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# Role of Interleukin-6 as a Predictor in Assessing Severity of COVID-19 Patients: A Hospital Based Cross-Sectional Study

**Sumzida Afrin[1], Sadia Sharmin[2]**

[1]Resident Medical Officer, Dhaka Central International Medical College, Bangladesh.
[2]Lecturer, Anower Khan Modern Medical College, Bangladesh.

Corresponding Author: Sumzida Afrin

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## ABSTRACT

The investigation is centered on evaluating the impact of interleukin-6 (IL-6) on determining the seriousness of COVID-19 among individuals in Bangladesh, a nation grappling with substantial challenges due to the outbreak. Given the absence of specific therapies for COVID-19, grasping biomarkers such as IL-6 becomes pivotal for prognosis and treatment. The primary objective of the study is to outline the socio-demographic attributes of COVID-19 patients, ascertain IL-6 concentrations, evaluate the disease's severity based on IL-6 levels, and recognize correlated comorbidities. Through the analysis of 90 patients in specialized COVID-19 facilities in Dhaka, information regarding IL-6 levels, socio-demographics, clinical characteristics, and comorbidities was gathered. The conclusions of the research contribute to enhancing the comprehension of the connection between IL-6 and COVID-19 severity, potentially facilitating early prognosis and intervention strategies. Such perceptions are imperative for healthcare practitioners to implement practices grounded on evidence and alleviate the repercussions of the outbreak. This particular Hospital-Based Cross-sectional Study delves into the function of Interleukin-6 (IL-6) as an indicator for evaluating the severity of COVID-19 patients. A total of 90 participants from COVID dedicated hospitals were examined, with demographic characteristics scrutinized alongside COVID symptoms, oxygen saturation levels, and IL-6 concentrations. The results indicate a notable correlation between IL-6 levels and COVID severity, with heightened IL-6 levels corresponding to severe instances. Suggestions encompass the utilization of IL-6 and other inflammatory markers for predicting severity and advocating for further extensive studies to guide policymaking. Despite drawbacks such as limitations in sample size, IL-6 emerges as a promising indicator for early identification of COVID-19 severity.

***Keywords:*** COVID-19, IL-06, X-Ray, Patients

## 1. INTRODUCTION

Corona Virus Disease (COVID-19) is an irresistible sickness brought about by a newly found strain of corona Virus (Wu and McGoogan, 2020). A great many people contracted the COVID-19 infection will encounter moderate to severe respiratory sickness and most of them recover without requiring extraordinary therapy. More seasoned individuals, and those with basic clinical issues like cardiovascular sickness, diabetes, ongoing respiratory infection, and malignancy are bound to foster genuine ailment. The most ideal approach to forestall

and hinder transmission is to be all around knowledge about the COVID-19 infection, the sickness it causes and how it spreads. As the infection attacks the respiratory system and spreads via airborne droplets so shielding one's face with appropriate face mask and avoiding contact with general masses unless its absolute necessary, can play a vital role slowing down the spread of the disease. The COVID-19 infection spreads fundamentally through respiratory droplets while coughing or sneezing or through beads of spit, when a tainted individual hacks or wheezes. So, it's significant that you additionally practice respiratory manners as well. Most patients with Covid-19 experience mild self-limiting disease. However, up to 20% of known cases of Covid-19 are complicated by severe pneumonia which might result in acute respiratory distress syndrome (ARDS) which consequences acute hypoxemic respiratory failure (Zhou *et al.*, 2020). Coronaviruses may activate deregulated host immune responses. As exploratory studies have suggested that interleukin-6 (IL-6) levels are elevated in cases of complicated Covid-19 (Coomes and Haghbayan, 2020). In the current situation, identification of COVID-19 disease progression mainly depends on the clinical manifestation. On the other hand, no effective biomarker has been proposed yet. It has been suggested that one of the possible mechanisms underlying rapid disease progression is a cytokine storm. Furthermore, the level of inflammatory cytokine Interleukin-6 in critically ill patient has been found elevated significantly (Li, 2020). So, it could be a potential therapeutic target for critically ill patients with an exaggerated inflammatory response. The World Health Organization (WHO) declared the COVID-19 outbreak a Public Health Emergency of International Concern on 30 January 2020, and a pandemic on 11 March 2020. On the background of the ongoing pandemic, the spreading of Covid-19 in LTCF might significantly burden the local health care system and markedly contributes to mortality. Timely and effective intervention is essential to reduce morbidity and mortality during the Covid-19 outbreak in the LTCF. Such intervention consists of quick identification of cases, immediate introduction of infection control measures, initial triage, and daily monitoring of patients. An effective screening tool is essential to identify the patients at risk for severe illness and death. Such patients need close monitoring and early transfer to the hospital. Various biomarkers, especially inflammatory markers like C-reactive protein (CRP), ferritin, fibrinogen, D-dimer and Interleukin 6 (IL-6) are associated with Covid-19 progression (Ponti *et al.*, 2020).

In another study reveals that around (53%) patients developed hypoxemia during the course of the disease of COVID-19 (Sabaka *et al.*, 2021a). Patients with hypoxemia had significantly higher concentrations of IL-6, C-reactive protein, pro-calcitonin, fibrinogen, total bilirubin, aspartate aminotransferase and alanine aminotransferase at initial screening and IL-6 is the most robust predictor of hypoxemia (Sabaka *et al.*, 2021a). So, the role of systematic measurement of IL-6 in the initial assessment of Covid-19 and its ability to predict the severe course of disease is yet to be determined.

## 2. JUSTIFICATION OF THE STUDY

Coronavirus disease 2019 (Covid-19) is a disease caused by the zoonotic novel Coronavirus called SARS-CoV-2(Wu and McGoogan, 2020). Day by day COVID-19 has becoming a disease of high mortality and morbidity specially among elderly patients throughout world. On the contrary, there is no specific treatment of this disease has not established yet while most of its management is symptomatic.

In addition to this nowadays, identification of COVID-19 disease advancement mainly depends on the clinical manifestation. On the other hand, no effective biomarker has been proposed yet. It is evident that one of the underlying pathologies of COVID 19 is cytokine storming (F. Liu *et al.*, 2020). Various biomarkers, especially inflammatory markers like C-reactive

protein (CRP), ferritin, fibrinogen, D-dimer and Interleukin 6 (IL-6) are associated with Covid-19 progression (Ponti *et al.*, 2020). Among these inflammatory markers, IL-6 is the most significant predictor of hypoxemia (Sabaka *et al.*, 2021a). So in terms of, severity assessment or even early prediction of complicated COVID-19 measurement of interleukin-6 could be a great prospect.

On the contrary, so far reviewed not that much studies have been found regarding this issue specially in Bangladesh. Therefore, this study will be attempted to find out the level of interleukin-6 among COVID-19 infected patients with view to assessing its relationship with severity of COVID-19 status.

