
**ASSOCIATION BETWEEN CT SEVERITY SCORE AND
BIOMARKERS FOR EVALUATION OF PROGNOSIS IN
PATIENTS WITH COVID-19 INFECTION-
A RETROSPECTIVE OBSERVATIONAL STUDY.**

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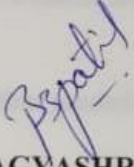
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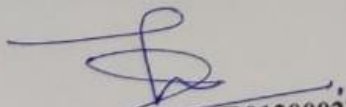
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LIST OF ABBREVIATIONS

WHO	: World Health Organization
SARS-CoV-2	: Severe Acute Respiratory Syndrome Corona Virus -2
MERS	: Middle East Respiratory Syndrome
RAAS	: Renin-Angiotensin-Aldosterone System
NIH	: National Institutes of Health
ARDS	: Acute Respiratory Distress Syndrome
CRP	: C-reactive proteins
LDH	: Lactate Dehydrogenase
Hscrp	: High sensitivity C -reactive protein
FDA	: Food and Drug Administration
EUA	: Emergency use authorizations
IL-6	: Interleukin -6
HRCT	: High Resolution computed tomography
CT	: Computed Tomography
CT Severity Score:	Computed tomography severity scoring.
ACE2	: Angiotensin-converting enzyme.
TNF	: Tumour necrosis factor
T2DM	: Type 2 Diabetes mellitus
HTN	: Hypertension

ABSTRACT

ASSOCIATION BETWEEN CT SEVERITY SCORE AND BIOMARKERS FOR EVALUATION OF PROGNOSIS IN PATIENTS WITH COVID-19 INFECTION- A RETROSPECTIVE OBSERVATIONAL STUDY.

Background and Objective:

In COVID19, high levels of inflammatory markers have been related to endothelial dysfunction, cytokine storm, and coagulopathy. There is increasing data to suggest that these results impact the mortality rate in patients with severe Covid-19. The current study evaluates patients' clinical outcomes by correlating their inflammatory indicators and CT Severity Score (CTSS).

Method: A retrospective, single-center, observational study was carried out on patients with COVID-19 infection who were admitted to the KLES Dr Prabhakar Kore Hospital & MRC Belagavi, Karnataka between August 1, 2020, and October 31, 2020.

Results: 912 patients were included based on inclusion and exclusion criteria, with 80% being males and 20% being females. In the mortality group, they had a mean age of 62.5 ± 12.4 and in the survival group, it was 51.1 ± 16.2 . The severity of COVID-19 infection was higher in patients with one or more co-morbidities, predominantly in those with T2DM. A significant positive correlation was found between serum ferritin, LDH, hsCRP, IL-6, and d-dimer and CT Severity Score ($p < 0.001$). A ROC analysis was performed, and the serum ferritin value was 331 ng/ml, with a sensitivity of 72.2% and a specificity of 56.3%; the LDH value was 375.5 U/L, with a sensitivity of 70.5% and a specificity of 63.3%. HsCRP-85.5 mg/ltr has a sensitivity of 72.2% and a specificity of 52%; IL-6 has a sensitivity of 60.2% and specificity of 60.8%; and D-dimer has a sensitivity of 70.5% and specificity of 65.2% at 643.5 ng/ml Was obtained. These values can be used to screen patients and predict their prognosis.

Conclusion: In our study of 912 patients, we observed that severe COVID-19 infection was more common in elderly-aged males. The severity of the covid-19 disease was higher in patients with one or more co-morbidities, predominantly in those with T2DM. The severity of the disease, as reflected in the HRCT, positively correlated with an increase in the levels of biomarkers. Hence it is concluded that the CT Severity Score and biomarker levels can be used as markers of prognosis in the patient with covid -19 infection.

Keywords: Covid-19 infection, Mortality, Biomarkers, Prognosis.

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INTRODUCTION:

On January 1, 2019, the China Health Authority reported several pneumonia cases in Wuhan City, Hubei Province, central China. Instances have been tracked since December 8, 2019, and many of those afflicted worked at or lived near the nearby Hunan Seafood Wholesale Market¹. Later then The World Health Organization (WHO) verified it as a novel coronavirus, previously known as 2019-nCoV, that was found in a patient's throat swab sample on January 7². The Coronavirus Study Group has designated SARS-CoV-2 as the pathogen, and the World Health Organization has named the virus Coronavirus Disease-19 (COVID-19). Authorities in China reported 7736 confirmed cases and 12,167 suspected cases on January 30. Additionally, 82 confirmed cases were reported in 18 other countries³. The World Health Organization declared the SARS-CoV-2 pandemic a worldwide public health emergency the same day (PHEIC).

In COVID-19, high levels of inflammatory markers have been related to endothelial dysfunction, cytokine storm, and coagulopathy. There is rising data to suggest that these results impact the mortality rate in patients with severe Covid-19. The current study is carried out to evaluate patients' clinical outcomes by correlating their inflammatory indicators and CT Severity Score (CTSS).

OBJECTIVE OF THE STUDY

To assess the association between CT Severity Score with biomarkers for evaluation of prognosis in patients with Covid -19 infection

REVIEW OF LITERATURE

Virology

Veterinarians used to know a lot about coronaviruses since they may cause a variety of illnesses in the respiratory, digestive, and central neurological systems of a broad variety of animal hosts. In the 1960s, coronaviruses were discovered to cause infection in humans. They usually infected youngsters and the elderly with upper respiratory tract illnesses. Only in the past 20 years has it been evident that coronaviruses may transmit deadly infections⁴.

The end of 2002 saw the arrival of three new zoonotic coronaviruses that produced devastating human diseases. Since its detection in September 2012 in Jeddah, Saudi Arabia, MERS-CoV has produced sporadic and isolated outbreaks; and since its discovery in October 2015, SARS-CoV-2 has been the source of the continuing worldwide COVID-19 pandemic⁴.

The virus: classification and origin

The coronaviruses are a group of enclosed, single-stranded, positive-sense RNA viruses that may cause respiratory illness and other organ system diseases in a variety of animal species, including humans. They belong to the order Nidovirales, family Coronaviridae, and subfamily Coronavirinae. There are four genera in the subfamily Coronavirinae, and they are called Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus, respectively³. Betacoronavirus species were formerly divided into lineages A, B, C, and D. The Embecovirus (lineage A), Sarbecovirus (lineage B), Mercovirus (lineage C), and Nobecovirus (lineage D) subgenera of Betacoronavirus have been formed from these lineages³.

Prior to the 2003 SARS epidemic, two betacoronavirus (CPV-1 and CPV-2) and two alphacoronaviruses (HCoV-229E and HCoV-NL63) were the most prevalent coronaviruses that caused respiratory diseases in humans (HCoV-OC43 and HCoV-HKU1, which was discovered in January 2004). In March 2003, SARS-CoV-1, a brand-new betacoronavirus belonging to group 2b, was discovered to be the disease's primary cause^{3, 4}. A betacoronavirus is a coronavirus that causes SARS (SARS-CoV-1 and SARS-CoV-2) and MERS (MERS-CoV). MERS-CoV is a member of lineage C, while SARS-CoV-1 and SARS-CoV-2 are members of lineage B⁵.

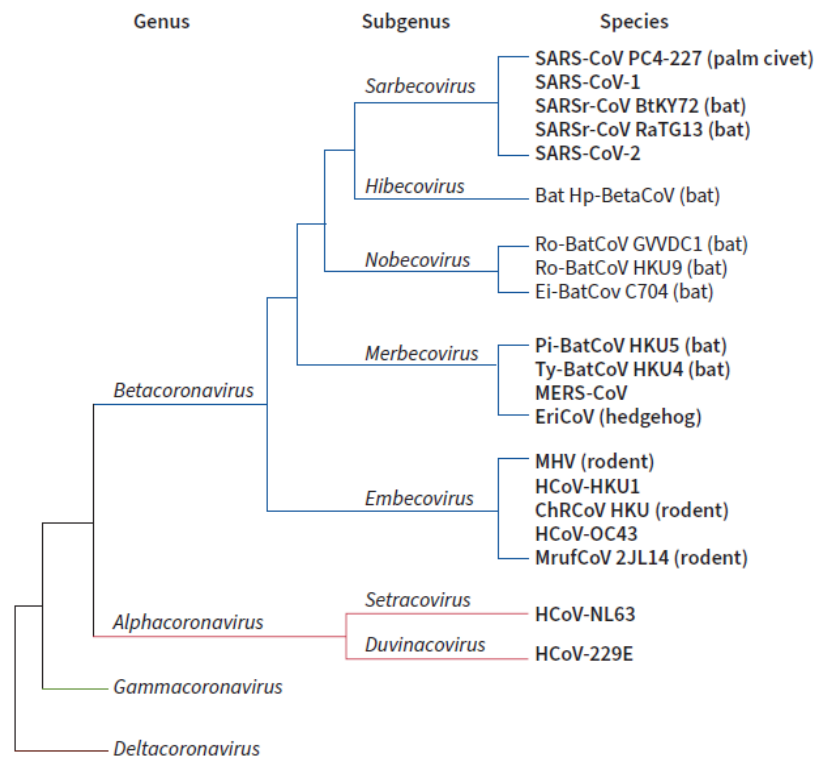


Figure 1: Taxonomy of SARS-CoV2

SARS-CoV-2 virus structure.

A coronavirus's four main structural proteins are the nucleocapsid (N), spike (S), membrane (M), and envelope (E).

S Glycoprotein.

A large, adaptable class I viral transmembrane protein is known as S, is found in coronaviruses. The size of this very prevalent S protein varies from 1,160 to 1,400 amino acids. Its primary role is to facilitate the attachment to and activation of certain receptors on the surfaces of host cells, so allowing infectious virion particles to enter the cell⁶.

M Protein.

The M protein is the most abundant viral protein and giving the viral envelope a distinct shape⁷. It attaches to the nucleocapsid and serves as the main organizer when the coronavirus is put together⁷. Although the structural characteristics of several coronavirus families are similar, their M proteins are quite varied⁸. The three transmembrane domains of the M protein are separated by long carboxy termini within the virion and short amino termini outside. As a whole, M-M interaction serves to preserve the viral scaffold. Although SARS-M CoV-1's protein has an amino acid substitution, SARS-M CoV-2's protein is unchanged.

E Protein.

When compared to the other major structural proteins, the E protein of a coronavirus is the smallest and least understood. It performs other functions in addition to contributing to the pathogenesis, assembling, and release of the virus. It's a small ion channel (viroporin) that's an integral membrane polypeptide. Coronavirus pathogenicity is changed when this protein is inactive or absent, probably because of structural and tropism changes. A short hydrophilic amino terminus, a sizable hydrophobic transmembrane domain, and an effective C-terminal domain make up the three different parts of the E protein⁶. The amino acid composition of the SARS-CoV-1 and SARS-CoV-2 E proteins is identical.

N Protein.

The N protein of coronaviruses has several roles. "Among its various roles, it forms a complex with the viral genome, helps the M protein bind during virion formation, and improves viral transcription efficiency^{9,10}. The RNA-binding domain (RBD) or linker region (LKR), the carboxy-terminal domain (CTD), and the N-terminal domain (NTD) are all separate and highly conserved domains¹⁰.

nsps and Accessory Proteins.

The SARS-CoV-2 genome contains 8 auxiliary proteins in addition to the 15 nsps (nsp1-nsp10 and nsp12-nsp16), including 3a, 3b, p6, 7a, 7b, 8b, and 9b¹¹. These proteins have many functions and are necessary for the transmission of viruses. In contrast to SARS-CoV-2, which lacks both, SARS-accessory CoV possesses both a shorter 3b protein and a longer 8b protein¹¹. When compared to other coronavirus sequences, there are no known amino acid alterations in the nsp7, nsp13, envelope, matrix, and p6 and 8b auxiliary proteins.

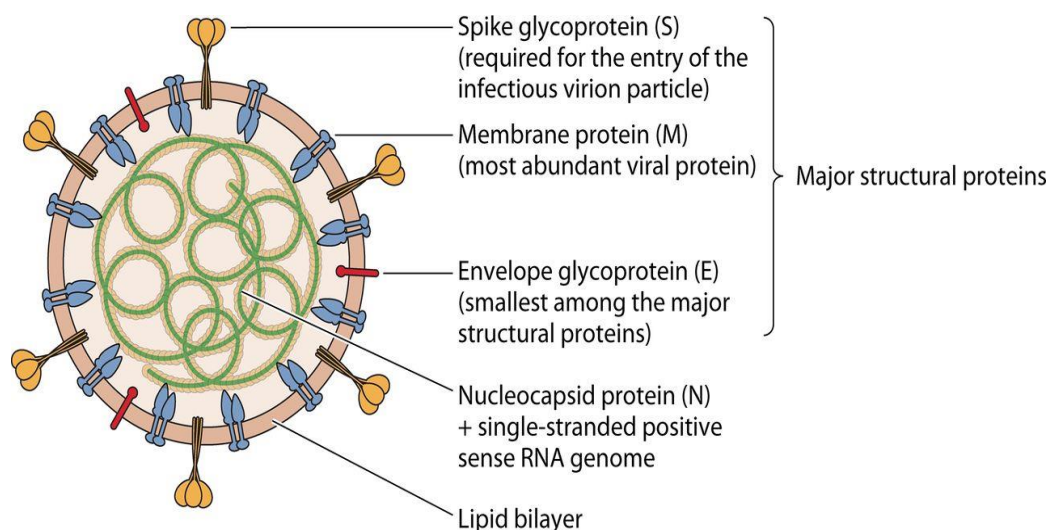


Figure 2: Structure of SARS-CoV-2

The life cycle of SARS-CoV-2

The life cycle of SARS-CoV-2 is considered comparable to that of SARS-CoV and other coronaviruses. The receptor protein angiotensin-converting enzyme 2 (ACE2) on the surface of the viral particle binds to the spike protein. Transmembrane serine protease 2 cleaves the viral spike protein to start endocytosis, which is subsequently used to internalize the virus¹³. The viral genome is translated into a polyprotein by host machinery, which is then cleaved by both host and viral proteases; the viral RNA-dependent RNA polymerase amplifies the genome virions produced and discharged by exocytosis. The ACE2 receptor is found in a variety of tissues, including the lungs (alveolar epithelial cells), upper airway, heart, gastrointestinal tract, kidneys, and vascular endothelial cells in the majority of tissues¹⁴. This possibly explains some of the extensive clinical symptoms of COVID-19.

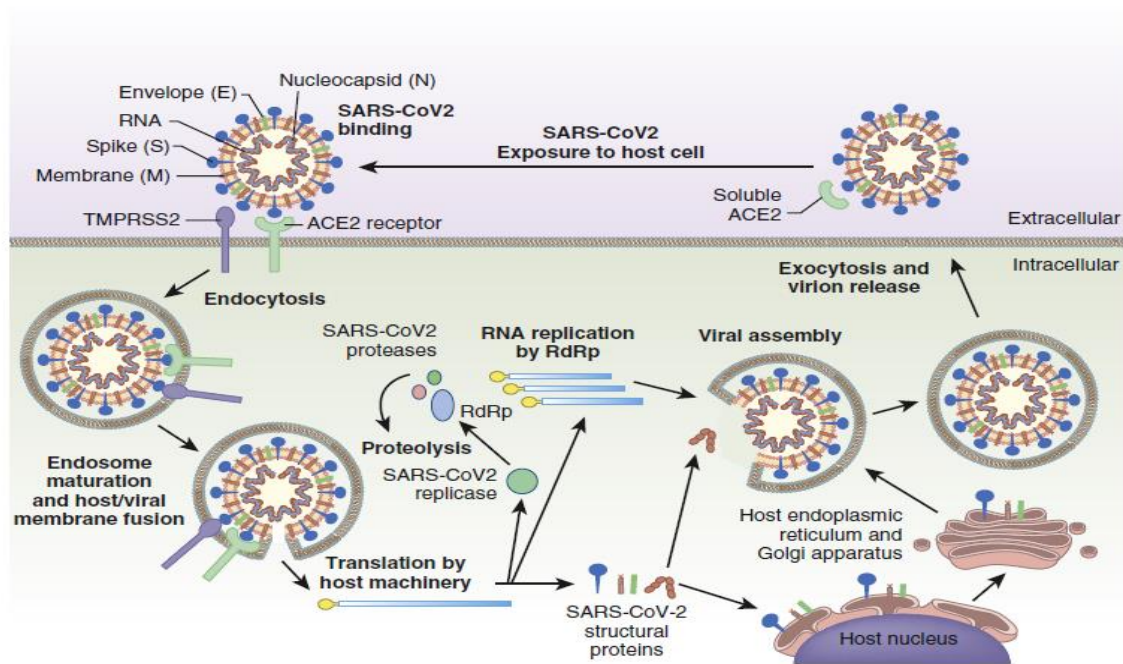


Figure 3: Life cycle of SARS-CoV-2

TRANSMISSION

Respiratory droplets are the primary vector for virus transmission. Specifically, this is thought to happen when respiratory droplets larger than $5\ \mu\text{m}$ in diameter are close by (less than 6 feet, or 2 m)¹⁵.

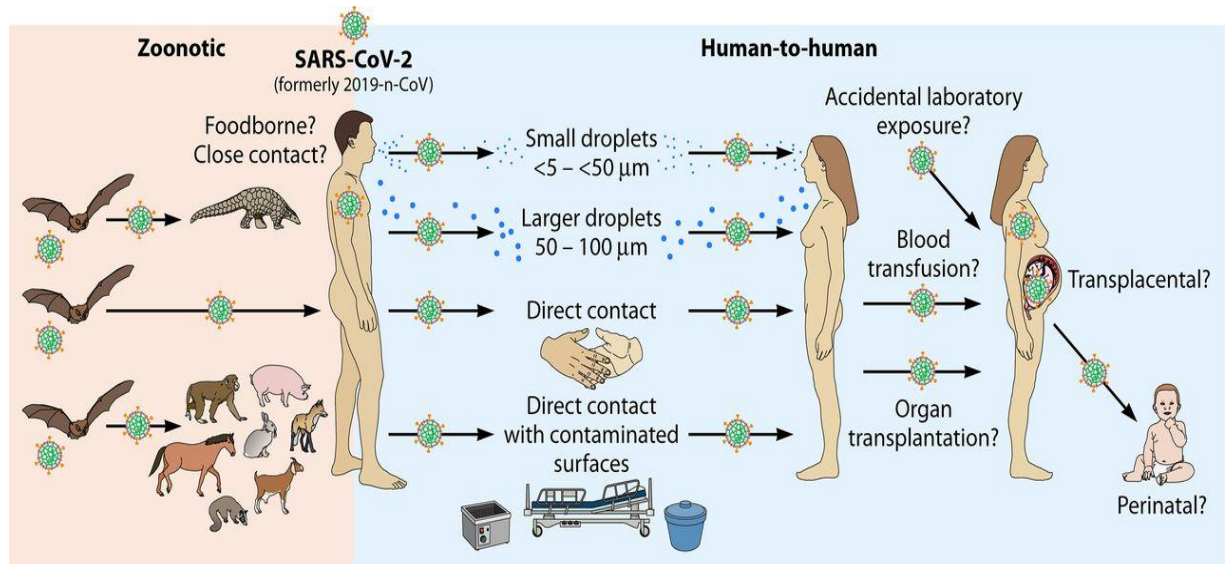


Figure 4: Transmission of SARS-CoV-2

PATHOGENESIS.

SARS-CoV-2 is identical to SARS-CoV and MERS-CoV in terms of phylogeny and structure. Each of the three has 5-8 auxiliary proteins in addition to 16 nonstructural proteins, 4 structural proteins (spike (S), envelope (E) glycoprotein, nucleocapsid (N), and membrane (M) protein), and 16 non-structural proteins. The carboxyl (C)-terminal S2 subunit comprises a fusion peptide, a single transmembrane, and a cytoplasmic domain that facilitates the fusing of the virus with the cell membrane. The amino (N)-terminal S1 subunit aids in the incorporation of the virus into the host cell.

The receptor-binding domain (RBD) and the N-terminal domain (NTD), which make up the two different portions of the S1 subunit, both let viruses enter their host cells and may be neutralized by antibodies or vaccinations¹⁷. The RBD is a crucial peptide domain in the

pathophysiology of infection because it functions as a receptor binding site for the human angiotensin-converting enzyme 2 (ACE2). It was originally believed that inhibiting the renin-angiotensin-aldosterone system (RAAS) would raise the risk of COVID-19 and severe illness requiring hospitalization¹⁸. The SARS-CoV-2 spike, also known as the S protein (S1), binds to ACE2 receptors on respiratory epithelial cells, such as type II alveolar epithelial cells, enabling the virus to enter host cells. Together with the upper oesophagus and enterocytes from the ileum, the bladder's urothelial cells, and the kidney's proximal tubular cells are two further examples of tissues that express ACE2 receptors. The host transmembrane serine protease 2 (TMPRSS2) priming the S2 component of the spike protein facilitates viral entry, endocytosis, and virion generation^{19,20}.

PATHOGENESIS OF SARS-COV-2-INDUCED PNEUMONIA

The pathophysiology of pneumonia caused by SARS-CoV-2 may be divided into early and late stages. In the first phase, the virus multiplies and immediately damages tissue. Recruited T cells, monocytes, and neutrophils produce cytokines such tumor necrosis factor (TNF), granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-1 (IL-1), interleukin-6 (IL-6), IL-1, IL-8, and IL-12 at the final stage. Massive levels of cytokines, particularly IL-6 and TNF-, are released into the bloodstream in severe COVID-19 instances by an overactive immune system, resulting in both local and systemic inflammation. "Cytokine storm" is the term used to describe this phenomenon^{21,22}. In patients with severe COVID-19, increased vascular permeability and the ensuing development of pulmonary edema can be attributed to a number of different mechanisms, including a) endotheliitis brought on by direct viral damage and perivascular inflammation, which causes the deposition of microvascular and microthrombi; b) fast contraction of the epithelium, which causes cell swelling and disruption of the intercellular

connections; c) stimulation of the kallikrein-bradykinin pathway, which increases vascular permeability; and d) dysregulation of the RAAS as a result of increased viral binding to ACE2 receptors. When SARS-CoV-2 activates toll-like receptors (TLRs), pro-IL-1 is produced. This pro-IL-1 is subsequently cleaved into active mature IL-1, which induces fibrosis and lung inflammation^{23,24,25,26}.

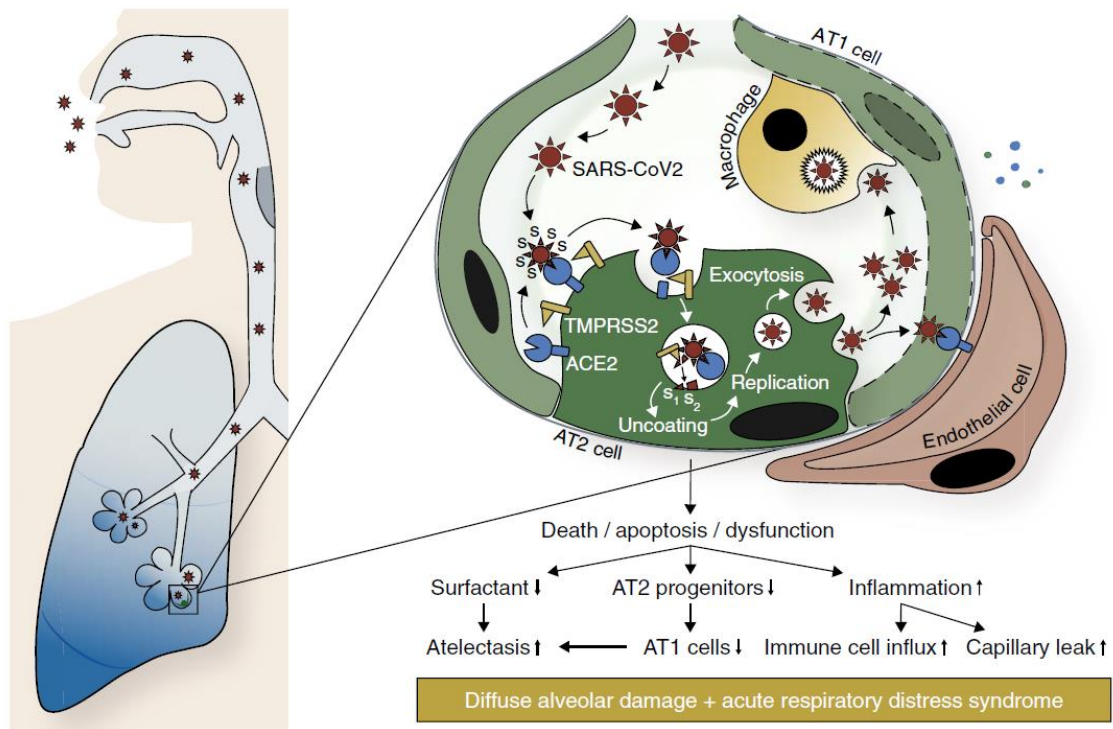


Figure 5: Pathophysiology of COVID-19 infection

Angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMSP2) must be expressed for SARS-CoV-2 to enter hosts via the alveolar epithelium (TMPRSS2). Coronavirus attaches to alveolar type 2 (AT2) cells by glycoprotein S, one of its four structural proteins, when virus-host cell membrane fusion may take place (spike). Second, TMPRSS2 cleaves ACE2, allowing ACE2 to be removed from the cell surface and the viral glycoprotein S subunits S1 and S2 to be released. This causes the viral coat to come off and the DNA to be released into the cytoplasm. The host cell's machinery then aids in the virus's replication by translating the S, M, N, and E viral core

proteins in the endoplasmic reticulum, assembling virus particles in the Golgi intermediate compartment, and packaging the virus particles into tiny vesicles for exocytosis. A variety of negative effects of SARS-CoV-2 infection on the damaged lung include AT2 cell death or injury. The risk of atelectasis and alveolar collapse is increased by a variety of circumstances, including: Surfactant deficiency increases this risk; AT2 progenitor cell deficiency resulting in faulty alveolar type 1 (AT1) cell replacement, compromising alveolar repair and potentially accelerating fibrosis; ACE2 down-regulation encourages spatially constrained overactivity of the ACE-angiotensin II-AT1 cell receptor axis, exacerbating the tissue-destructive impact of the inflammatory; and (4) the virus-induced release of cytokines by AT1 and AT2 cells results in capillary leakage and immune cell infiltration of the alveolar interstitium.

CLINICAL PRESENTATION.

The majority of infected people will see symptoms within 11 days, while the median incubation period for SARS-CoV-2 is thought to be 5 days²⁷. Septic shock, multiple organ failure, and acute respiratory failure requiring mechanical ventilation are all included in the COVID-19 clinical spectrum, as well as asymptomatic and paucisymptomatic variations of these illnesses. Between 18.1 and 33.3 percent of infected people show no signs of illness^{28,29}.

Clinical symptoms of the patient, biochemical and radiographic anomalies, hemodynamics, and organ function are all examined to gauge the severity of the presenting disease. According to NIH-provided criteria, COVID-19 is divided into five distinct groups (NIH).

