383	.022	0.697
	yes	0.00	0.000	0.000	
Generalized body ache	no	0.71	1.319	.077	***<0.001***
	yes	0.00	0.000	0.000	
Cyanosis	no	0.02	.141	.008	0.651
	yes	0.00	0.000	0.000	
Crackles on auscultation	no	0.21	.405	.024	***0.04***
	yes	0.60	.516	.163	
Wheezing	no	0.31	.492	.029	***<0.001***
	yes	1.00	.667	.211	
Bronchial breath sounds	no	0.19	.392	.023	***0.033***
	yes	0.60	.516	.163	

The table above shows the association between the duration of patient's signs and symptoms and patient deaths. Out of 306 patients 296 patients survived while 10 patients died. From the table, it can be observed that a significant difference was found between mean duration of symptoms between patients who died and patients who survived for the variables fever ($p<0.001$), cough ($p=0.011$), dyspnea ($p=0.031$), altered taste ($p=0.001$), fatigue ($p=0.009$), confusion (0.045) and generalized body ache ($p<0.001$). Patients who died had a significantly prolonged mean duration of these symptoms. In case of signs, a significant difference was observed between mean duration of signs such as crackles ($p=0.04$), wheezing ($p<0.001$) and bronchial breath sounds ($p=0.033$).

Table 4.4: Association of vital signs of patients with patient outcome (N=306)

Variables	Patient expired	No. of patients	Mean	Std. Deviation	Std. Error of Mean	P value
SpO_2 on admission	no	296	93.71	4.60	.27	***0.004***
	yes	10	84.00	8.08	2.56	
SpO_2 after O_2 therapy	no	296	97.54	1.97	.11	***<0.001***
	yes	10	95.00	2.00	.63	
Glasgow Coma Scale (GCS)	no	296	14.86	.48	.03	***0.018***
	yes	10	14.00	.94	.30	
Temperature	no	296	100.17	.99	.06	0.438
	yes	10	99.92	.66	.21	
Heart rate	no	296	94.39	11.06	.64	***0.005***
	yes	10	107.00	10.91	3.45	
Systolic blood pressure	no	296	131.77	14.11	.82	***<0.001***
	yes	10	114.00	27.16	8.59	
Diastolic blood pressure	no	296	87.18	9.50	.55	***<0.001***
	yes	10	75.00	15.63	4.94	
Respiratory rate	no	296	21.08	1.96	.11	***0.008***
	yes	10	23.80	2.53	.80	

The table above displays the vital signs of the patients and their association with patient outcome. As observed, all the variables, except for temperature, showed a significant difference between patients who survived and patients who died. Patients who expired had a significantly lower SPO_2 on admission ($p=0.004$), lower SPO2 after oxygen therapy ($p<0.001$), lower GCS ($p=0.018$), lower systolic ($p<0.001$) and diastolic blood pressure ($p<0.001$), higher heart rate ($p=0.005$) and higher respiratory rate ($p=0.008$). A student's t-test was conducted for analysis.

4.4 Hematological and biochemical parameters of the study subjects

The various investigations conducted on the study subjects were evaluated and the results were compared between patients who survived and patients who expired. The mean values of serum electrolytes, hematological and biochemical markers were all compared by univariate analysis using student's t test and their results are presented in **Tables 4.5, 4.6** and **4.7** respectively.

Table 4.5: Association of serum electrolytes with patient outcome (n= 176)

Serum Electrolytes	Patient expired	No of patients	Mean	Std. Deviation	Std. Error of Mean	P-value
Sodium	no	166	134.04	3.906	.303	***0.002***
	yes	10	130.00	3.197	1.011	
Potassium	no	166	4.314	4.7971	.3723	***0.011***
	yes	10	3.320	.3360	.1062	
Chloride	no	166	98.55	3.313	.259	0.437
	yes	10	98.00	2.000	.632	
Bicarbonate	no	166	23.25	1.613	.125	***0.001***
	yes	10	21.40	1.578	.499	

The table above shows the association of serum electrolytes with patient outcome. From the table, it is observed that mean levels of sodium (p=0.002), potassium (p=0.011) and bicarbonate (p=0.001) were significantly lower among patients who expired.

Table 4.6: Relationship of hematological markers with patient outcome (N=306)

Hematological markers	Patient expired	No. of patients	Mean	Std. Deviation	Std. Error of Mean	p value
Hemoglobin in g/dl	no	296	11.127	1.4271	.0829	***<0.001***
	yes	10	8.820	.7729	.2444	
ESR	no	296	44.50	12.692	.775	***0.013***
	yes	10	54.80	14.718	4.654	
WBC	no	296	8.524	11.0264	.6409	***0.02***
	yes	10	17.260	24.1174	7.6266	
Neutrophil percentage	no	296	74.97	7.120	.414	***0.02***
	yes	10	82.80	5.095	1.611	
Lymphocyte percentage	no	296	19.01	6.224	.362	***0.001***
	yes	10	11.80	4.780	1.511	
Neutrophil: Lymphocyte ratio	no	296	4.5727	2.17399	.12636	***<0.001***
	yes	10	8.2171	3.37743	1.06804	
Platelet	no	296	187.50	51.580	2.998	***0.001***
	yes	10	130.80	8.979	2.839	

The table above displays the hematological markers among the two groups of patients. On conducting a univariate analysis, it was observed that all the parameters showed a

significant difference among patients who survived versus patients who died. Patients that expired had a significantly lower hemoglobin level (p<0.001), lymphocyte percentage (p=0.001), and platelet count (p=0.001); and a significantly higher ESR (p=0.013), total WBC (p=0.02), neutrophil percentage (p=0.02) and neutrophil: lymphocyte ratio (p<0.001).