This study aimed to describe the characteristics of confirmed COVID-19 patients and establish the association with the level of Interleukin-6 and COVID-19 severity among the COVID-19 patients. The main objective of this study was to find out the level of IL-6 among COVID-19 infected patients and to explore the association of altered IL-06 level with adverse outcome of COVID-19. This study will help to assess the association of altered IL-6 status with adverse outcome of COVID-19 and taking appropriate measures accordingly and also preventing disease severity thereby. In addition to this the study findings will help to health professionals to follow evidence-based practice as well. Moreover, the study findings will help to increase academic knowledge as well.

## 3. RESEARCH QUESTION

What is the role of interleukin-6 in assessing severity of COVID-19 patients?

## 4. STUDY OBJECTIVES

1. To determine the socio-demographic characteristics of the respondents
2. To determine the level of interleukin-6 among COVID patients
3. To assess the severity of COVID-19 patients by level of Interleukin-6
4. To identify the comorbidities associated with interleukin-6 level.

## 5. REVIEW OF LITERATURE

### 5.1 COVID-19

In late 2019, coronavirus disease-2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged from Wuhan, China, and became a new worldwide public health concern. In Bangladesh, COVID-19 was first reported on 8 March 2020 (Islam et al., 2021). Since then the number COVID-19 cases are rising gradually. Till date around 1.51 million people has been affected with COVID-19 infection and total 26,362 people died with this particular infection. Most importantly most of the people died due to COVID-19 had multiple comorbidities like Diabetes Mellitus, Bronchial Asthma so and so forth. According to a study conducted in Bangladesh, a case of metabolic syndrome that remained positive for SARS-CoV-2 RNA over a prolonged period. On clinical and laboratory examination, the patient was diagnosed with obesity, raised blood pressure, dyslipidemia, and uncontrolled glycaemia. However, upon taking appropriate measures and controlling the plasma sugar level, he tested negative for SARS-CoV-2 RNA on the 72nd day since illness onset(Islam et al., 2021). This finding suggests that various commodities not only worsening the severity of the disease but also increase the period of communicability of the infection which allows disease transmission for a prolong period. Another study conducted in Bangladesh which reveals around 19.8% of patients had diabetes and 76% of the COVID-19 patients were male (Akter et al., 2020).

### 5.2 Severity of COVID-19

Coronavirus dis- ease 2019 (COVID-19) is a major infectious disease that seriously endangers people's life and health due to its high incidence and high infectivity. About 81% of patients with novel coronavirus infection were mild. However, 14% were severe and 5% were critical. Severe illness often experienced dyspnea and/or hypoxemia after 1 week. Critically ill patients progressed rapidly to acute

respiratory distress syndrome, metabolic acidosis, coagulopathy, and septic shock as well (Shang et al., 2020). Patients with severe disease have high mortality and poor prognosis. Patients with SARS-CoV-2 infection can experience a range of clinical manifestations, from no symptoms to critical illness. In general, adults with SARS-CoV-2 infection can be grouped into the following severity of illness categories. However, the criteria for each category may overlap or vary across clinical guidelines and clinical trials, and a patient's clinical status may change over time.

- **Asymptomatic or Presymptomatic Infection**: Individuals who test positive for SARS-CoV-2 using a virology test (i.e., a nucleic acid amplification test [NAAT] or an antigen test) but who have no symptoms that are consistent with COVID-19.
- **Mild Illness**: Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.
- **Moderate Illness**: Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation ($SpO_2$) ≥94% on room air at sea level.
- **Severe Illness**: Individuals who have $SpO_2$ <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen ($PaO_2/FiO_2$) <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50%.
- **Critical Illness**: Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

### 5.3 Factors predisposing to severity of COVID-19

Among biochemical parameters, plasma glucose, D-dimer, and Troponin-I levels were significantly elevated amidst the cohort with diabetes. The frequency of patients requiring insulin increased threefold during infection with SARS CoV-2. 1.4% patients developed new onset of diabetes mellitus (Akter et al., 2020). The current coronavirus disease 2019 (COVID-19) outbreak was reported to cause significantly higher mortality and morbidity among patients with diabetes mellitus (DM) (Morshed, Al Mosabbir and Hossain, 2021). The death rate among all hospitalized patients (with and without DM) was 2.8% compared to 11.3% among diabetic patients (Morshed, Al Mosabbir and Hossain, 2021). So, in patients with COVID-19 glycemic control management is very essential to prevent potential adverse consequences. Glycemic control in COVID-19 patient was significantly worse in the early months of the pandemic as com- pared with the same months in 2019 (Ledford et al., 2021).
Furthermore, COVID-19 might also predispose infected individuals to hyperglycemia. Interacting with other risk factors, hyperglycemia might modulate immune and inflammatory responses, thus predisposing patients to severe COVID-19 and possible lethal outcomes (Lim et al., 2021). Another study reveals both hyperglycemia and hypoglycemia were associated with poor outcomes in patients with COVID-19 (Klonoff et al., 2021). Admission glucose was a strong predictor of death among patients directly admitted to the ICU (Klonoff et al., 2021).

### 5.4 IL-6 and severity of COVID-19

The outbreak of the COVID-19 due to the SARS-CoV-2 was firstly reported in Hubei province, Wuhan, China (Rahman et al., 2021). The SARS-CoV-2 is a high transmissible virus that spread across the world within a short period. Therefore, on March 12, 2020, the world health organization (WHO) declared COVID-19 a pandemic for the world. The COVID-19 primarily targets the lungs of the patients. However, it can damage other organs in severe cases. Therefore, hematological abnormalities and their intensities are