1. **Asymptomatic or Presymptomatic Infection:** individuals who test positive for COVID-19 but don't exhibit any symptoms of having SARS-CoV-2.
2. **Mild illness:** The COVID-19 virus is thought to be present in people who don't have chest pain or shortness of breath but nonetheless display symptoms including a fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhoea, anosmia, or dysgeusia.
3. **Moderate illness:** those who show milder radiological or clinical signs of a respiratory infection but who also have an oxygen saturation level (SpO₂) of less than 94 percent while breathing room air.
4. **Severe illness:** Hypoxemia is characterized by a patient's oxygen saturation (SpO₂) on room air falling below 94 percent, a low arterial oxygen partial pressure to inspired oxygen fraction (PaO₂/FiO₂) of less than 300, a high respiratory rate of greater than 30 breaths per minute or a high proportion of lung infiltrates.

5. **Critical illness:** Acute respiratory failure, septic shock, or multiple organ dysfunction sufferers. Patients with severe COVID-19 disease may develop acute respiratory distress syndrome around a week after the onset of symptoms, which may lead to critical illness (ARDS).

Respiratory failure of any severity, or a marked deterioration in an already compromised respiratory state, characterizes acute respiratory distress syndrome (ARDS). One of the required clinical and ventilatory criteria is chest imaging (chest x-ray, CT scan, or lung ultrasound) demonstrating bilateral opacities (lung infiltrates > 50%) not entirely explained by effusions, lobar collapse, or collapse of both lobes of the lung. Before making a diagnosis of ARDS based only on clinical and radiologic symptoms, it's crucial to rule out conditions including fluid overload, heart failure, and pulmonary edema. According to the Berlin classification, ARDS may be divided into one of three kinds depending on how severe the hypoxia is as determined by the PaO₂/FiO₂ or P/F ratio³⁰.

- **Mild ARDS:** Patients not receiving mechanical ventilation should have a PaO₂/FiO₂ of 200 mmHg \leq FiO₂ 300 mmHg. Patients receiving non-invasive ventilation (NIV) using positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) should also have a PaO₂/FiO₂ of 200 mmHg \leq FiO₂.
- **Moderate ARDS:** 100 mmHg < PaO₂/FiO₂ \leq 200 mmHg
- **Severe ARDS:** PaO₂/FiO₂ \leq 100 mmHg.

An ARDS diagnosis may be made in the absence of PaO₂ if the ratio of SpO₂/FiO₂ is less than 315³¹.

Extrapulmonary Manifestations.

Technically, SARS-CoV-2 is a systemic viral infection since it produces COVID-19, a disease that primarily affects the respiratory system but may potentially lead to the failure of other organs.

Renal manifestations: A common complication for hospitalized COVID-19 patients is acute kidney injury (AKI). Although the exact causes of AKI in this group are unknown, they may include hypervolemia, pharmacological side effects, vascular damage from medication, and other medication-related injuries, as well as potential viral cytotoxicity³². The most prevalent extrapulmonary complication of COVID-19 is acute kidney injury (AKI), which is linked with a high mortality rate. The incidence of AKI among hospitalized COVID-19 patients was 36.6%, with 1993 patients (14.3% of the total) needing renal replacement therapy during their stay, according to the results of a large multicentre cohort study encompassing 5,449 patients (RRT)³³. Proteinuria, haematuria, irregular electrolytes (such as hyperkalemia and hyponatremia), and acid-base balance issues are some of the clinical and laboratory symptoms (e.g., metabolic acidosis)³⁴.

Cardiac manifestations: COVID-19 is known to cause damage to the heart tissue, including myocardial ischemia/infarction (MI) and myocarditis. Cardiogenic shock, cardiomyopathy, and arrhythmias are some of the most prevalent heart symptoms. In retrospective research done at a single institution, 27.8% of the 187 patients with a diagnosis of COVID-19 had high troponin levels that suggested myocardial damage. Patients with raised troponin levels also had a greater number of malignant arrhythmias and a faster rate of mechanical breathing than those with normal troponin levels³⁴. A meta-analysis of 198 published studies including 159,698 COVID-19 participants found a strong correlation between acute myocardial injury and a high burden of pre-existing cardiovascular disease and increased mortality and ICU admission³⁵.

Hematologic manifestations: The majority of COVID-19 patients have unusually low-test lymphocyte levels. Leukocytosis, thrombocytopenia, leukopenia, increased ESR levels, C-reactive protein (CRP), lactate dehydrogenase (LDH), and a low white blood cell count are some other abnormalities seen in the lab. Despite using systemic anticoagulation for therapeutic or preventative purposes, patients with COVID-19 nevertheless have a high risk of venous and thromboembolic events, including PE, DVT, MI, ischemic strokes, and arterial thromboses. Notably, COVID-19 is linked to considerably higher D-dimer and fibrinogen levels, as well as longer prothrombin time (PT) and partial thromboplastin time, among those at risk of arterial and venous thrombosis (aPTT) ^{34,36}.

Gastrointestinal manifestations: According to a meta-analysis study by Tariq et al. that looked at 78 trials comprising 12, 797 individuals, up to 20% of patients with COVID-19 infection report gastrointestinal (GI) symptoms include diarrhoea, nausea and/or vomiting, anorexia, and abdominal discomfort^{37,38}.

Hepatobiliary manifestations: IN 14–53% of those with COVID-19 infection, liver function tests often show a sharp rise in aspartate transaminase (AST) and alanine transaminase (ALT)³⁹. Hepatic impairment occurs more often in those with severe COVID-19 infection.

Endocrinologic manifestations: Patients infected with this virus who already suffer from endocrinologic disorders like diabetes mellitus are at a higher risk for having life-threatening complications. COVID-19 individuals hospitalised with clinical signs such as abnormal blood glucose levels, euglycemic ketosis, and diabetic ketoacidosis³⁴.

Neurologic manifestations: Other neurological symptoms include headache, stroke, loss of consciousness, seizure disorder, and toxic metabolic encephalopathy. Northern Italian researchers reported five COVID-19 individuals who developed Guillain-Barré syndrome (GBS)^{40,41}.

Cutaneous manifestations: A meta-analysis of 34 papers reporting 996 cases of COVID-19 found that the most common cutaneous symptom was acral lesions resembling pseudo chilblains, seen in 40.4% of patients. The other frequent skin signs were erythematous maculopapular rash (21.3%), vesicular rash (13%) and urticarial rash (10.9%). It was interesting to see that the onset of a certain rash appeared to depend on the patient's age. Vascular rashes (4%) that resembled livedo or purpura and were more prevalent in the elderly as well as erythema multiforme-like eruptions (3.7%) that were more prevalent in the young were other rare rashes⁴².

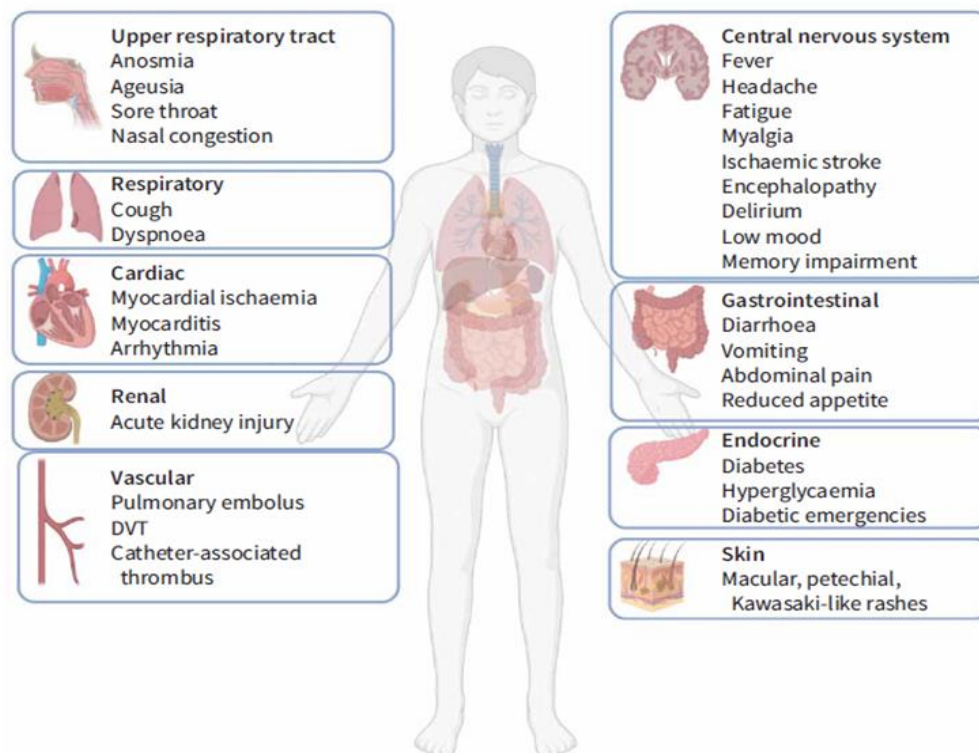


Figure 6: Clinical features of COVID-19 infection

Diagnostic Testing In COVID-19.

Molecular Testing.

- The typical diagnostic procedure involves nasopharyngeal swabbing and real-time polymerase chain reaction (PCR) screening for SARS-CoV-2 nucleic acid. The US Food and Drug Administration (FDA) has validated commercial PCR tests for the

qualitative detection of SARS-CoV-2 nucleic acid from nasopharyngeal swabs and other locations, such as oropharyngeal, anterior/mid-turbinate nasal swabs, nasopharyngeal aspirates, bronchoalveolar lavage (BAL), and saliva and granted emergency use authorizations (EUAs). Only patients receiving mechanical breathing should have their BAL samples obtained in order to guarantee the longest time of positive.

- The sensitivity of PCR testing is affected by a number of factors, such as the quality of the material, how it was collected technically, how long it has been since the patient was exposed, and where the specimen came from⁴³. The specificity of the majority of commercially available SARS-CoV-2 PCR tests is close to 100%, albeit, provided there is no cross-contamination during specimen processing.
- SARS-CoV-2 antigen testing is quicker than molecular PCR but has lower sensitivity⁴⁴. Patients meeting the criteria should also be tested for other viral infections of the respiratory tract.

Serology Testing

- The presence of disease antibodies may be discovered using antibody testing. For determining the existence of antibodies against SARS-CoV-2, several commercially manufactured antibody testing kits are now available. These tests are essential for the global surveillance of COVID-19.
- Despite the large number of antibody tests that have been developed to date, serologic testing has limits in terms of specificity and sensitivity, and test results might vary. However, a test for antibodies developed by the Centres for Disease Control and Prevention (CDC) may be able to detect earlier SARS-CoV-2 infection with a specificity of higher than 99% and a sensitivity of 96%.

Lymphopenia (in 68% of cases) and mild thrombocytopenia (in 52% of cases) are the most common anomalies seen in a complete blood count (36.2 percent of the time). Thrombocytopenia does not add much to the prognosis.

Hs-C-reactive protein

The liver produces CRP in response to stimulation from IL-6 and other inflammatory mediators; the plasma protein is then secreted. Because a rise in CRP levels is associated with an increase in sickness severity, this acute phase reactant is used therapeutically as a biomarker for a number of inflammatory conditions despite its lack of specificity⁴⁵.

Interleukin-6

The pleiotropic proinflammatory cytokine interleukin (IL)-6 is produced by lymphocytes, monocytes, and fibroblasts. In a dose-dependent fashion, bronchial epithelial cells generate IL-6 in response to SARS-CoV infection. Increased cytokine release, as shown by elevated IL-6 levels in the blood, has been related to systemic inflammation and hypoxemic respiratory failure caused by COVID-19^{45,46,47}.

Lactate dehydrogenase

In the process of breaking down glucose, the enzyme LDH changes pyruvate into lactate. Necrosis of the cell membrane causes LDH to be released. This is a symptom of lung injury or infection, such as SARS-CoV-2 pneumonia. There are strong reasons to believe that LDH levels cause COVID-19 disease⁴⁷.

D-dimer.

The hyperinflammatory and hypoxic damage brought on by SARS-CoV-2 infection may result in endothelial cell failure, thrombosis, and increased D-dimer levels.

Increased levels of D-dimers show that coagulation and fibrinolysis have been activated since they are formed during the lysis of cross-linked fibrin.

Due to the development of pulmonary microthrombus, deep venous thrombosis, and disseminated intravascular coagulopathy, high levels of D-dimer have been associated with poor outcomes^{48,49}.

Radiological findings

Radiological evidence can support a COVID-19 diagnosis. Up to seventy-five percent of symptomatic individuals have abnormal chest radiographs. Bilateral patchy ground-glass change or consolidation is typical, typically in the peripheries and with a basal predominance.

HRCT

By determining the degree of lung involvement, detecting co-occurring illnesses, and assisting in the creation of a treatment plan, a high-resolution computed tomography (HRCT) chest scan may aid in the diagnosis of COVID-19. Bilateral multifocal peripheral ground-glass opacities are the most common HRCT chest findings in COVID-19 pneumonia⁵⁰. It is crucial to remember that a negative result from a regular HRCT does not mean that the disease does not exist; rather, it shows that the lung parenchyma is not implicated in the study at hand.

With the use of the CO-RADS scale, a radiological diagnosis of COVID-19 illness was suspected. Lung involvement severity was characterized using a total severity rating, which ranged from 0 to 25. The CT scan was assessed according to the degree of lung involvement using a severity index^{50,51,52}.

Table No 1: CO-RADS Scoring System

CO-RADS score	Level of suspicion	Findings
CO-RADS 0	Not interpretable	Scan technically insufficient for assigning a score
CO-RADS 1	Very low	Normal or non-infectious
CO-RADS 2	Low	Typical for other infections but not COVID-19
CO-RADS 3	Equivocal/unsure	Features compatible with COVID-19, but also other diseases
CO-RADS 4	High	Suspicious for COVID-19
CO-RADS 5	Ver high	Typical for COVID-19
CO-RADS 6	Proven case	RT-PCR positive for SARS-CoV-2

Lung involvement is quantified using the COVID-19 CT Severity Score index. Three of the right and two of the left lobes of each of the five lobes of the lungs were visually rated, and a score between 1 and 5 was assigned.

Table No 2: CT Severity Score distribution.

% Involvement (single lobe)	Score
0-5 % lung involvement	1
5-25 % lung involvement	2
25-50 % lung involvement	3
50-75 % lung involvement	4
75-100 % lung involvement	5

Table No 3: CT Severity Score Index

CT severity	SCORE
Mild	< 8
Moderate	9 - 15
Severe	> 15
Total score	~ 25

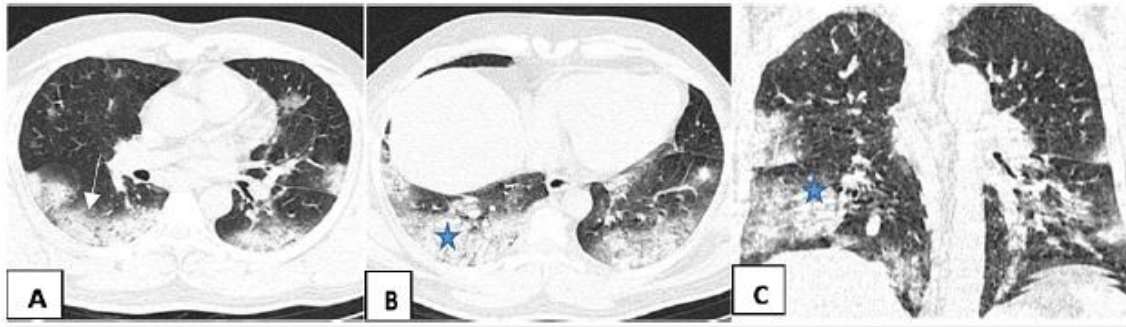


Figure 7: HRCT Thorax of COVID -19 patients.

HRCT thorax axial and coronal reformatted images of 60 year old male patient demonstrate a few patchy crazy pavement appearance (white arrow) and multiple peripheral area of patchy consolidation (Blue star),predominantly involving bilateral lower lobe with CT severity score of 11/25 (moderate disease)

Treatment

During the early stages of the pandemic, when very little was known about COVID-19 and its clinical treatment, the utilization of experimental medicines and pharmaceutical repurposing was crucial for mitigating the impact of this unique viral illness. Since then, a lot has changed due to the efforts of clinical researchers all across the globe. These discoveries have accelerated the discovery of novel drugs and vaccines and increased our knowledge of COVID-19 and its treatment.

Pharmacologic Therapies in The Management Of Adults With COVID-19

Antiviral drugs (such as molnupiravir, paxlovid, and remdesivir), anti-SARS-CoV-2 monoclonal antibodies (such as bamlanivimab/etesevimab, casirivimab/imdevimab, sotrovimab, and bebtelovimab), anti-inflammatory drugs (such as dexamethasone), and immunomodulators (such as baricitinib, tocilizumab) are available under FDA issued Emergency Use Authorization(EUA) or being evaluated in the management of COVID-19⁴⁴."

COVID-19 treatment varies with illness severity. The initial stage of COVID-19 infection, which starts before to or shortly after the beginning of symptoms, must be distinguished from the second stage, which takes place later. Antiviral drugs and antibody-based treatment are most likely to be effective at this phase since viral replication has already started. Hyperinflammation brought on by cytokine production and activation of the coagulation system results in a prothrombotic condition in the latter stages of the illness. Antiviral treatments may not be as effective at treating this hyperinflammatory condition as anti-inflammatory drugs such as corticosteroids or immunomodulating therapy, or a combination of these therapies. The most recent prospective therapeutic options for clinical application in COVID-19 management are summarized in the section that follows^{44,53}.

Antiviral Therapies

- **Molnupiravir** is an oral route, a broadly-effective antiviral medication that inhibits the RdRp enzyme. Initial research focused on its potential as an antiviral treatment for influenza and alphaviruses, such as the Venezuelan equine encephalitic virus and We know that Molnupiravir medication substantially lowers hospitalization and death in individuals with mild COVID-19 disease based on a meta-analysis of phase 1-3 research. Early Molnupiravir medication reduced hospitalization and mortality rates in unvaccinated individuals with moderate to severe COVID-19^{53,54}.
- **Paxlovid:** (ritonavir in combination with nirmatrelvir) An interim review of phase 2-3 data comprising 1219 patients indicated that individuals who were administered Paxlovid within three days of symptom start were 89% less likely to have hospitalization or all-cause death compared to placebo. The Food and

Drug Administration approved Paxlovid for the treatment of mild to moderate COVID-19 on December 22, 2021⁵⁵.

- **Remdesivir:** an antiviral drug with a broad spectrum of effects, has been shown to be effective against SARS-CoV-2 in vitro. Remdesivir has been given FDA clearance for the treatment of COVID-19 in hospitalized adults and kids (over 12 years of age and weighing 40 kilograms or more). Remdesivir was shown to shorten hospital stays for patients with moderate-to-severe COVID-19 compared to a placebo in three randomized, controlled clinical trials. The WHO SOLIDARITY Trial, which was conducted at 405 institutions in 40 countries, included 11,330 inpatients with COVID-19. Overall mortality, the need for mechanical ventilation, and hospital stay lengths were not substantially different between the remdesivir (2750) and placebo (4088) groups. Those who got a 3-day course of remdesivir had an 87% decreased chance of hospitalization or mortality compared to placebo, according to a new randomized, double-blind, placebo-controlled research conducted on non-hospitalized COVID-19 patients^{58,59,60}.
- **Chloroquine and hydroxychloroquine Antiviral** therapy for COVID-19 during the pandemic initially included hydroxychloroquine and chloroquine. Clinical status and overall mortality did not improve with the addition of hydroxychloroquine alone or in combination with azithromycin in randomized controlled trials of hospitalized patients. Postexposure prophylaxis with hydroxychloroquine did not protect against SARS-CoV-2 or COVID-19 in randomized controlled trials^{63,64}. Patients diagnosed with COVID-19 in either an inpatient or outpatient setting should not use hydroxychloroquine or chloroquine at this time.

- **Lopinavir/ritonavir:** was advised as an antiviral therapy for COVID-19 at the start of the pandemic. The FDA has recently approved this combo drug for the management of HIV. Randomized controlled research comparing lopinavir-ritonavir treatment to the standard of care in hospitalised patients with severe COVID-19 revealed no effect. It is currently not approved to combine the use of lopinavir and ritonavir for the treatment of COVID-19 in either inpatient or outpatient settings.
- **Ivermectin:** The Food and Drug Administration-approved anti-parasitic medication ivermectin is extensively used to treat COVID-19 in different parts of the world. In vitro testing has shown that it lessens SARS-CoV-2 proliferation. In a single-center, double-blind, randomised control research, treatment with ivermectin at a dosage of 300 mcg/kg body weight for five days did not significantly lessen or abate symptoms in 476 adult patients with mild COVID-19 illness. Patients with COVID-19 who are either inpatients or outpatients should not use ivermectin at this time due to its lack of efficacy⁶⁷.

The Omicron subvariants BA.2.12.1, BA.4, and BA.5 may respond well to the combination of remdesivir, nirmatrelvir, and Molnupiravir, according to the results of many studies⁶⁸.

Anti-SARS-CoV-2 Neutralizing Antibody Products

Although it is known that people who recover from COVID-19 produce antibodies effective against SARS-CoV-2, how long these antibodies remain effective is unclear. Lots of ongoing clinical studies continue to investigate their potential as treatment agents for treating COVID-19.

- During the SARS, MERS, and Ebola pandemics, researchers looked at convalescent plasma therapy, but they couldn't find any evidence of its effectiveness from randomized controlled studies. EUA given by the FDA, patients with severe, life-threatening COVID-19 have access to convalescent plasma treatment^{69,70,70}. Investigations assessing the use of convalescent plasma in the potentially deadly COVID-19 have shown mixed outcomes, despite early promise. According to a retrospective study based on a US national registry, patients with COVID-19 who were not receiving mechanical ventilation and who received a transfusion of convalescent plasma with higher anti-SARS-CoV-2 IgG antibody levels fared better than those who received a transfusion of convalescent plasma with low antibody levels. In three short randomized controlled studies, there were no significant differences in clinical improvement or overall mortality between patients treated with convalescent plasma and those treated with usual treatment^{71,72,73}. In in-vitro research, convalescent plasma from individuals infected with the original SARS-CoV-2 strains showed significantly decreased neutralization against SARS-CoV-2 variant B.1.351/501Y.V2. In another in vitro investigation, the B.1.351 variety was substantially more resistant to neutralization compared to the B.1.1.7 variation, which was readily neutralized by convalescent plasma from patients who had previously been infected with the original SARS-CoV-2 strains⁷⁵.
- **REGN-COV2 (Casirivimab and Imdevimab):** The SARS-CoV-2 spike protein RBD is the target of REGN-COV2, a combination of two non-competing IgG1 antibodies (casirivimab and imdevimab). When tested on non-human primates, this combination was shown to decrease viral load in vivo, protecting them against the virus's pathogenic consequences⁷⁶. The REGN-COV2 antibody cocktail reduced

viral load in comparison to the placebo, according to an interim analysis of 275 outpatients with COVID-19 treated with 2.4 g of REGN-COV2 (casirivimab 1,200 mg and imdevimab 1,200 mg) or 8 g of REGN-COV2 (casirivimab 2,400 mg and imdevimab 2,400 mg). The fact that this antibody combination was equally as risk-free as the placebo group was also supported by our halfway research⁷⁷. According to early results from a Phase 3 trial of REGN-COV (casirivimab/imdevimab), patients with COVID-19 who were not previously hospitalized had a 70% lower probability of being hospitalized or passing away. In vitro investigations on the effects of REGN-COV2 reveal that the two new SARS-CoV-2 variants of concern, B.1.1.7 and B.1.351, nevertheless maintain viral activity. Based on their in-vitro testing, Wilhelm et al. revealed in a recent preprint that the SARS-CoV-2 Omicron strain was resistant to both casirivimab and imdevimab.

- **Bamlanivimab and Etesevimab (LY-CoV555 or LY3819253 and LY-CoV016 or LY3832479).**

Two monoclonal antibodies have been developed to counteract the effects of spikes. The plasma of a recovered COVID-19 patient is used to create the monoclonal antibody known as bamlanivimab. In nonhuman primates, it has been shown to inhibit the spread of SARS-CoV-2 and other coronaviruses (such as REGN-CoV2), suggesting it possesses antiviral properties⁷⁸. In vitro analysis showed that etesevimab neutralizes resistant variants with epitope changes because it binds to a different epitope than bamlanivimab. The combination of bamlanivimab and etesevimab substantially reduced SARS-CoV-2 viral load in Phase 2 of the BLAZE-1 investigation as compared to the placebo⁷⁹. The Phase 3 section of the data is presently being revealed, but preliminary findings from the Phase 2 component of the BLAZE-1 research show that therapy lowered the risk

of hospitalization and death by 87 percent. In vitro testing of bamlanivimab/etesevimab against B.1.1.7 and B.1.351, two of the most concerning developing SARS-CoV-2 variants, indicated continued activity⁸⁰.

The potent anti-spike neutralizing monoclonal antibody sotrovimab (VIR-7831) has been shown to have activity against the four volatile organic compounds (VOCs) alpha (B.1.1.7), beta (B.1.351), gamma (P1), and delta in vitro (B.1.617.2). Results from a planned follow - up assessment of the Phase 3, multicenter, double-blind, placebo-controlled COMET-ICE trial showed that one dose of sotrovimab (500 mg) reduced the risk of hospitalization or death in high-risk non-hospitalized patients with mild to moderate COVID-19 by 85% compared to placebo.

- **The monoclonal antibody bebtelovimab (LY-CoV1404, 1404)** neutralizes SARS-CoV-2 by attaching to the RBD of the virus' spike(S) protein. The neutralization of Omicron VOC and its subvariants, as well as all other known types of SARS-CoV-2 VOCs, has shown the high efficacy of bebtelovimab⁸¹. Study by Doughan et al. indicated that bebtelovimab, either alone or in combination with bamlanivimab and etesevimab, resulted in better viral clearance and speedier system resolution in ambulatory individuals with moderate to severe COVID-19 . Under an Emergency Use Authorization (EUA) granted by the US Food and Drug Administration, patients with mild to moderate COVID-19 and laboratory-confirmed SARS-CoV-2 infection who are at high risk of developing severe illness, hospitalization, or death may be eligible to receive bebtelovimab (FDA). These individuals need to be ambulatory, above 40 kg in weight, and at least 12 years old.

Specifically, the FDA approved the clinical use of REGN-COV2 (casirivimab and imdevimab) and sotrovimab in two further EUAs issued in November 2020 and May 2021. The only patients for whom these EUAs permitted the use of these medications were those with laboratory-confirmed SARS-CoV-2 infection with mild to moderate COVID-19 who are at high risk of developing worse and who are not in an inpatient setting (aged 12 years or older and weighing more than 40 kg). On March 25, the US authorities stopped giving patients bamlanivimab alone because of the results of a recent therapy study. According to them, the treatment is impractical due to the rising number of coronavirus variants. To ascertain if antibody treatments are still effective, it will be critical to track the incidence of new mutations in each area.