Table 4.7: Relationship of biochemical markers with patient outcome

Biochemical markers	Patient expired	No. of patients	Mean	Std. Deviation	Std. Error Mean	P value
C reactive protein	no	296	122.79	123.12	7.16	***<0.001***
	yes	10	307.60	163.82	51.81	
PT	no	161	14.60	0.95	0.08	0.263
	yes	8	15.00	1.31	0.46	
Ferritin	no	247	384.27	258.56	16.45	***<0.001***
	yes	10	946.20	298.09	94.26	
D-dimer	no	294	1.54	8.61	0.50	***<0.001***
	yes	10	42.10	82.18	25.99	
procalcitonin	no	257	0.08	0.10	0.01	***0.037***
	yes	10	0.15	0.19	0.06	
Random blood sugar	no	266	9.61	3.61	0.22	***<0.001***
	yes	10	15.50	3.90	1.23	
SGPT/ALT	no	238	44.65	13.07	0.85	0.066
	yes	10	52.40	10.86	3.44	
SGOT/AST	no	183	49.77	12.21	0.90	***0.001***
	yes	8	64.25	9.08	3.21	
serum creatinine	no	276	1.16	0.79	0.05	***0.019***
	yes	10	1.76	0.69	0.22	
NT Pro BNP	no	135	218.00	107.63	38.05	***0.045***
	yes	8	316.79	271.10	23.33	
Troponin I	no	139	5.00	4.34	1.54	***0.001***
	yes	8	51.63	153.49	13.02	
Glycosylated hemoglobin	no	296	0.81	2.34	0.14	0.28
	yes	10	1.64	3.46	1.09	

*All biochemical parameters were not investigated for all 306 patients in the study

Table 4.7 above demonstrates the difference in biochemical markers among patients that survived as compared to the ones who died. A significant difference was found in all but

three of the parameters, namely prothrombin time, alanine aminotransferase and glycosylated hemoglobin. Patients who expired in hospital exhibited a significantly higher mean for NT Pro BNP (p= 0.045) and Troponin I (p=0.001). Such patients also displayed a significantly higher mean for C - reactive protein (p<0.001), serum ferritin (p<0.001), d-dimer (p<0.001), procalcitonin (p=0.037), random blood sugar (p<0.001), Aspartate transaminase (p=0.001) and serum creatinine (p=0.019).

4.5 Management of study subjects during hospital admission

The figure below shows the various measures taken in managing patients with a confirmed diagnosis of COVID-19. Out of 306 patients, 181 (59.2%) patients received oxygen through a nasal cannula. Intravenous fluids were given to 119 (38.9%) patients. Forty-seven (15.4%) patients needed B.P support using medications, 42 (13.7%) needed high flow nasal cannula to maintain their oxygenation, 33 (10.8%) patients were managed with CPAP, 16 (5.2%) with BiPAP, 6 (2%) required mechanical ventilation as a last resort and 2 (0.7%) patients had to undergo dialysis.

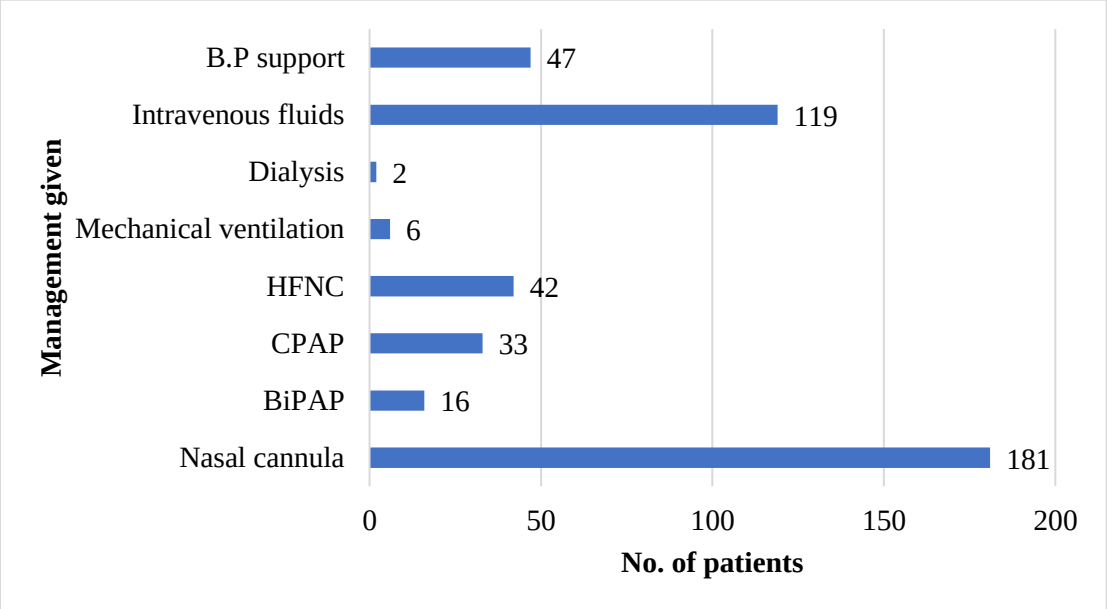

Figure 4.4: Management given to study subjects based on requirement

Table 4.8: Medications used by the study subjects

Medications used	Frequency	Percentage
Ivermectin	4	1.3
Enoxaparin	235	76.8
Favipiravir	2	0.7
Remdesivir	52	17.0
Dexamethasone	127	41.5
Methylprednisolone	23	7.5

Among the medications that were prescribed for the patients, the most common was enoxaparin (76.8%), followed by the glucocorticoid dexamethasone (41.5%), the antiviral Remdesivir (17%), methylprednisolone (7.5%), Ivermectin (1.3%) and Favipiravir (0.7%)

4.6 Outcome of the study subjects

The pie chart below shows the outcome of the study subjects. Out of a total of 306 patients, 88.9% recovered, 5.9% took discharge on risk bond, 2 % were referred to other hospitals and 3.3% died.

