Dissertation on

STUDY OF ASSOCIATION OF BIOCHEMICAL MARKERS AND RADIOLOGICAL FINDINGS WITH THE SEVERITY OF COVID-19 INFECTION IN DIABETIC PATIENTS

Submitted in partial fulfillment of the

Requirement for the award of the Degree of

DOCTOR OF MEDICINE

BRANCH I - GENERAL MEDICINE

MADURAI MEDICAL COLLEGE, MADURAI.

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI-600 032. TAMILNADU

APRIL 2022

CERTIFICATE FROM THE DEAN

This is to certify that this dissertation entitled **"STUDY OF ASSOCIATION OF BIOCHEMICAL MARKERS AND RADIOLOGICAL FINDINGS WITH THE SEVERITY OF COVID-19 INFECTION IN DIABETIC PATIENTS"** submitted by **Dr.A.SUGANTHI,** Post graduate in Madurai Medical College, Madurai to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment of the requirement for the award of degree of **Doctor of Medicine (M.D), Branch-I - General Medicine,** is a bonafide research work carried out by her under my direct supervision & guidance.

Dr.A.RATHINAVEL M.S.,Mch.,Ph.D.,
Dean,
Madurai Medical College,
Madurai.

CERTIFICATE FROM HEAD OF DEPARTMENT

This is to certify that the dissertation entitled **"STUDY OF ASSOCIATION OF BIOCHEMICAL MARKERS AND RADIOLOGICAL FINDINGS WITH THE SEVERITY OF COVID-19 INFECTION IN DIABETIC PATIENTS"** submitted by **Dr.A.SUGANTHI,** Post graduate in Madurai Medical College, Madurai to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment of the requirement for the award of degree of **Doctor of Medicine (M.D) Branch-I - General Medicine,** is a bonafide research work carried out by her under my direct supervision & guidance.

Dr. M. NATARAJAN M.D.,
Professor and HOD,
Department of General Medicine,
Madurai Medical College, Madurai

CERTIFICATE FROM GUIDE

This is to certify that the dissertation entitled **"STUDY OF ASSOCIATION OF BIOCHEMICAL MARKERS AND RADIOLOGICAL FINDINGS WITH THE SEVERITY OF COVID-19 INFECTION IN DIABETIC PATIENTS"** submitted by **Dr.A.SUGANTHI**, Post graduate in Madurai Medical College to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment of the requirement for the award of degree of **Doctor of Medicine (M.D) Branch-I - General Medicine,** is a bonafide research work carried out by her under my direct supervision & guidance.

Dr. K. SENTHIL M.D.,
Professor of Medicine,
Madurai Medical College, Madurai

CERTIFICATE - II

This is to certify that this dissertation work titled "**STUDY OF ASSOCIATION OF BIOCHEMICAL MARKERS AND RADIOLOGICAL FINDINGS WITH THE SEVERITY OF COVID-19 INFECTION IN DIABETIC PATIENTS"** of the candidate **Dr.A.SUGANTHI** with registration Number **201911122** for the award of **DOCTOR OF MEDICINE** in the branch of **GENERAL MEDICINE.** I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **0% (Zero percentage)** of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

URKUND REPORT

Curiginal

Document Information

Analyzed document	STUDY OF ASSOCIATION OF BIOCHEMICAL MARKERS AND RADIOLOGICAL FINDINGS WITH THE SEVERITY OF COVI-19 INFECTION IN DIABETIC PATIENTS.docx (D123206853)
Submitted	2021-12-20T13:05:00.0000000
Submitted by	A. SUGANTHI
Submitter email	sugudoctor@gmail.com
Similarity	0%
Analysis address	sugudoctor.mgmu@analysis.urkund.com