- **Tixagevimab and Cilgavimab (AZD7442):** two potent anti-spike monoclonal antibodies, are made by separating antibodies from B cells of people who have SARS-CoV-2 infection. Through their attachment to certain areas of the viral spike protein's RBD, the antibodies deactivate SARS-CoV-2^{82,83}. An ongoing multicenter, double-blind, randomized, placebo-controlled trial has assessed the safety and effectiveness of a single dose of these two monoclonal antibodies for preexposure prophylaxis against COVID-19 in high-risk patients who did not respond well to the COVID-19 vaccine or was unable to receive the vaccine⁸⁴. The US Food and Drug Administration gave this monoclonal antibody combination an emergency use license in December 2021 for the aim of COVID-19 preexposure prophylaxis in adults and paediatric population (12 years of age and older, weighing at least 40 kg) who have no current evidence of SARS-CoV-2 infection and who have not recently been exposed to SARS-CoV-2 positive persons AND

who are moderately or severely immunocompromised owing to a variety of diseases and therapies.

Immunomodulatory Agents

- **Corticosteroids:** Lung inflammation from severe COVID-19 is associated with the production of cytokines and an increase in inflammatory markers. Early on in the pandemic's course, it was unclear whether or not glucocorticoids would be effective in treating COVID-19. According to the Randomized Evaluation of Covid-19 Therapy (RECOVERY) trial, which enrolled hospitalised patients with clinically suspected or laboratory-confirmed SARS-CoV-2 and randomly assigned them to receive dexamethasone (n=2104) or usual care (n=4321), dexamethasone use was associated with lower 28-day mortality in patients receiving invasive mechanical ventilation or oxygen support but not in patients receiving no respiratory support⁸⁵. According to the results of this crucial investigation, dexamethasone alone or in combination with remdesivir is now frequently used to treat patients in hospitals who need more oxygen or non-invasive or invasive mechanical ventilation.
- **Interferon- β -1a (IFN- β -1a):** SARS-CoV-2 inhibits the generation of interferons, a kind of cytokine essential for the immune system to react to a virus, in the laboratory⁸⁶. Patients with acute respiratory distress syndrome (ARDS) haven't reacted well to IFN-1a, nevertheless⁸⁷. In a small randomized, double-blind, placebo-controlled study, inhaled IFN-1a was more likely to lead to clinical improvement and recovery than the control. Another small rerandomized clinical investigation found that the clinical response to inhaled IFN-1a was not significantly different from the response in the control group. According to the

scientists, utilizing this medication sooner rather than later decreased hospital stays and death after 28 days. Data for four treatment group patients who passed away before finishing therapy, however, were not included. It is thus difficult to infer inferences from these results⁸⁸. At this time, it is uncertain if interferon-1a is effective against the four SARS-CoV-2 VOCs, Alpha (B.1.1.7), Beta (B.1.351), Gamma(P1), and Delta (B.1.617.2). Therapy with this medication is not indicated for treating COVID-19 infection because of the lack of data on its safe and effective usage and the potential for adverse effects.

- **Interleukin (IL)-1 Antagonists:** The Food and Drug Administration has authorized interleukin-1 receptor antagonists like Anakinra for the treatment of rheumatoid arthritis. A short case-control research trial examined its off-label usage in severe COVID-19. These measures were taken because cytokines like interleukin are responsible for the severe forms of COVID-19. According to this trial, anakinra dramatically reduced mortality risk and the rate at which patients with severe COVID-19 needed invasive mechanical ventilation⁸⁹. Since interleukin-1 receptor antagonists have not been tested against the three novel SARS-CoV-2 types, we are unsure of their effectiveness (B.1.1.7; B.1.351, and P.1). At this moment, this therapy is not advised for COVID-19 infection since it has only been studied in case series.
- **Anti-IL-6 receptor Monoclonal Antibodies:** Interleukin-6 (IL-6), a pro-inflammatory cytokine, is often blamed for the high degree of inflammation seen in COVID-19. By eliminating certain cells, targeting the IL-6 receptor may reduce inflammation. This is based on accounts of a limited number of individuals who had effective therapy for severe COVID-19⁹⁰. Tocilizumab and sarilumab are examples of IL-6 receptor inhibitors that the Food and Drug Administration (FDA)

has approved for use in treating cancer and the very rare disorder Castleman's syndrome (Siltuximab)⁹¹.

- **Tocilizumab:** Patients with acute respiratory distress syndrome (ARDS) haven't reacted well to IFN-1a, nevertheless⁹¹. In a small randomized, double-blind, placebo-controlled study, inhaled IFN—1a was more likely to lead to clinical improvement and recovery than the control. Another small randomized clinical investigation found that the clinical response to inhaled IFN-1a was not significantly different from the response in the control group. According to the scientists, utilizing this medication sooner rather than later decreased hospital stays and death after 28 days. Data for four treatment group patients who passed away before finishing therapy, however, were not included. It is thus difficult to draw inferences from these results⁹². At this time, it is uncertain if interferon-1a is effective against the four SARS-CoV-2 VOCs, Alpha (B.1.1.7), Beta (B.1.351), Gamma(P1), and Delta (B.1.617.2) .Tocilizumab did not reduce the need for a ventilator or the number of deaths in this study⁹³.
- **Sarilumab and Siltuximab** - IL-6 receptor blockers Tocilizumab may have a similar effect on the inflammatory response to COVID-19 as sarilumab and siltuximab. There are no published clinical trials that support the use of siltuximab for severe COVID-19 at this time. Although 431 patients were monitored for 60 days in a worldwide, randomized, double-blind, placebo-controlled phase 3 trial of sarilumab, neither the clinical status nor the death rate showed any statistically significant changes⁹⁴.

Janus kinase (JAK) inhibitors

- **The Janus kinases (JAKs) 1 and 2:** are specifically inhibited by the orally accessible drug baricitinib. It is recommended for those with moderately active to severely active rheumatoid arthritis (R.A.). Baricitinib was regarded as a possible treatment for COVID-19 because of its effects on in vitro SARS-CoV-2 endocytosis and the intracellular signaling cascade of cytokines responsible for the late-onset hyperinflammatory state that culminates in severe illness^{95,96}. The drug has considerable promise as a possible therapy for all kinds of COVID-19 because to its dual activity. The combination therapy of baricitinib plus remdesivir was superior to remdesivir therapy alone at reducing recovery time and accelerating clinical improvement in hospitalized patients with COVID-19, according to the results of the ACTT-2 trial, which was a double-blind, randomized, placebo-controlled study of baricitinib plus remdesivir in adult patients with COVID-19⁹⁷. Under an FDA EUA, baricitinib and remdesivir may be combined for therapy in hospitalized COVID-19 patients. The effectiveness of baricitinib alone or in combination with remdesivir has not been studied in SARS-CoV-2 variations, and it is yet unclear how the drug interacts with dexamethasone.
- **Ruxolitinib:** an oral selective inhibitor of JAK 1 and 2, may be used to treat graft-versus-host disease (GVHD) that does not respond to steroids, polycythemia vera, and myeloproliferative disorders. It has been hypothesized that, like baricitinib, it may interfere with the cytokine's intracellular signaling pathway, making it a potent COVID-19 treatment option. Ruxolitinib's effectiveness and safety were evaluated in a small prospective multicenter randomized controlled phase 2 research, which demonstrated no appreciable advancement above the industry

standard. However, the majority of patients' chest CT scans revealed significant improvement, and they recovered from lymphopenia more rapidly⁹⁸.

- **Tofacitinib:** is used to treat moderate to severe instances of RA, psoriatic arthritis, and ulcerative colitis, the same as other oral selective JAK1 and JAK3 inhibitors. It was believed that by preventing the chain of inflammatory reactions, its medication would help people with severe COVID-19, whose lung damage was brought on by viral inflammation. In a small randomized controlled research with 289 individuals, tofacitinib was shown to lower the risk of respiratory failure or fatality.
- **Bruton's tyrosine kinase inhibitors:** including acalabrutinib, ibrutinib, and rilzabrutinib aim to regulate macrophage signaling and activity. They may be used to treat certain types of blood cancer, according to the Food and Drug Administration. The activation of macrophages is likely a component of the immune response to inflammation found in severe COVID-19. The results of a small, off-label study in which 19 hospitalized patients with severe COVID-19 received acalabrutinib offered evidence for the potential therapeutic efficacy of BTK inhibition⁹⁹. The effectiveness of these medications in treating severe cases of COVID-19 disease is now being tested in clinical studies.

Oxygenation and Ventilation Management In COVID-19

Conventional Oxygen Therapy

For individuals with COVID-19 who also have respiratory issues, continuous pulse oximetry is advised. The oxygen saturation (SpO₂) must be maintained between 92 and 96 percent by utilizing a nasal cannula or a Venturi mask to provide more oxygen (or between 88 and 90 percent if the individual has COPD). If the clinical condition and

oxygen saturation levels improve, oxygen should be given for a while before being tested again. If after using traditional medical therapy there is no improvement in symptoms or oxygen saturation, High-Flow Nasal Cannula (HFNC) or Noninvasive Positive Pressure Ventilation (NIPPV) is advised.

Management of Acute Hypoxemic Respiratory Failure in COVID-19

Traditional oxygen treatment is unable to address the oxygen needs of adult patients with COVID-19, whose most common complication is acute hypoxemic respiratory failure. High-flow nasal cannulas (HFNC), noninvasive high-pressure ventilation (NIPPV), endotracheal intubation, invasive mechanical ventilation (IMV), or extracorporeal membrane oxygenation are among the advanced respiratory support procedures that are necessary for these patients (ECMO)

High-Flow Nasal Cannula (HFNC) and Noninvasive Positive Pressure Ventilation (NIPPV)

Acute hypoxemic respiratory failure brought on by COVID-19 may be treated with the noninvasive respiratory support techniques HFNC and NIPPV. They help patients avoid the need for invasive mechanical ventilation in certain situations. A meta-analysis comparing the outcomes of patients treated with HFNC to those treated with standard oxygen therapy and noninvasive positive pressure ventilation (NIPPV) prior to mechanical breathing found that HFNC was superior to both of these treatments¹⁰⁰. With a properly fitted interface, HFNC or NIPPV reduces the amount of air that escapes from the patient's mouth and nose. As a result, the likelihood of the virus spreading from patient to patient in the hospital is decreased¹⁰¹. However, because of the increased potential for the creation of aerosols, these treatment procedures should be limited to low-pressure environments¹⁰².

Noninvasive Positive-pressure Ventilation (NIPPV)

- The management of acute hypoxemic respiratory failure brought on by COVID-19 requires non-invasive positive pressure ventilation (NIPPV; bilevel positive airway pressure [BiPAP]/continuous positive airway pressure [CPAP]), which may assist some patients to avoid invasive mechanical ventilation.
- Only COVID-19 hospital patients who are having trouble breathing because of COPD, cardiogenic pulmonary edema, or obstructive sleep apnea (OSA) should get NIPPV.
- Avoiding aerosolization is easier if you wear a helmet. When using NIPPV while wearing a face mask, it is advised that you use one that has an expiratory valve attached to an antibacterial filter (full-face or oronasal).
- In COVID-19 patients hospitalised with moderate to severe hypoxemia, the HENIVOT trial, an open-label multicentre randomised clinical trial in Italy, did not find a significant difference in the number of days free of respiratory support when comparing helmet non-invasive ventilation treatment with high flow nasal oxygen.

Endotracheal Intubation and Lung Protective Invasive Mechanical Ventilation

- Preoxygenation should be done with HFNC (100% O₂ for 5 minutes).
- For COVID-19 patients with acute hypoxemic respiratory failure and ARDS, reduced tidal volumes (V.T.) (4 to 8 ml/kg projected body weight, PBW) and inspiratory pressures that attain a plateau pressure (P_{plat}) of less than 30 cm H₂O are advised¹⁰³.

- PEEP should be increased because the driving pressure (P_{plat}-PEEP) should be maintained as low as possible (14 cmH₂O).
- In order to promote lung-protective breathing, neuromuscular blocking agents (NMBA) may be given as required.
- Patients with persistent hypoxemia are especially advised to use a conservative fluid management strategy for ARDS patients without tissue hypoperfusion and prone breathing for more than 12 to 16 hours per day (PaO₂:FiO₂ of 150 mm Hg).
- By minimizing the likelihood of ventilator-induced hemodynamic effects, lung-protective ventilation may lessen the likelihood of the development of or worsening of AKI.
- A need for ECMO should be assessed in a subset of patients who have chronic hypoxemia despite lung-protective ventilation and in patients who do not respond to prone position ventilation.

Management Of COVID-19 Based on The Severity of Illness

- **Asymptomatic or Presymptomatic Infection**
 - People who test positive for SARS-CoV-2 but don't have the other symptoms of COVID-19 should nevertheless be isolated for monitoring.
- **Mild Illness**
 - The National Institutes of Health recommends that people with minor illnesses may be cared for in the community with isolation and supporting services.

- Routinely, diagnostic tests in the lab or at the radiology department are unnecessary.
 - Those patients who are elderly or who have pre-existing conditions need careful observation until clinical recovery is achieved".
 - The National Institutes of Health (NIH) Covid-19 treatment recommendations panel suggests using Paxlovid or Remdesivir, in that order of preference, as recommended medicines for those with a high risk of developing a disease and a low threshold to consider being hospitalised for closer monitoring.
 - The panel only supports using non - preferred medicines like Bebtelovimab or Molnupiravir in the clinic if the preferred medications are unavailable, impractical, or unsuitable.
 - The National Institutes of Health (NIH) Covid-19 Treatment Guidelines Panel warns against taking dexamethasone for mild sickness.
- **Moderate Illness**
 - Patients with significant COVID-19 disease need thorough monitoring and should be hospitalized.
 - When interacting with or caring for a patient, medical professionals should always wear the necessary PPE.
 - Patients in hospitals should get resuscitation with isotonic fluids if they are volume deficient, and supplemental oxygen treatment should be started if the patient's saturations (SpO₂) rise over 96%.

- If a bacterial infection is suspected, empiric antibiotic treatment should begin, but if it isn't needed, it should be stopped as soon as feasible.
- Since patients with COVID-19 are at risk for both venous and thromboembolic events, they should be maintained on thromboembolic prophylaxis with the appropriate anticoagulation.
- Patients who are hospitalized and need oxygen therapy may be candidates for a combination of remdesivir and dexamethasone.
- The National Institutes of Health (NIH) Covid-19 treatment guidelines panel advises using either remdesivir alone, dexamethasone plus remdesivir, or dexamethasone alone in hospitalized patients who require supplemental oxygen but are not receiving HFNC, NIPPV, IMV, or ECMO because combination therapy (remdesivir and dexamethasone) is not available.
- **Severe/Critical Illness** ^{103,104}
 - Hospitalization is necessary for patients with a severe/critical case of COVID-19.
 - Due to their increased risk of prolonged critical illness and death, patients with severe COVID-19 should discuss the goals of their treatment, consider their advance directives, and name substitute medical decision-makers.
 - Since COVID-19 is linked to a prothrombotic condition, it is recommended that preventive anticoagulation be continued indefinitely for all patients.
 - Endotracheal intubation, bronchoscopy, tracheostomy, manual ventilation prior to intubation, physical pronation of the patient, and nebulization, as

well as upper airway suctioning, removing the patient from the ventilator, and non-invasive ventilation are all procedures that produce aerosols on COVID-19 patients in the intensive care unit.

- Clinicians and other healthcare workers are required to put on the proper PPE, such as gowns, gloves, N95 masks, and eye protection.
- When renal failure is present, dialysis or a kidney transplant may be necessary.
- A decision to use HFNC or NIPPV in patients who do not need intubation should be evaluated.
- When endotracheal intubation is not required, oxygenation may be enhanced by having an awake patient self-prone while receiving HFNC. However, further evidence from clinical studies is required to determine whether or if this procedure is effective when performed on conscious individuals.
- Patients who are admitted to the hospital and have to use oxygen via non-invasive or invasive ventilation are encouraged to take dexamethasone, as per the recommendations of the NIH's Covid-19 Treatment Guidelines Panel. In patients hospitalized with HFNC or NIPPV who are showing signs of disease progression, it is suggested that they get combination treatment consisting of dexamethasone plus baricitinib or tocilizumab.
- If respiratory collapse is imminent, endotracheal intubation with IMV should be started as soon as feasible.

- By starting vasopressors, the mean arterial pressure (MAP) should be maintained between 60 and 65mm Hg. When starting a vasopressor, norepinephrine is often the drug of choice.
- If a subsequent bacterial infection is suspected, empiric antibiotic treatment may be warranted. De-escalation of antibiotic usage is a daily concern, and the diagnosis should inform the treatment's duration.
- The Surviving Sepsis Campaign recommends treating COVID-19-related ARDS with the same standard care given to patients with ARDS from other causes, including prone posture.
- Patients with refractory respiratory failure, as indicated above, may benefit from extracorporeal membrane oxygenation (ECMO).

Prevention of COVID-19

- **Vaccination to prevent SARS-CoV-2 infection**

The single most crucial step in preventing this global pandemic is vaccination against SARS-CoV-2 infection in communities throughout the globe, together with the deployment of public health and infection control measures to stop or slow the spread of SARS-CoV-2. Clinical researchers from all over the world have devoted countless hours to finding effective vaccinations to stop the spread of SARS-CoV-2. The SARS-CoV-2-neutralizing antibodies are created as a result of vaccination. According to the WHO Coronavirus (COVID-19) Dashboard, more than 12 billion doses of the vaccine have been administered.

BNT162b2 vaccine: Results from an ongoing global, placebo-controlled, observer-blind, pivotal effectiveness study showed that a two-dose regimen of the experimental vaccine

BNT162b2 (mRNA-based, BioNTech/Pfizer) given 21 days apart provided 95% protection against COVID-19 with a safety profile similar to previous viral vaccines¹⁰⁵. Following the first EUA being issued in August 2021, the US FDA awarded a license for the clinical use of the BNT162b2 vaccine for the prevention of COVID-19.

mRNA-1273 vaccine: In a randomized, observer-blinded, placebo-controlled research encompassing various centers, two doses of mRNA-1273 (mRNA based, Moderna) vaccination given 28 days apart were proven to be 94.1 percent effective for avoiding COVID-19 illness. (106) In January 2022, the US FDA approved the clinical use of the mRNA-1273 immunization to prevent COVID-19 after a first Expanded Use Authorization (EUA).

Ad26.COV2.S vaccine: Based on the findings of a phase 3 trial that demonstrated that a single dose of the Ad26.COV2.S vaccine prevented COVID-19 in 73.1 percent of adult participants randomly assigned to receive the vaccine compared to a control group that received a placebo, the FDA granted EUA for the third COVID-19 vaccine, Ad26.COV2.S, on February 27, 2021¹⁰⁷.

ChAdOx1 nCoV-19 vaccine: According to an intermediate analysis of an ongoing multicenter randomized control research, clinical efficacy against symptomatic COVID-19 after two doses was 70.4 percent, while protection against COVID-19 after at least one standard dosage was 64.5 percent¹⁰⁸. The ChAdOx1 nCoV-19 vaccine for the prevention of COVID-19 has received authorization or emergency use authorization in several countries, however, the FDA has not yet approved its use in the United States.

NVX-CoV2373 vaccine: In a phase 2 trial that was randomized, observer-blinded, and placebo-controlled, the NVX-CoV2373 (Novavax) vaccine, a recombinant SARS-CoV-2 nanoparticle genetically modified vaccine, was shown to be efficacious in preventing

COVID-19¹⁰⁹. The country was experiencing a second wave of infection at the time of the experiment because of the Beta(B.1.351) variant, indicating that the therapy was successful. A single dose of NVX-CoV2373, an adjuvanted recombinant spike protein nanoparticle vaccine, proved effective against any variant of concern, according to the findings of a randomized, placebo-controlled research including nearly 29,000 people from the United States and Mexico (92.6 percent confidence interval [CI], 83.6 to 96.7).

In addition to the vaccinations previously described, other vaccines, both protein-based and inactivated, have been created and authorized for emergency use in numerous nations worldwide to prevent COVID-19. These vaccinations were produced in China, India, and Russia, under the brand name Covaxin (CoronaVac).

Early in 2021, many people who had received the Ad26.COV2. S vaccination and the ChAdOx1 nCoV-19 vaccine had a unique clinical syndrome that included thrombocytopenia and thrombosis in unusual places (cerebral venous sinus thrombosis/splanchnic venous thrombosis). Despite its apparent resemblance to HIT, this unique clinical disease was given the label vaccine-induced immune thrombotic thrombocytopenia because it occurred in patients who had never been exposed to heparin (VITT). On the other hand, VITT operates with a management style fairly similar to HIT¹⁰⁵.

Due to research indicating a decline in immunity after the first two doses and a boost from the third dosage delivering increased protection, several countries have added a third dose (booster dose) to their vaccination schedule¹¹⁰.

Mixing vaccine types enhanced antibody and neutralizing responses for all seven vaccinations evaluated; this includes most major commercially available vaccines. This

conclusion comes from a phase 2 randomized controlled experiment conducted in the United Kingdom¹¹¹.

Preexposure Prophylaxis (PrEP) to prevent SARS-CoV-2 infection

Vaccination is recommended as the primary method of protection against this virus; however, not everyone has a favorable reaction to the COVID-19 vaccine, and it is not recommended for individuals who have experienced a severe allergic reaction to earlier doses of the vaccine or any of its components. The US Food and Drug Administration (FDA) authorized an EUA for the emergency use of this Tixagevimab and in combination with Cilgavimab for use in pre-exposure prophylaxis of COVID-19 in adults and pediatric populations (12 years of age and older being at least 40 kg in weight) with no evidence of SARS-CoV-2 infection and no recent exposure to SARS-CoV-2 positive people AND who have moderate to severe immunocompromised due to a variety of conditions and treatments OR are on immunosuppressive medications and may not mount an adequate immune response to COVID-19 vaccination OR in individuals in whom COVID-19 vaccination is contraindicated due to history of severe adverse reaction to the vaccine components.

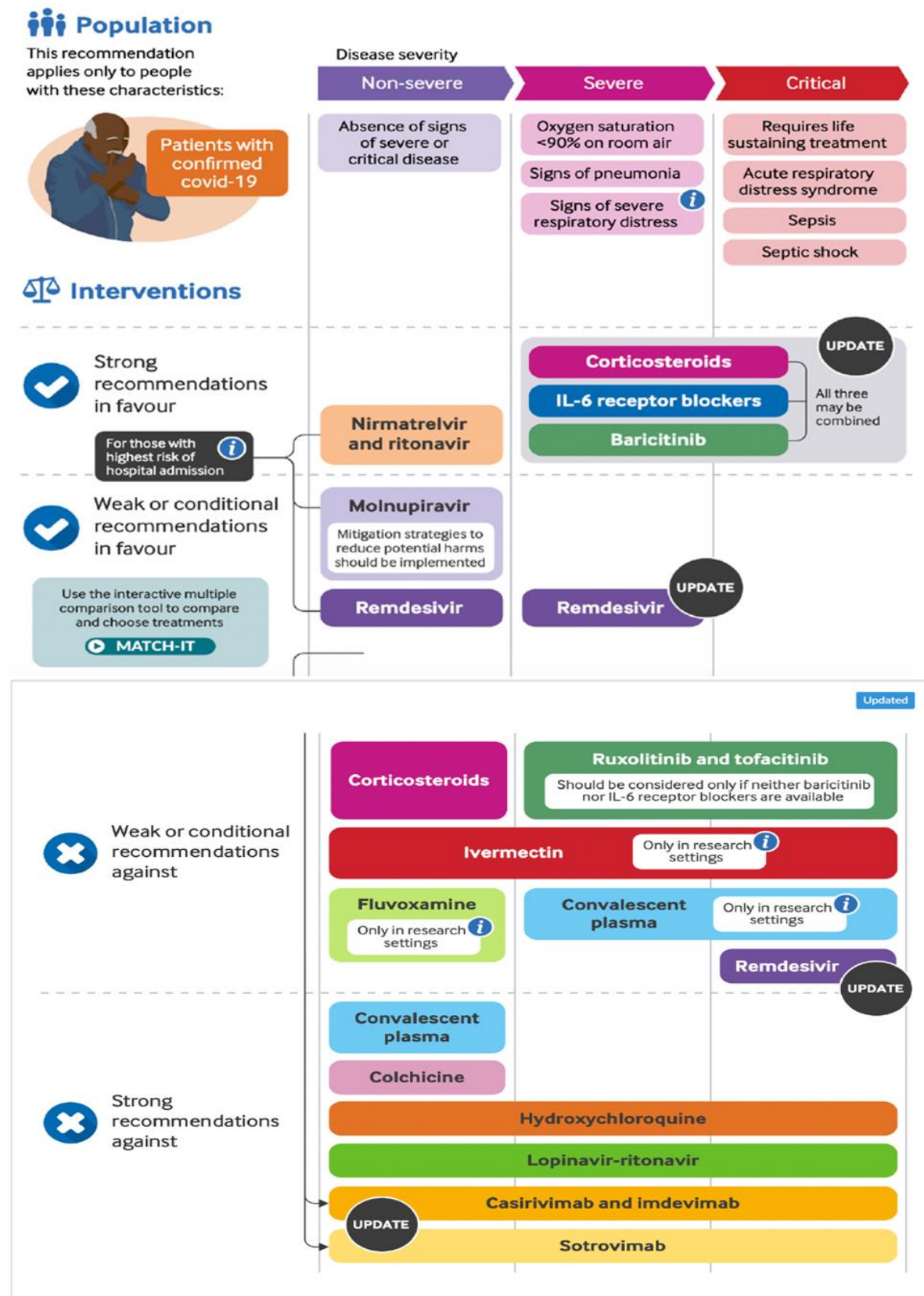


Figure 8: WHO Recommendations for treatment of COVID-19 based on the severity



AIIMS/ ICMR-COVID-19 National Task Force/Joint Monitoring Group (Dte.GHS)
Ministry of Health & Family Welfare, Government of India
CLINICAL GUIDANCE FOR MANAGEMENT OF ADULT COVID-19 PATIENTS

22nd April 2021

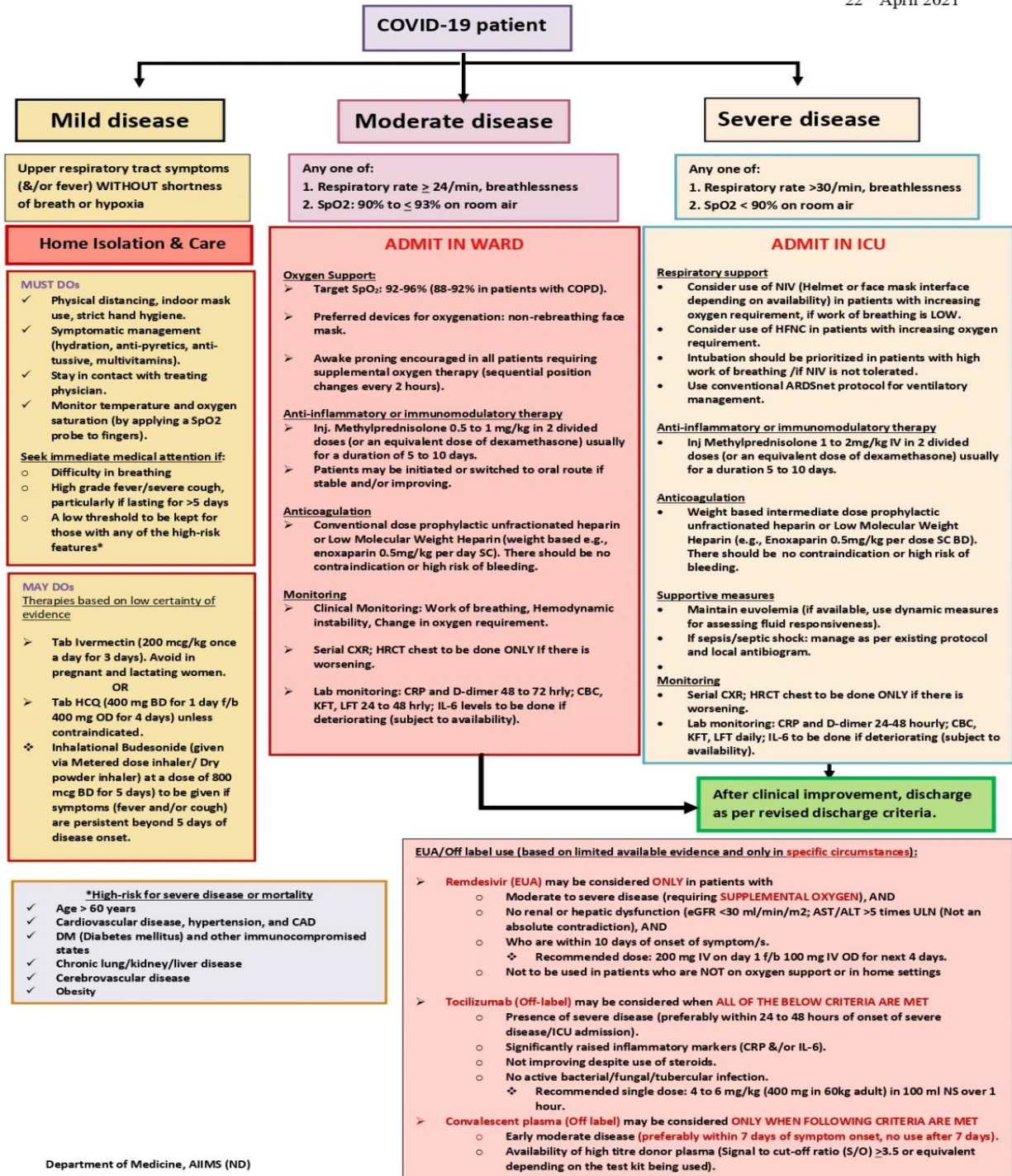


Figure 9: COVID-19 Management, AIIMS Protocol 2021

ROLE OF CT SEVERITY SCORE AND BIOMARKERS FOR PREDICTION AND PROGNOSIS IN COVID-19 INFECTION.