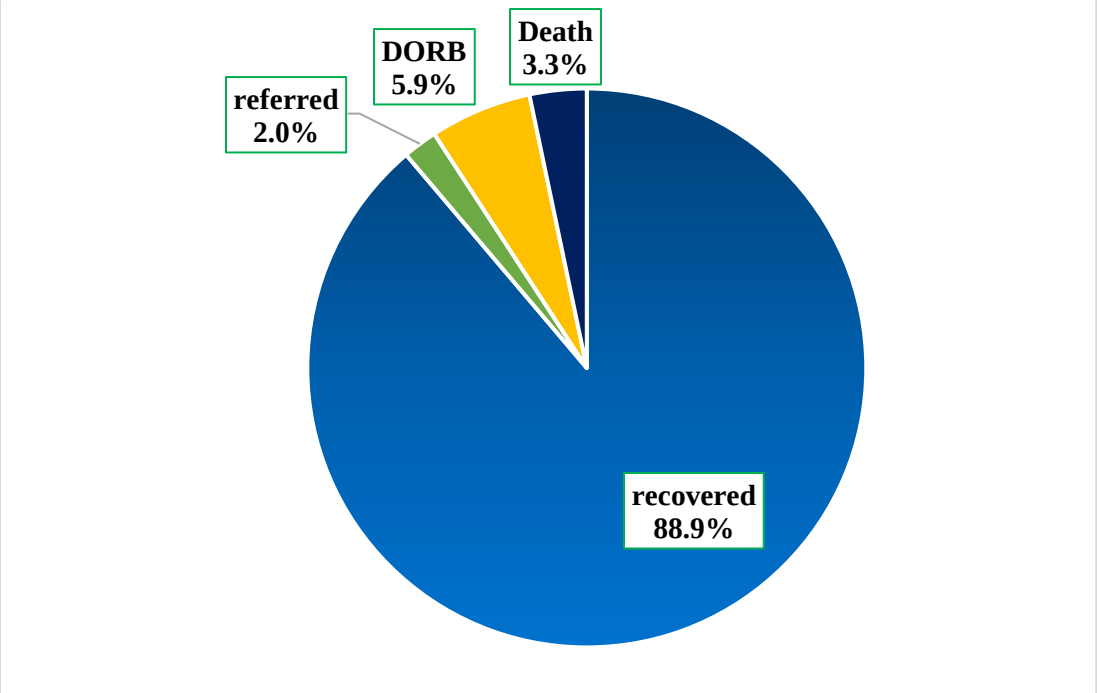

Figure 4.5: Outcome of the study subjects

Chapter 5- Discussion

As the coronavirus disease 2019 (COVID-19) pandemic continues to evolve, modifications in epidemiological and clinical features among different cohorts of patients have been noticed across different countries(Rodriguez-Morales, et al., 2020). Although multiple studies have been done internationally regarding the clinical features of COVID-19, few were conducted nationally (Chowdhury et al.,2021; Biswas et al., 2021). Hence, this study aims to shed light on the clinical presentation and outcome of hospitalized COVID-19 patients in the city of Chattogram, Bangladesh. The study undertaken was a prospective observational type of study where patients admitted to a private hospital with a diagnosis of COVID-19 were followed from their time of admission until their discharge or death.

The predominance of the male population in this study was found to be much higher than many other studies conducted both nationally (Biswas, et al., 2021) and internationally (Chen, et al., 2020). In a study conducted by (Tian, et al., 2020) in China, the median age of the patients was 47.5 years. However, contrary to our study, the proportion of male patients (48.5%) admitted was much lower than our study. This variation in admission could be due to the increased prevalence of certain risk factors, such as smoking among the male gender as compared to female gender in Bangladesh (Sultana et al.,2015). Nevertheless, according to another study by (Vahey, et al., 2021), male gender and older age (>65 years) showed significant association with hospitalization which is consistent with our study.

For occupation, job holders made up the highest proportion of enrolled study subjects while students made up the least proportion. According to a study published by (Mutambudzi, et al., 2021), essential workers are more likely to get infected by COVID-19 as compared to non-essential workers. Although our study did not precisely mention the occupation of the job holders, it is comprehendible that this cohort of study subjects had to go to work and hence were more likely to have been exposed to infection. As for students, since schools were shut down to limit spread of infection, these individuals were less likely to get infected unless through their family members.

In case of vaccination status, only 5 (1.6%) cases received at least one dose of vaccine. This agrees with the study by Havers, et al., (2021) where vaccinated people were less likely to get admitted unless they were old or had at least three underlying medical conditions. The Havers study also reports that unvaccinated people are 17 times more likely to be admitted for COVID-19 than unvaccinated people. Common comorbidities observed among the study subjects were hypertension, diabetes, smoking, obesity, bronchial asthma and so on. Vahey, et al., (2021) reports that taking opioids, having metabolic syndrome, obesity, hypertension and arrhythmia is significantly associated with hospitalization of COVID-19 patients. Another study by Wang, et al., (2020), reports patients with pre-existing diabetes mellitus, hypertension, cardiovascular diseases, or respiratory diseases to be more critically ill requiring hospital admissions. Yet another Brazilian study by Soares et al (2020) reported that cardiovascular diseases and diabetes were the two most common comorbidities among the patients hospitalized for COVID-19. The association between smoking and increased severity of COVID-19 has been reported in multiple studies (Reddy, et al., 2021; Patanavanich and Glantz, 2020). While a history of smoking increases the risk of hospitalization during COVID 19, current smoker usually have a worse prognosis and past smokers(Reddy, et al., 2021). For chronic kidney disease, one meta-analysis conducted by (Henry and Lippi, 2020) found a significant association between chronic kidney disease and severe COVID-19. Hence, it is not astonishing to find such patients admitted to hospital for COVID-19.

The proportion of patients exhibiting these symptoms in much higher in this study than the one published by Tian, et al., (2020). Common symptoms reported in that study were fever, cough, fatigue, dyspnea and headache. In another study by (Soares, et al., 2020) common clinical symptoms were cough, fever, headache, runny nose, sore throat, shortness of breath and diarrhea. While proportion of patients with fever, cough and shortness of breath were higher in our study, proportion of patients with headache, frequency of patients with nasal congestion was higher in their study.

Patients in our study presented with signs of wheezing, crackles and bronchial breath sounds on pulmonary auscultation. Wang, et al. (2020) reported similar findings in their study on the characteristics of pulmonary auscultation in patients with COVID-19.

Cyanosis was another sign observed in 2% of the patients in our study. In case of clinical management, patients mostly received IV fluids, followed by medications to support blood pressure. Supplemental O_2 was given to 89.8% of the study respondents. Some of these patients had received noninvasive therapy followed by invasive therapy based on their oxygen requirements. This is similar to another study conducted in Chattogram where 82.8% patients needed supplemental oxygen (Biswas, et al., 2021).