Sources included in the report

SA	**Pramodh kumar.pdf** Document Pramodh kumar.pdf (D111622716)	1

INSTITUTIONAL ETHICS COMMITTEE MADURAI MEDICAL COLLEGE & GOVT. RAJAJI HOSPITAL, MADURAI
CDSCO:Reg.No.ECR/1365/Inst/TN/2020 & DHR Reg.No.EC/NEW/INST/2020/484

Title of work	:	STUDY OF ASSOCIATION OF BIOCHEMICAL MARKERS AND RADIOLOGICAL FINDINGS WITH THE SEVERITY OF COVID-19 INFECTION IN DIABETIC PATIENTS
Principal Investigator	:	Dr.A.SUGANTHI
Designation	:	PG in MD., GENERAL MEDICINE (2019 – 2022)
Co-Investigators	:	Guide:Prof.Dr.K.SENTHIL,M.D.,Gen.Medicine Professor of General Medicine
Department	:	Department of General Medicine , Govt. Rajaji Hospital attached to Madurai Medical College, Madurai

The request for an approval from the Institutional Ethics Committee (IEC) was considered on the IEC meeting held on 16.12.2020 at Auditorium, Govt. Rajaji Hospital, Madurai at 10.00 AM.

The Members of the committee, the Secretary and the Chairman are pleased to inform you that your proposed project mentioned above is **Approved.**

You should inform the IEC in case of any changes in study procedure, methodology, sample size investigation, Investigator or guide or any other changes.

1. You should not deviate from the area of work for which you had applied for ethical clearance.

2. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions. If encountered during from study.

3. You should abide to the rules and regulations of the institution(s)

4. You should complete the work within the specific period and if any extension is required, you should apply for the permission again for extension period.

5. You should submit the summary of the work to the ethical committee on completion of the study.

MEMBER SECRETARY,
IEC, Madurai Medical College,
Madurai

Dr.K.RAADHIKA, M.D(Pharm)
Associate Professor
Member Secretary
IEC - Madurai Medical College
Madurai.

29 DEC 2020

CHAIRMAN,
IEC, Madurai Medical College,
Madurai

Prof. Dr.V. Nagaraajan
MD.,MNAMS.,DM.,DSC(Neuro).,DSC(Hon)
CHAIRMAN
IEC Madurai Medical College
Madurai

DECLARATION

I, **Dr.A.SUGANTHI** solemnly declare that, this dissertation **"STUDY OF ASSOCIATION OF BIOCHEMICAL MARKERS AND RADIOLOGICAL FINDINGS WITH THE SEVERITY OF COVID-19 INFECTION IN DIABETIC PATIENTS"** is a bonafide record of work done by me at the Department of General Medicine, Madurai Medical College, Madurai under the guidance of Professor **Dr. K. SENTHIL M.D,** Department of General Medicine, Madurai Medical college, Madurai from January 2021 to June 2021. I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree or diploma to any other University, Board either in India or abroad. This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the award of Degree of Doctor of Medicine (M.D.), general Medicine Branch-I examination to be held in April 2022.

PLACE: MADURAI **Dr. A.SUGANTHI**

DATE:

ACKNOWLEDGEMENT

I would like to thank the Dean, Professor. **Dr.A.RATHINAVEL M.S.,Mch.,Ph.D.,** Madurai Medical College, for permitting me to utilize the hospital facilities for the dissertation.

I also extend my sincere thanks to **Dr.M.NATARAJAN M.D.,** Head of the Department and Professor of Medicine for his constant support during the study.

I would like to express my deep sense of gratitude and thanks to my unit Chief, Professor. **Dr. K. SENTHIL M.D,** my guide and Professor of Medicine, for his valuable suggestions and excellent guidance during the study.

I am greatly indebted to my beloved Professors **Dr. G. BAGIALAKSHMI, M.D., Dr. C. DHARMARAJ, M.D. DCH, Dr. DAVID PRADEEP KUMAR, M.D. Dr. SENTHAMARAI, M.D., Dr. VIVEKANANTHAN M.D.,DTCD., Dr. V.N ALAGAVENKATESAN M.D., and Dr. J. SANGUMANI, M.D.,** for their valuable suggestions throughout the course of study.