Francone et al¹¹² did a retrospective single-centre analysis of 130 SARS-CoV-2 patients with symptoms. They found that ground glass opacities were a sign of early-phase illness (up to 7 days after the first symptoms), while crazy-paving pattern, consolidation, and fibrosis were signs of late-phase illness (more than 7 days). Critical and severe stages had much higher CT scores than mild stages, and patients in the late phase had higher CT scores than patients in the early phase. CT score was linked to CRP and D-dimer levels in a big way. Both univariate and multivariate analyses showed that a CT score of less than 18 was associated with an increased risk of mortality.

The COVID-19 clinical features of lung illness and the chest CT Severity Score were studied by Sharma S. et al¹¹³ in a tertiary care hospital. Overall, 150 COVID-19-infected individuals were evaluated. Participants' mean ages were 54.46, with 62.7% being male and 37.3% female. 17.3% of patients in the study group had diabetes mellitus, making it the most frequent co-morbidity. The age of the patient had a substantial impact on the illness's severity. Significant correlations were seen between lymphopenia and serum ferritin, C-reactive protein, and D-dimer levels as well as the CT Severity Score. Shorter survival periods were substantially linked with the severity of CT. The tertiary care hospital in India was the setting for this extensive study. It looked at 150 COVID-19 pneumonia patients to find out how the CT Severity Score relates to a number of clinical and lab indicators. The severity score from a chest CT has a good relationship with lab variables and can help predict how COVID-19 illness will progress.

Study by Zhou et al¹¹⁴ had 134 participants. The levels of serum ferritin, interleukin (IL)-2, and IL-6, as well as leukocytes, neutrophils, high-sensitivity C-reactive protein

(hsCRP), prothrombin, and D-dimer, were all significantly higher in the group that had died than in the group that had recovered at different points. In the group that did not recuperate, the peak CT score was lower than in the group that died (20 vs. 11 points).

Jain et al¹¹⁵ demonstrate that levels of CRP, D-Dimer, and CT Severity Score alone may predict the outcome of mortality using a sample size of 735. The cut off for CRP was 45 mg/L (Sn 0.8, Sp 0.56) whereas the cut off for D-dimer was 1000 µg/l (Sn:0.8, Sp: 0.9).

The average age of the 902 patients in a study by Saeed et al¹¹⁶ was 44.2 years old, with a standard deviation of 11.9 years (85.3 percent male and 14.7 percent female). Patients with a higher CT Severity Score were found to have substantially higher serum levels of C-reactive protein, d-dimer, and ferritin ($p < 0.001$). Patients needed more oxygen and stayed in the hospital longer as the scan's intensity rose.

Dagher et al¹¹⁷, using a research population of 761 individuals, observed that if a CT scan was not performed, the findings advised using LDH, CRP, or NLR as prognostic tools in COVID-19 patients if they had previously been done, since these biomarkers were also shown to be predictive in COVID-19 patients.

CT Severity Score on HRCT thorax and inflammatory markers were shown to have an association with mortality from COVID-19, according to study conducted by Ravindra et al¹¹⁸ in 2343 patients. People who test positive for COVID-19 can thus be recognized and quickly treated if the virus is found in their system. "Mean ferritin levels were 321.83 ± 266.42 ng/ml," "Mean D-dimer levels were 1.51 ± 0.85 mg/l," and "Mean interleukin-6 (IL-6) levels were 323.05 ± 95.52 pg/ml"¹⁸⁷.

The findings of a study that was carried out by Bukkaraju et al¹¹⁹, using a sample size of 100 patients. Along with other biochemical markers including IL-6, CRP, Ferritin, and D-dimer, the CT chest severity score was shown to be linked with reduced SpO₂, decreased

PaO₂/FiO₂, and increased RR. Patients diagnosed with moderate and severe cases of COVID-19 exhibited levels of IL-6, D-Dimer, and CRP that were considerably greater than those of patients diagnosed with mild cases of COVID-19 and of controls ($P < 0.001$).

METHODOLOGY

Source of data: Patients receiving care at KLES Dr Prabhakar Kore & Charity Hospital, Belagavi.

Study Design: A retrospective observational study.

Study Period: January 2021 to December 2021.

Sample Size: 200

The minimum sample size formula based on the prevalence rate is

$$n = \frac{z_{\alpha}^2 P(1-P)}{d^2}$$

In this formula, P represents the prevalence and d the likely variation in prevalence.

Z α is linked with the level of significance. For 5% level the significance $z\alpha = 1.96$.

Reference:

With P = 35% and d = 20% of P = 7%, the sample size is 178.

To get more confirmative results the sample size was raised to **200**

Sample Method: A Retrospective observational study, all consecutive patients fulfilling the inclusion criteria were included in the study, and statistical analysis was done by SPSS using descriptive analysis and chi-square test.

Inclusion Criteria

- RT-PCR /CBNAAT/RAT Positive for SARs CoV-2.
- Adults between 18- 95 years

Exclusion Criteria

- Pregnant Women.
- Post Covid patients.
- Lactating women.
- Children below 18 years.

METHODOLOGY

- A one-year Hospital based retrospective study
- Study from January 2021 to December 2021 at KLE's Prabhakar Kore Hospital and Medical Research Centre, Belagavi.
- The data was collected from Hospital Medical records with written permission.
- RT-PCR /CBNAAT/ RAT Positive COVID-19 patients with the fulfilment of the inclusion criteria and exclusion criteria were included in the study.
- The COVID-19 biomarkers is compared with the CT Severity Score.

CT Severity Score

Total score	CT Severity
<8	Mild
8-15	Moderate
16-25	Severe

Biomarkers

The normal range of biomarkers was determined in accordance with laboratory results from the Prabhakar Kore Hospital and Medical Research Centre in Belagavi, KLE.

Table No 4: Normal values of Biomarkers.

Sl.no	Biomarkers	Normal Range
1	Serum Ferritin	30 - 400 ng/ml
2	HsCRP	0.0 - 5.0 mg/ltr
3	IL-6	0 - 7 pg/ml
4	D-dimer	0.0 - 200 ng/ml
5	LDH	135 - 225 U/L

STATISTICAL ANALYSIS

The data collected was entered in the MS Excel master sheet. Data was tabulated and analyzed using the software OpenEpi version 3.01 and Statistical Package for Social Sciences (SPSS) version 22. Categorical data have been presented as numbers and percentages (%) and quantitative data in terms of mean and standard deviation. Categorical variables have been analyzed using Pearson's chi-square test and Fisher exact tests (when the expected count of 20% of cells is less than 5). Quantitative variables have been analyzed using the Student T test and ANOVA. Receiver Operator Curve (ROC) has been used for the calculation of sensitivity and specificity. A p-value of <0.05 has been considered statistically significant.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram.

Sensitivity: Defined as ability of a test to identify correctly all those who have the disease i.e. true positive.

Specificity: It is the ability of test to identify correctly those who do not have the disease i.e. true negative.

Positive predictive value (PPV): The proportion of patients who test positive who actually have the disease.

Negative predictive value (NPV): The proportion of patients who test negative who are actually free of the disease.

Diagnostic accuracy: Is the ability of screening test to detect true positives and true negatives in the total population studied.

ROC curve (receiver operating characteristic curve): Is a graph showing the performance of a classification model at all classification thresholds.

p-value (Probability that the result is true) of < 0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

RESULTS

Table 5: Age-wise distribution of patients

Age group	Outcome	
	Death No (%)	Survival No (%)
20-29 years	02 (1.1%)	101 (13.7%)
30-39 years	05 (2.8%)	87 (11.8%)
40-49 years	18 (10.2%)	133 (18.1%)
50-59 years	44 (25.0%)	170 (23.1%)
60-69 years	50 (28.4%)	135 (18.3%)
70-79 years	42 (23.9%)	86 (11.7%)
≥ 80 years	15 (8.5%)	24 (3.3%)
Total	176 (100%)	736 (100%)
Mean	62.5	51.1
Standard deviation	12.4	16.2
P value	<0.001	

In the present study, the age of patients ranged from 20-99 years. i.e., the youngest was 20 years old. The oldest was 93 years old. Around 44 patients (25.0%) in the age group of 50-59 years in the mortality group, and in the survival group, it's about 170 patients (23.1%). It has been observed that as age advances mortality rate increases and the survival rate decreases. In the age group above 60 years, 107 patients were in the mortality group, and 245 were in the survival group. The mean age in the mortality group was 62.5 ± 12.4 , and the survival group was 51.1 ± 16.2 .

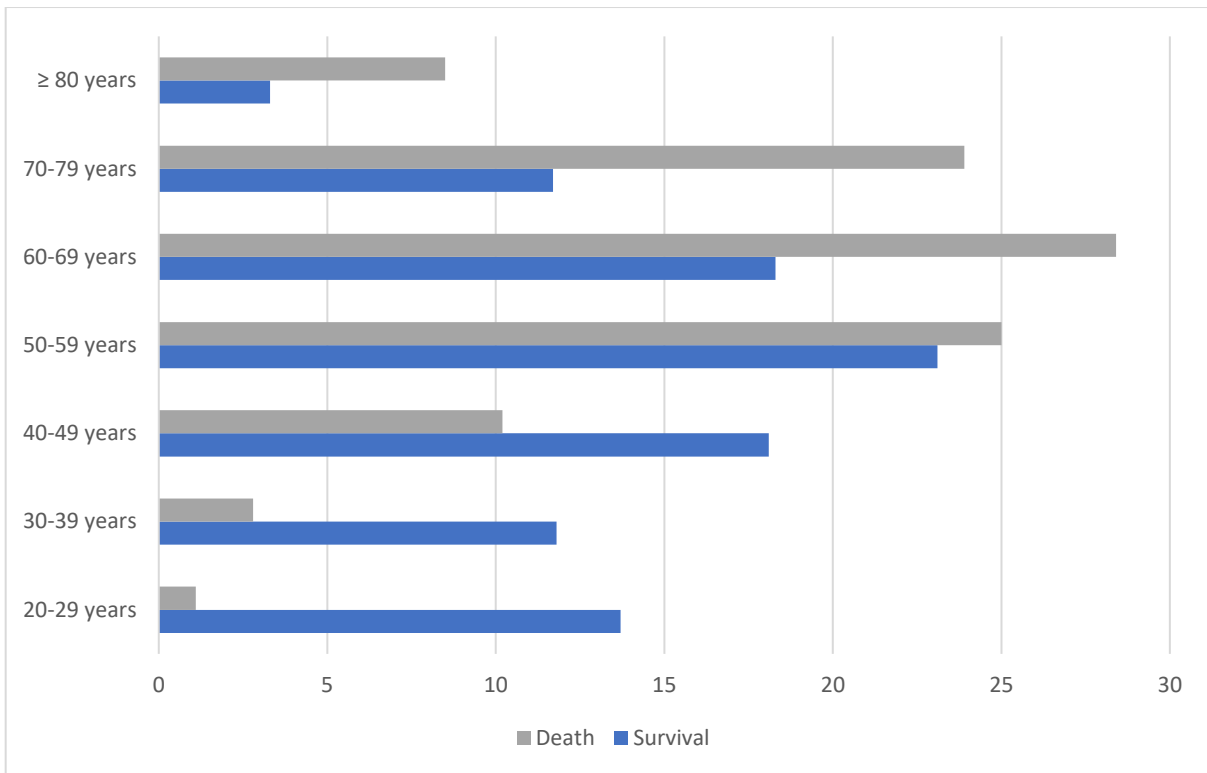
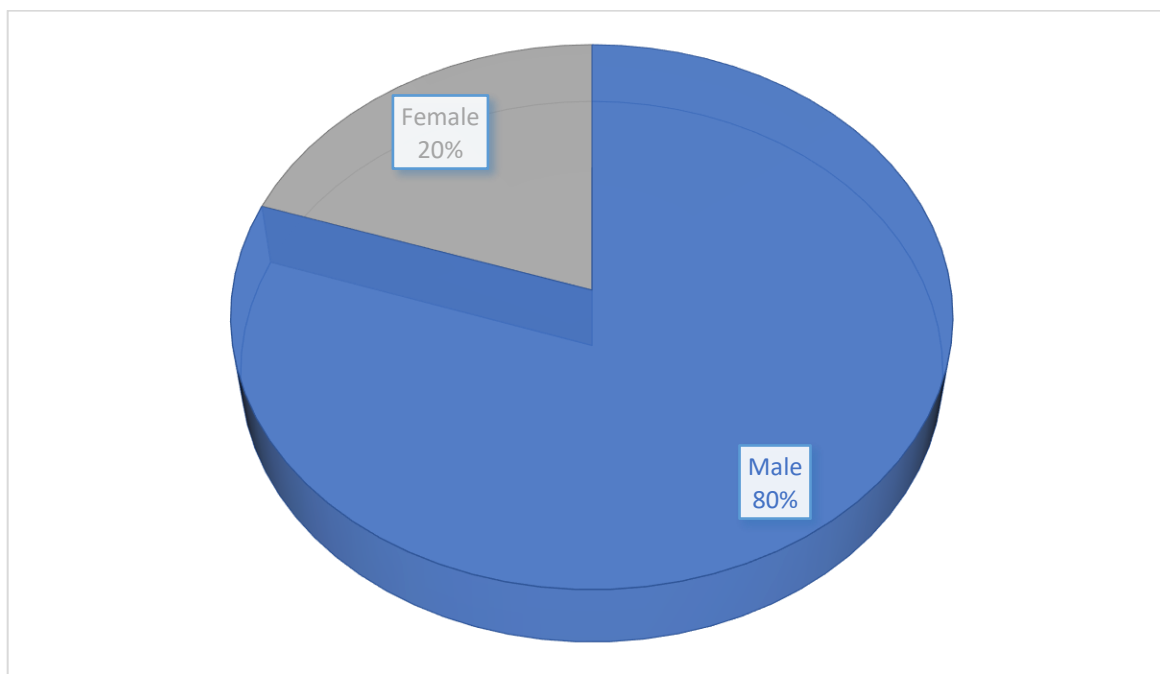
Graph No.1: Age-wise distribution of patients.

Table 6: Sex-wise distribution of patients

Gender	No of patients	(%)
Male	731	80.2
Female	181	19.8
Total	912	100.00

Graph No.2: Sex-wise distribution of patients

There were 731 male patients in our study; the remaining 181 were females. There was male preponderance observed in our study with a ratio of male: female 4.03:1

Table 7: Symptomatology of Patients

Symptoms	No of patients	(%)
Cough		
Absent	314	34.4
Present	598	65.6
Fever		
Absent	321	35.2
Present	591	64.8
Myalgia		
Absent	758	83.1
Present	154	16.9
Breathlessness		
Absent	327	35.8
Present	585	64.2

In our study, patients presented with various symptoms of Covid-19, the most typical symptom was Cough (65.6%), fever (64.8%), Breathlessness (64.2%), Myalgia (16.9%), other symptoms like altered sensorium, diarrhoea, vomiting etc (6.2%)

Table 8: Distribution of patients with co-morbidities

Co-morbidities	No. of Patients	(%)
T2DM	308	33.8
Hypertension	274	30.0
IHD	78	8.5
CKD	18	2
Asthma	20	2.19

The most common comorbidity observed in our present study was diabetes mellitus which was 33.8%, Hypertension in 30%, 8.5% of patients with ischemic heart disease, 2% of patients with chronic kidney disease, and 2.19% of patients were in Asthma.

Table 9: Comparison of CT Severity Score with co-morbidities among study participants.

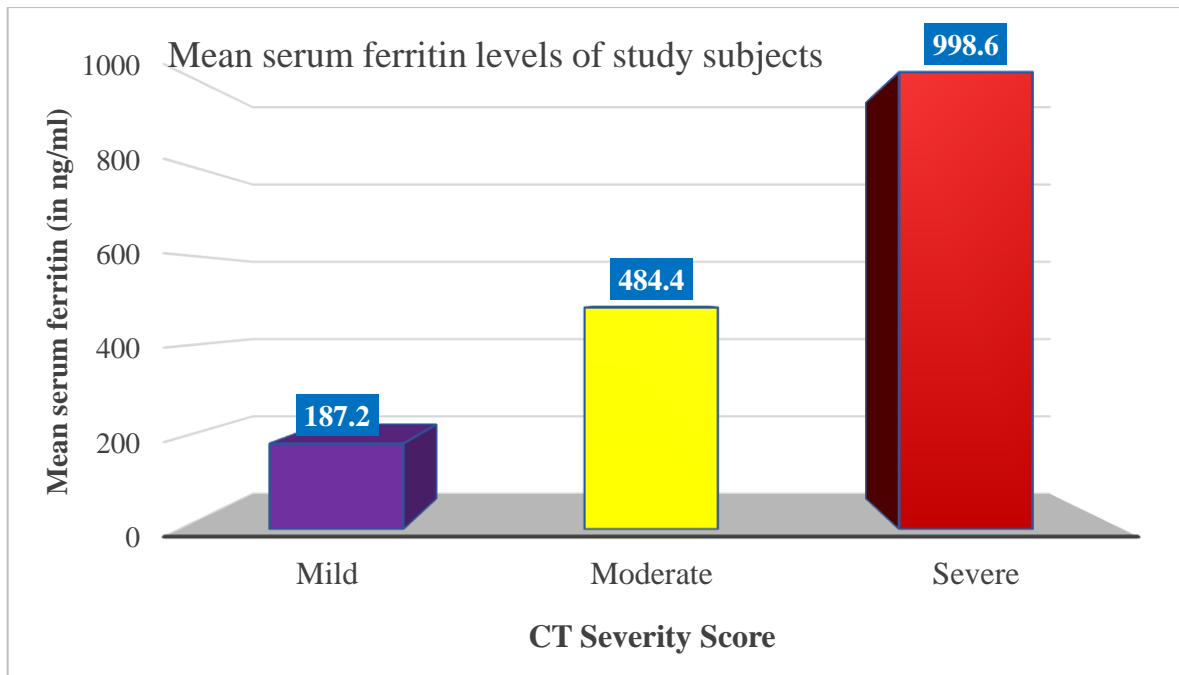
Co-morbidity	CT Severity Score			p-value
	Mild	Moderate	Severe	
Diabetes Mellitus type II				
Absent	182 (30.1%)	261 (43.2%)	161 (26.7%)	0.006
Present	65 (26.1%)	138 (44.8%)	105 (34.1%)	
Hypertension				
Absent	186 (29.2%)	268 (42.0%)	184 (28.8%)	0.086
Present	61 (22.3%)	131 (47.8%)	82 (29.9%)	
Ischemic heart disease				
Absent	233 (27.9%)	359 (43.0%)	242 (29.0%)	0.149
Present	14 (17.9%)	40 (51.3%)	24 (30.8%)	
Chronic kidney disease				
Absent	246 (27.5%)	391 (43.7%)	257 (28.7%)	0.053
Present	01 (5.6%)	08 (44.4%)	09 (50.0%)	
Asthma				
Absent	242 (27.1 %)	390 (43.7%)	260 (29.1%)	0.978
Present	05 (25.0%)	09 (45.0%)	06 (30.0%)	

When we compare the Co-morbidities with the CT Severity Score, T2DM is present in 44.8 % of the moderate group and 34.1% in the severe group with P value (0.006) which has a strong correlation. Hypertension, on the other hand, is the second most co-morbidities in our study

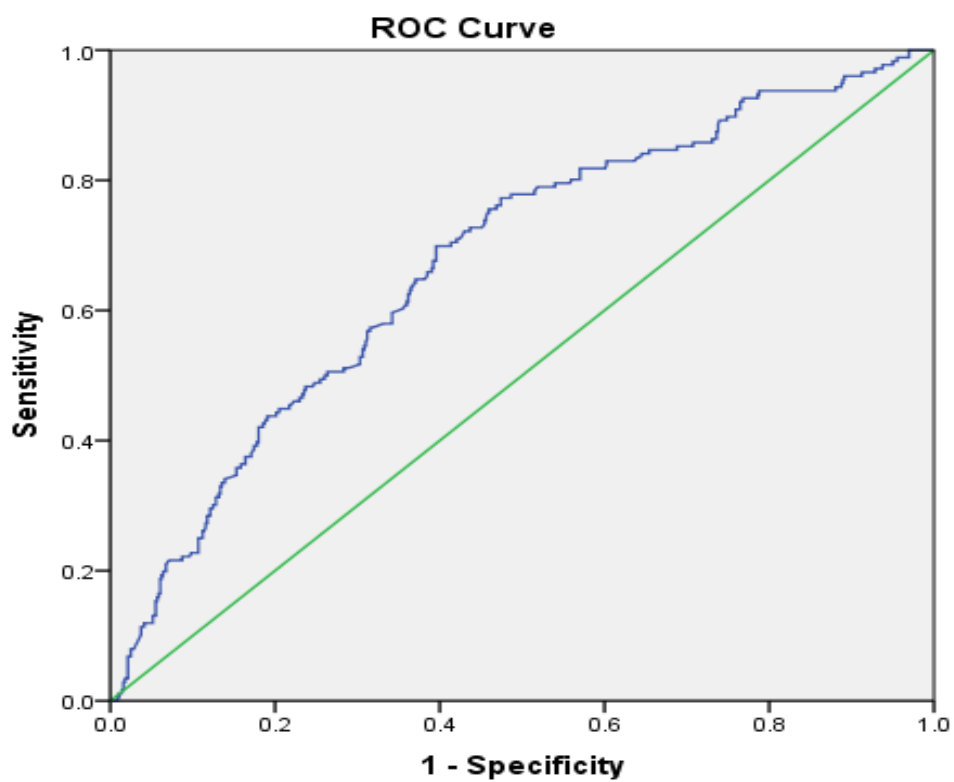
Table 10: Comparison of CT Severity Score with serum ferritin levels among study subjects

Serum Ferritin	CT Severity Score		
	Mild	Moderate	Severe
Minimum	4.8	4.0	13.6
Maximum	1656.0	5374.0	10223.0
Mean	187.2	484.4	998.6
Std Deviation	208.8	649.1	1048.9
p value	<0.001		

HRCT scan of COVID-19 were correlated with serum ferritin with each group mild, moderate, severe were assessed. It shows to P value significant and mean value in mild-187.2, moderate-484.4, severe -998.6. The values increase with increase in CT Severity Score



Graph 3: Comparison of CT Severity Score with serum ferritin levels among study subjects



Graph No.4: ROC curve for serum ferritin as predictor of outcome.

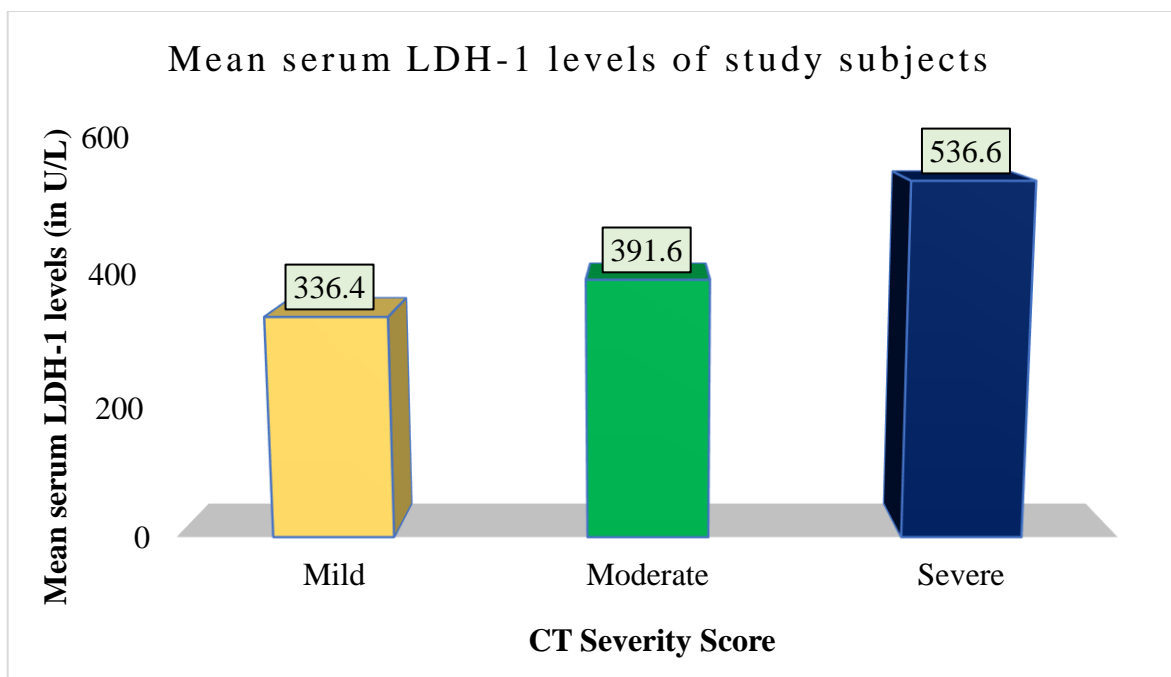
Area	95 % CI		p value
	Lower bound	Upper bound	
0.676	0.631	0.721	<0.001
Co-ordinates of the curve			
Serum ferritin level	Sensitivity		Specificity
331.0	72.2%		56.3%

The ROC curve shows area under the curve AUC-0.676 and P value <0.001 with the cut of value of 331.0 has a sensitivity of 72.2% and a specificity of 56.3%.