The most common drugs used for COVID-19 treatment were enoxaparin (76.8%), followed by the dexamethasone (41.5%), Remdesivir (17%), methylprednisolone (7.5%), Ivermectin (1.3%) and Favipiravir (0.7%). Biswas, et al., (2021) reported treatments using Favipiravir in 59(28.2%), Remdisivir in 111(53.1%), Methylprednisolone in 87(41.6%), Dexamethasone in 93(44.5%), Antibiotics in 204(97.60%), Toccilizumab in 34(16.3%), plasma in 18(8.6%) and LMWH in 200(95.7%) patients. In our study no patient was given Tocilizumab or plasma therapy since one was very expensive and the other was controversial. As for patient outcome 88.9% recovered, 5.9% took DORB, 2 % were referred to other hospitals and 3.3% died. This fatality rate is higher than that observed in China(Tian, et al., 2020). However, nationally, it is much lower than two other studies conducted in Bangladesh(Biswas, et al., 2021)(Chowdhury, et al., 2021).

On comparing the different parameters between the patients who expired as compared to survived, significant differences were found in many parameters. For demographic profile, the age ($p=0.007$) and number of affected family members ($p=0.046$) were significantly associated with adverse patient outcome. Majority of deaths were reported in the >55 year old age group and no deaths reported under age 35. Most of the patients who died were male patients with a male: female ratio of 4:1. According to a study by (Wang, et al., 2020), patients who die due to COVID-19 are more likely to be aged and be male. For occupation, patients who were retirees were more likely to have an adverse outcome since they were aged. As for affected family members, patients with a history of one affected family member had a significantly higher chance of death ($p=0.046$). In case of vaccination, no deaths were observed among the vaccinated cases. Patients with a history of diabetes ($p<0.001$), hypertension ($p= 0.003$), bronchial asthma ($p= 0.041$) and use of suppressive therapy ($p=0.024$) had a significant association with adverse patient outcome. This is

somewhat similar to a study by (Wang, et al., 2020) where patients who died were more likely to have hypertension, cardiovascular diseases or diabetes. The present study found a significant difference between mean duration of symptoms for the variables fever ($p<0.001$), cough ($p=0.011$), dyspnea ($p=0.031$), altered taste ($p=0.001$), fatigue ($p=0.009$), confusion (0.045) and generalized body ache ($p<0.001$) among patients who survived versus those who died. One study by Verity, et al., (2020) estimates the mean duration from onset-of-symptoms to death to be 17.8 days. Another study by Islam, et al., (2020) claims that among the various clinical characteristics such as fever, cough, myalgia, diarrhea, abdominal pain, dyspnea, fatigue, sputum production, chest tightness headache and nausea or vomiting, only fatigue and dyspnea increased the death significantly.

A significant increase between mean duration of specific signs such as crackles ($p=0.04$), wheezing ($p<0.001$) and bronchial breath sounds ($p=0.033$) was also observed among patients who died. This is expected, as patients who died from the disease could not recover from the illness and hence the symptoms remained until death. Additionally, patients who expired had a significantly lower SPO_2 on admission ($p=0.004$), lower SPO_2 after oxygen therapy ($p<0.001$), lower GCS ($p=0.018$), lower systolic ($p<0.001$) and diastolic blood pressure ($p<0.001$), higher heart rate ($p=0.005$) and higher respiratory rate ($p=0.008$). Pan, et al., (2020) identified SPO_2 and diastolic pressure, to be significantly different between patients who survived and patients who died.

In the present study, levels of sodium, potassium and bicarbonate were significantly low among patients who expired. According to a study by (Tezcan, et al., 2020), hyponatremia was one of the independent factors related to COVID-19 mortality. Unlike our study, hypochloremia and hypocalcemia were also related to adverse patient outcome. For hematological markers, patients that expired had a significantly lower hemoglobin level ($p<0.001$), lymphocyte percentage ($p=0.001$), and platelet count ($p=0.001$); and a significantly higher ESR ($p=0.013$), total WBC ($p=0.02$), neutrophil percentage ($p=0.02$) and neutrophil: lymphocyte ratio ($p<0.001$). Our findings are similar to another study conducted by (Henry, et al., 2020) where a significant increase in white blood cells, and decrease in neutrophils and platelets were observed. A raised ESR was also observed in that study. However, unlike our study, no significant difference was observed between

levels of hemoglobin among patients who survived versus patients who died. A decreased hemoglobin levels was found in another study by Selçuk, et al. (2020) along with an increase in WBC count.

For biochemical markers, among patients that died, a significantly higher mean for NT Pro BNP ($p= 0.045$) and Troponin I ($p=0.001$) were observed. At the same time, a significantly higher mean for C - reactive protein ($p<0.001$), serum ferritin ($p<0.001$), d- dimer ($p<0.001$), procalcitonin ($p=0.037$), random blood sugar ($p<0.001$), aspartate transaminase ($p=0.001$) and serum creatinine ($p=0.019$) were also observed. Similar results were reported in the study by Henry, et al., (2020), where a significantly raised CRP, ferritin and procalcitonin were reported. Another study by (Gao, et al., 2020), reports the NT-Pro BNP to be significantly raised among patients who have an adverse outcome for COVID-19- a finding similar to our study. One other study by (Selçuk, et al., 2021) reported elevated levels of glucose, Troponin I, NT-Pro BNP and creatinine levels, all of which were consistent in our study.

Chapter 6- Conclusion

The study indicated certain demographic factors and comorbidities were more common in patients that had an adverse outcome of COVID-19. Factors that determined adverse patient outcome were older age, comorbidities like diabetes, hypertension and asthma, patients on immunosuppressive therapy, etc. Significant variations in hematological and biochemical parameters were also observed when cases were compared based on patient survival. While the case fatality rate in this study was much higher than a few neighboring countries, it was comparatively lower than studies conducted and published nationally. Improved management of patients with COVID-19 can limit disease related complications and untimely loss of life. That being stated, identification of specific indicators that can help detect potentially fatal cases earlier can further improve patient outcome.

Chapter 7- Limitations

This study, like many others, had many limitations that needs to be mentioned.

- Owing to time limitations and a single center for data collection, this study fell slightly short of the targeted number of 354 participants.
- The participants could not be categorized as mild, moderate or severely ill due to their health statuses changing constantly in hospital admission. To avoid confusion, this parameter was skipped altogether.
- To improve accuracy of results, only patients who had a positive confirmatory RT-PCR test for COVID-19 were included in our study. This has caused symptomatic false negative cases to be excluded from our study.
- Outcome of some patients whose symptoms have deteriorated during hospital stay could not be observed due to lack of available seats at the hospital ICU due to which they had to be referred elsewhere.
- Since this is a single center study, data might not be representative of the entire population. For more precise results, a multi-center approach involving many COVID-19 dedicated hospitals in the city was not possible due to hindrances in obtaining permission from respective hospital authority.
- Since the collection of data and publication of the results, newer medications have been introduced. At the same time, the coronavirus has also undergone mutations to develop a more virulent strain. As the result, patient outcome may be different than what is observed in this study.