I offer my special thanks to **Dr.P.MOHAN KUMARESH.M.D.,** the Head of department of Biochemistry, **Dr.K.RANI.M.D.,** the Head of department of Pathology, **Dr.S.SUMATHY, MDRD., DGO.,** the Head of department of Radiodiagnosis for their kind co-operation and valuable guidance.

I thank all my Associate Professors **Dr.K.MURALIDHARAN M.D., Dr.S.KRISHNASAMY PRASAD M.D., Dr.R.PANDICHELVAN M.D.,** and all the Assistant Professors of my Unit **Dr.V.MANIKANDAN.M.D., Dr.C.RAMANAN.M.D.,** and **Dr.S.SARAVANAMADAV.M.D.,** for their help and constructive criticisms.

I sincerely thank all the staffs of department of Medicine, biochemistry, pathology and Radiodiagnosis for their timely help rendered to me, whenever and wherever needed.

I extend my love and express my gratitude to my Co PGs, Dr. Sai Sathish, Dr.Mudavath Vinay naik Chauhan, Dr.John Bill Clinton, Dr.Mukeshwar Dr.Gopinathan and Dr.Mimi Janet for their constant support during my study period.

I also thank all the patients who participated in this study for their extreme patience and kind co-operation.

I’m grateful to my parents and friends who have helped making this study a reality.

Above all, I thank the almighty God who has showered blessings on me and guided me in every step of the dissertation.

LIST OF ABBREVIATIONS

ACE	-	Angiotensin converting enzyme
ARDS	-	Acute respiratory distress syndrome
COVID-19	-	Corona virus disease 2019
CRP	-	C-Reactive protein
CT	-	Computed tomography
ELISA	-	Enzyme linked immuno sorbent assay
IL-6	-	Interleukin-6
LDH	-	Lactate dehydrogenase
MERS CoV	-	Middle East Respiratory Syndrome Corona virus
NCDC	-	National Centre for Disease Control
NLR	-	Neutrophil Lymphocyte Ratio
NSAID	-	Non Steroidal Anti Inflammatory Drugs
PNC	-	Platelet Neutrophil Complexes
SARS-CoV-2	-	Severe acute respiratory syndrome corona virus – 2
RT-PCR	-	Reverse transcriptase polymerase chain reaction

TABLE OF CONTENTS

INTRODUCTION

During December 2019, cluster of cases of pneumonia of unknown cause reported in Wuhan city, located in Hubei province of China. Later they identified these pneumonia as caused by a novel coronavirus. Initially this virus was called as 2019 novel coronavirus. Then these viruses are named by International committee on Taxonomy of viruses as Severe Acute Respiratory Syndrome Corona Virus – 2 (SARS-CoV-2). Coronavirus disease 2019 also known as COVID-19, was declared by World Health Organization, on February 11, 2020.

The COVID-19 infection more likely affects the persons with advanced age or with other comorbidities. COVID-19 infection mostly produces fever, dry cough, malaise, fatigue, diarrhoea and other nonspecific symptoms of upper respiratory tract. But in some patients, the infection can result in severe pneumonia and even fatal respiratory diseases known as acute respiratory distress syndrome (ARDS). Patients with severe infection had dyspnea, and they required ICU admission and oxygen therapy.

Diabetes is the most common non-communicable disease, characterized by chronic hyperglycaemia, either due to absolute or relative deficiency of insulin secretion or by its action. Diabetes can be divided into two types. Type I diabetes mellitus is also known as insulin dependent diabetes mellitus. Type II diabetes mellitus is also known as Non-insulin diabetes mellitus. Patients with diabetes are at higher risk of all infections. Because of defect innate immunity, impaired

phagocytosis and bactericidal activity, they are more prone for high risk of both infection and severity of the disease.