involved in the severity ofCOVID-19 (Rahman et al., 2021). The systematic review and meta- analysis of interleukin (IL)-6 in COVID-19, by Daniel Leisman and colleagues, provides a crucial comparison with other inflammatory syndromes, showing that IL-6 is more markedly elevated in conditions such as sepsis and acute respiratory distress syndrome (ARDS) (Chen et al., 2021).It is evident that, COVID-19 infection may lead to Acute respiratory distress syndrome and even in severe cases sepsis and multi-organ dysfunction as well. So, raised level of IL-06 could be a very important prognostic factor COVID-19 infection. Interleukin-6 (IL-6), a pro-inflammatory cytokine, has been reported to be associated with disease severity and mortality in patients with coronavirus disease 2019 (COVID-19). According to a study conducted in China, the mortality rate was higher in the elevated IL-6 group than in the normal IL-6 group (0.16 vs 5%) (Z. Liu et al., 2020). In another study, sixty-nine severe COVID-19 patients were included. Patients with severe disease showed significant lymphocytopenia. Elevated level of lactate dehydrogenase (LDH), C-reactive protein (CRP), ferritin, and D-dimer was found in most severe cases. Baseline interleukin-6 (IL-6) was found to be associated with COVID-19 severity. Indeed, the significant increase of baseline IL-6 was positively correlated with the maximal body temperature during hospitalization and with the increased baseline of CRP, LDH, ferritin, and D-dimer. High baseline IL-6 was also associated with more progressed chest computed tomography (CT) findings (T. Liu et al., 2020). A retrospective data analysis of cases of COVID-19 revealed, 53% of the patient's developed hypoxemia during the course of disease. Patients with hypoxemia had significantly higher concentrations of IL-6, C-reactive protein, procalcitonin, fibrinogen, total bilirubin, aspartate aminotransferase and alanine aminotransferase at initial screening (Sabaka et al., 2021b). Cytokines are vital in regulating immunological and inflammatory responses. Among them, IL-6 is of major importance because of its pleiotropic effects. It seems that the highly pathogenic SARS-CoV-2 is associated with rapid virus replication and a tendency to infect the lower respiratory tract, resulting in an elevated response of IL-6-induced severe respiratory distress (Ulhaq and Soraya, 2020). A hospital based prospective cohort study reveals that maximal IL-6 level before intubation showed the strongest association with the need for mechanical ventilation, followed by maximal CRP level (Herold et al., 2020). A systematic review and meta-analysis to assess the evidence of association between COVID-19 and IL-06 reveals that, interleukin-6 (IL-6) levels are elevated in cases of complicated Covid-19 cases mostly (Coomes and Haghbayan, 2020). Acute respiratory distress syndrome (ARDS) and multi-organ dysfunction are among the leading causes of death in critically ill patients with COVID-19. The elevated inflammatory cytokines suggest that a cytokine storm, also known as cytokine release syndrome (CRS), may play a major role in the pathology of COVID-19 (B. Liu et al., 2020). IL-06 is an important inflammatory cytokine among them. A retrospective cohort study among Mild and severe COVID-19 patients shown that, the levels of IL-6, CRP, and PCT increased in 95 (67.9 %), 91 (65.0 %), and 8 (5.7 %) patients on admission, respectively. The proportion of patients with increased IL-6, CRP, and PCT levels was significantly higher in the SG (Severe group) than in the MG (Mild group). Another retrospective Cohort analysis of COVID-19 patients revealed around fifty-three patients (11 men, 42 women) with diagnosed Covid-19 were included in the analysis and (53%) patients developed hypoxemia during the disease. Patients with hypoxemia had significantly higher concentrations of IL-6, C-reactive protein, procalcitonin, fibrinogen, total bilirubin, aspartate aminotransferase and alanine aminotransferase at initial screening. ROC analyses identified IL-6 as the most robust predictor of hypoxemia (Sabaka et al., 2021a).

## 6. METHODOLOGY

### 6.1 Study Design

The study was a cross-sectional. Selected COVID dedicated tertiary level Hospital where COVID-19 affected patients admitted in Dhaka city. The selected study places are (i) Anwer Khan Modern Medical College Hospital, (ii) Dhaka Central International Medical College & Hospital (DCIMCH). Study duration was four months from 1st September to 31st December 2021. COVID-19 Patients admitted in the Hospital at Dhaka City.

### 6.2 Selection Criteria

**Inclusion criteria:**

COVID-19 patients admitted in the Hospital. Patients who have given informed consent. Both male and female patients was included in the study. Patients >18 years (adults) was included in the study.

**Exclusion Criteria:**

Mentally unstable persons were excluded.

### 6.3 Sampling Technique and Sample Size

Simple random sampling technique was used in this study. Sample size was calculated by applying following formula

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

Here,

n = desired sample size

z = Standard normal deviate; set at 1.96 which correspond at 95% Confidence Interval.

q = 1-p

d = allowable error = 10% = 0.1

p = Proportion in the population

According to a study in China, among 140 patients infected with COVID, increased proportion of Interleukin-6 level is 67.9% (F. Liu et al., 2020)

So, p = 0.679

q = (1-0.679) = 0.321

So, according to the equation,

$n = \{(1.96)^2 \text{ X } 0.679 \text{ X } 0.321\} / (0.1)^2$

$= (0.837/ 0.01)$

$= 89.7 \approx 90$

So, our sample size was 90.

### 6.4 Data Collection Method and Tool

Data were collected by cross-sectional survey and reviewing medical records of the COVID-19 patients. Semi-structured questionnaire was prepared for collecting data from the respondents. A checklist was also developed for data collection

### 6.5 Data management Plan

Initially data was checked for its completeness and correctness in order to exclude missing or inconsistent data. Corrected data then was entered into the computer.

### 6.6 Data Analysis Plan

The data were analyzed by using the software Statistical Package for the Social Sciences (SPSS: Version 25). Descriptive data were analyzed by the simple frequency distribution (Mean, Percentage and standard deviation). Cross tabulation was done to find out the relationship between dependent and independent variables. Statistical significance will be set at 95% Confidence Interval. Data were presented by using frequency curve, graph and charts.

### 6.7 Ethical Issues

Approval from Ethical Review committee of State University of Bangladesh was taken. Permission was taken from Hospital Director. Verbal informed consent was taken from the respondents before enrolling for the study. Confidentiality was maintained strictly. Respondents had every right to withdraw themselves from the study at any time during the data collection period.

## 7. RESULTS

### 7.1 Socio-Demographic Findings of the COVID-19 Patients

#### 7.1.1 Sex distribution of COVID-19 patients

Around 58% of the respondents are male and rest are female

**Table 1: Distribution of the respondents by sex (n= 90)**

| Sex | Frequency | Percentage (%) |
|---|---|---|
| **Male** | 52 | 58.0 |
| **Female** | 38 | 42.0 |
| **Total** | 90 | 100 |

### 7.1.2 Age distribution of COVID-19 patients

**Table 2: Distribution of the respondents by age (n=90)**

| Age (in years) | Frequency | Percentage |
|---|---|---|
| 20-29 | 6 | 6.0 |
| 30-59 | 41 | 46.0 |
| 60+ | 43 | 48% |
| **Total** | **90** | **100%** |

**Mean age:** 48.25 years
**SD**: ± 5.92

### 7.1.3 Marital status of COVID-19 patients

Around 60% of the respondents are married and rests 16%, 24% are unmarried and widowed respectively

**Table 3: Distribution of the respondents by marital status (n=90)**

| Marital Status | Frequency | Percentage (%) |
|---|---|---|
| Married | 52 | 58.0 |
| Unmarried | 14 | 16.0 |
| Separated | 2 | 1.0 |
| Widowed | 22 | 24.0 |
| Total | 90 | 100 |

### 7.1.4 Religion of COVID-19 patients

More than 90% of the respondents were Muslim and Hindus.

**Table-04: Distribution of the respondents by Religion (n=90)**

| Religion | Frequency | Percentage |
|---|---|---|
| Islam | 78 | 87.0 |
| Hindu | 8 | 9.0 |
| Christian | 2 | 2.0 |
| Buddist | 2 | 2.0 |
| Total | 90 | 100% |

### 7.1.5 Educational qualification of COVID-19 patients

More than half of the respondents were educated up to Bachelors, Masters and above level.

**Table 5: Distribution of the respondents by educational qualification (n=90)**

| Educational qualification | Frequency | Percentage (5%) |
|---|---|---|
| Illiterate | 5 | 6.0 |
| Primary | 3 | 3.0 |
| Secondary | 8 | 9.0 |
| HSC | 23 | 25.0 |
| Bachelors | 33 | 36.0 |
| Masters and above | 18 | 20.0 |
| Total | 90 | 100% |

### 7.1.6 Monthly income of COVID-19 patients

Around 77% of respondent's monthly income is up to 50,000 takas.