Chapter 8- Recommendations

This study is an initial step in exposing the characteristics of COVID-19 patients in Bangladesh. Further studies need to be conducted on the prevention and control of COVID-19 based on the risk factors mentioned in this study and outside. Studies need to be conducted on the impact vaccinations have on patient outcome among hospitalized COVID 19 patients. All cases that were included had a confirmatory test for COVID-19. A comparative study between RTPCR positive and RTPCR negative patients that are symptomatic for COVID 19 should be done to observe any variations in outcome. In addition, conducting a study comparing symptomatic patients with an initial RT-PCR negative COVID-19 test result followed by a repeated test that came back positive; with that of symptomatic patients who had an initial RT-PCR positive test result can help us understand, the impact a delayed confirmatory diagnosis has on treatment and patient outcome.

References

Anand, K. B., Karade, S., Sen, S. and Gupta, R. M., 2020. SARS-CoV-2: camazotz's curse. Medical Journal Armed Forces India, 76(2), p. 136-41.

Biswas, R.S.R., Nath, J.D., Barua, P.K., Karim, M.R., Islam, M.S. and Ahmed, K.F., 2021. Clinicopathological features and outcome of COVID-19-early experiences from three covid hospitals, Chittagong, Bangladesh. medRxiv, Volume In press.

Boopathi, S., Poma, A. B. and Kolandaivel, P., 2021. Novel 2019 coronavirus structure, mechanism of action, antiviral drug promises and rule out against its treatment. Journal of Biomolecular Structure and Dynamics, 39(9), p. 3409-18.

Braciale, T. J. and Hahn, Y. S., 2013. Immunity to viruses. Immunological reviews, 255(1), p. 5.

Brian, D. A. and Baric, R. S., 2005. Coronavirus Replication and Reverse Genetics. 1 ed. Heidelberg: Springer Berlin.

Cai, Q., Huang, D., Yu, H., Zhu, Z., Xia, Z., Su, Y., et al., 2020. COVID-19: Abnormal liver function tests. J Hepatol, 73(3), p. 566.

Charan, J. and Biswas, T., 2013. How to calculate sample size for different study designs in medical research? Indian journal of psychological medicine, 35(2), p.121-26.

Chen L, Liu HG, Liu W, Liu J, Liu K, Shang J, et al., 2020. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. Chinese journal of tuberculosis and respiratory diseases, 43, p. E005.

Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., Han, Y., et al., 2020. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet, 395(10223), p. 507-513.

Chowdhury, A.T.M.M., Karim, M.R., Mehedi, H.H., Shahbaz, M., Chowdhury, M.W., Dan, G. et al., 2021. Analysis of the primary presenting symptoms and hematological findings of COVID-19 patients in Bangladesh. The Journal of Infection in Developing Countries, 15(02), p.214-223.

De Groot RJ, Baker SC, Baric RS, Brown CS, Drosten C, Enjuanes L, et al., 2013. Commentary: Middle east respiratory syndrome coronavirus (mers-cov): announcement of the coronavirus study group. Journal of virology, 87(14), p. 7790-7792.

DGHS, 2021. COVID-19 Dynamic Dashboard for Bangladesh. [Online] Available at: http://103.247.238.92/webportal/pages/covid19.php[Accessed 15 9 2021].

DGHS, 2021. National Guidelines on COVID-19. Dhaka: Communicable Disease Control, Directorate General of Health Services.

Diao, B., Wang, C., Wang, R., Feng, Z., Zhang, J., Yang, H., et al., 2021. Human kidney is a target for novel severe acute respiratory syndrome coronavirus 2 infection. Nature Communications, 12(1), p.1-9.

Fiske, A., Schönweitz, F., Eichinger, J., Zimmermann, B., Hangel, N., Sierawska, A., et al., 2022. The COVID-19 Vaccine: Trust, doubt, and hope for a future beyond the pandemic in Germany. Plos one, 17(4), p.e0266659.

Fung, T. S. and Liu, D. X., 2019. Human Coronavirus: Host-Pathogen Interaction. Annu. Rev. Microbiol, 73, p. 529–557.

Gao, L., Jiang, D., Wen, X.S., Cheng, X.C., Sun, M., He, B., et al., 2020. Prognostic value of NT-proBNP in patients with severe COVID-19. Respiratory research, 21(1), p. 1-7.

Hamming, I., Timens, W., Bulthuis, M.L.C., Lely, A.T., Navis, G.V. and van Goor, H., 2004. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. The Journal of Pathology: A Journal of the Pathological Society of Great Britain and Ireland, 203(2), p. 631-7.

Havers, F.P., Pham, H., Taylor, C.A., Whitaker, M., Patel, K., Anglin, O., et al., 2021. COVID-19-associated hospitalizations among vaccinated and unvaccinated adults≥ 18 years–COVID-NET, 13 states, January 1–July 24. medRxiv, p. In Press.

Henry, B.M., De Oliveira, M.H.S., Benoit, S., Plebani, M. and Lippi, G., 2020. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID- 19): a meta-analysis. Clinical Chemistry and Laboratory Medicine (CCLM), 58(7), p. 1021-8.

Henry, B. M. and Lippi, G., 2020. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. International urology and nephrology, 52(6), p. 1193-4.

Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., et al., 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet, 395(10223), p.497-506.

Islam, M.S., Barek, M.A., Aziz, M.A., Aka, T.D. and Jakaria, M., 2020. Association of age, sex, comorbidities, and clinical symptoms with the severity and mortality of COVID-19 cases: a meta-analysis with 85 studies and 67299 cases. medRxiv. Issue In press.

Jiang, S., Du, L. and Shi, Z., 2020. An emerging coronavirus causing pneumonia outbreak in Wuhan, China: calling for developing therapeutic and prophylactic strategies. Emerging microbes and infections, 9(1), p. 275-277.