Diabetic patients with COVID-19 infection had higher levels of inflammatory biomarkers like C-reactive protein, serum ferritin, lactate dehydrogenase, high neutrophil-lymphocyte ratio than those without diabetes. Severity of pneumonia and need for oxygen support also is higher in diabetic patients.

The Novel corona virus nucleic acids are detected in nasopharyngeal and throat swabs, sputum, blood and lower respiratory secretions. Hence viral nucleic acid testing by RT-PCR is used for diagnostic purpose. The Clinical history, symptoms, laboratory findings like lymphopenia, elevated CRP, LDH, along with chest imaging play a vital role in diagnosis of COVID-19 infection. Computed tomography of chest is helpful in early detection and diagnosis of COVID-19 infection, which shows multiple patchy areas of ground glass opacity in the periphery of the lungs.

Due to advancement in transport facilities across the world and easy mode of spread, there was rapid spread of COVID-19 infection and resulted in high mortality. The spread of disease and mortality can be better prevented by breaking the chain of transmission of the virus by social distancing, use of face mask, early identification and isolation of the patients and adequate tertiary treatment. Most of the countries affected by COVID-19 imparted the complete lockdown to prevent the spread and mortality of the disease.

Though COVID-19 infection affects the people of middle age to elderly, the association of co-morbidities is one of the most important factor for the severity, prognosis and mortality of the patients. Of those other co-morbidities, diabetes is considered to be the most potential for the severity of any infection including COVID-19 infection. The prevalence of diabetes is more in developing countries like India, and so there is need for early identification of the diabetic patients who may progress for mortality of the disease. The pandemic of COVID-19 may lead to high mortality which reflects in terms of socioeconomic problems to the family as well as the country.

Hence we made an attempt to study the association of biochemical markers and radiological findings with the severity of COVID-19 infection in diabetic patients. The present study will be useful to the clinicians for treating the diabetic patients in COVID-19 care centres. The knowledge of the association of the biochemical markers and radiological findings will also help in early identification of severe patients and prevent the mortality of the patients.

AIM AND OBJECTIVES

This study is aimed at observation and analysis of the biochemical and radiological markers that have association with the severity of COVID-19 in diabetic and non-diabetic patients with the following objectives.

1. Evaluation of biochemical markers in diabetic and non-diabetic patients with COVID-19 infection.
2. Evaluation of imaging findings in diabetic and non-diabetic patients with COVID-19 infection and analysing the pattern of involvement.
3. Correlation of degree of association of these biochemical markers and the imaging with severity of COVID-19 infection.

REVIEW OF LITERATURE

HISTORY OF COVID-19

During 20th century, two strains of human coronaviruses identified to cause human diseases are 22E (HCov-229E), OC43 (HCov-OC43). SARS associated corona viruses (SARS-CoV) are causing infection in animals and also in humans. One of the major devastating epidemic occurred in November 2002 to July 2003. It causes mortality rate of 10% across the world.

The COVID-19 infection, declared as a public health emergency of international concern on 30th January, 2020 was also declared as a pandemic disease on 11th March, 2020. Novel coronavirus has spread beyond China to other countries and other continents like South Korea, Japan, Italy, Iran, United States, India, etc. causing pandemic outbreak.

Corona viruses are positive strand RNA viruses belongs to Coronaviridae family. It is a lipid enveloped virus with helical capsid symmetry. Genome size is about 16-21kb. Corona virus and its members of the genus causes respiratory illness. Non-segmented virus with petal /club shaped projections. Corona viruses also affects animals.

The route of entry for SARS-COV is through respiratory tract and causing viral pneumonia and other systemic illness. But it lacks upper respiratory symptoms. Most of the patients presented with cough and dyspnea. Many patients typically presented with fever, myalgia and watery diarrhoea.