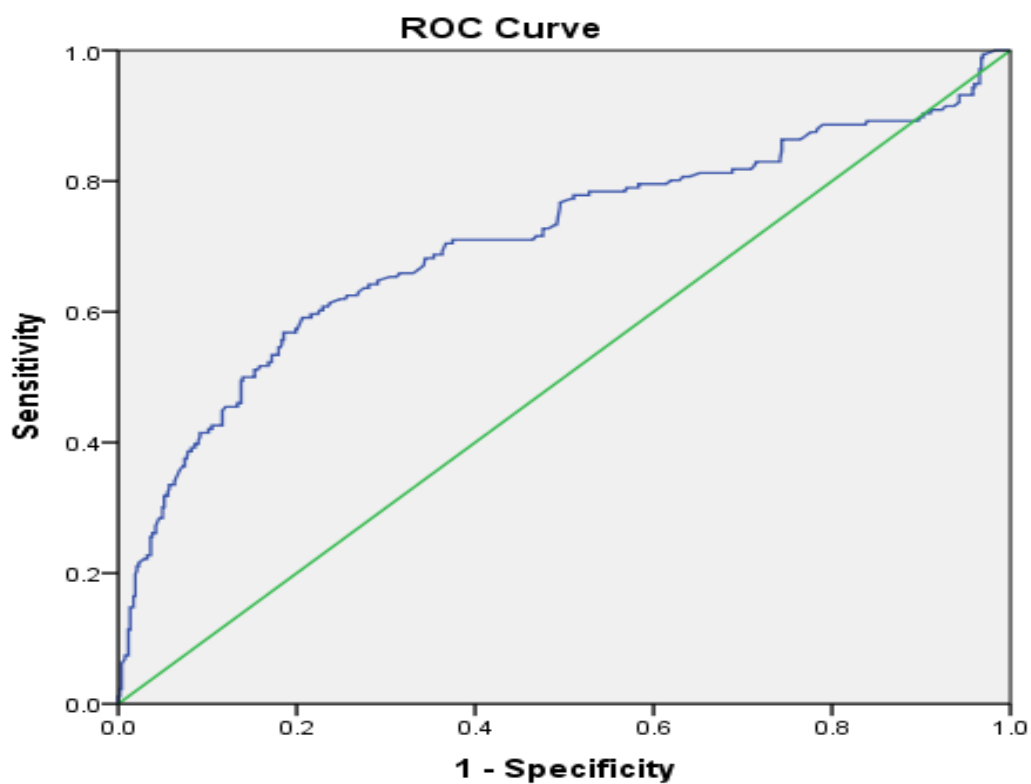
Table 11: Comparison of CT Severity Score with serum LDH levels among study subjects

Serum LDH	CT Severity Score		
	Mild	Moderate	Severe
Minimum	27.0	4.9	5.07
Maximum	1623.0	3650.0	2394.0
Mean	336.4	391.6	536.6
Std Deviation	196.5	280.0	311.4
p value	<0.001		

HRCT scans of COVID-19 was correlated with LDH with each group mild, moderate and severe were assessed. It shows to P value significant and mean value in mild-336.4, moderate-391, severe -536.6. The value increases with increase in Ct Severity Score.



Graph No.5: Comparison of CT Severity Score with serum LDH-1 levels among study subjects



Graph No.6: ROC curve for serum LDH as predictor of outcome.

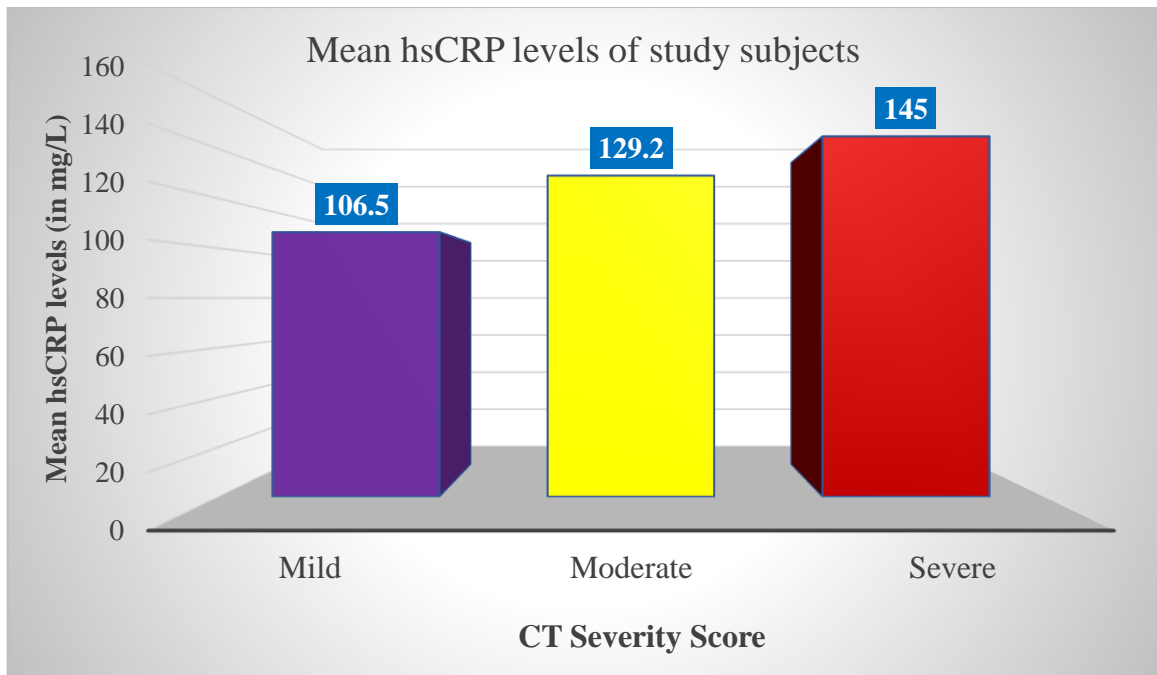
Area	95 % CI		p value
	Lower bound	Upper bound	
0.707	0.657	0.757	<0.001
Co-ordinates of the curve			
Serum LDH level	Sensitivity		Specificity
375.5	70.5%		63.3%

The ROC curve shows area under the curve AUC-0.707 and P value <0.001 with the cut of value of 375.5 has a sensitivity of 70.5% and a specificity of 63.3%.

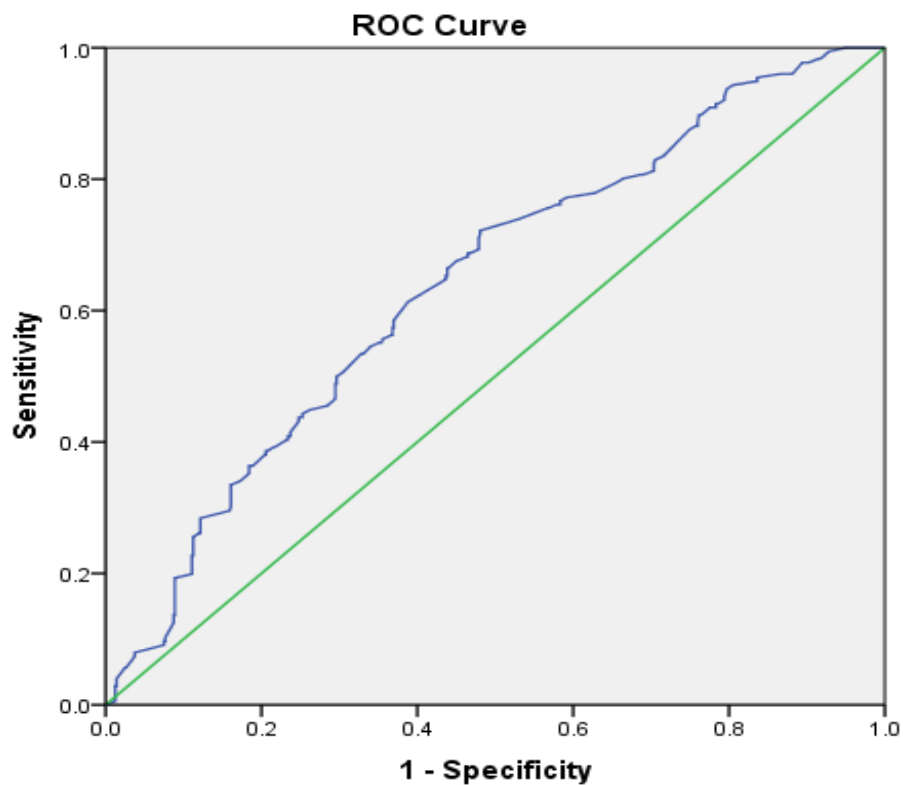
Table 12: Comparison of CT Severity Score with serum hsCRP levels among study subjects

Serum hsCRP	CT Severity Score		
	Mild	Moderate	Severe
Minimum	0.4	1.4	0.6
Maximum	772.0	2699.0	649.8
Mean	106.5	129.2	145.0
Std Deviation	109.4	184.5	100.5
p value	0.017		

HRCT scan of COVID-19 were correlated with hsCRP with each group mild, moderate, severe were assessed. It shows to P value significant and mean value in mild-106.5, moderate-129.2, severe -145. The values increases with increase in CT Severity Score.



Graph No.7: Comparison of CT Severity Score with serum hsCRP levels among study subjects



Graph No.8: ROC curve for serum hsCRP as predictor of outcome.

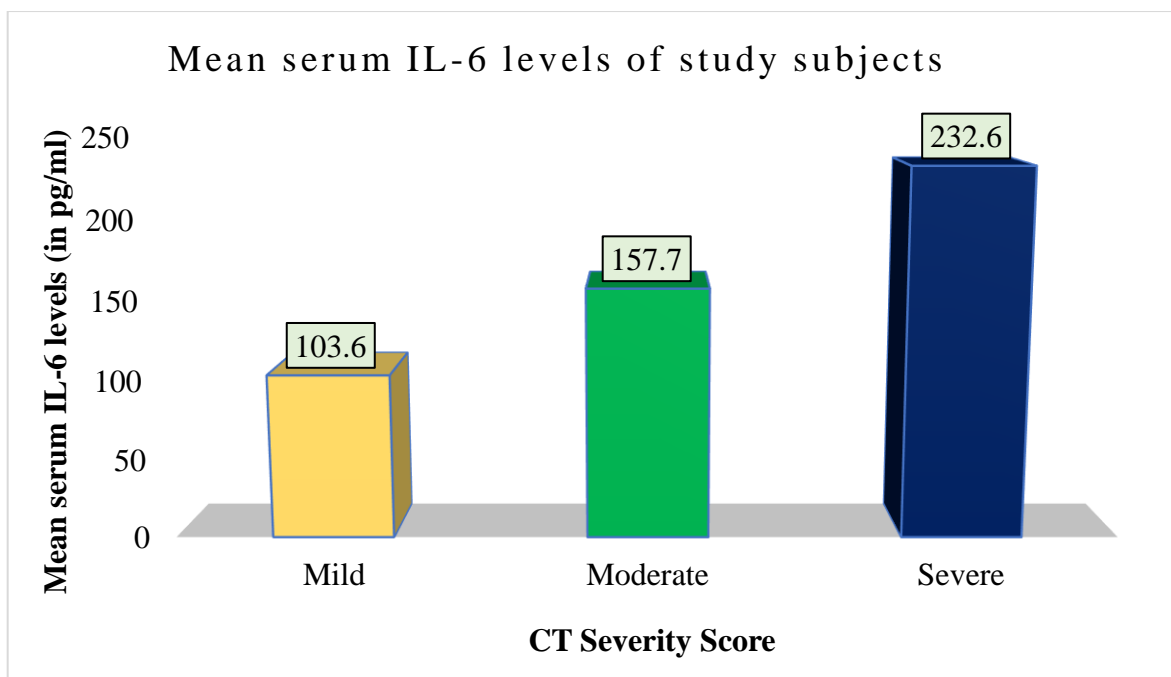
Area	95 % CI		p value
	Lower bound	Upper bound	
0.641	0.596	0.686	<0.001
Co-ordinates of the curve			
Serum hsCRP level	Sensitivity		Specificity
85.5	72.2%		52.0%

The ROC curve shows area under the curve AUC-0.641 and P value <0.001 with the cut of value of 85.5 has a sensitivity of 72.2% and a specificity of 52.0%.

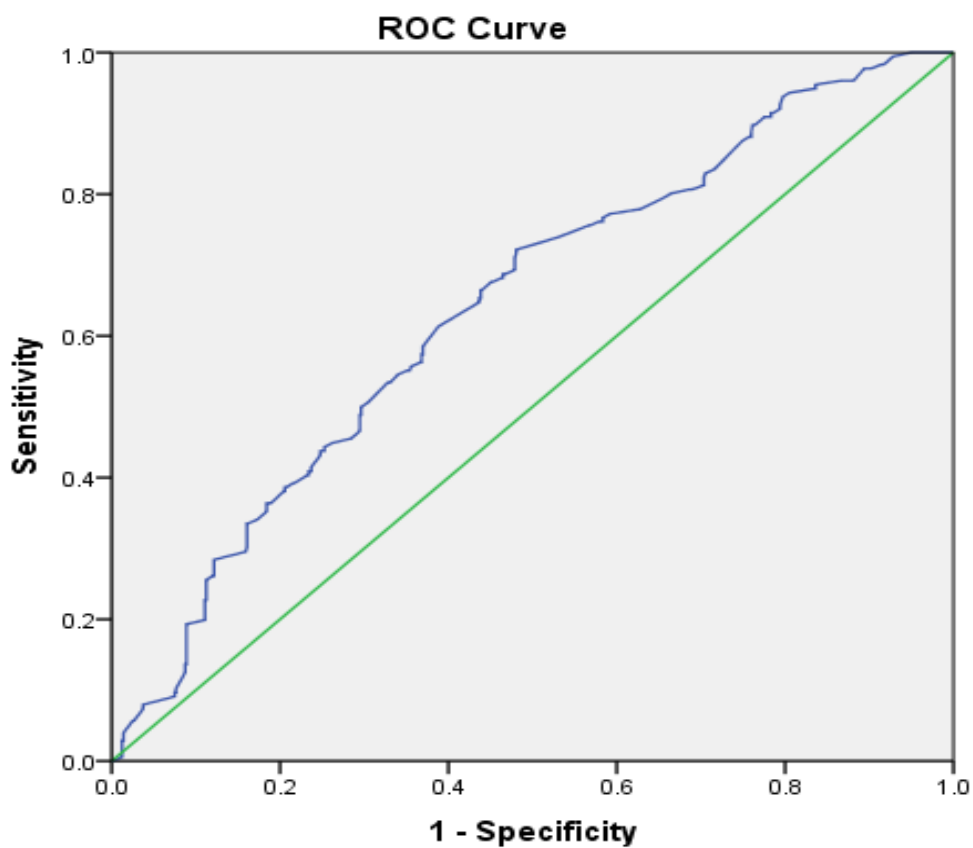
Table 13: Comparison of CT Severity Score with serum IL-6 levels among study subjects

Serum IL-6	CT Severity Score		
	Mild	Moderate	Severe
Minimum	1.0	1.5	1.5
Maximum	4754.0	3950.0	5000.0
Mean	103.6	157.7	232.6
Std Deviation	383.3	340.2	569.3
p value	0.011		

HRCT scan of COVID-19 was correlated with IL-6 with each group mild , moderate, severe were assessed. It shows to P value significant and mean value in mild-103.6, moderate-157.7, severe -232.6. The values increases with increase in CT Severity Score.



Graph No.9: Comparison of CT Severity Score with serum IL-6 levels among study subjects



Graph No.10: ROC curve for serum IL-6 as predictor of outcome.

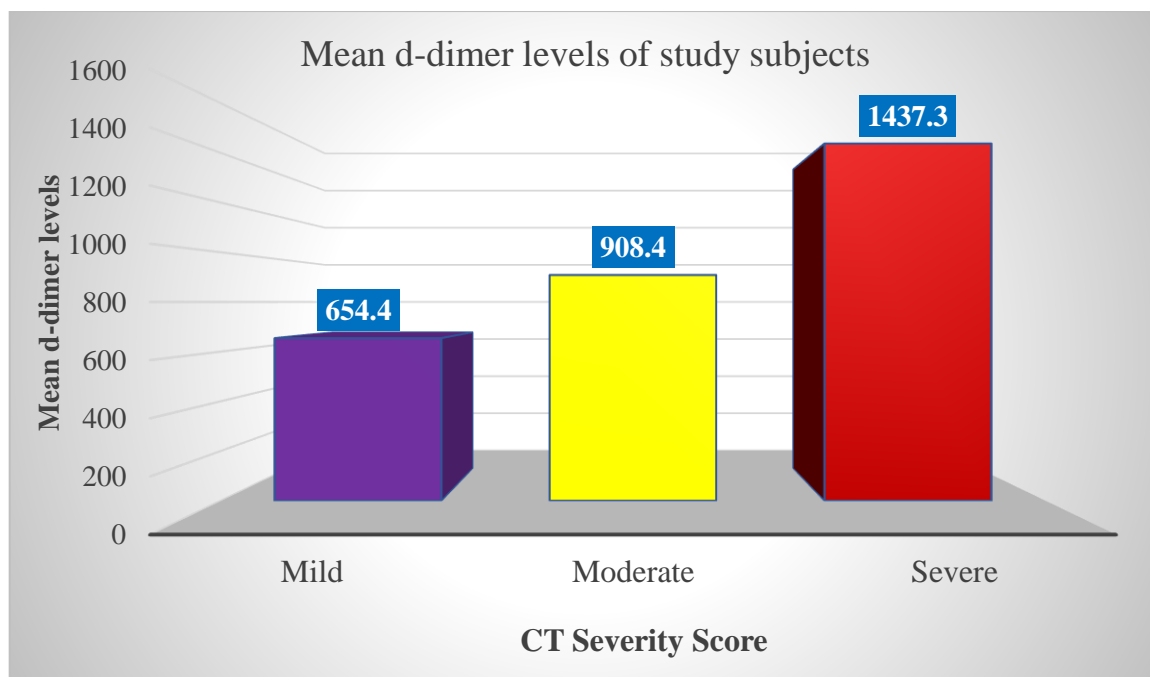
Area	95 % CI		p value
	Lower bound	Upper bound	
0.673	0.631	0.716	<0.001
Co-ordinates of the curve			
Serum IL-6 level	Sensitivity		Specificity
76.3	60.2%		60.8%

The ROC curve shows area under the curve AUC-0.673 and P value <0.001 with the cut of value of 76.3 has a sensitivity of 60.2% and a specificity of 60.8%.

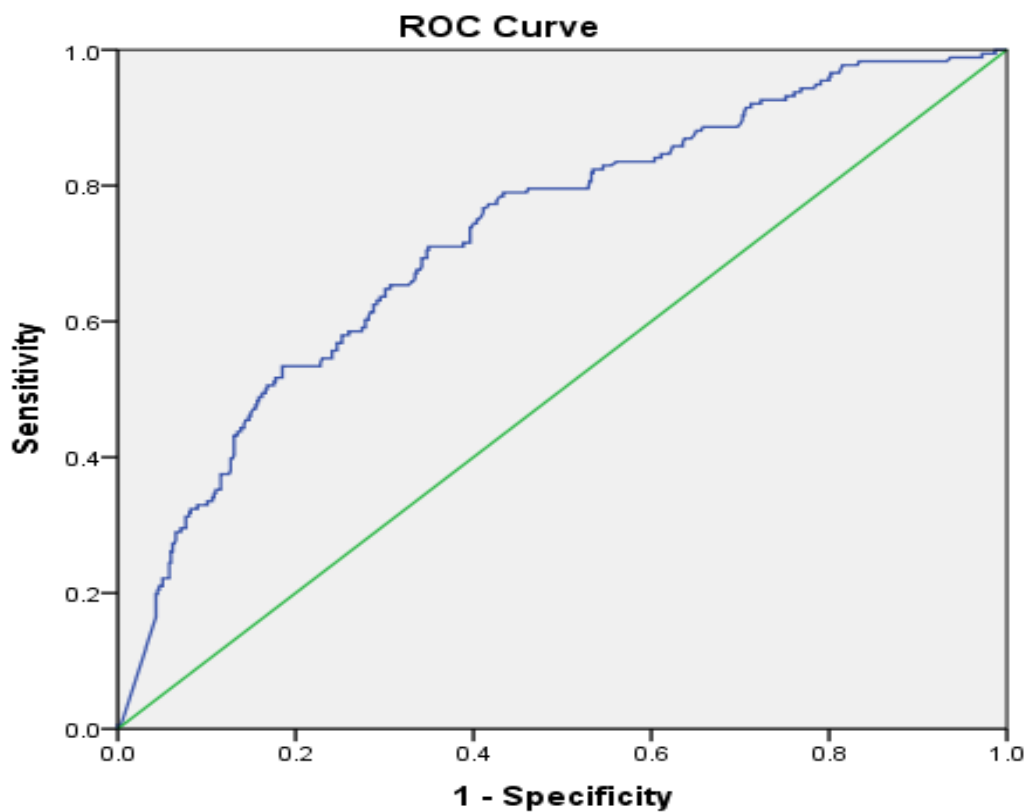
Table 14: Comparison of CT Severity Score with serum d-dimer levels among study subjects

Serum d-dimer	CT Severity Score		
	Mild	Moderate	Severe
Minimum	7.7	67.0	6.6
Maximum	5000.0	5937.0	7673.0
Mean	654.4	908.4	1437.3
Std Deviation	901.4	1164.9	1605.1
p value	<0.001		

HRCT scan of COVID-19 were correlated with d-Dimer with each group mild, moderate, severe were assessed. It shows to P value significant and mean value in mild-654.4, moderate-908.4, severe -1437.3. The values increase with increase in CT Severity Score.



Graph No.11: Comparison of CT Severity Score with serum d-dimer levels among study subjects



Graph No.12: ROC curve for d-dimer as predictor of outcome.

Area	95 % CI		p value
	Lower bound	Upper bound	
0.728	0.685	0.771	<0.001
Co-ordinates of the curve			
d-dimer	Sensitivity		Specificity
643.5	70.5%		65.2%

The ROC curve shows area under the curve AUC-0.728 and P value <0.001 with the cut of value of 643.5 has a sensitivity of 70.5% and a specificity of 65.2%.

DISCUSSION

We analyzed the records of 912 patients with COVID-19 infection who were studied for biomarkers level and co-related with HRCT thorax findings to predict the prognosis.

In our study, the patient's age range was 20-99 years (youngest 20 and oldest 93); there were almost 365 patients between the age group of 41-60 years, 195 patients below the age group of 40, and 352 patients above 60 years.

The mean age in the mortality group is 62.5 ± 12.4 , and the survival group is 51.1 ± 16.2 .

Zhao et al¹²⁰ observed 44 patients between the ages of 21 and 40, 41 between the ages of 41 and 60, and 14 patients over 70 years.

In another study of 902 individuals, Saeed et al¹²¹ found that the average age of the patients was 44.2 ± 11.9

According to Gupta et al³⁴ study, the mean age in their sample population was 43.3 years, with patients ranging in age from 16 to 73 years.

Male preponderance was observed in our current study (n = 731) compared to female preponderance (n = 181), with a male-to-female ratio of 4.03:1.

In their study sample of 902 individuals, Saeed et al⁶³ discovered a male prevalence of over 85% compared to 14.7% of female patients.

Another study by Gupta et al³⁴ found a 66.7% male predominance in their sample.

Even in our analysis, a male predominance was noted, accounting for about 80% (M: F; 4.03:1) for obvious reasons. We conclude that males are affected more than females.

A study by Saeed et al¹²¹ discovered a higher proportion of males, 93.4%, than females, possibly due to the protective effect of estrogen in female patients.

Further analysis shows that patients presented with various symptoms of Covid-19; the most typical symptom was Cough (65.6%), fever (64.8%), Breathlessness (64.2%), and Myalgia (16.9%).

In our study, the cough had a slight predominance over the fever, followed by breathlessness.

Cough is closely associated with the virus' propagation by respiratory droplets. In addition to inflammatory factors, such as accumulated secretions, postnasal drip, and infections, the cough reflex facilitates the release of fluids and particles from the airways.

There was an overlapping of symptoms in our study population.

Bhandari et al¹²² conducted a study with a sample size of 80 patients. They also observed that the most prevalent symptoms were fever, cough, and myalgia, with other symptoms such as headache and diarrhoea being seen in more than half of their patients.

According to Huang et al¹²³, the most prevalent symptoms noticed in their study population were fever, cough, and dyspnoea.

We considered comorbidities, the most common comorbidity observed in our study population was type II diabetes mellitus (n = 308), hypertension (n = 274), ischemic heart disease (n = 78), chronic kidney disease (n = 18), asthma (n=20), and other comorbidities (hypothyroidism, seizures, cerebrovascular accident, etc. n= 7).

In a study of 80 patients by Bhandari et al¹²², the most common comorbidity reported was type II diabetes mellitus, hypertension, and ischemic heart disease.

Wei-jie Guan et al¹²⁴ study showed that most people had hypertension (16.9%), followed by diabetes (8.2%), in a 1590 study population.

Jain et al¹¹⁵ in a study population of 735, observed that Diabetes (42.85%) and hypertension (39.86%) to be the most common co-morbidities

Numerous studies^{120,123,124,125} indicate that comorbidities such as hypertension, type II diabetes, and coronary artery disease are related to an increased risk of infection and a poor prognosis; the risk of infection also increases if there are several comorbidities.