King, J., Kosinski-Collins, M. and Sundberg, E., 2020. Coronavirus Structure, Vaccine and Therapy Development. [Online] Available at: https://www.biophysics.org/blog/coronavirus-structure-vaccine-and-therapy-development [Accessed 23 April 2021].

Letko, M., Marzi, A. and Munster, V., 2020. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. Nat. Microbiol, 5(4), p. 562-569.

Lippi, G. and Plebani, M., 2020. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. Clinical Chemistry and Laboratory Medicine, 58(7), p. 1063-9.

Liu, X., Wang, J., Xu, X., Liao, G., Chen, Y. and Hu, C.H., 2020. Patterns of IgG and IgM antibody response in COVID-19 patients. Emerging microbes & infections, 9(1), p.1269-1274.

Li, W., 2005. Bats Are Natural Reservoirs of SARS-Like Coronaviruses. Science, 310, p. 676-679.

Lu, R., Zhao, X., Li, J., Niu, P., Yang, B., Wu, H., et al., 2020. Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. The lancet, 395(10224), p.565-574.

MOHFW, 2020. National guidelines on clinical management of COVID-19, Dhaka: MOHFW.

Mohiuddin, A. K., 2020. A Brief Review of Covid-19 Situation in Bangladesh, Tejgao, Dhaka: Preprints.

Mutambudzi, M., Niedzwiedz, C., Macdonald, E.B., Leyland, A., Mair, F., Anderson, J., et al., 2021. Occupation and risk of severe COVID-19: prospective cohort study of 120 075 UK Biobank participants. Occupational and environmental medicine, 78(5), p.307-314.

National Health Commission of the People's Republic of China, 2020. Covid-19's Diagnosis and Treatment Plan (Trial Eighth Edition). Infect Dis Immun, 1(1), p. E1.

Na, W., Moon, H. and Song, D., 2021. A comprehensive review of SARS-CoV-2 genetic mutations and lessons from animal coronavirus recombination in one health perspective. Journal of Microbiology, 59(3), p. 332-40.

Pan F, Yang L, Li Y, Liang B, Li L, Ye T, et al., 2020. Factors associated with death outcome in patients with severe coronavirus disease-19 (COVID-19): a case-control study. International journal of medical sciences,17(9):1281.

Patanavanich, R. and Glantz, S. A., 2020. Smoking is associated with COVID-19 progression: a meta-analysis. Nicotine and Tobacco Research, 22(9), p. 1653-6.

Patel, M., Chaubey, A.K., Pittman Jr, C.U., Mlsna, T. and Mohan, D., 2021. Coronavirus (SARS-CoV-2) in the environment: Occurrence, persistence, analysis in aquatic systems and possible management. Science of The Total Environment, 765, p.142698.

Peiris, J.S.M., Lai, S.T., Poon, L.L.M., Guan, Y., Yam, L.Y.C., Lim, W, et al., 2003. Coronavirus as a possible cause of severe acute respiratory syndrome. The Lancet, 361(9366), p.1319-25.

Pradhan, D., Biswasroy, P., Naik, P.K., Ghosh, G. and Rath, G., 2020. A review of current interventions for COVID-19 prevention. Archives of medical research, 51(5):363-74.

Ragab, D., Salah Eldin, H., Taeimah, M., Khattab, R. and Salem, R., 2020. The COVID-19 cytokine storm; what we know so far. Frontiers in immunology, p.1446.

Ramírez-Truque, M. and Herrera-Morice, M., 2020. Role of the clinical laboratory in the COVID-19 epidemic: review of available diagnostic methods and their limitations. 86(629).

Rana, E.A., Chowdhury, N.S., Islam, M.S., Ara, J., Nasrin, S.S., Dutta, P., et al., 2020. Molecular detection and prevalence of SARS-CoV-2 during the early outbreak in Southern Bangladesh. Int. J. One Health, 6(2), p.153-59.

Reddy, R.K., Charles, W.N., Sklavounos, A., Dutt, A., Seed, P.T. and Khajuria, A., 2021. The effect of smoking on COVID-19 severity: A systematic review and meta-analysis. Journal of medical virology, 93(2), p.1045-56.

Rehman, S.U., Shafique, L., Ihsan, A. and Liu, Q., 2020. Evolutionary trajectory for the emergence of novel coronavirus SARS-CoV-2. Pathogens, 9(3), p.240.

Rodriguez-Morales, A. J., Rodriguez-Morales, A. G., Méndez, C. A. and Hernández-Botero, S., 2020. Tracing new clinical manifestations in patients with COVID-19 in Chile and its potential relationship with the SARS-CoV-2 divergence. Current Tropical Medicine Reports, 7(3), p. 75-8.

Rokni, M., Ghasemi, V. and Tavakoli, Z., 2020. Immune responses and pathogenesis of SARS-CoV-2 during an outbreak in Iran: Comparison with SARS and MERS. Reviews in medical virology, 30(3), p.e2107.

Ruan, Q., Yang, K., Wang, W., Jiang, L. and Song, J., 2020. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive care medicine, 46(5), p.846-48.

Schulte-Schrepping, J., Reusch, N., Paclik, D., Baßler, K., Schlickeiser, S., et al., 2020. Severe COVID-19 is marked by a dysregulated myeloid cell compartment. Cell, 182(6), p.1419-40.

Selçuk, M., Keskin, M., Çınar, T., Günay, N., Doğan, S., Çiçek, V., et al., 2021. Prognostic significance of N-Terminal Pro-BNP in patients with COVID-19 pneumonia without previous history of heart failure. Journal of Cardiovascular and Thoracic Research, 13(2), p.141.

Shimizu, M., 2019. Clinical features of cytokine storm syndrome. In: R. Cronand E. Behrens, eds. Cytokine storm syndrome. Cham: Springer, p. 31-41.

Siordia Jr, J. A., 2020. Epidemiology and clinical features of COVID-19: A review of current literature. Journal of Clinical Virology, 127, p. 104357.

Soares, R. D., Mattos, L. R. and Raposo, L. M., 2020. Risk factors for hospitalization and mortality due to COVID-19 in Espírito Santo State, Brazil. The American Journal of Tropical Medicine and Hygiene, 103(3), p. 1184.

Sultana, P., Akter, S., Rahman, M.M. and Alam, M.S., 2015. Prevalence and predictors of current tobacco smoking in Bangladesh. J Biostat Biometric App, 1(1), p.102.