HCoV-NL63, is a group 1 corona virus causing both upper and lower respiratory illness. HCoV-HKU1 was first identified in 2005, belongs to group 2 coronaviruses. MERS-CoV, Middle East Respiratory Syndrome Corona Virus identified in 2012 is with 35% mortality in humans. It is emerged from bats.

There were 6 genotypes of human corona viruses identified until December 31st, 2019. Novel coronaviruses/SARS CoV-2 was identified during December, 2019.

Types of coronaviruses:

1. 229E (Alpha coronavirus)
2. NL63 (Alpha coronavirus)
3. OC43 (Beta coronavirus)
4. HKU1 (Beta coronavirus)
5. MERS-CoV (Beta coronavirus)
6. SARS-CoV (Beta coronavirus)
7. SARS CoV-2 (Novel coronavirus)

SARS-CoV-2 has beta corona virus linkage, under sarbecovirus subgenus. These viruses has 79% of sequence similarity with SARS-CoV and 50% sequence similarity with Middle East Respiratory Syndrome Corona Virus (MERS-CoV).

Alpha (α, B.1.1.7), beta (β, B.1.351), gamma (γ, P1) and delta (δ, B.1.617.2) are the four genera of corona viruses. Among them alpha or beta group of viruses causing infection in humans, Gamma and delta viruses to infect birds. SARS CoV, MERS CoV and SARS CoV-2 are the highly pathogenic viruses. They produce severe

pneumonia in humans in the form of diffuse alveolar damage, ARDS, Respiratory failure ultimately leading to increased morbidity and mortality.

The coronaviruses can cause respiratory and enteric infections. This COVID-19 outbreak is believed to be a zoonotic origin. SARS-CoV-2 is highly contagious, thus early detection and diagnosis and isolation of cases is very important public health issue in control of outbreak.

ETIOLOGY

Civet cats and Dromedary were the intermediate host for SARS-CoV and MERS-CoV respectively. There were no known intermediate host for SARS-CoV-2. Human to human transmission of SARS-CoV-2 (COVID-19) mainly spreads through respiratory droplets and contact.

Virus	Genus	Reservoir host	Receptor	Origin of virus
SARS-CoV-2	Beta coronavirus	Bat	ACE-2	Wuhan, china
SARS-CoV	Beta coronavirus	Bat	ACE-2	Guangzhou, china
MERS-CoV	Beta coronavirus	Bat	CD26/DPP4	Saudi Arabia

Many studies reported that patients with pre-existing co-morbid illness developed severe disease. In patients with severe disease had elevated levels of CRP, lymphopenia due to reduction in CD3+, CD4+, and CD8+T cells.

STRUCTURE OF CORONA VIRUS

The nCOVID-19 virus is an enveloped virus with 80 to 120nm in diameter. It has a positive single stranded RNA genome of 31kb size. This genome, contain a basic nucleocapsid (N) protein in a complex form, forms a helical viral protein called spike protein (S). Spike protein is a type-1 glycoprotein forms a peplomer on the surface of the virion gives rise to crown-like appearance.