The comorbidities, particularly type II diabetes mellitus, and the severity of Covid -19 infection in these individuals may result from compromised immunity, overexpression of ACE, and glycation of ACE. The COVID-19 virus attaches to ACE II in pancreatic islet cells, causing damage that may lead to acute hypoglycemia. It was also noted that type II diabetes mellitus worsens in these patients, whereas those with type I diabetes mellitus may present with diabetic ketoacidosis. As a result of hyperglycemia, alterations in coagulation abnormalities, endothelial dysfunction, and the release of inflammatory cytokines may occur, which may account for the increased severity and mortality. In patients with type II diabetes, insulin resistance may result in disrupted glucose haemostasis, which may cause inflammation-related microvascular damage and interstitial fibrosis.

We analyzed the HRCT findings of all the patients and categorized them according to CT Severity Score - < 8 is mild, 9-15 is moderate, and >15 is severe.

In our study, we observed that in mild 27.0 %(n=247), moderate 43.7 % (n=399), and severe 29.1 %(n=266), the mortality was high in patients with high severity scores.

Ravindra et al¹¹⁸, with a 2343 study population, observed that patients' CT Severity Scores were normal in 147 (6.27%), mild in 724 (30.90%), moderate in 903 (38.54%), and severe

in 569 (24.29%). Of 2343 subjects, 569 had severe CT Severity Scores, with 205 (36.03%) dying and 364 (63.97%) surviving. The findings of this study were similar as in our study.

Zhou et al¹¹⁴ with a 134-study population, also observed that patients with COVID-19 who had total CT scores of 16 or more were more likely to have poor survival than those with 15 or less.

We analyzed for any co-relation of CT Severity Score with each biomarker, i.e., serum ferritin, LDH, IL-6 d-dimer, and hs-CRP levels.

We compared CT Severity Score with serum Ferritin levels among our study population which showed a significant P value <0.001, the mean value of serum Ferritin in mild - 187.2, moderate - 484.4, and in severe - 998.6. As the CT Severity Score increases, the mean values of serum ferritin also increase, which shows a positive correlation with the CT Severity Score. We analyzed the ROC curve of (AUC-0.676) and P value <0.001 with the cut-off value of 331.0, which has a sensitivity of 72.2% and a specificity of 56.3%.

Similarly, we compared serum LDH with CT Severity Score and this showed a positive correlation with a significant P value <0.001. The mean value for mild was 336.4, moderate-391.6 and severe -536.6. As the CT Severity Score increase, the mean values increase. AUC shows 0.7 and P value <0.001 with a cut-off value of 375.5, a sensitivity of 70.5%, and a specificity of 63.3%.

We compared hs-CRP with CT Severity Score, and this showed a positive co-relation with a significant P value of 0.017. The mean value for mild was -106.5, moderate-129.2, and severe -145 As the CT Severity Score increase, the mean values increase. AUC shows 0.6 and P value <0.001 with a cut-off value of 85.5, has a sensitivity of 72.2%, and a specificity of 52.0%.

We correlated IL-6 and d-Dimer with CT Severity Score, and this showed a positive correlation with a significant P value of 0.011 and for d-Dimer <0.001. The mean value for IL6 for mild was -103.6, moderate-157.7, and severe -232.6, and in d-Dimer mild -654.4, moderate-908.4 and severe -1437 as the CT Severity Score increased, the mean values also increase. AUC for IL6 shows 0.6, d-dimer 0.7, and P value <0.001 for both IL-6 and d-dimer, with a cut-off value of 76.3, has a sensitivity of 60.2%, and a specificity of 60.8% and for the d-Dimer cut-off value of 643.4, has a sensitivity of 70.5%, and a specificity of 65.2%.

Various other studies showed similar significant findings as in our study.

Zhou et al¹¹⁴ studied 134 COVID-19-infected patients. At various phases, the deceased group had significantly higher levels of leukocytes, neutrophils, high-sensitivity C-reactive protein (hsCRP), prothrombin, D-dimer, serum ferritin, interleukin (IL)-2, and IL-6 than the recovered group. In the deceased group, the overall CT score at the peak stage was substantially higher than in the recovered group (20 vs. 11 points).

Jain et al¹¹⁵ with a patient population of 735, demonstrated that only CRP, D-Dimer, and CT Severity Score levels may predict the outcome of death Cut off for CRP was 45 mg/L (Sn 0.8, Sp 0.56), D-dimer was 1000µg/L (Sn:0.8, Sp: 0.9).

Abd El Megid et al¹²⁶ studied 305 COVID-19-infected patients and observed a significant positive correlation with CRP, ferritin, and d-dimer levels.

We believe it is important to study a large number of patients addressing confounding factors such as age, sex, symptoms, and comorbidities at the time of presentation, as there was little understanding of this new pandemic. During the first wave of the pandemic, cases were more severe and had a higher mortality rate. This could be due to awareness and knowledge of infection, CT abnormalities, treatment, and vaccination, all of which

have impacted patient severity. Now, we may not have the same virulent strain; the strain may have mutated and become less virulent however, a large number of patients must be studied in order to address these challenges, thus we need to conduct research on a large sample size.

LIMITATIONS.

- It was a retrospective, single-center study, therefore the findings cannot be applied to the wider population. More cohort studies are required.
- "Most patients in the recovered group were mild to moderate illness; the predictive value of selected risk factors may be overestimated. Therefore, well-matched groups in disease severity should be investigated to more accurately evaluate the risk factors related to the mortality of COVID-19."
- The assessment of disease severity on CT images could be subjective.

CONCLUSION

In our study of 912 patients, we observed that severe COVID-19 infection was more common in elderly-aged males. The severity of the covid-19 disease was higher in patients with one or more co-morbidities predominantly in those with T2DM

The severity of the disease as reflected on the HRCT score positively correlated with an increase in the levels of various biomarkers. Hence it can be concluded that the CT Severity Score and biomarker levels can be used as markers of prognosis in the patient with covid -19 infection.

SUMMARY

In our study, we compared biomarkers with CT severity in COVID-19-infected patients.

- The age of patients ranged from 20-99 years. i.e., the youngest was 20 years old. The oldest was 93 years old. The mean age in the mortality group was 62.5 ± 12.4 years, and in the survival group, it was 51.1 ± 16.2 years. Mortality and morbidity increased with age.
- There were 731 male patients in our study; the remaining 181 were female patients. Male predominance was observed in our study with an M: F of 4.03:1.
- The most common symptoms in our study were cough (65.6%) followed by fever (64.8%) and breathlessness (64.2%).
- Comorbidities such as hypertension, type II diabetes mellitus, and ischemic heart disease enhance both the risk of infection and the severity of infection. It was observed that patients with type II diabetes mellitus were more likely to experience COVID-19 infection of a severe nature.
- After co-relating serum ferritin with CT Severity Score, it was observed that there was a significant positive correlation ($p < 0.001$) with a mean value of 187.2ng/ml in the mild group and 484.4 ng/ml in the moderate and 998.6ng/ml in the severe group of CT Severity Score. The ROC curve showed that the area under the curve (AUC) of 0.676 and with the cut value of 331ng/ml, has a sensitivity of 72.2% and a specificity of 56.3%.
- Serum LDH co-related with CT Severity Score and it was observed there was a significant positive correlation ($p < 0.001$) with a mean value of 336.4 U/L in the mild group and 391.6 U/L in the moderate and 536.6 U/L in the severe group of CT Severity Score. The mean values increased with CT Severity Score. The ROC

curve showed that the area under the curve (AUC) of 0.707 and with the cut value of 375.5 U/L, has a sensitivity of 70.5% and a specificity of 63.3%.

- There was a significant correlation between serum hs-CRP and CT Severity Score. It was observed that there was a significant positive correlation ($p < 0.017$) with a mean value of 106.5mg/ltr in the mild group and 129.2mg/ltr in the moderate and 145mg/ltr in the severe group of CT Severity Score. The ROC curve showed that the area under the curve (AUC) of 0.641 and with the cut value of 85.5mg/ltr, has a sensitivity of 72.2% and a specificity of 52%.
- IL-6 and CT Severity Score showed good correlation and it was observed that there was a significant positive correlation ($p < 0.011$) with a mean value of 103.6pg/ml in the mild group and 157.7pg/ml in the moderate and 232.6pg/ml in the severe group of CT Severity Score. The ROC curve showed that the area under the curve (AUC) of 0.673 and with the cut value of 76.3pg/ml, has a sensitivity of 60.2% and a specificity of 60.8%.
- Similarly, D-dimer and CT Severity Score showed good correlation and it was observed that there was a significant positive correlation ($p < 0.001$) with a mean value of 654.4ng/ml in the mild group and 908.4ng/ml in the moderate and 1437.3ng/ml in the severe group of CT Severity Score. The ROC curve showed the area under the curve (AUC) of 0.728 and with the cut value of 643.5ng/ml, has a sensitivity of 70.5% and a specificity of 65.2%.
- Serum ferritin, LDH, hs-CRP, IL-6, and d-dimer with cut-off values of 331 ng/ml, 375.5 U/L, 85.5 mg/ltr, 76.3 pg/ml, 643.5 ng/ml repetitively obtained from ROC curve can be used as a screening tool for the COVID-19 infected patients and can help predict the prognosis of the disease.

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ANNEXURE I

PROFORMA

CASE NO	
NAME	
IP NO	
AGE	YEARS
SEX	
ADDRESS	
OCCUPATION	

Presenting Complaints				
COMORBIDITIES	HYPERTENSION	DIABETES	CARDIOVASCULAR DISEASE	OTHERS
YES/NO				
SINCE				
ON TREATMENT				

Vitals:

Temperature	
Pulse	
Respiratory Rate	
Blood Pressure	
SpO2	

INVESTIGATIONS:

	Corads score	CT Severity Score	IL-6	D-dimer	Ferritin	Hscrp	LDH
AT ADMISSION							

CLINICAL OUTCOME	
DISCHARGED	
AMA(DISCHARGED AGAINST MEDICAL ADVISE)	
DEATH	
COMPLICATIONS, IF ANY	

ANNEXURE II – KEY TO MASTERCHART

- T2DM- Type II Diabetes Mellitus
- IHD – Ischemic heart disease.
- CKD- Chronic Kidney Disease

ANNEXURE III – MASTERCHART

MASTER CHART

IP No	Age	Sex	fever	cough	pleural effusion	myalgia	TDM	HTN	IHD	CKD	ASTHMA	CT severity score(--/25)	Ferritin 1	LDH 1	hsCRP (value)	IL-6 1	d-Dimer 1	OUTCOME	
																		Improved and discharged	DIED
1024932	49	M	1	1	0	0	1	0	0	0	1	MODERAT	651	573	135	17.4	5000	YES	
1023058	74	M	1	1	1	1	0	0	0	0	0	MODERAT	267	240	102	31.6	938	YES	
1021470	48	F	1	0	1	0	0	0	0	0	0	MILD	180	232	14	26	344	YES	
1024346	78	M	1	1	1	0	0	0	0	0	0	SEVERE	1115	792	57	126	455	YES	
1024283	72	M	1	0	1	0	1	0	0	0	0	MODERAT	316	252	5.4	10.6	105	YES	
1023950	55	M	1	1	1	0	0	0	0	0	0	MODERAT	606	332	19	89	859	YES	
1021418	42	M	0	1	1	0	0	0	0	0	0	MILD	554	411	168	121	759	YES	
1023907	67	M	1	1	1	0	0	0	0	0	0	MODERAT	434	401	75	14	517	YES	
1024635	52	M	1	1	1	0	0	0	0	0	0	SEVERE	917	353	56	173	346	YES	
1020024	60	M	1	1	0	0	0	0	0	0	0	MODERAT	56.9	244	23	3.79	363	YES	
1022622	39	M	0	1	0	0	0	0	0	0	0	MODERAT	74.3	123	33	3.79	147	YES	
1022763	70	M	0	1	0	0	0	0	0	0	0	MODERAT	161	516	123	176	661	YES	
1024049	50	M	1	0	0	0	0	0	0	0	0	MODERAT	326	289	2.1	4.54	248	YES	
1021264	43	M	1	0	0	1	0	0	0	0	0	SEVERE	778	433	119	120	1045	YES	
1022375	30	M	1	1	1	0	0	0	0	0	0	MILD	27.4	234	95	12	531	YES	
1021495	75	M	0	1	0	0	1	1	1	0	0	MILD	33	343	13	1.56	182	YES	
1022667	59	M	1	1	1	0	0	0	0	0	0	MILD	372	1012	78	11.3	5000	YES	
1022797	64	M	1	1	1	1	0	0	0	0	0	MILD	133	196	83	1.6	120	YES	
1022395	66	M	0	1	1	0	0	0	0	0	0	MILD	36.2	145	90	32	581	YES	
1018721	25	M	1	1	1	1	0	0	0	0	0	MODERAT	218	219	194	123	867	YES	
1022636	54	M	1	1	1	0	0	0	0	0	0	MODERAT	443	334	60	58.8	206	YES	
1018431	74	M	1	1	1	1	0	0	0	0	0	MODERAT	1054	345	56	432	1087	YES	
1021041	33	M	1	1	1	1	0	0	0	0	0	MODERAT	744	646	103	6.04	996	YES	
1019405	24	M	1	1	1	0	0	0	0	0	0	MILD	88	358	124	23	1244	YES	
1023483	57	M	1	1	1	0	0	0	0	0	0	MILD	356	355	772	21	647	YES	
1021292	23	F	1	1	1	0	0	0	0	0	0	MODERAT	46	375	299	12.2	390	YES	
1024867	60	M	0	1	0	1	0	0	0	0	0	SEVERE	1355	306	335	432	1573	YES	
1019869	26	F	0	1	1	0	0	0	0	0	0	SEVERE	1435	467	124	120	1759	YES	
1021570	56	F	1	1	1	0	0	0	0	0	0	SEVERE	327	340	343	243	686	YES	
1017889	41	M	0	1	0	0	0	0	0	0	0	MODERAT	345	35	157	6.04	1996	YES	
1019413	27	F	0	1	1	1	0	0	0	0	0	MODERAT	80	358	44	6.04	996	YES	
1020943	48	M	0	1	1	1	0	0	0	0	0	MODERAT	163	232	10	23	457	YES	
1021531	54	M	0	0	1	0	0	0	0	0	0	MODERAT	342	342	94	13	435	YES	
1025361	61	M	1	1	0	0	0	0	0	0	0	MILD	534	135	103	4.02	319	YES	
1020424	45	F	1	1	0	0	0	0	0	0	0	MILD	139	176	66	10	933	YES	
1024956	60	M	1	1	1	0	0	0	0	0	0	SEVERE	1146	484	126	6.04	996	YES	
1020649	54	F	1	1	1	0	0	0	0	0	0	MODERAT	86	358	174	34	467	YES	
1021443	27	F	1	1	1	1	0	0	0	0	0	MODERAT	421	145	218	6.04	855	YES	
1023840	26	M	0	1	1	0	0	0	0	0	0	SEVERE	996	358	25	40.9	217	YES	
1020811	41	M	1	0	1	0	0	0	0	0	0	MODERAT	80	358	102	96	996	YES	
1019609	24	M	1	0	1	0	0	0	0	0	0	MODERAT	44	342	34	44	546	YES	
1022727	25	M	1	1	1	1	0	0	0	0	0	MILD	77	232	55	32	465	YES	
1020584	71	M	1	1	0	0	0	0	0	0	0	SEVERE	825	502	323	2629	1356		YES
1024639	44	F	1	1	0	0	0	0	0	0	0	MODERAT	306	404	92	105	448	YES	
1020488	39	M	1	0	0	1	0	0	0	0	0	MODERAT	234	454	75	245	678	YES	
1017707	45	M	1	0	1	1	1	0	0	0	0	MODERAT	344	684	102	33	957	YES	
1023711	71	F	1	1	0	0	0	0	1	0	0	MILD	608	274	13	24	338	YES	
1021836	59	M	1	1	1	0	1	1	0	0	0	SEVERE	542	674	124	234	1532	YES	
1021845	52	M	1	1	1	0	1	0	0	0	0	MILD	211	660	12	33.5	5000	YES	
1023488	64	M	1	1	1	0	1	1	0	1	0	MODERAT	2000	433	103	218	775	YES	
1020455	60	M	1	1	1	0	1	1	0	0	0	MILD	264	235	66	46.2	282	YES	
1019426	65	M	1	1	0	0	1	1	0	0	0	MILD	429	242	126	32.5	746	YES	
1023326	85	M	1	0	0	0	1	1	0	0	0	MODERAT	61.5	251	174	75	661	YES	
1024174	60	F	1	0	0	0	0	0	0	0	0	MODERAT	22.4	397	218	49.8	472	YES	
1021407	20	M	1	1	1	0	0	0	0	0	0	SEVERE	674	545	25	45	968	YES	
1022906	78	M	0	1	1	0	1	0	0	0	0	SEVERE	1254	45	102	574	5000		YES
1025516	82	M	1	0	1	0	1	1	1	0	0	SEVERE	193	368	34	136	864		YES
1020680	70	M	0	1	1	0	1	1	0	0	0	MODERAT	276	259	55	45	276	YES	
1024333	26	F	0	1	1	1	0	0	0	0	0	MODERAT	152	168	9.3	15.2	140	YES	
1023878	72	F	1	1	1	0	1	1	0	0	0	MODERAT	532	504	56	186	1451	YES	
1024659	23	F	1	1	0	1	0	0	0	0	0	SEVERE	428	635	64	465	794	YES	
1024370	54	M	1	1	1	0	0	1	0	0	0	MILD	125	456	235	137	386	YES	
1023727	60	M	1	1	0	0	0	0	0	0	0	SEVERE	1152	573	145	40.3	5000	YES	
1020944	39	M	1	1	1	0	0	0	0	0	0	SEVERE	2000	458	74	52.8	437	YES	
1021397	56	M	0	0	1	0	0	0	0	0	1	SEVERE	262	397	169	1.54	1519		YES
1020473	33	F	1	1	1	0	0	0	0	0	0	SEVERE	260	53	102	35.9	427	YES	
1019423	70	M	1	0	1	0	1	1	0	0	0	MODERAT	645	673	121	76	374	YES	
1020361	50	M	1	1	0	0	0	0	0	0	0	MILD	56	54	79	47	156		YES
1023886	59	M	0	0	1	1	0	1	0	0	0	MILD	359	515	83	14	605	YES	
1023858	66	M	1	1	1	1	1	1	0	0	0	SEVERE	661	546	210	12	588	YES	
1024081	70	M	1	1	1	0	1	1	1	0	0	SEVERE	640	457	327	6.77	1617	YES	
1024337	30	M	0	1	1	0	0	0	0	0	0	MILD	7.09	207	171	1.15	162	YES	
1022372	70	M	1	0	0	0	1	1	0	0	0	MODERAT	478	266	71	317	556	YES	
1021314	70	M	1	1	1	0	0	0	0	0	0	MODERAT	967	647	167	353	3524	YES	
1023275	75	M	1	0	0	0	1	1	0	0	0	MODERAT	108	269	134	135	5000	YES	
1023734	58	F	1	0	1	1	0	0	0	0	0	MODERAT	433	301	192	32.7	1247	YES	
1019966	36	F	1	0	0	0	0	0	0	0	0	MODERAT	80	339	110	12	996	YES	
1019037	32	M	1	1	1	0	0	0	0	0	0	MODERAT	533	268	178	45	102	YES	
1021329	67	M	0	1	1	1	1	1	0	0	0	MILD	41	358	12	45	996	YES	
1021013	25	M	1	1	0	0	0	0	0	0	0	SEVERE	80	358	89	6.04	2451	YES	

1021509	75	M	1	0	1	0	0	0	0	0	0	MILD	1656	589	126	251	465	YES	
1011581	45	M	1	1	1	0	1	0	0	0	0	MILD	5725	45	174	126		YES	
1020037	51	M	0	0	1	0	1	1	0	0	0	MODERAT	142	444	218	85	788	YES	
1022355	52	M	0	0	1	0	1	0	0	0	0	MODERAT	452	645	25	152		YES	
1022414	85	M	1	0	0	0	1	0	0	0	0	MILD	94.9	694	102	42.3	1179	YES	
1022680	63	M	1	1	1	0	1	0	0	0	0	MILD	190	198	34	10.1	84	YES	
1021413	28	F	1	1	0	0	0	0	0	0	0	MILD	163	286	55	15.3	340	YES	
1023021	28	M	1	0	0	0	0	0	0	0	0	MODERAT	45	453	41	212	2000	YES	
1024852	45	M	1	1	1	0	0	0	0	0	1	MODERAT	390		53	12.5	605	YES	
1024101	45	M	0	1	0	0	0	1	0	0	0	MILD	532	294	24		871	YES	
1022442	55	M	1	1	1	0	1	1	0	0	0	MILD	74.7	250	102	45	303	YES	
1023502	59	M	1	1	0	0	0	0	0	0	0	MODERAT	64.6	115	21	1.68	67	YES	
1022840	37	M	1	0	0	1	0	0	0	0	0	MILD	159	242	79	1.5	268	YES	
1024054	67	M	1	0	0	0	1	1	1	0	0	MODERAT	43.1	214	83	3.77	162	YES	
1022899	25	F	1	1	1	0	0	0	0	0	0	MILD	80	358	210	6.04	996	YES	
1019402	25	F	1	1	0	0	0	0	0	0	0	MILD	80	358	327	6.04	996	YES	
1020548	26	F	1	1	1	0	0	0	0	0	0	MILD	80	358	71	6.04	996	YES	
1019115	54	F	0	0	1	0	0	0	0	0	0	SEVERE	684	331	67	334	273	YES	
1023631	44	M	1	1	1	0	0	1	0	0	1	SEVERE	543	242	344	9.19	488	YES	
1022222	65	M	1	1	1	0	1	1	0	0	0	MODERAT	557	534	34	283	1251	YES	
1023031	60	M	1	1	0	1	0	1	0	0	1	MODERAT	125	229	53	16.9	345	YES	
1021471	57	M	1	1	1	0	1	1	0	0	0	SEVERE	3036	401	119	2445	1189	YES	
1024210	78	F	1	1	0	0	1	1	0	0	0	MILD	341		11	15.9	389	YES	
1024654	61	M	0	0	1	0	1	1	0	0	0	MILD	87.3	166	102	183	1487	YES	
1021775	80	M	1	1	1	0	1	0	0	0	0	MILD	322		121	521	876	YES	
1024132	35	M	0	1	0	0	0	0	0	0	0	MILD	500	295	79	21	264	YES	
1024854	40	M	1	1	0	0	0	0	0	0	0	MILD	115	105	83	45	198	YES	
1022122	34	M	1	0	1	0	0	0	0	0	0	SEVERE	670	751	210	537	1117	YES	
1019409	26	M	1	0	1	1	0	0	0	0	0	SEVERE	6442	451	327	412	5000	YES	
1019608	32	M	1	1	0	0	0	0	0	0	0	SEVERE	454		171	245	554	YES	
1021009	53	M	0	1	1	1	1	0	0	0	0	MILD	25	746		25.8	688	YES	
1020547	24	F	1	1	1	0	0	0	0	0	0	MILD	80	412	452	6	996	YES	
1026090	84	M	0	0	1	1	1	1	0	0	0	MODERAT	51.5	212	3.8	9.06	191	YES	
1019307	30	M	1	0	1	0	0	0	0	0	0	MODERAT	37.5	192	24	24	101	YES	
1019730	78	M	0	1	1	1	0	0	0	0	0	MILD	770	776	102	45	366	YES	
1022988	32	M	0	1	1	0	0	0	0	0	0	MILD	292	42	21	12	5000	YES	
1021752	62	M	1	0	1	0	1	1	0	0	0	MODERAT	3243	436	79	2.49	763	YES	
1023279	39	M	0	1	1	0	0	1	1	0	0	MODERAT	170		83	1.5	396	YES	
1023629	70	M	0	0	1	0	0	0	1	0	0	SEVERE	292	348	210	45.2	856	YES	
1019116	23	M	0	1	0	0	0	0	0	0	0	MODERAT	43	240	327	222		YES	
1019044	46	F	1	1	1	0	1	1	0	0	0	MODERAT	424		71	124		YES	
1019120	22	F	1	1	0	1	0	0	0	0	0	MILD	51.5	217	67	142	122	YES	
1019490	60	M	1	0	0	1	0	0	0	0	0	MILD	11.4	321		19.6	135	YES	
1019890	38	M	1	1	1	0	0	0	0	0	0	MILD	422	22	26	164		YES	
1019984	38	M	1	1	0	0	0	0	0	0	0	MODERATE		457	178	16		YES	
1019414	23	M	1	0	0	0	0	0	0	0	0	MODERAT	113	372	56	46	832	YES	
1018384	23	F	0	1	0	1	0	0	0	0	0	MODERAT	44	45	146	64		YES	
1019406	25	M	1	0	0	0	0	0	0	0	0	MILD	141		24	768	102	YES	
1022244	64	M	0	1	0	0	0	0	0	0	0	MILD	489	373	102	127	326	YES	
1020485	65	M	1	0	1	0	1	0	0	0	0	MILD	145	390	21	201	496	YES	
1020991	55	M	0	1	1	0	1	0	0	0	0	MODERAT	603	239	79	475	1029	YES	
1021918	72	M	1	0	1	0	1	1	0	0	0	SEVERE	800	124	83	87.9		YES	
1026279	52	M	1	1	1	0	0	0	0	0	0	MILD	55	282	210	3.92	161	YES	
1025636	58	M	1	1	1	0	0	0	0	0	0	SEVERE	591	406	327	1.5	406	YES	
1020115	60	M	0	1	0	0	1	0	0	0	0	SEVERE	665	479	71	5.71	348	YES	
1026255	60	M	0	1	1	0	0	1	0	0	0	MODERAT	64.6	412	67		243	YES	
1020756	29	M	1	1	0	0	0	0	0	0	0	MODERAT	422	305	134	101		YES	
1023606	30	F	1	1	0	0	0	0	0	0	0	MODERAT	112	201	192		217	YES	
1023102	42	M	0	1	1	1	1	0	0	0	0	MODERAT	134	357	110	113	886	YES	
1026716	47	M	1	0	1	0	0	0	0	0	0	MODERAT	42		178			yes	
1020650	58	M	1	1	0	1	0	0	0	0	0	MILD	80	358	119	6.4	996	YES	
1022267	82	M	0	1	0	1	1	1	0	0	0	MILD	378		95	163	491	YES	
1026176	46	M	1	1	1	0	0	0	0	0	0	MILD	162	198	13	26.1	158	YES	
1026260	61	M	0	0	1	0	1	1	0	0	0	MODERAT	342		78	41.7		YES	
1019025	27	M	0	1	1	1	0	0	0	0	0	SEVERE	416	287	83	45	144	YES	
1018385	24	F	1	1	0	0	0	0	0	0	0	MODERAT	432	325	90		2000	YES	
1019462	52	M	1	1	0	0	0	0	0	0	0	SEVERE	552	303	194	84.3	437	YES	
1019487	23	F	0	1	0	0	0	0	0	0	0	MILD	23.3		60		128	YES	
1025147	75	M	0	1	1	0	1	1	1	0	0	MODERAT	155	301	56	360	4225	YES	
1021466	59	M	1	0	1	0	1	1	0	0	0	MILD	54	24	103	452		YES	
1023182	58	M	1	1	1	0	1	0	0	0	0	MILD	44	204	124		416	YES	
1023186	42	M	1	0	0	0	1	0	0	0	0	MODERAT	68.1	185	772	9.62	179	YES	
1022920	70	M	1	0	1	1	0	1	0	0	0	MODERAT	213		299		1470	YES	
1023301	65	F	1	1	1	0	0	0	1	0	1	MODERAT	123	125	335	2041	2457	YES	
1019411	25	M	1	1	0	0	0	0	0	0	0	MODERAT	80	358	124	6.04		YES	
1021473	62	M	1	1	0	0	0	0	0	0	0	MILD	148	208	343		248	YES	
1022805	58	M	1	0	1	0	0	0	0	0	0	MILD	87	381	157	103	339	YES	
1022804	36	M	1	1	1	0	0	0	0	0	0	MILD	112	78	44			YES	
1022158	71	M	1	1	0	0	0	1	0	0	0	MILD	71.6	297	10	73.7		YES	
1022987	52	M	1	0	1	0	0	0	0	0	0	MODERAT	718	518	94	24	281	YES	
1023875	58	M	0	0	1	0	0	0	0	0	0	MODERAT	234		24			YES	
1020880	65	M	0	1	1	0	0	0	1	0	0	MILD	284	415	102	16.6	405	YES	
1020427	67	M	1	1	1	0	0	0	0	0	0	MODERAT	332	42	21			YES	
1020388	50	M	0	0	1	0	0	0	0	0	0	SEVERE	1080	87	79	1.5	630	YES	
1022489	68	M	1	0	1	0	0	0	0	1	0	SEVERE	228	872	83	107	1305	YES	
1022915	78	M	1	0	0	0	0	0	0	0	0	SEVERE	178		210	52.4	1339	YES	
1021406	33	M	1	1	1	0	0	0	0	0	0	MODERAT	621	392	327	578		YES	
1020631	60	M	1	1	0	0	0	0	0	0	0	MODERAT	440		71	535	338	YES	
1020624	41	M	1	0	1	0	0	0	0	0	0	MODERATE		343	67	245	410	YES	
1022272	25	M	1	0	1	0	0	0	0	0	0	MODERAT							