Tezcan, M.E., Gokce, G.D., Sen, N., Kaymak, N.Z. and Ozer, R.S., 2020. Baseline electrolyte abnormalities would be related to poor prognosis in hospitalized coronavirus disease 2019 patients. New Microbes and New Infections, 37, p.100753.

Thompson, M. R., Kaminski, J. J., Kurt-Jones, E. A. and Fitzgerald, K. A., 2011. Pattern recognition receptors and the innate immune response to viral infection. Viruses, 3(6), p. 920-940.

Thrusfield, M. & Brown, H., 2017. Surveys. In: F. Edition, ed. Veterinary Epidemiology: Wiley-Blackwell, p. 270-295.

Tian, S., Hu, N., Lou, J., Chen, K., Kang, X., Xiang, Z., et al., 2020. Characteristics of COVID-19 infection in Beijing. Journal of infection, 80(4), p.401-06.

Tyrrell, D. A. and Bynoe, M. L., 1965. Cultivation of a novel type of common-cold virus in organ cultures. British Medical Journal, 1(5448), p. 1467.

Vahey, G.M., McDonald, E., Marshall, K., Martin, S.W., Chun, H., Herlihy, R., et al., 2021. Risk factors for hospitalization among persons with COVID-19—Colorado. PloS one, 16(9), p. e0256917.

Verity, R., Okell, L.C., Dorigatti, I., Winskill, P., Whittaker, C., Imai, N., et al., 2020. Estimates of the severity of COVID-19 disease. MedRxiv. Volume: In Press

Vijgen, L., Keyaerts, E., Moës, E., Thoelen, I., Wollants, E., Lemey, P., et al., 2005. Complete genomic sequence of human coronavirus OC43: molecular clock analysis suggests a relatively recent zoonotic coronavirus transmission event. Journal of virology, 79(3), p.1595-604.

Wang, B., Liu, Y., Wang, Y., Yin, W., Liu, T., Liu, D., et al., 2020. Characteristics of pulmonary auscultation in patients with 2019 novel coronavirus in China. Respiration, 99(9), p.755-63.

Wang, F., Cao, J., Yu, Y., Ding, J., Eshak, E.S., Liu, K., et al., 2020. Epidemiological characteristics of patients with severe COVID-19 infection in Wuhan, China: evidence from a retrospective observational study. International journal of epidemiology, 49(6), p.1940-50.

Wang, F., Wang, H., Fan, J., Zhang, Y., Wang, H. and Zhao, Q., 2020. Pancreatic injury patterns in patients with coronavirus disease 19 pneumonia. Gastroenterology, 159(1), p.367-70.

Wang, L.F., Shi, Z., Zhang, S., Field, H., Daszak, P. and Eaton, B.T., 2006. Review of Bats and SARS. Emerging infectious diseases,12, p. 1834–1840.

Wang, M.Y., Zhao, R., Gao, L.J., Gao, X.F., Wang, D.P. and Cao, J.M., 2020. SARS-CoV-2: Structure, Biology, and Structure-Based Therapeutics Development. Frontiers in cellular and infection microbiology, p. 724.

Worldometer, 2021. Covid-19 coronavirus pandemic. [Online]. Available at: https://www.worldometers.info/coronavirus/?utm_campaign=homeAdvegas1? [Accessed 17 7 2021].

Yan, Y., Shin, W.I., Pang, Y.X., Meng, Y., Lai, J., You, C., et al., 2020. The first 75 days of novel coronavirus (SARS-CoV-2) outbreak: recent advances, prevention, and treatment. International journal of environmental research and public health, 17(7), p. 2323.

Yin, Y. and Wunderink, R. G., 2018. MERS, SARS and other coronaviruses as causes of pneumonia. Respirology, 23(2), p. 130-7.

Zhang, W., Du, R.H., Li, B., Zheng, X.S., Yang, X.L., Hu, B., et al., 2020. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerging microbes and infections, 9(1), p. 386-9.

Zhou, H., Zhang, Z., Dobrinina, M., Dong, Y., Kang, Z., Chereshnev, V., et al., 2022. Urinalysis, but not blood biochemistry, detects the early renal-impairment in patients with COVID-19. medRxiv, p. 1-19.

Zhou, X. and Ye, Q., 2021. Cellular Immune Response to COVID-19 and Potential Immune Modulators. Frontiers in Immunology. Frontiers in Immunology, 12, p.1566.

Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., et al., 2020. A novel coronavirus from patients with pneumonia in China, 2019. New England Journal of Medicine, 382, p. 727–733.

Annexure 1

Title: "Analysis of Clinical features of COVID-19 patients in Chattogram, Bangladesh."

সম্মতি পত্র (Consent Form)

আমি……বয়স……...

এই মর্মে সম্মতি প্রদান করছি যে, এ যে তথ্য দেয়া হয়েছে তা পড়েছি ।

১। আমাকে গবেষণা সম্বন্ধে বিস্তারিত জানান হয়েছে।

২। আমি লিখিতভাবে আমার তথ্য লিপিবদ্ধ করার ব্যাপারে সম্মতি প্রদান করেছি।

৩। আমি এই গবেষণার একটি কপি আমার কাছে রাখতে পারব।

৪। আমি এই মর্মে অবগত আছি যে–

- এই গবেষণা দ্বারা আমি সরাসরি উপকৃত নাও হতে পারি।
- আমি যেকোনো সময় আমার সম্মতি প্রত্যাহার করতে পারব।
- গবেষণার কোন জায়গায় আমার নাম প্রকাশ করা হবেনা।
- আমি গবেষণায় থাকি বা না থাকি আমার চিকিৎসায় কোন পরিবর্তন হবেনা।
- গবেষণার যেকোনো সময় আমি আমার নাম পরিবর্তন করতে পারব।

৫। আমি গবেষণার ফল অন্য গবেকদের মধ্যে প্রকাশ করার অনুমতি প্রদান করছি।

৬। আমি গবেষণার ফল আমার পরিবার ও বন্ধুদের মধ্যে প্রকাশ করতে পারব।

অংশগ্রহনকারীর সাক্ষর ……. তারিখ ……..