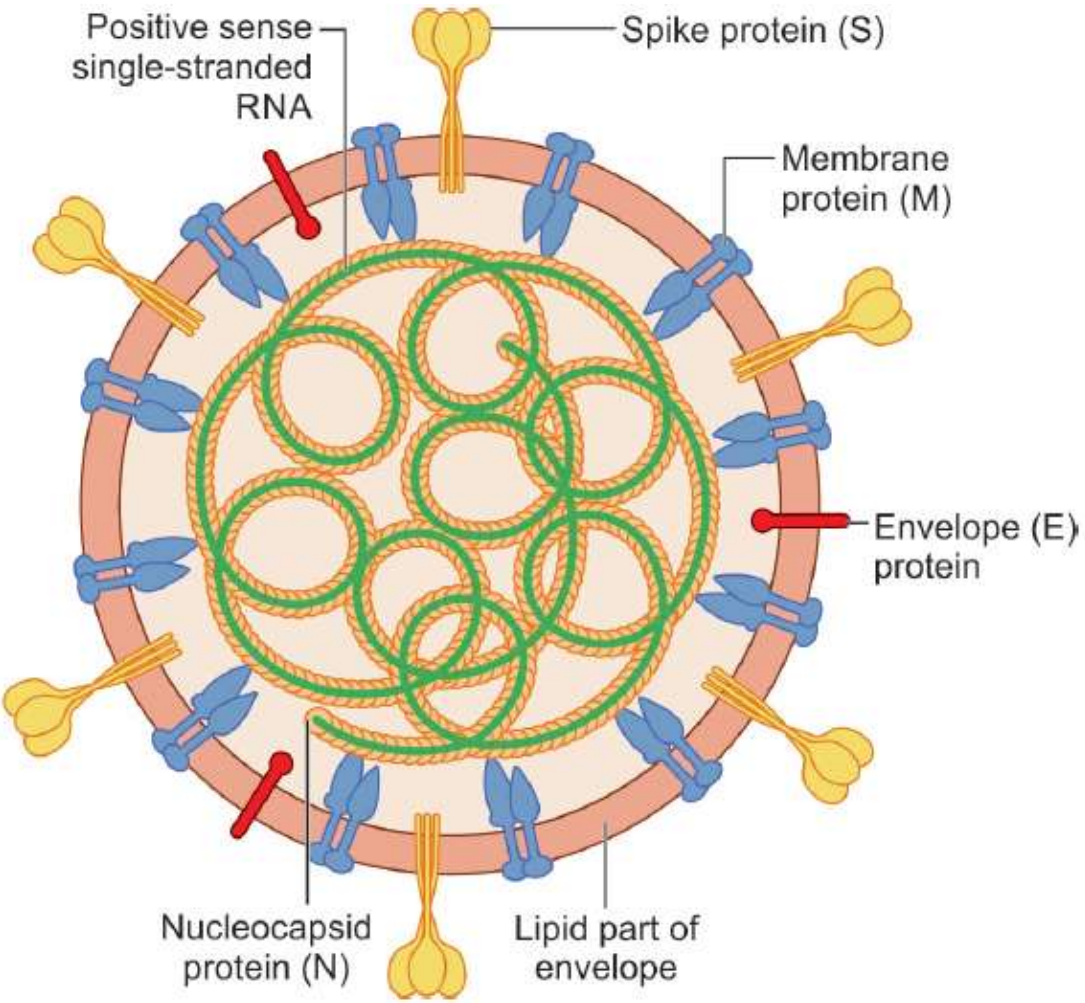
The coronaviruses comprise of specific genes in open reading frames (ORF1) regions which encode proteins used for viral replication, spike formation, and the formation of nucleocapsid. The coronavirus also has receptor binding domain, through which it affects the multiple host. Most coronaviruses recognize carbohydrates or amino peptidases receptor for entry to the host cells, while MERS-CoV and SARS-CoV recognize exopeptidases.

The cellular proteases including cathepsins, HAT (Human Airway Trypsin like protease), and TMPRSS2 (Trans Membrane Protease Serine-2), which splits up the spike protein facilitate the entry of virus. MERS coronavirus uses DPP4 (Di-Peptidyl Peptidase 4) receptors. ACE-2 (Angiotensin Converting Enzyme-2) is the specific receptor for SARS-CoV-2. ACE-2 is mainly expressed in type II alveolar epithelial cells. Primary target for COVID-19 is the type II alveolar cells.

The structure of nCOVID-19 consists of typical spike glycoproteins (S) which facilitates the entry of viruses by attachment with ACE-2 receptors. It is also referred to as CoV S protein and determines the infectious nature, virus virulence, host specificity and tissue tropism. Spike protein has two subunits. S1 subunit is

responsible for binding to ACE-2 in the host cell facilitating viral attachment to the surface of target cells. S2 subunit favours the fusion of viral and host cell membranes. Nucleocapsid (N) protein interfere with host immune responses. Membrane glycoproteins (M) is mainly for budding and transport of nutrients.