1024202	82	M	1	0	0	0	0	0	0	0	0	MILD	10.7	207	1.8	40.8	1444	YES	
1020439	41	M	0	0	1	0	0	0	0	0	0	MILD	43	542	56		308	YES	
1024420	66	F	0	0	1	1	0	0	0	0	0	MILD	231	5436	244	45	500	YES	
1019947	26	F	0	0	0	1	0	0	0	0	0	MILD	98.5	289	415	38.2	617	YES	
1020219	56	M	1	1	0	0	0	0	0	0	0	SEVERE	1870	180		1.5		YES	
1021759	56	M	0	1	1	0	0	0	0	0	0	SEVERE	453	252	156	35.9	5	YES	
1022168	51	M	1	1	1	0	0	0	0	0	0	SEVERE	455	452		61.7	559	YES	
1023888	55	F	1	1	0	0	0	0	0	0	0	SEVERE	304	344	164	130	709	YES	
1024044	34	M	1	1	1	1	0	0	0	0	0	MODERAT	1769	555	23	58.6	407	YES	
1023645	60	M	1	1	1	1	0	0	0	0	0	MODERAT	223	342	45	78	746	YES	
1024379	54	M	1	1	1	0	0	0	0	0	0	MODERAT	31.3	304	75	66	435	YES	
1023274	50	M	0	0	1	0	0	0	0	0	0	SEVERE	390	376	342	646	1421	YES	
1022960	30	F	1	1	1	0	0	0	0	0	0	MILD	9.06	248	12	1.5	188	YES	
1022751	31	M	1	1	0	0	0	0	0	0	0	MILD		211	9.3		608	YES	
1024146	72	M	1	1	0	0	0	0	0	0	0	SEVERE	824		56	153	877	YES	
1022520	29	F	1	1	0	0	0	0	0	0	0	MILD	39.3	160	64	5.98		YES	
1021608	45	M	1	1	1	0	0	0	0	0	0	MODERAT	211	412	235	11.3	386	YES	
1021899	38	M	1	1	0	0	0	0	0	0	0	MODERAT	116	240	145	14.3	472	YES	
1021699	30	M	1	1	1	0	0	0	0	0	0	MILD	145	56	178	72	400	YES	
1021933	72	F	1	1	1	0	0	1	0	0	0	MODERAT	20.4	320	56	29.6	271	YES	
1021094	38	M	0	1	1	0	0	0	0	0	0	MODERAT	451	291	146	33.3	221	YES	
1021588	22	F	1	0	0	1	0	0	0	0	0	MODERAT	345	245	24	76.6	233	YES	
1021727	80	M	0	1	0	0	0	0	0	0	0	MODERAT	535	423	102	115	436	YES	
1021818	44	M	0	1	1	0	0	0	0	0	0	MODERAT	355	245	21	251	644	YES	
1018883	22	M	0	1	1	0	0	0	0	0	0	MODERAT	116	172	79	126	324	YES	
1020850	50	M	1	1	1	0	1	1	0	0	0	MODERAT	83.6	181	83	85	174	YES	
1020897	70	M	1	1	0	1	1	1	0	0	0	MODERAT	38.8	663	210	9.01	121	YES	
1023969	51	M	0	0	1	1	0	0	0	0	0	MODERAT	345	546	327	64		YES	
1024507	40	M	1	0	1	0	0	0	0	0	0	MODERAT	45	672	71	61.8	327	YES	
1020105	36	M	0	0	1	0	0	0	0	0	0	MODERAT	323	296	67	64	185	YES	
1019961	42	M	1	0	0	0	0	0	0	0	0	MODERATE			134	36	124	YES	
1022649	30	M	1	1	1	0	0	0	0	0	0	MODERAT	246	323	192	123	589	YES	
1024098	35	M	1	0	0	0	0	0	0	0	0	MILD	314		110	1.5	97	YES	
1021418	42	M	0	1	1	0	0	0	0	0	0	SEVERE	554	411	178	121	399	YES	
1023186	42	M	1	0	0	0	0	0	0	0	0	MILD	68.1	189	12	9.62	179	YES	
1022926	75	M	1	0	1	1	0	0	0	0	0	MODERATE		85	119		1470	YES	
1023031	66	M	0	0	1	0	0	0	0	0	0	MILD	124	54	95	16.9		YES	
1022837	67	M	1	1	0	0	0	0	0	0	0	MODERAT	152	330	13	94	1111	YES	
1021775	80	F	1	1	1	0	1	1	1	0	0	MODERAT	322	330	78	17.8	876	YES	
1024314	43	M	1	0	1	0	0	0	0	0	0	SEVERE		423	83	17.7	671	YES	
1023275	75	M	1	0	0	1	0	0	0	0	0	SEVERE	108	269	90		5000	YES	
1024334	56	M	0	1	0	1	0	0	0	0	0	SEVERE	187	340	194	35.1	258	YES	
1023540	58	M	1	1	0	0	0	0	0	0	0	SEVERE	741	525	60	1.56	5000	YES	
1024783	38	F	0	0	1	0	0	0	0	0	0	SEVERE	246	345	56	1.5	482	YES	
1022275	54	M	1	1	0	0	0	0	0	0	0	MODERATE		375	103	133	607	YES	
1024933	40	M	1	1	1	0	1	1	0	1	0	SEVERE	1918	390	124	390		YES	
1024859	50	M	1	0	0	0	0	0	0	0	0	MILD	357	227	772	3.17	394	YES	
1020591	65	M	0	1	1	0	0	0	0	0	0	MODERAT	122	257	299		730	YES	
1022022	60	M	0	1	0	0	0	0	0	0	0	MILD		258	335	19.3	865	YES	
1022012	43	M	1	0	0	0	0	0	0	0	0	MODERAT	461	45	124			YES	
1022453	63	M	0	1	1	0	0	0	0	0	0	MODERAT	95.8	576	343	548	634	YES	
1021492	40	M	1	1	1	0	0	0	0	0	0	SEVERE	819	782	157	75.4	1229	YES	
1021237	60	M	1	1	0	0	0	0	0	0	0	MODERAT	412	45	44	21	563	YES	
1021390	23	M	0	1	1	0	0	0	0	0	0	MODERAT	122	542	10	25	458	YES	
1024155	37	M	0	1	0	1	0	0	0	0	0	MODERAT	140	228	94		370	YES	
1021016	58	M	1	1	1	0	0	0	0	0	0	MODERAT	158	612	56	88	602	YES	
1022846	75	M	1	1	0	1	0	0	0	0	0	MILD	91.9	27	146	119		YES	
1020723	47	M	1	1	0	0	0	0	0	0	0	MILD			24	56.7	136	YES	
1020366	62	M	1	1	1	0	0	1	0	0	0	MODERAT	644	727	102		1378	YES	
1020416	30	M	1	1	0	0	0	0	0	0	0	MILD	455	454	21	42		YES	
1020936	68	F	1	1	1	0	1	0	0	0	0	MODERAT	306	265	79	80.1	524	YES	
1020845	45	F	1	0	1	0	1	0	0	0	0	MODERAT	673	308	83		1033	YES	
1020953	43	F	0	0	1	0	0	0	0	0	0	MILD	451	440	210	123		YES	
1020595	47	M	1	0	1	0	0	1	0	0	0	MODERAT	613	398	327	64.6	537	YES	
1020676	37	M	1	1	1	0	1	0	0	0	0	MILD		301	71	222	239	YES	
1020922	45	F	1	1	1	0	0	0	0	0	0	MILD	85.5	204	67	124	194	YES	
1020609	48	F	1	0	0	1	0	1	0	0	0	MODERAT	302	454	134	142	309	YES	
1021012	62	M	1	1	1	0	1	1	0	0	0	MILD	44.1	221	192	19.6	306	YES	
1020643	71	M	1	1	1	0	1	1	0	0	0	MILD	121	452	110	164	1374	YES	
1020233	21	F	0	1	1	0	0	0	0	0	0	mild	450		178	16		YES	
1020920	71	F	0	1	1	0	0	1	0	0	0	MODERAT	494	296	12	46	851	YES	
1019618	87	M	1	0	0	0	0	0	0	0	0	SEVERE	2833		93	64	707	YES	
1020077	46	M	1	0	1	0	0	0	0	0	0	MODERAT	319	419	40	768	179	YES	
1021423	50	M	0	0	0	1	0	0	0	0	0	MILD				127		YES	
1020386	50	M	1	1	0	0	0	0	0	0	0	MODERAT	213	576	107	60.4		YES	
1020618	43	M	0	1	1	1	0	0	0	0	0	SEVERE	1096			24.3	296	YES	
1021165	71	M	1	1	0	0	0	0	0	0	0	MILD	129	415	2.1	4754	387	YES	
1023853	40	M	1	0	1	1	1	1	1	0	0	MILD	306	467	11		125	YES	
1020061	34	M	0	0	0	1	0	0	0	0	0	MODERATE		247	102	8.45	166	YES	
1020831	35	M	1	0	1	0	0	0	0	0	0	SEVERE	1608	625	121	14.6	471	YES	
1020774	50	M	1	0	1	0	0	1	0	0	0	MODERATE		240	79		295	YES	
1020450	56	M	1	1	1	0	1	0	0	0	0	MODERAT	1128		83	6.61		YES	
1020358	74	M	1	1	0	0	0	0	0	0	0	MODERAT	184	258	210	49.5	164	YES	
1020639	62	M	0	1	1	0	0	0	0	0	0	MODERATE			327	46	1205	YES	
1020799	55	M	1	1	1	0	1	0	0	0	0	MODERAT	455	305	171			YES	
1020309	44	M	1	1	1	0	1	1	0	0	1	MODERAT	277	288	232	13.1	564	YES	
1020867	73	M	1	1	1	0	1	1	0	0	0	MODERAT	289	253	213	523	565	YES	
1020314	55	M	1	0	0	0	0	0	0	0	0	SEVERE	421	42	142	32	425	YES	
1020448	64	M	0	1	1	0	1	1	0	0	0	MODERAT	872	432	422	421	1399	YES	
1024077	69	M	0	0	1	0	0	1											

1019809	32	F	0	0	1	0	0	0	0	0	0	SEVERE		358	44	6.04	996	YES	
1023722	62	M	1	0	1	0	0	0	0	0	0	SEVERE	911		10	262	791	YES	
1021693	68	M	1	1	0	0	0	0	0	0	0	SEVERE	1245	456	94	784	5000	YES	
1021074	60	M	0	0	0	0	0	0	0	0	0	SEVERE	667		9.3		456	YES	
1020929	25	M	0	1	1	0	0	0	0	0	0	MODERATE		358	56	6.04	996	YES	
1024048	52	M	1	0	1	0	0	1	0	0	0	MODERAT	659		64		5263	YES	
1022995	63	M	1	1	0	0	0	0	0	0	0	MODERAT	172	266	235	6.28	471	YES	
1022086	74	M	1	1	1	0	0	0	0	0	0	SEVERE	529		145	257	154	YES	
1020694	60	F	0	1	0	0	0	0	0	0	0	MODERAT	668	565	74			YES	
1024619	48	M	1	1	1	0	0	1	0	0	0	SEVERE	1107	385	169	6.24	443	YES	
1021303	68	M	1	1	0	0	0	0	0	0	0	SEVERE	970		175	49.2		YES	
1020136	48	M	1	1	0	0	0	0	0	0	0	SEVERE	1150	684		166	1237	YES	
1024646	23	F	1	0	1	0	0	0	0	0	0	MILD	24	196	1.2	1.5	163	YES	
1023909	51	M	1	1	0	0	0	0	0	0	0	MILD	33	192		1.4	132	YES	
1021563	49	M	0	1	1	0	0	0	0	0	0	MODERAT	564	887		784	5000	YES	
1024050	45	M	1	1	0	1	0	0	1	0	0	MODERAT	1582		###	17.7	1071	YES	
1021172	68	M	0	1	0	1	0	1	0	0	0	SEVERE	532	402	9.3	76.6	304	YES	
1028512	50	F	1	1	0	0	0	0	0	0	0	SEVERE	482	402	56	115	554	YES	
1026814	55	F	1	1	0	0	0	0	0	0	0	SEVERE	849	93	64	251	6456	YES	
1025585	55	M	0	0	1	1	0	1	0	0	0	SEVERE	457	430	235	126		YES	
1020524	34	M	1	1	1	0	0	0	0	0	0	SEVERE	455	234	145	85	5000	YES	
1020218	33	M	1	1	0	0	0	0	0	0	0	MODERATE		394	74	18	431	YES	
1023425	44	M	1	0	0	0	0	0	0	0	0	MODERAT	4624	390	169	24.7	463	YES	
1023106	34	M	1	1	1	0	0	0	0	0	0	MODERAT	320	295	9.3	16.3	440	YES	
1026783	25	M	1	0	0	0	0	0	0	0	0	MODERATE		227	56	1.5	111	YES	
1025268	23	M	0	1	0	1	0	0	0	0	0	MODERAT	4.7		64	1.56		YES	
1023932	60	F	1	1	1	0	0	0	0	0	0	MODERAT	159	258	235	106	1013	YES	
1022722	55	M	1	0	0	1	1	1	0	0	0	MILD	236	282	145	96.4	193	YES	
1020487	64	F	1	1	1	0	0	0	0	0	0	MILD	235	55	45	140	1098	YES	
1021325	58	M	0	0	1	0	0	1	0	0	0	MILD	94.4	546	448	24	514	YES	
1022117	30	M	1	1	0	0	1	1	0	0	0	MILD	138	312	9.2	50.3	358	YES	
1021488	54	M	1	1	1	0	0	1	0	0	0	MODERAT	314	497	9.3		532	YES	
1021286	73	M	0	1	1	0	0	0	0	0	0	MODERAT	836		56	58.2	547	YES	
1025129	51	F	0	1	1	0	0	0	0	0	0	MILD	96	184	64	14.7	138	YES	
1026447	51	M	1	1	0	0	0	0	0	0	0	SEVERE			235		1424	YES	
1023265	53	M	1	0	1	1	0	0	0	0	0	SEVERE	250	258	145	21.8		YES	
1021419	69	M	1	0	1	0	1	0	0	0	0	SEVERE	312			54.5	1399	YES	
1021604	47	M	1	1	0	0	0	0	0	0	0	SEVERE	834	507		5.54	952	YES	
1023043	64	M	0	0	1	0	1	1	0	0	0	MILD	127	271		24	597	YES	
1026252	48	M	1	1	1	0	0	0	0	0	0	SEVERE	954	408	44	820	1410	YES	
1020297	58	M	1	0	0	0	0	0	0	0	0	MODERAT	456	82	24	452	307	YES	
1021724	60	M	0	0	1	0	1	1	0	0	0	MODERAT	1459	796	102	297	5000	YES	
1025455	43	M	0	1	1	0	0	0	0	0	0	MILD	72.6		21	1.5		YES	
1024118	55	M	1	0	0	1	0	0	0	0	0	MODERAT	730		79	1.5	563	YES	
1022668	55	F	1	0	1	0	0	0	0	0	0	SEVERE	136	591	83	71.2	620	YES	
1020483	71	M	1	1	0	0	0	0	0	0	0	SEVERE		415	210	23.4	345	YES	
1022664	35	F	0	1	0	0	0	0	0	0	0	MILD			327			YES	
1023024	62	F	1	1	1	0	0	0	0	0	0	SEVERE	561	864	71	81.1	5000	YES	
1013501	61	M	0	0	0	0	0	0	0	0	0	MILD	87.3	388	67		525	YES	
1023428	48	M	0	0	1	0	0	0	0	0	0	MILD		1623	9.3	183	1463	YES	
1022117	71	M	0	1	1	0	1	0	0	0	0	MODERAT	138	312	56	50.3		YES	
1025149	60	M	1	0	0	0	0	0	0	0	0	MODERAT	588	536	64	85	5000	YES	
1020393	30	M	0	0	1	0	0	0	0	0	0	MODERAT	614	398	235	64.6	537	YES	
1019932	42	M	1	1	0	0	0	0	0	0	0	MILD	359	364	145		284	YES	
1020932	53	M	1	0	1	0	0	0	0	0	0	MILD	336	465	91		515	YES	
1024289	29	M	0	1	1	0	0	0	0	0	0	MILD	108	184	4.1	1.5		YES	
1024235	72	M	1	0	1	0	1	1	0	0	0	MODERAT	425			11.9	1030	YES	
1023083	40	M	0	0	1	0	1	0	0	0	0	SEVERE	559	310	5.7		861	YES	
1023257	57	M	1	1	0	1	0	0	0	0	0	MODERAT	541	356	45	86		YES	
1023561	88	M	0	1	1	1	1	1	1	0	0	SEVERE	1183	230		46	294	YES	
1024608	20	F	0	0	0	0	0	0	0	0	0	MILD	36	487	13	119	1335	YES	
1024885	24	F	0	1	1	1	0	0	0	0	0	MILD	80	358	6.1	6.04	996	YES	
1024282	50	M	0	1	1	0	0	0	0	0	0	MODERAT	210	231		754	134	YES	
1024883	23	M	0	0	1	0	0	0	0	0	0	MILD	22.5	220	1.7	2.98	120	YES	
1024888	24	F	0	1	1	1	0	0	0	0	0	MILD	29	225	16	2.09	218	YES	
1021244	36	M	1	1	0	1	0	0	0	0	0	MODERATE		617	102	17.7	298	YES	
1021634	38	M	1	1	1	0	0	0	0	0	0	SEVERE	1175	458	121	59	381	YES	
1021245	62	F	1	0	1	0	0	1	0	0	0	SEVERE	371	368	79	76.6		YES	
1019902	68	M	1	0	0	0	0	1	0	0	0	SEVERE	327		83	115	234	YES	
1021589	28	F	1	0	0	0	0	0	0	0	0	SEVERE			210	251		YES	
1024280	47	F	1	1	0	0	0	0	0	0	0	MODERAT	28.7	228	327	126	330	YES	
1024300	25	M	1	0	0	0	0	0	0	0	0	MODERAT	198	261	171	85	193	YES	
1024705	27	F	1	1	1	0	0	0	0	0	0	SEVERE	13.6	240	3.6	1.5		YES	
1025563	55	M	1	0	1	0	0	0	0	0	0	SEVERE	1560	631		4532	956	YES	
1020042	60	M	0	0	0	0	0	0	0	0	0	MILD	84.4	207	0.5	1.54		YES	
1020044	53	M	0	1	0	0	0	0	0	0	0	MILD	14.8	205	3.3			YES	
1021628	58	M	0	0	0	0	0	0	0	0	0	SEVERE	2002	455	455	51	354	YES	
1023817	65	M	1	1	0	1	1	1	1	0	0	MODERAT	266	233	15	55	273	YES	
1021510	67	M	0	1	1	0	1	0	0	0	0	MILD	452		72	54	1355	YES	
1020527	43	M	1	1	1	0	1	0	0	0	0	MODERAT	808		986	78	787	YES	
1024649	49	M	1	1	0	0	1	1	0	0	0	MILD	17.6	247	41	65.2	331	YES	
1021295	57	M	0	1	1	0	1	1	0	0	0	MODERAT	5374	707		14.7	145	YES	
1015136	42	M	0	1	0	0	1	0	0	0	0	MODERAT	95.2	402	876		952	YES	
1019566	69	M	1	1	0	0	1	0	0	0	0	MODERATE		93	113	15.4	412	YES	
1021988	69	M	1	0	0	0	1	1	1	0	0	MODERATE		430	78	525	896	YES	
1020036	49	M	1	0	1	0	1	1	0	0	0	SEVERE	928	234	886		328	YES	
1026262	76	M	0	0	1	0	1	1	0	1	0	MODERAT	548	394	123	488	1298	YES	
1025578	55	F	1	0	0	1	1	0	0	0	0	MODERAT	646	56	786		786	YES	
1022364	53	F	1	0	1	0	1	0	0	0	0	MODERAT	238	454	127	64.4	499	YES	
1023190	35	M	0	1	0	1	1	1	0	0	1	MILD	6.84	176	1				

1020038	75	M	1	1	0	0	1	0	0	0	0	MODERAT	637	442	376		243	YES	
1020702	62	M	1	0	0	1	1	1	0	0	0	MODERAT	512		102	23.2	279	YES	
1022005	36	M	0	1	1	0	1	1	0	0	0	MODERAT	185	205	121	9.62	170	YES	
1021569	58	M	0	1	1	0	1	1	0	1	0	SEVERE	4526	384	79	1169	1252	YES	
1019892	58	M	0	1	0	0	1	0	0	0	0	MODERAT	546	5663	83		5000	YES	
1024673	28	M	1	0	0	0	0	0	0	0	0	MILD	32.6	209	210	1.5	135	YES	
1024706	27	M	0	1	1	0	0	0	0	0	0	MILD	88.4	207	327	3.8		YES	
1020762	26	F	0	1	0	0	0	0	0	0	0	MODERATE		241	171			YES	
1022713	70	M	0	0	1	0	0	0	0	0	0	MODERATE				1.5	251	YES	
1024607	31	F	0	0	0	0	0	0	0	0	0	MODERAT	216	377		27.8		YES	
1024334	56	M	0	1	0	1	0	1	0	0	0	SEVERE	188	340	18	33.1	258	YES	
1021098	40	M	1	1	1	0	0	0	0	0	0	SEVERE		622	9.3	156	533	YES	
1020927	57	F	0	1	1	0	0	0	0	0	0	MODERAT	260	194	56	8.89	804	YES	
1024770	58	M	1	1	1	0	0	1	0	0	0	SEVERE	486	804	64		1520	YES	
1029510	27	F	1	1	0	1	0	0	0	0	0	MODERATE			235			YES	
1025945	27	M	1	1	1	0	0	0	0	0	0	MODERAT	565	370	145	844	382	YES	
1022108	58	M	1	1	1	0	0	0	0	0	0	SEVERE	1059	528	105	34.2	741	YES	
1024491	45	M	0	1	0	0	0	1	0	0	0	MODERAT	680	205	18	24.9	205	YES	
1020434	26	F	0	1	1	1	0	0	0	0	0	MODERAT	344			360		YES	
1021312	32	M	1	1	0	0	0	0	0	0	0	MODERAT	1186		1.4	419		YES	
1020638	64	M	1	1	0	0	0	0	0	0	1	SEVERE	269			1352		YES	
1020136	48	M	1	1	0	0	0	0	0	0	0	MODERAT	1150	684	174	166	1237	YES	
1024721	56	F	1	1	0	0	0	0	0	0	0	MODERATE						YES	
1023556	64	M	1	1	0	0	0	0	0	0	0	MODERAT	1045	307	95	18.7	504	YES	
1020516	30	M	1	0	0	0	0	0	0	0	0	MODERATE		154		5.21	119	YES	
1024885	23	M	0	1	1	0	0	0	0	0	0	MILD	22.5	220	1.7	2.98	120	YES	
1019840	32	M	1	1	1	0	0	0	0	0	0	MILD		340				YES	
1022836	67	M	0	1	0	0	0	1	0	0	0	MILD	208	354		40.5	240	YES	
1019496	34	M	1	1	1	0	1	0	0	0	0	MILD	222		36			YES	
1018929	58	F	1	1	0	0	1	0	0	0	0	MILD	41.2	216	60	1.2	210	YES	
1019878	75	M	1	1	1	0	1	1	0	0	0	MILD	667	249				YES	
1017909	71	F	0	1	1	0	1	0	0	0	0	MODERATE						YES	
1019223	57	F	0	1	0	1	1	0	0	0	0	MODERAT	112			2.1	400	YES	
1020036	49	F	1	0	1	0	1	1	0	0	0	SEVERE	929	561	42	20.6	328	YES	
1024532	26	F	0	1	1	0	0	0	0	0	0	MODERAT	80	358		6.05	996	YES	
1025463	28	F	0	1	0	0	0	0	0	0	0	MODERATE		220			695	YES	
1024529	22	M	0	1	1	0	0	0	0	0	0	MODERATE					142	YES	
1023615	52	F	1	0	0	0	0	1	0	0	1	MILD	81.6	217	8.6	10.2	195	YES	
1024707	28	F	0	1	1	0	0	0	0	0	0	MILD	80	358	24	6.04	996	YES	
1023713	59	F	1	0	1	0	1	0	0	0	0	MODERAT	334	284	102	16.4		YES	
1020988	44	F	1	0	0	0	1	0	0	0	0	MODERATE		269	21	7.19		YES	
1020163	55	F	1	1	0	0	1	0	0	0	0	MODERAT	249	317	79	49	308	YES	
1020374	82	M	1	1	0	0	1	1	0	0	0	SEVERE			83	12	131	YES	
1027075	55	F	1	1	0	0	1	0	0	0	0	SEVERE			210			YES	
1020299	65	M	1	0	0	0	1	1	0	0	0	MODERAT	712	226	327	46	310	YES	
1025471	37	M	1	0	0	0	0	0	0	0	0	SEVERE	547	864	71	133	846	YES	
1025865	23	F	1	0	0	0	0	0	0	0	0	SEVERE	447	856	67	4.57	190	YES	
1021592	23	F	1	1	1	1	0	0	0	0	0	MILD	75	647	436	1.5	80	YES	
1024528	23	M	0	1	0	0	0	0	0	0	0	MILD	78.6	200	324	1.5	79	YES	
1024913	26	M	1	1	1	1	0	0	0	0	0	MILD	57.1	148	0.4	1.5	102	YES	
1021638	46	M	1	0	1	0	0	0	0	0	0	MODERAT	532	402	62	621	654	YES	
1021552	36	M	0	1	1	0	0	0	0	0	0	MODERAT	482	93	15	63		YES	
1027471	54	M	0	0	1	0	0	1	0	0	0	MODERAT	849	430	34	123		YES	
1021773	42	M	1	1	0	0	0	0	0	0	0	MODERAT	457	234	26	89.4	399	YES	
1020423	71	M	0	0	1	0	0	0	0	0	0	MODERATE		394	178	360		YES	
1020367	62	M	1	1	0	0	0	0	0	0	0	MILD	427	514	56	419	251	YES	
1020990	54	F	0	1	0	0	0	0	0	0	0	MODERAT	99.7	148	146	1352	158	YES	
1022506	39	M	1	1	1	0	0	0	0	0	0	MODERAT	58.9	395	24	237	417	YES	
1022675	42	M	1	1	1	0	1	0	0	0	0	SEVERE	212	555	102	4.46		YES	
1025372	55	M	1	1	0	0	0	0	0	0	0	MODERATE			21			YES	
1021702	73	M	1	1	0	0	1	1	1	0	0	MODERAT	147	202	79	2.08	270	YES	
1023295	50	M	1	1	1	0	0	0	0	0	0	MILD	36.8	252	83		494	YES	
1021462	38	M	1	1	0	0	0	0	0	0	0	SEVERE	577		210	50.6	1345	YES	
1023896	70	M	0	1	1	0	1	1	0	0	0	SEVERE			327		2642	YES	
1022452	45	M	1	0	1	0	0	1	0	0	0	MODERAT	422	1036	71	296	3451	YES	
1021590	27	F	1	1	1	1	1	1	0	0	0	MODERAT	532		67		1000	YES	
1021715	41	M	1	0	0	0	0	0	0	0	0	MILD	482	225	134	8.87	344	YES	
1020940	58	M	0	0	0	0	0	1	0	0	0	MILD	849	402	192		657	YES	
1020395	64	M	0	0	1	1	0	1	0	0	0	MODERAT	457	93	110		345	YES	
1019649	55	F	1	1	1	0	0	0	0	0	0	MODERAT	320	430	178	44	365	YES	
1020704	42	M	0	1	1	0	0	1	0	0	0	MODERATE		234	12			YES	
1019927	79	M	0	0	1	0	1	1	0	0	0	SEVERE	110	394	16	10.1	412	YES	YES
1021590	27	F	1	1	1	1	0	0	0	0	0	MODERATE			119	222		YES	
1019967	56	M	1	0	0	1	0	0	0	0	0	MODERAT	184		95	124	98	YES	
1019335	57	M	0	1	1	0	0	1	0	0	0	MILD	14.8	228	13	142	501	YES	
1019656	55	M	1	1	0	0	0	0	0	0	0	MILD	782		78	19.6	231	YES	
1020138	57	M	1	1	0	0	0	0	0	0	0	SEVERE	1286	254	90	16	261	YES	
1019117	43	F	1	0	0	0	0	0	0	0	0	MILD	91	159	194	46	121	YES	
1019777	26	M	0	1	0	0	0	0	0	0	0	MILD	23.6	651	60	64	130	YES	
1019593	48	M	1	0	0	0	0	0	0	0	0	MILD	32	45	56	768	187	YES	
1020143	27	M	1	1	0	0	0	0	0	0	0	MILD	245		103	127	165	YES	
1020896	58	F	1	0	0	0	0	0	0	0	0	MILD	302	24	124	9.17	144	YES	
1020923	45	M	1	0	0	0	0	0	0	0	0	MODERAT	360	340	772	12.5	701	YES	
1026900	41	F	1	0	1	0	0	1	0	0	0	MILD	11	359	299		1378	YES	
1020420	64	M	1	1	0	0	0	0	0	0	0	MODERAT	344	270	335	17.3	173	YES	
1018864	33	M	1	1	0	0	0	0	0	0	0	MODERAT	26.3	200	124	345	3443	YES	
1020375	57	M	1	0	1	1	0	1	0	0	0	MILD	160	290	343	9.37	113	YES	
1020848	40	M	1	1	1	0	0	1	0	0	0	MODERAT	655	435	157	76.6		YES	
1020106	36	F	0	1	0	0	0	0	0	0	0	MODERAT	532	215	44	115	100	YES	
1025446	36	M	0	1	0	0	0	0	0	0	0	MODERAT	482	432	10	251		YES	