আমি এই মর্মে ঘোষণা করছি যে আমি গবেষণার ব্যাপারে উনাকে জানিয়েছি-

গবেষকের নাম…….. তারিখ……

Annexure 2

Title: "Analysis of Clinical features of COVID-19 patients in Chattogram , Bangladesh"

Case Record Form (CRF)

Case no:							**Date of entry:……./……./202**		
Patient code number/hospital Registration number:									
Name(name will not be used in public domain) :									
Age (completed years)	**Below 12 =0**	**13-17 =1**	**18-24 =2**	**25-34 =3**	**35-44 =4**	**45-54 =5**	**55-64=6**	**65-74=7**	**75 or older =8**
Sex :	**Male=0**		**Female=1**						
Address:	**Division…….. District…… Union…….**		**Ward No: House No: National ID (If known):**						
Occupation:									
Contact Number:									
Date of Symptom onset:			**Date of Sample collection:**						
Date of admission (only for admissible patient):									
Any contact of COVID -19 patient in last 14 days: No=0 Yes=01									
Ay History of Travelling or residing in area reporting CoVID-19: No=0 Yes=01									
Family members affected: No=0 Yes=01 If yes ,number:									

Asymptomatic /Mild/Moderate/Severe/Critical

1. General Symptoms(Please tick all the symptoms present in the patient	**If yes , duration in days**

Fever	**No=0 Yes=1**	
Cough	**No=0 Yes=1**	
Difficulty breathing(dyspnea)	**No=0 Yes=1**	
Altered sense of smell	**No=0 Yes=1**	
Altered sense of Taste	**No=0 Yes=1**	
Fatigue	**No=0 Yes=1**	
Sore throat	**No=0 Yes=1**	
Diarrhoea	**No=0 Yes=1**	
Vomiting	**No=0 Yes=1**	
Anorexia	**No=0 Yes=1**	
Headache	**No=0 Yes=1**	
Confusion	**No=0 Yes=1**	
Nasal Congestion	**No=0 Yes=1**	
Conjunctivitis	**No=0 Yes=1**	
Dizziness	**No=0 Yes=1**	
Chest Pain	**No=0 Yes=1**	
Others (Mention):		

2. Sign (Tick) : (Please tick all the symptoms present in the patient)

Cyanosis	**No=0 Yes=1**	
Crackles	**No=0 Yes=1**	
Wheeze	**No=0 Yes=1**	

Bronchial Breath sound on auscultation	**No=0 Yes=1**	
SpO2	%	
GCS	/15	

3. Vital signs during admission:

Temperature (axillary)	**0 F**
Heart rate	**b/min**
Blood Pressure	**mmHg**
Respiratory Rate	**/min**
SpO2	**/%**

4. RT_PCR test

Negative = 0	**Positive=01**
Date of sample collection: / /202	**Date of Result: / /202**

5. Lab Investigations:

Date							
Hemoglobin (%)							
CRP Titer							
CBC	**ESR**						
	WBC	**Total**					
		DC	**Neutrophil (%)**				
			Lymphocyte (%)				
Platelet count							
Prothrombin Time							
S Ferritin							
D-Dimer							
S Procalcitonin							
RBS							
SGPT							
SGOT							
S Creatinine							
NT-pro BNP							
Hs Trop I							
INTERLEUKIN-6(IL-6)							
S LDH							
HbA1C							
S Electrolytes	**Na**						
	K						
	Cl						
	HCO3						
	pH						

ABG	**HCO3**					
	PO2					
	CO2					
	Alkalosis					
	Acidosis					

6.Imaging:

Chest X-ray P/A view (Pneumonitis)	**No=0**	**Yes=1**	
HRCT	**No=0**	**Yes=1**	

7. Risk Factors of Co morbidities (please tick)

Diabetes Mellitus	**No=0 Yes=1**	
Hypertension	**No=0 Yes=1**	
Chronic kidney disease	**No=0 Yes=1**	
Bronchial asthma	**No=0 Yes=1**	
COPD	**No=0 Yes=1**	
Chronic Heart Disease	**No=0 Yes=1**	
CVD	**No=0 Yes=1**	
Chronic Liver Disease	**No=0 Yes=1**	
Smoking	***No=0 Yes=1***	
Obesity	***No=0 Yes=1***	
Chemotherapy	**No=0 Yes=1**	
Surgery	**No=0 Yes=1**	
HIV	**No=0 Yes=1**	

8.H/O suppressive therapy **No=0 Yes =1 If yes duration:**

9.Treatment (Please tick):

	OXYGEN THERAPY	***No=0 Yes=1***
	I/V FLUID	***No=0 Yes=1***
	BLOOD PRESSURE SUPPORT REQUIRED	**No=0 Yes=1**
	MECHANICAL VENTILATION REQUIRED	**No=0 Yes=1**
	DIALYSIS REQUIRED	**No=0 Yes=1**
	STEROID	***No=0 Yes=1***

10. If in Intensive care Unit (ICU):

OXYGEN THERAPY	**DURATION**	**HOURS/DAY**	
	FLOW	**L/MIN**	
		BIPAP	**No=0 Yes=1**

	NIV TYPE:	CPAP	No=0 Yes=1	
		HFNC	No=0	
			Yes=1	If yes=flow ……..L/min
MECHANICAL VENTILATION	NO=0 YES= 1		DURATION	

	NAME	DOSE	Starting date	ENDING DATE
Drugs	IVERMECTIN			
	ENOXAPARIN			
	FAVIPIRAVIR			
	REMDESIVIR			
	ORADEXON			
	METHYLPRED			

11. For Mild /Moderate case(if not admitted):

HOME ISOLATION	No=0 Yes=1	
INSTITUTIONAL ISOLATION	No=0 Yes=1	DATE OF ISOLATION : / /202

12. Repeat PCR:

DATE	RESULT
1ST DATE: . ……/ /202	NEGATIVE =0 POSITIVE =1
2ND DATE: ……/……/202	NEGATIVE =0 POSITIVE =1

13. Date of Discharge;……./……../202

14.Date of End of Isolation……../……./202

15. Outcome:

RECOVERED	*No=0 Yes=1*
REFERRED	No=0 Yes=1
LEFT BY OWN(DORB)	No=0 Yes=1
DEATH	No=0 Yes=1

16.Contact tracing (to be done by the local heath authority) informed:
yes=1 no=0

17.Followup:
a) Day 5 0f admission.
b)Day 14 of admission.

Signature of the researcher /concerned physician