**Table 6: Distribution of the respondents by Monthly Income (n=90)**

| Monthly Income | Frequency | Percentage (%) |
|---|---|---|
| 5000-10,000 | 21 | 23.0 |
| 11,0000-20,000 | 04 | 4.0 |
| 21,000-50,000 | 43 | 48.0 |
| 51,000-70,000 | 22 | 25.0 |
| Total | 90 | 100 |

### 7.1.7 Occupation of COVID-19 patients

About 40%,29% and 21% respondents Occupation Were Service, Business and housewife respectively

**Table 7: Distribution of the respondents by Occupation (n=90)**

| Monthly Income | Frequency | Percentage (%) |
|---|---|---|
| Service | 36 | 40.0 |
| Business | 26 | 29.0 |
| Agriculture | 1 | 1.0 |
| Day laborer | 3 | 3.0 |
| Housewife | 19 | 21.0 |
| Others | 5 | 6.0 |
| Total | 90 | 100% |

### 7.1.8 Family type of COVID-19 patients

More than half of the respondents belong to joint or extended families.

**Table 8: Distribution of the respondents by Family type (n=90)**

| Family Type | Frequency | Percentage |
|---|---|---|
| Nuclear | 39 | 43% |
| Joint or extended | 51 | 57% |
| Total | 90 | 100% |

### 7.1.9 Number of children of COVID-19 patients

Around 29% of the respondents had at least one child.

**Table 9: Distribution of the respondents by number of children (n=90)**

| Number of Children | Frequency | Percentage (%) |
|---|---|---|
| No child | 20 | 22.0 |
| One child | 26 | 29.0 |
| Two child | 25 | 28.0 |
| Three or above | 19 | 21.0 |
| Total | 90 | 100.0 |

## 7.2 COVID-19 Related Findings of the Participants

### 7.2.1 Clinical findings of the patients

**Table 10: Distribution of the respondents by clinical findings (n= 90)**

| Clinical Features | Frequency | | Percentage (%) | |
|---|---|---|---|---|
| | Present | Absent | Present | Absent |
| Features of shock | 37 | 53 | 41.0 | 59.0 |
| Features of Respiratory failure | 39 | 51 | 43.0 | 57.0 |

### 7.2.2 Chest X-Ray findings of theCOVID-19 patients

Around 58% respondents presented with ground glass opacities on their Chest X-ray findings.

**Table 11: Distribution of the respondents by feature of Chest X-ray Findings (n=90)**

| Chest X-ray Findings | Frequency | Percentage |
|---|---|---|
| Normal | 38 | 42.0 |
| Ground glass opacities | 52 | 58.0 |
| Total | 90 | 100% |

### 7.2.3 Chest X-Ray findings of theCOVID-19 patients:

Around 42% and 20% of the respondents presented with ground glass opacities and bilateral involvement respectively.

**Table 12: Distribution of the respondents by feature of HRCT Findings (n=90)**

| HRCT Findings | Frequency | Percentage |
|---|---|---|
| Ground glass opacities | 38 | 42.0 |
| Vascular engorgements | 9 | 10.0 |
| Normal | 25 | 28.0 |
| Bilateral involvement | 18 | 20.0 |
| Total | 90 | 100% |

### 7.2.4 Chest X-Ray findings of theCOVID-19 patients:

Near about 60% of the respondents have Interleukin-06 level >24 pg/mL.

**Table 13: Distribution of the respondents by Interleukin-06 level Findings (n=90)**

| Interleukin-06 level (pg/mL) | Frequency | Percentage (%) |
|---|---|---|
| 0-16.4 pg/mL | 1 | 1.0 |
| 16.5-20 pg/mL | 18 | 20.0 |
| 20.1-24 pg/mL | 19 | 21.0 |
| >24 pg/mL | 52 | 58.0 |
| Total | 90 | 100% |

### 7.2.5 COVID-19 severity of participants:

About 57% of the respondents were suffering from severe form of COVID.

**Table 14: Distribution of the respondents by Severity of COVID-19 (n=90)**

| Severity of COVID | Frequency | Percentage |
|---|---|---|
| Mild | 16 | 18.0 |
| Moderate | 23 | 25.0 |
| Severity | 51 | 57.0 |
| Total | 90 | 100.0 |

### 7.2.6 Oxygen saturation level of COVID-19 patients:

About 58% of the respondent's oxygen saturation level is below 90%.

**Table 15: Distribution of the respondents by Oxygen saturation level (n=90)**

| Oxygen Saturation Level | Frequency | Percentage (%) |
|---|---|---|
| <90% | 52 | 58.0 |
| >90% | 38 | 42.0 |
| Total | 90 | 100.0 |

### 7.2.7 COVID symptoms of the participants:

Around 17%, 14%, and 10% of the respondents presented with fever, sore throat and respectively. While 16% of the respondents presented with loss of smell sensation and loss of taste sensation.

**Table 16: Distribution of the respondents by COVID symptoms (n = Multiple response)**

| COVID symptoms | Frequency | Percentage (%) |
|---|---|---|
| Fever | 79 | 17.0 |
| Sore throat | 67 | 14.0 |
| Headache | 46 | 10.0 |
| Diarrhea | 33 | 7.0 |
| Loss of smell sensation | 36 | 8.0 |
| Cough | 66 | 14.0 |
| Malaise | 37 | 8.0 |
| Vomiting | 12 | 3.0 |
| Loss of taste sensation | 39 | 8.0 |
| Shortness of breath | 48 | 10.0 |
| Total | 463 | 100.0 |

### 7.2.8 Associated Co-morbidities of the participants:

Around 27%, 13% and 23% of the respondents had co-morbidities like Diabetes, COPD and Bronchial Asthma respectively.

**Table 17: Distribution of the respondents by associating Co-morbidities (n=90)**

| COVID symptoms | Frequency | Percentage (%) |
|---|---|---|
| Diabetes | 43 | 27.0 |
| COPD | 21 | 13.0 |
| Bronchial Asthma | 37 | 23.0 |
| Hypertension | 39 | 24.0 |
| Ischemic Heart Disease | 20 | 12.0 |
| Total | 160 | 100.0 |

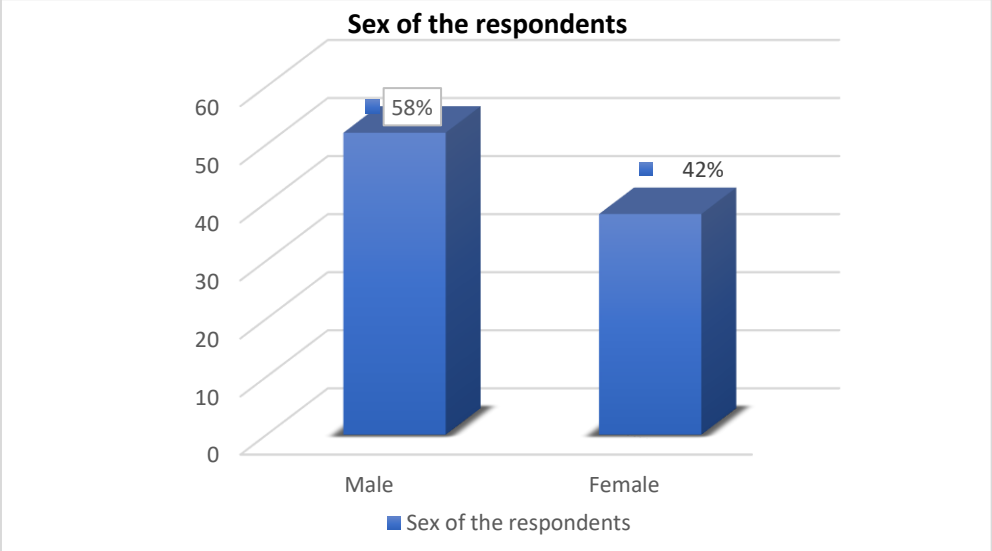
## 7.3 Interleukin-06 Related Findings of the Respondents