1019892	58	M	0	1	1	0	1	0	0	0	0	MODERATE			83			YES	
1021009	53	M	0	1	1	1	1	0	0	0	0	MILD	25	746	210	25.8	688	YES	
1022158	71	M	1	1	0	0	0	1	0	0	0	MILD	71.6	297	327	73.7		YES	
1022489	68	M	1	1	1	0	0	0	0	0	0	MODERATE	228	872	71	107	1305	YES	
1023631	44	M	1	1	1	0	0	1	0	0	1	MODERATE			67	9.19	488	YES	
1021253	49	M	1	1	0	0	0	0	0	0	0	MILD	334	331				YES	
1024109	85	F	0	0	1	0	0	1	1	0	0	MILD	285	327	1.4	3.53	1446	YES	
1021495	75	F	0	1	0	0	0	1	0	0	0	MILD	783	210	12	1.5	180	YES	
1020850	50	M	1	1	1	0	1	0	0	0	0	MODERATE	83.6	181			174	YES	
1022846	75	M	1	1	1	0	0	0	0	0	0	MILD	91.9	27		119		YES	
1025516	82	M	0	0	1	0	1	1	1	0	0	SEVERE	193	368		136	864		YES
1025502	82	M	0	1	1	0	1	1	0	0	0	MODERATE	257	291	117			YES	
1022668	55	F	1	0	1	0	0	0	0	0	0	MODERATE	136	591	24	71.2	620	YES	
1019116	23	M	0	1	0	0	0	0	0	0	0	MILD	43	240	102			YES	
1019869	26	F	0	1	1	0	0	0	0	0	0	SEVERE			21	120	759	YES	
1017707	45	M	1	0	1	1	1	0	0	0	0	MILD			79			YES	
1021411	43	M	0	0	1	0	0	0	0	0	0	MODERATE	80	358	83		500	YES	
1019545	52	M	0	0	1	1	1	0	0	0	0	MILD	247	354	210	94.6	725	YES	
1019822	50	M	0	1	1	0	0	0	0	0	0	SEVERE	1577		327	5.22	321	YES	
1023888	55	F	1	1	0	0	0	0	0	0	0	MODERATE	304	344	71	1320	709	YES	
1027075	55	F	1	0	0	0	1	0	0	0	0	SEVERE			67	360		YES	
1021836	59	M	1	1	1	0	1	1	0	0	0	MODERATE	542	674	9.3	419	1532	YES	
1020455	60	M	1	1	1	0	1	1	0	0	0	MODERATE	264		56	1352	282	YES	
1020680	70	M	0	1	1	0	1	1	0	0	0	MODERATE	276	259	64	213	276	YES	
1019423	70	M	1	0	1	0	1	1	0	0	0	MODERATE	645	673	235		548	YES	
1023950	55	M	1	1	1	0	0	0	0	0	0	MODERATE	606	332	145		438	YES	
1024635	52	M	1	1	1	0	0	0	0	0	0	SEVERE	917	353	74	73.3	346	YES	
1024174	60	F	1	0	0	0	0	0	0	0	0	MILD	22.4	397	169	49.8	472	YES	
1023907	67	M	1	1	1	0	0	0	0	0	0	MODERATE			9.3	360	517	YES	
1021836	59	M	1	1	1	0	1	1	0	0	0	MODERATE	542	674	56	419	1532	YES	
1027471	54	M	0	0	1	0	0	1	0	0	0	MODERATE			64	1352	547	YES	
1021295	57	M	0	1	1	0	1	1	0	0	0	MODERATE	5374	707	235	14.7	649	YES	
1021625	74	M	1	0	1	0	1	0	0	0	0	Moderate	1349	701	147	3950	948		YES
1019401	69	M	1	1	1	0	0	1	1	0	0	Moderate	387	386	26	33.4	572		YES
1019733	72	F	1	1	1	0	0	1	0	0	0	severe	4583	535	178	214	1094		YES
1013634	51	M	1	1	0	1	0	1	0	1	0	severe	1087	976	56	1023	483		YES
1019721	64	M	1	1	1	1	1	0	0	0	0	severe	421	649	146	628	1646		YES
1021469	85	M	0	0	1	0	1	1	0	0	0	Moderate	873	353	24	16	294		YES
1022318	66	F	1	0	1	1	1	1	0	0	0	severe	915	552	102	1935	1346		YES
1022362	58	M	1	0	1	0	1	0	0	0	0	mild	106	306	21	28.9	400		YES
1021169	70	M	0	0	0	1	0	0	0	0	0	Moderate	810	342	79	3.5	280		YES
1021530	57	M	0	1	1	0	0	0	1	0	0	severe	943	1756	83	27	5000		YES
1019598	60	M	1	1	1	0	1	0	0	0	0	severe	442	377	210	42.9	284		YES
1020782	82	M	1	1	0	1	1	1	0	0	0	severe	787	342	327	286	5000		YES
1021922	58	F	1	0	1	0	1	1	0	0	0	Moderate	156	631	71	49.3	5000		YES
1020039	73	M	0	1	1	0	1	1	0	0	0	Moderate	529	342	67	47	784		YES
1021593	65	M	1	0	1	0	1	0	0	0	0	severe	782	214	134	153	1649		YES
1022367	75	M	1	0	1	0	0	0	0	0	0	mild	439	866	192	37.3	676		YES
1020295	59	M	1	1	1	1	0	0	0	0	0	severe	231	509	110	199	1254		YES
1020750	64	M	1	1	0	0	1	1	1	0	0	severe	1014	1113	178	16.2	5000		YES
1022733	70	M	0	0	1	0	0	1	1	0	0	Moderate	104	402	12	11.5	103		YES
1020523	71	M	1	1	1	0	1	1	0	0	0	Moderate	344	93	89	32.2	290		YES
1019616	83	M	1	0	1	0	0	0	1	0	0	severe	1186	430	9.3	53	1043		YES
1022407	67	M	0	1	1	1	0	1	0	0	0	severe	269	234	56	46.8	1320		YES
1021629	73	F	1	1	1	0	1	1	0	0	0	mild	80.2	394	64	45.8	360		YES
1023926	72	M	1	0	1	0	1	1	0	0	0	severe	202	371	235	64	419		YES
1022264	60	M	1	1	1	0	0	0	0	0	1	severe	1013	969	145	946	1352		YES
1022671	39	M	0	1	1	0	0	0	0	0	0	mild	240	456	74	13	213		YES
1023965	70	M	1	1	1	0	1	1	0	0	0	severe	1434	709	169	8.48	644		YES
1022916	50	M	0	1	1	0	1	0	0	0	0	severe	1308	933	650	347	1392		YES
1022775	44	M	0	0	1	1	0	0	0	0	0	Moderate	20.3	244	26	115	244		YES
1022462	51	M	1	0	1	0	1	0	0	0	0	Moderate	2318	476	178	113	1349		YES
1022738	63	M	1	1	1	1	1	0	0	0	0	Moderate	413	750	56	26.6	1482		YES
1019602	68	M	1	1	1	0	1	0	0	0	0	severe	738	966	46	97.5	5000		YES
1020598	49	M	1	0	0	1	1	0	0	0	0	severe	1349	826	124	17.5	5000		YES
1022740	74	M	0	0	1	0	1	1	0	0	0	Moderate	499	3650	102	677	5000		YES
1023029	73	M	1	1	1	0	1	1	0	0	0	severe	745	456	121	18.8	4636		YES
1023296	66	M	1	1	1	0	1	1	0	0	0	severe	848	329	234	222	1573		YES
1023272	52	M	1	1	1	0	0	1	0	0	0	severe	517	819	219	124	1217		YES
1021459	56	M	0	1	0	1	1	0	0	0	0	severe	923	842	89	142	1765		YES
1021997	71	M	1	1	1	0	0	0	1	0	0	Moderate	271	854	32	19.6	660		YES
1021081	66	F	1	1	1	0	1	0	0	0	0	mild	82.9	280	13	164	328		YES
1021843	84	M	0	1	1	0	1	1	1	0	0	mild	385	489	102	16	898		YES
1021421	64	M	0	1	1	0	0	0	0	0	0	severe	1507	975	121	46	5000		YES
1021050	32	M	1	1	1	0	0	0	0	0	0	severe	759	579	79	64	1467		YES
1022051	65	M	1	1	1	0	1	1	0	0	0	severe	2000	670	83	768	346		YES
1024591	60	F	1	0	1	0	0	0	0	0	0	severe	978	156	210	127	847		YES
1021386	36	M	1	0	1	1	0	0	0	0	0	severe	466	143	327	20	975		YES
1020930	68	M	1	0	1	0	1	1	0	0	0	severe	632	732	171	57	1242		YES

1020766	56	M	0	0	1	1	1	1	1	0	0	Moderate	229	243	67	25	187		YES
1020760	56	M	0	0	1	0	1	1	0	0	0	Moderate	459	392	134	47	1858		YES
1019711	77	M	1	1	1	1	0	0	0	0	0	severe	1015	245	192	153	431		YES
1021514	65	F	0	1	1	0	1	1	0	0	0	severe	432	629	243	37.3	1528		YES
1021972	69	M	0	1	1	0	1	1	0	1	0	severe	904	415	353	199	509		YES
1021262	68	M	0	1	0	0	0	0	0	0	0	severe	2000	855	317	16.2	5000		YES
1020855	81	M	1	1	1	0	1	1	0	0	0	severe	465	527	232	11.5	5000		YES
1021636	61	M	1	1	1	0	1	0	0	0	0	severe	1341	416	262	43.4	1350		YES
1021999	50	M	0	1	1	0	1	0	0	0	0	severe	505	424	215	175	1770		YES
1021950	58	M	1	1	1	0	1	1	0	0	0	severe	529	683	224	43	1327		YES
1021326	57	M	0	1	1	1	0	0	1	0	0	severe	1133	538	250	8.69	4746		YES
1022949	84	M	1	1	1	0	0	1	0	0	0	severe	567	885	299	175	1580		YES
1021523	52	M	0	1	1	0	0	1	0	0	0	severe	317	820	335	135	5000		YES
1023099	81	M	1	0	1	0	0	1	0	0	0	severe	320	157	124	128	1245		YES
1021174	67	M	1	1	1	0	0	1	0	0	0	severe	38.9	435	343	136	425		YES
1022015	46	M	0	0	1	0	0	0	0	0	0	severe	937	2394	157	98	257		YES
1020115	78	M	0	0	1	0	1	1	1	0	0	Moderate	230	244	133	35	3427		YES
1019681	75	M	1	1	1	0	1	1	1	0	0	Moderate	2924	457	127	23.2	5000		YES
1020763	60	F	0	1	1	0	0	0	0	0	0	Moderate	341	231	56	550	424		YES
1023505	90	M	0	0	1	0	0	0	0	0	0	severe	1290	971	103	88.8	5000		YES
1022988	60	M	1	1	1	0	1	0	0	0	0	severe	615	613	246	110	1193		YES
1022752	38	M	1	1	1	0	0	0	0	0	0	severe	347	1089	89	55	1258		YES
1020910	59	M	1	1	1	0	1	0	0	0	0	severe	875	442	102	203	1416		YES
1021528	70	M	1	1	1	0	1	1	0	0	0	Moderate	2574	135	56	49.4	968		YES
1023093	70	M	1	1	0	0	1	0	0	0	0	Moderate	48.9	195	48	65	368		YES
1022908	55	F	1	0	1	0	0	0	0	0	0	severe	450	653	105	142	666		YES
1020525	50	M	0	0	1	0	0	0	0	0	0	severe	3037	140	213	579	5000		YES
1020446	46	M	0	0	1	1	0	0	1	0	0	mild	23.9	712	10	35	216		YES
1021029	75	M	1	1	1	0	0	0	0	0	0	severe	810	765	209	2353	5000		YES
1021362	52	M	0	1	1	0	0	0	0	0	0	Moderate	2839	1911	79	56	786		YES
1023170	47	M	1	1	0	0	0	0	0	0	0	severe	673	854	59	10.1	1141		YES
1019888	62	M	1	1	1	1	1	1	1	1	0	severe	46.3	634	59	105	1509		YES
1023297	49	M	1	1	1	0	0	0	0	0	0	Moderate	759	576	302	72.3	757		YES
1021203	60	M	0	1	1	0	0	0	0	0	0	Moderate	89.4	346	229	60.1	1301		YES
1021494	81	M	1	0	1	1	1	0	0	0	0	severe	513	476	119	80.4	1496		YES
1021238	74	M	0	0	1	1	1	1	1	0	0	severe	603	197	95	34	5000		YES
1023059	77	M	0	0	1	1	1	0	1	0	0	severe	387	410	13	62.9	999		YES
1020214	74	M	1	0	1	0	1	1	1	0	0	severe	305	511	78	116	517		YES
1020620	54	M	1	0	1	0	0	0	0	0	0	severe	90.6	289	83	135	5000		YES
1020695	70	M	0	1	1	0	1	1	0	0	0	severe	642	1478	90	79	5000		YES
1023607	63	M	0	0	1	1	0	1	0	0	0	severe	489	126	194	579	881		YES
1022686	58	M	0	1	1	0	1	1	0	0	0	severe	322	673	60	147	1806		YES
1024925	85	M	0	0	1	0	1	1	1	0	0	Moderate	1576	581	56	188	635		YES
1024541	80	M	0	0	1	0	1	0	0	0	0	severe	93.4	733	103	152	5000		YES
1023176	70	M	1	1	1	0	0	0	1	0	0	Moderate	402	342	124	932	5000		YES
1024729	80	F	0	1	1	0	1	1	0	0	0	Moderate	161	184	772	72.9	655		YES
1024059	79	M	1	1	1	1	1	0	0	0	0	severe	321	175	299	134	895		YES
1022971	57	M	1	1	1	0	0	0	0	0	0	severe	254	257	335	12	573		YES
1019824	58	M	1	1	1	0	1	0	0	0	0	severe	2254	869	124	162	1237		YES
1021994	70	M	0	1	0	1	1	0	0	0	0	severe	1243	758	343	261	884		YES
1024951	62	M	0	0	1	0	0	0	0	0	0	mild	34	342	157	13	204		YES
1023084	48	M	0	1	1	0	1	1	1	0	0	mild	383	946	44	54	1004		YES
1021702	63	M	1	1	1	1	1	1	0	0	0	Moderate	97	128	10	10	249		YES
1021782	52	M	1	1	1	0	0	0	0	0	0	mild	452	432	94	9.6	1442		YES
1023547	50	M	1	1	1	0	0	0	0	0	0	severe	625	765	157	36.5	791		YES
1024640	53	M	0	1	1	0	1	0	0	0	0	Moderate	448	341	99	106	1541		YES
1025352	75	M	0	1	1	0	1	1	0	0	0	Moderate	304	234	46	73	203		YES
1019820	72	M	1	1	1	0	1	1	1	0	0	severe	850	1032	95	43	750		YES
1024217	50	M	0	1	1	0	1	1	0	0	0	Moderate	134	174	367	306	646		YES
1021332	53	M	1	1	1	0	0	0	0	0	0	mild	25.8	452	526	26.8	688		YES
1022477	68	M	0	1	0	1	1	1	0	0	0	severe	121	1300	296	76.6	125		YES
1022029	40	M	1	1	1	0	1	0	0	0	0	severe	864	752	74	115	760		YES
1024348	70	M	0	0	1	1	1	1	0	1	0	Moderate	540	532	209	251	546		YES
1024624	63	M	1	1	1	0	0	0	1	0	0	Moderate	827	243	175	126	431		YES
1024645	41	M	0	0	1	1	0	0	0	0	0	severe	1200	394	113	85	735		YES
1023808	56	M	1	1	1	0	1	1	0	0	1	severe	1941	403	219	157	571		YES
1025470	26	M	1	0	1	1	0	0	0	0	0	severe	2117	114	280	648	3545		YES
1023934	55	M	1	1	1	0	1	1	0	0	0	severe	1988	459	200	138	4356		YES
1022690	53	M	1	1	1	1	0	0	0	0	0	severe	962	745	104	66.8	1308		YES
1022661	83	M	0	1	1	1	1	1	0	0	0	severe	1034	398	262	134	1391		YES
1021552	65	M	1	1	1	0	1	1	1	0	0	severe	320	347	215	584	1407		YES
1020443	67	F	1	1	1	1	1	1	0	0	0	severe	103	190	224	227	1307		YES
1021989	58	M	1	0	1	0	1	1	0	0	0	Moderate	434	674	250	45	764		YES
1019622	73	M	0	0	1	0	1	1	0	0	0	severe	4445	546	299	134	552		YES
1021177	70	M	1	1	1	0	0	0	0	0	0	Moderate	496	230	57	420	1543		YES
1021936	59	M	1	1	1	0	0	0	0	0	0	Moderate	308	299	88	67.4	295		YES
1022057	65	M	1	1	1	0	1	1	0	0	0	severe	2000	670	204	769	346		YES
1022895	50	M	0	0	1	0	0	0	1	0	0	Moderate	1571	1147	186	557	563		YES
1023903	43	M	0	0	1	0	0	0	0	0	0	mild	106	479	103	13	1484		YES

1024601	60	M	0	1	1	0	1	1	0	1	0	Moderate	53	868	66	113	1576		YES
1023569	43	M	0	1	1	0	0	0	0	0	0	Moderate	658	485	126	152	5000		YES
1018945	61	M	0	0	1	0	0	1	1	0	0	severe	1445	857	174	640	538		YES
1021758	88	M	1	1	1	1	0	1	0	0	0	severe	719	506	218	537	5000		YES
1015945	56	M	1	1	1	0	1	1	0	0	0	mild	92	152	25	42	285		YES
1020510	65	M	1	0	1	1	1	1	0	0	0	Moderate	683	139	102	117	534		YES
1025672	72	M	1	0	1	0	1	0	0	0	0	Moderate	774	694	34	57	4439		YES
1019111	55	M	0	0	1	0	1	1	1	0	0	severe	2442	1227	55	115	819		YES
1021563	69	M	1	0	1	0	1	1	0	1	0	Moderate	500	483	131	251	84.6		YES
1020369	72	M	0	0	0	0	0	1	0	0	0	Moderate	749	674	92	126	324		YES
1022589	79	M	1	0	1	0	0	1	0	0	0	Moderate	358	577	36	85	520		YES
1022785	69	M	1	1	1	0	1	1	0	0	0	severe	2032	718	204	260	1000		YES
1022551	65	M	1	1	0	0	1	0	0	0	0	mild	109	243	104	866	1335		YES
1023361	44	F	1	1	1	0	0	0	0	0	0	severe	392	692	103	157	2548		YES
1023824	55	M	1	1	1	0	0	0	0	0	0	severe	921	804	201	356	335		YES
1023584	62	M	1	0	1	0	1	0	0	0	0	severe	2048	392	331	5000	5000		YES
1022527	43	M	1	0	1	0	0	0	0	0	0	Moderate	163	728	22	113	866		YES
1021550	46	M	1	0	1	0	0	1	0	0	0	Moderate	730	813	67	3.24	1330		YES
1021982	82	M	0	0	1	0	1	0	1	0	0	severe	1470	956	188	120	678		YES
1024504	70	M	1	0	1	0	0	0	0	0	0	severe	839	255	232	222	793		YES
1020934	48	M	0	0	1	0	1	0	0	0	0	severe	783	653	262	124	1634		YES
1024657	60	M	1	0	1	0	1	1	0	0	0	severe	1468	894	215	142	337		YES
1024119	61	F	0	0	1	0	1	1	0	0	1	Moderate	532	645	224	118	1510		YES
1023280	68	F	1	1	1	0	1	1	0	0	1	Moderate	482	376	250	222	595		YES
1024344	55	M	1	1	1	0	1	1	0	0	0	Moderate	849	344	299	124	5000		YES
1023073	65	M	1	1	1	0	0	1	0	0	0	Moderate	457	674	335	142	5000		YES
1026018	59	M	1	1	0	0	1	0	0	0	0	severe	2731	584	124	5000	7673		YES
1025663	74	M	1	1	0	0	1	0	0	1	0	severe	894	721	343	786	806		YES
1020566	56	M	1	1	1	1	1	0	0	0	0	severe	587	554	157	185	1225		YES
1021679	70	M	1	1	1	0	0	0	0	0	0	severe	516	378	133	126	547		YES
1021224	56	M	1	0	1	0	0	0	0	0	0	Moderate	560	711	127	43.2	1068		YES
1020524	34	M	1	1	1	0	0	0	0	0	0	Moderate	455	340	56	58.8	2475		YES
1025810	63	F	1	1	0	0	1	1	0	0	0	mild	90.4	139	103	45	274		YES
1021991	27	M	1	1	1	0	0	0	0	0	0	mild	20	176	246	105	327		YES
1025802	55	M	1	1	0	0	0	1	0	0	0	severe	1477	724	89	290	5000		YES
1023593	43	M	1	1	0	0	0	0	0	0	0	severe	2000	486	128	494	4316		YES
1022589	79	M	1	0	1	0	0	0	0	0	0	Moderate	102	560	102	222	234		YES
1027390	73	M	0	1	1	0	1	1	0	0	0	severe	1826	786	242	124	1402		YES
1019584	56	M	1	1	1	0	1	1	0	0	0	severe	49.2	762	105	142	5000		YES
1025000	77	F	1	1	1	0	1	1	0	1	0	Moderate	898	337	563	1369	1294		YES
1020217	60	M	1	0	1	0	0	0	0	0	0	mild	328	262	98	23	223		YES
1022452	45	M	1	0	1	0	0	1	0	0	0	Moderate	422	1036	44	296	659		YES
1021757	59	M	1	1	1	0	1	1	0	0	0	Moderate	293	968	231	27	580		YES
1020836	74	M	0	0	1	1	1	1	0	0	0	severe	1270	611	100	135	4894		YES
1021162	78	M	1	1	1	1	1	1	0	0	0	Moderate	651	483	56	102	1103		YES
1023054	68	M	1	0	1	0	0	0	0	0	0	mild	29.4	285	13	23	948		YES
1026323	65	M	1	0	0	0	0	0	0	0	0	severe	967	894	167	279	1379		YES
1019895	41	M	0	0	1	0	0	0	0	0	0	severe	984	985	201	77.6	411		YES
1019339	65	M	0	0	1	0	1	0	0	0	0	severe	2292	1200	513	345	5000		YES
1023500	65	F	1	1	0	0	1	0	1	0	0	moderate	203	478	156	1108	1379		YES