**Table 18: Association between severity of COVID-19 and Interleukin-06 level of the respondents**

| IL-6 level | Severity of COVID-19 | | | | p-value ($x^2$ test) |
|---|---|---|---|---|---|
| | Mild f (%) | Moderate f (%) | Severe f (%) | Total f (%) | |
| Normal | 01 (100%) | 0 (0%) | 0 (0%) | 1 (100%) | |
| Mildly raised | 8 (44.4%) | 7 (38.9%) | 3 (16.7%) | 18 (100%) | p = 0 .000 |
| Moderately raised | 6 (37.8%) | 8 (34.8%) | 5 (9.8%) | 19 (100%) | df = 4 |
| Severely raised | 1 (6.3%) | 8 (34.8%) | 43 (84.3%) | 52 (100%) | |

Table 16 shows, who had normal IL-06 level among them no one developed severe COVID-19 infection. On the other hand, around 84.3% of the severely raised IL-06 patients had developed severe form of COVID-19. Association between severity of COVID-19 and IL-06 was found highly significant (p<0.0001).

**Fig-01: Distribution of respondents by Sex**




Around 58% of the respondents are male and rest of female.

**Fig-02: Distribution of the respondents by educational qualification**

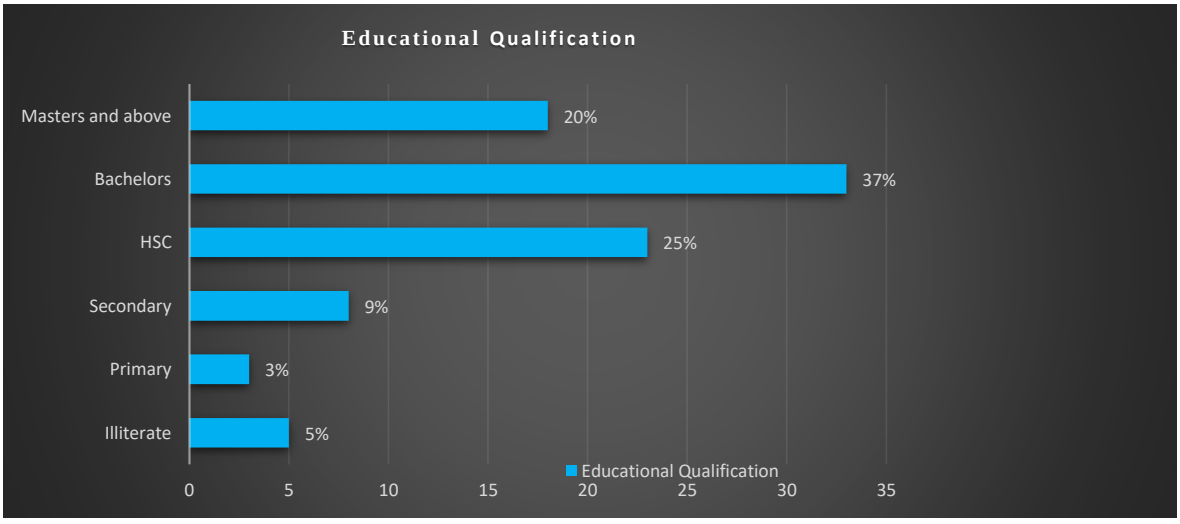


**Fig-03: Distribution of respondents by Religion.**

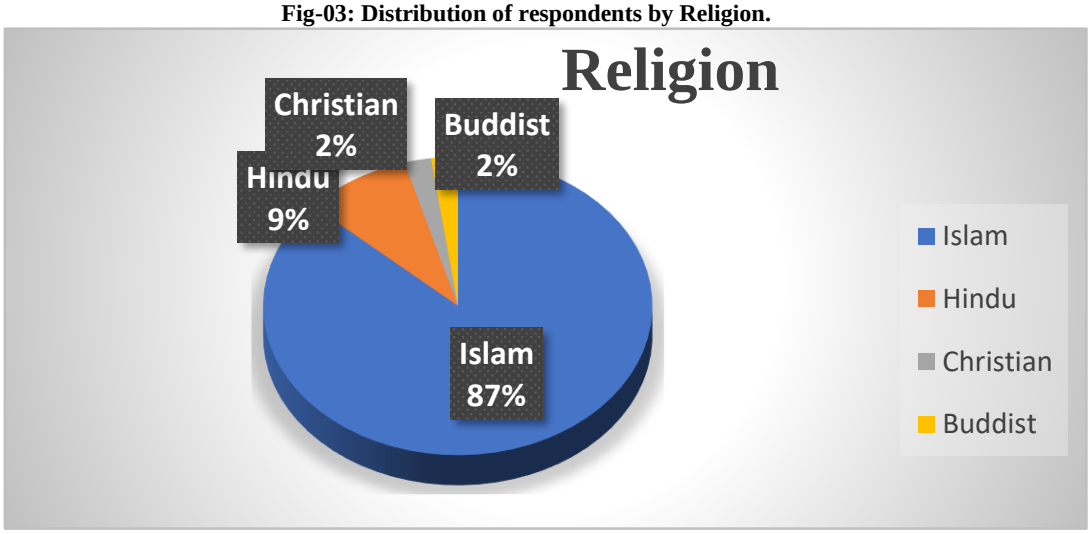



**Fig-04: Distribution of the respondents by number of children**

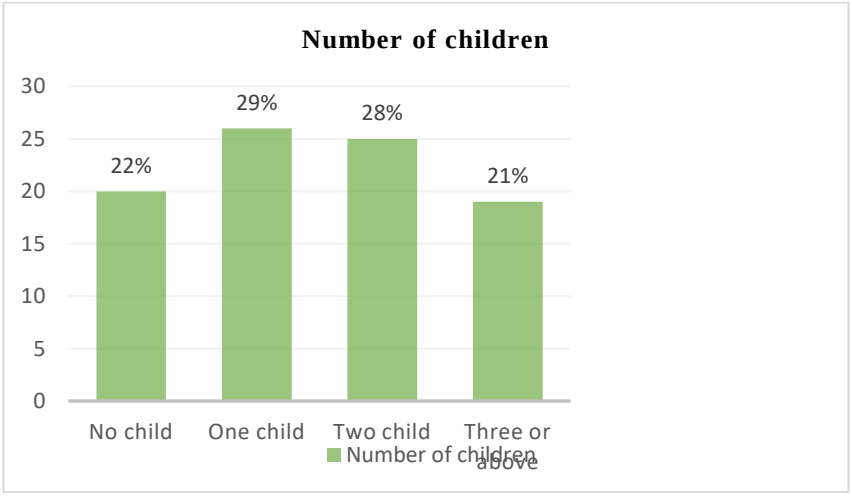



**Fig-05: Distribution of the respondents by level of Interleukin-06**

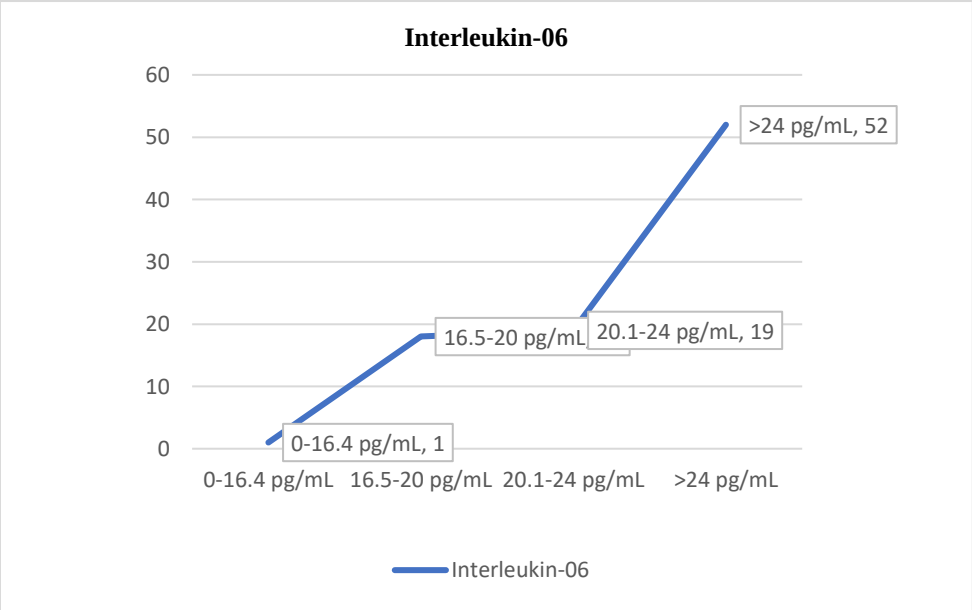


**Fig-06: Distribution of respondents by Oxygen saturation level**

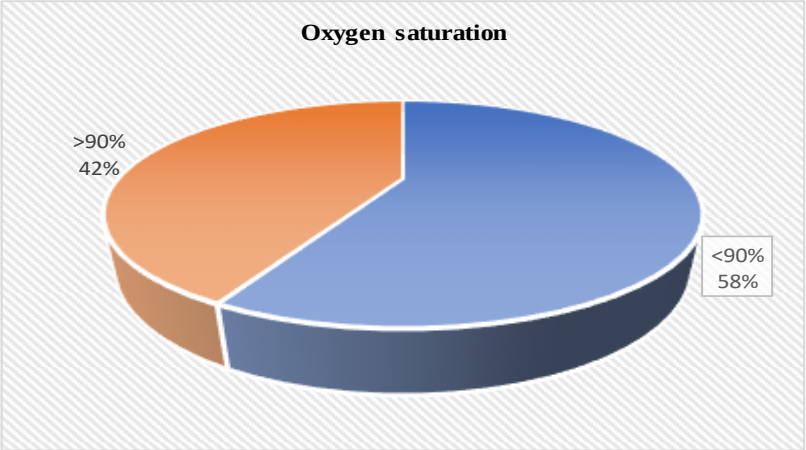



**Fig-07: Distribution of the respondents by COVID symptoms**

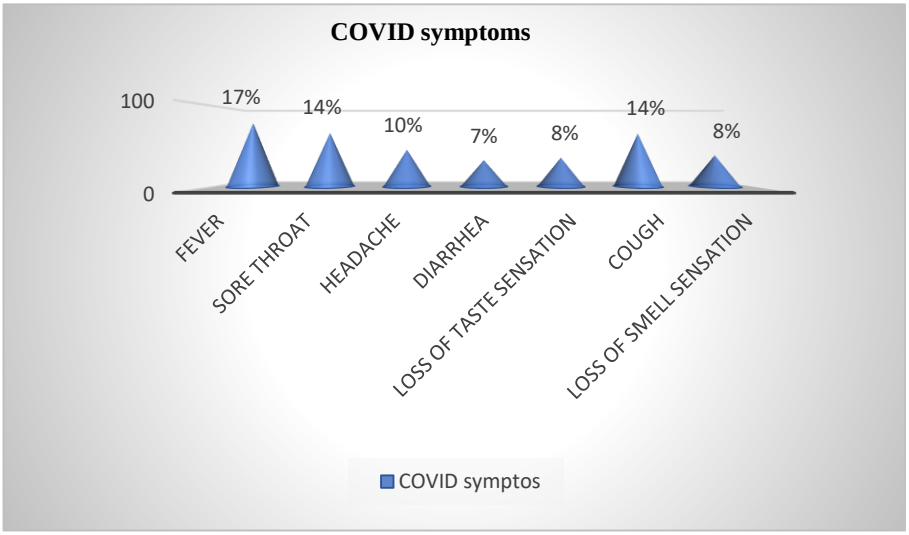



**Fig-08: Distribution of the respondents by HRCT Findings**

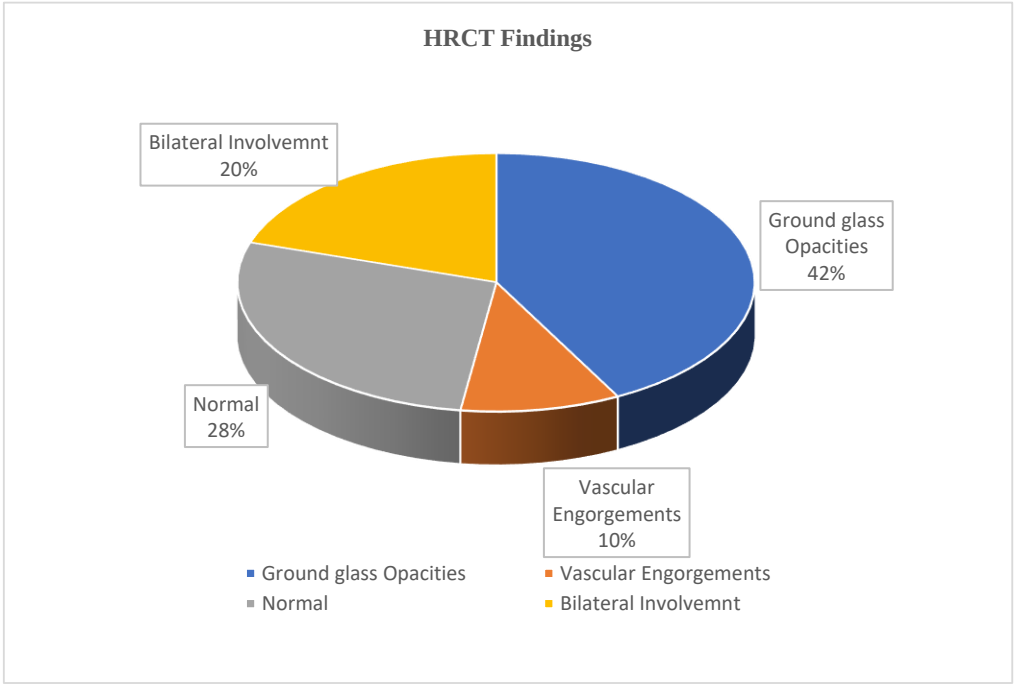


**Fig-09: Distribution of the respondents by Severity of COVID.**

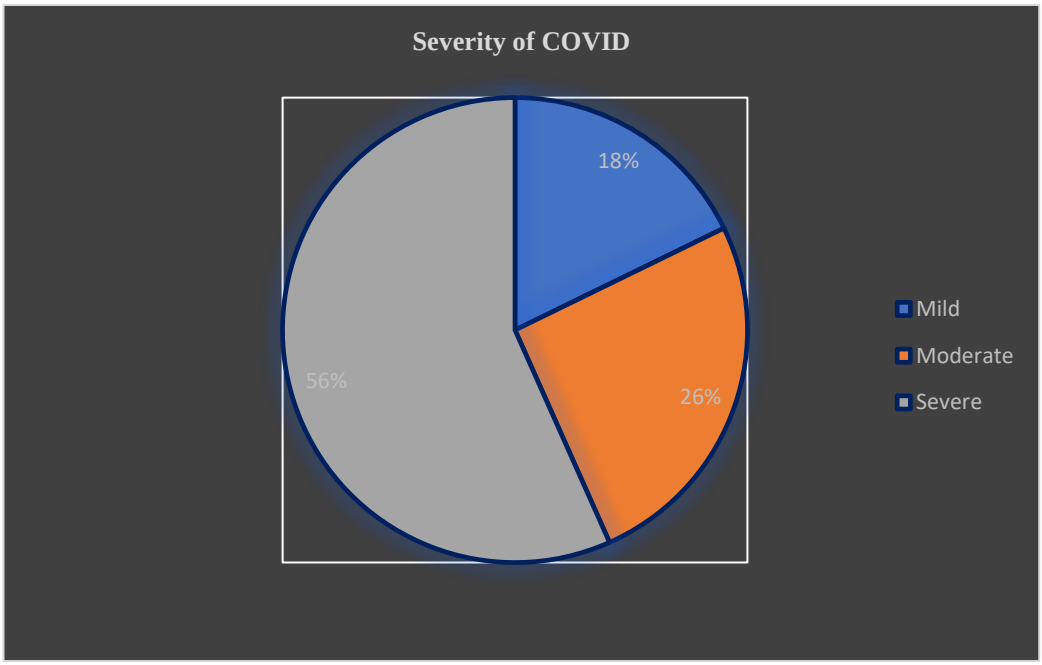



**Fig-10: Distribution of the respondents by associated Co-morbidities**

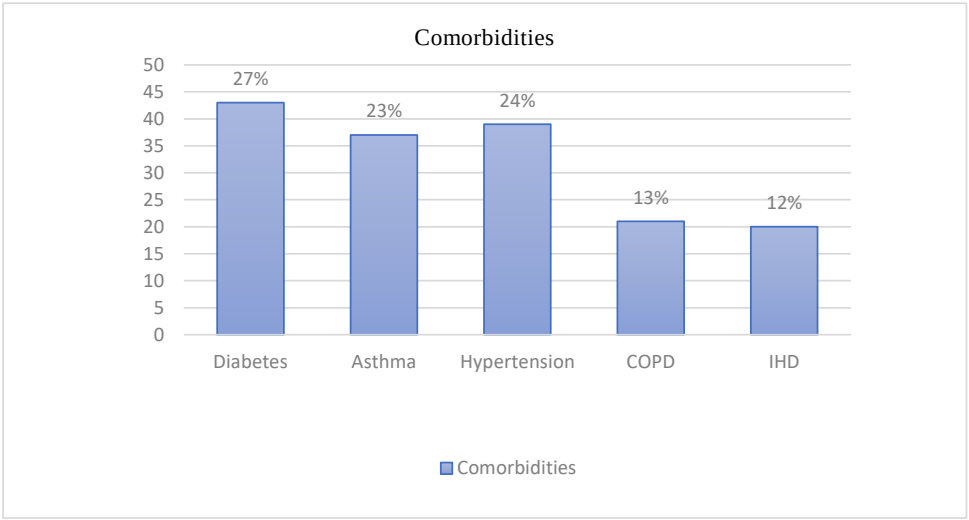



**Fig-11: Distribution of respondents by Chest X-ray Finding.**

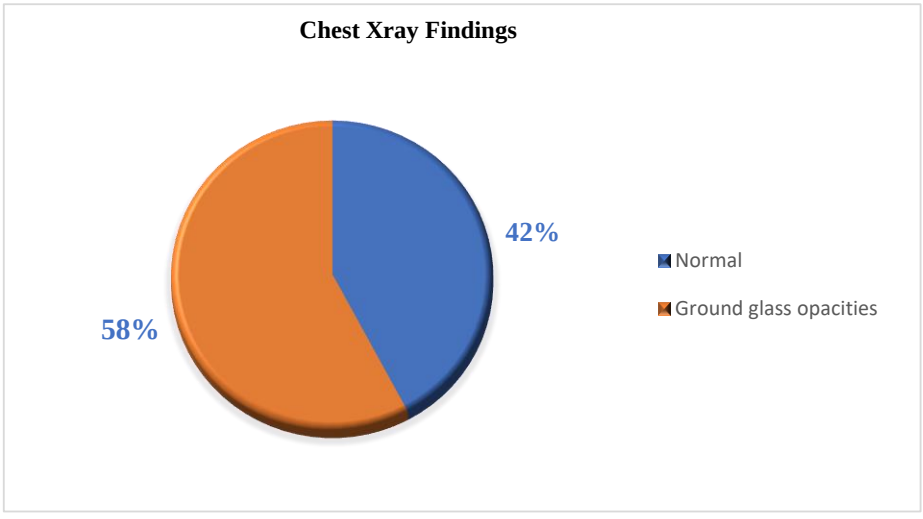
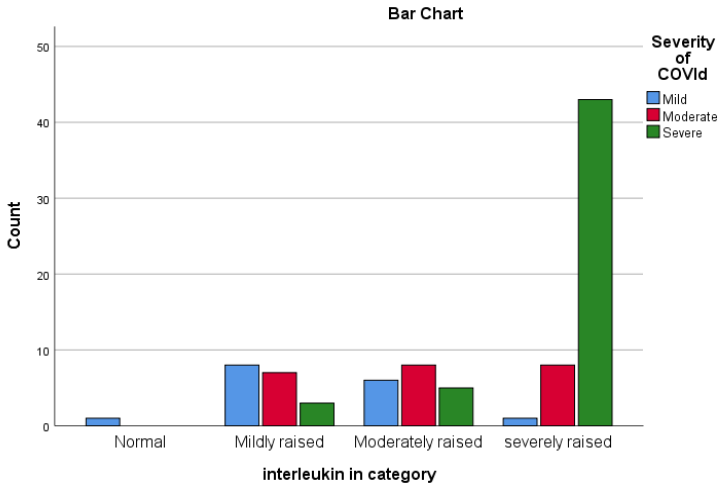


**Fig-12: Distribution of respondents by association between level of interleukin-06 and severity of COVID-19**




In this Bar diagram it has been clearly shown that severely raised interleukin-06 level patients are more likely to develop severe form of COVID.

## 8. DISCUSSION

COVID-19 has become an ongoing concerning almost last two and a half years globally. As time progresses newer variants are emerging day by day. So, its diagnosis as early as possible and treatment is important to prevent the community transmission of COVID-19. Interleukin-06 could be good prognostic marker in terms of COVID-19 management. This was a Hospital-Based Cross-sectional Study which was conducted to see the role of Interleukin-6 as a Predictor in assessing severity of COVID-19 patients. The inflammatory response plays a critical role in COVID-19, and inflammatory cytokine storm increases the severity of COVID-19 (F. Liu et al., 2020). Wan et al. found that cytokine storm is crucial to the progression of COVID-19 and can lead to severe complications and death. The fifth edition of "Diagnosis and Treatment of COVID-19" recommends monitoring the cytokine levels to improve treatment efficacy and reduce mortality (Wang et al., 2021). A total number of 90 respondents of this study were selected purposively from selected COVID dedicated tertiary level Hospital where COVID-19 affected patients were admitted in Dhaka city (Anwer Khan Modern Medical College Hospital, Kurmitola General Hospital, Dhaka Medical College Hospital).

Mean age of the respondents was 56.33 years and SD:± 10. Around 52% of the respondents age were within 20-60 years. Around 58% of the respondents are male and rest 42% are female. Around 60% of the respondents are married and rest 16%, 24% are unmarried and widowed respectively. More than 90% of the respondents were Muslim and Hindus. More than half of the respondents were educated up to Bachelors, Masters and above level. Around 77% of respondent's monthly income is up to 50,000 takas. Around 23% of the respondent's monthly income was about more than 50, 000 taka. Near about two tenth of the respondent's income was below 10,000tk. About 40%,29% and 21% respondents Occupation Were Service, Business and housewife respectively. On the contrary, around 9% of the respondents were from agriculture, day laborer and other occupation. occupation segregation may contribute to racial and ethnic disparities for COVID-19. Occupational segregation into high-risk industries and occupations likely contributes to differential risk with respect to COVID-19 (Hawkins, 2020). In this study, it has been found that more than half of the respondents belong to joint or extended families. Another important socio-demographic characteristic according to this study reveals around 29% of the respondents had at least one child. Surprisingly, 21% of

the respondents have three or more child. In this study each of the respondents who had suffered from COVID-19 evaluated in terms of different COVID-19 symptoms.

According to this study, most prevalent symptoms were fever, cough and sore throat and their percentage value includes 17%, 14% and 14% respectively. Apart from this, other symptoms include headache (10%), diarrhea (7%), loss of taste (8%) and loss of smell sensation (8%). A previous meta-analysis of 55 studies revealed clinical manifestation such as fever, cough, fatigue, anorexia, dyspnea, chest tightness, hemoptysis, diarrhea and abdominal pain were most prevalent symptoms of COVID-19 (Barek, Aziz and Islam, 2020). These findings are most similar with this study. It has been already proven that falling of oxygen saturation level is an important criterion for hospital admission of COVID-19 patient. In this study we recorded the oxygen saturation level of the respondents from retrospective medical data analysis of the patients. According to this study around 58% of the patient's oxygen saturation level was below <92%. Still now rt-PCR is the gold standard test for diagnosis of COVID. Philippe et al mentioned that diagnosis should rely on PCR and not on clinical presumption. Because of discrepancies between clinical symptoms, oxygen saturation or radiological signs on CT scans, pulse oximetry, and radiological investigation should be systematic (Gautret et al., 2020).

HRCT findings of the patients in this study reveals ground glass opacities (42%), bilateral involvement (20%) and vascular engorgements (10%) respectively. One of the main objectives of this study was to determine the role of interleukin-6 in assessing severity of COVID-19 patients. IL-6 is produced at the site of inflammation and is the chief stimulator of the acute phase response. Previous study has found that interleukin -06 level were significantly raised among the COVID-19 patients who were eventually developed more severity during their course of illness (Sabaka et al., 2021a).

Findings of this particular study reveals that around 18%, 25% and 57% of the respondents did suffer from mild, moderate and severe form of COVID-19 respectively. This study also found significant association between interleukin-06 level and severity of COVID-19 status (p value <0.0001). Previous study findings also quite similar with this finding. IL-6 appears as a potential predictor for the development of the severe Covid-19 and might serve for early identification of patients in need of hospitalization (Sabaka et al., 2021a). Another study findings revealed that, IL-6 levels were significantly increased in COVID-19-infected patients with severe condition compared with those with non-severe condition (SMD = 0.71, 95%CI −0.31–1.12, P = 0.0005) (Ulhaq and Soraya, 2020). Which also more likely similar to our study findings as well.

## 9. RECOMMENDATION

Efforts needed to increase knowledge, perception and practices regarding use of face mask and to follow all other preventive measures with a view to reducing transmission of COVID-19 and other respiratory infections as well.

Interleukin-06 and other inflammatory cytokines could be used as predictor of COVID-19 infection severity and thus help to manage appropriately.

Further large-scale in-depth study is needed to formulate policies in regards to prevent COVID-19 infections, associated comorbidities and complications as well.

## 10. LIMITATIONS OF THE STUDY

While conducting this study we do have some limitations as well. They are as follows:

1. Due to lack of availability of the COVID-19 patients as because prevalence of COVID-19 patients was decreasing at that time. Sample size was insufficient as well.
2. Due to time constrains we couldn't follow randomized sampling technique so there were chances of biasness

3. There were lack of previous research studies on this particular topic
4. Time constrain was another important limitation indeed.

## 11. CONCLUSION

The concentration of IL-6 at initial assessment predicted the development of hypoxemia i.e. reduced oxygen saturation level requiring hospitalization with excellent sensitivity and good specificity. IL-6 appears as a potential predictor for the development of the severe Covid-19 and might serve as good predictor for early identification of patients in need of hospitalization and appropriate management accordingly. In this study we have found that, IL-06 is significantly raised in case of severe COVID-19 infection. So, it could be determined as a potential predictor of severity assessment of COVID. Further in-depth large-scale studies are needed to evaluate the robustness of the use of IL-6 as an effective screening tool for the severe course of Covid-19.

### *Declaration by Authors*

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**Conflict of Interest:** The authors declare no conflict of interest.

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