The envelope protein (E) has a lipid bilayer. Other proteins are Chymotrypsin-like protease, RNA polymerase, Helicase and Papain-like protease.



STRUCTURE OF COVID-19

MODES OF TRANSMISSION OF COVID – 19

1. DROPLET TRANSMISSION

Direct transmission via cough, sneezing, speaking, spitting.

Limited to a distance of 6 feet or with in 2m

Particle size is about 5-10 micrometer in diameter.

2. FOMITE TRANSMISSION

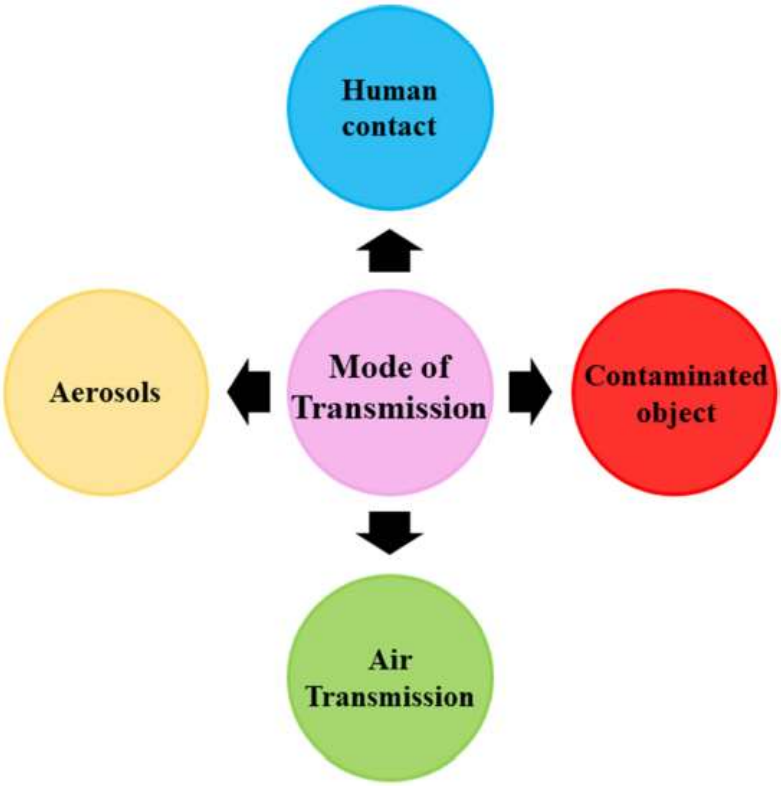
Indirect transmission through the contaminated surfaces of inanimate objects then touching the nose, eyes, mouth.

3. AIRBORNE – DROPLET NUCLEI TRANSMISSION

It is a type of indirect transmission. Particle size is about less than 5 micrometre. Aerosols, drops, direct contact with infected persons are the usual way of transmission. Hence aerosol producing processes likely to produce COVID-19 infection. They are

- Nebulisation
- Cardiopulmonary resuscitation
- Bronchoscopy
- Tracheostomy
- Endotracheal intubation
- Non-invasive positive pressure ventilation

Zoonotic mode of transmission also reported in China in the initial pandemic period.



MODE OF TRANSMISSION OF NOVEL COVID-19

INCUBATION PERIOD

The incubation period is the time interval between infectivity and onset of disease. The median incubation period for COVID-19 is 5-7 days but incubation period range varied from 1-14 days. Hence 14 days quarantine period is advised to limiting the movement of individuals at risk. COVID-19 outbreak is an example for propagated epidemic.

The National Centre for Disease Control (NCDC) defines the suspect case of SARS-CoV-2, as any person with acute onset of two or more of the following

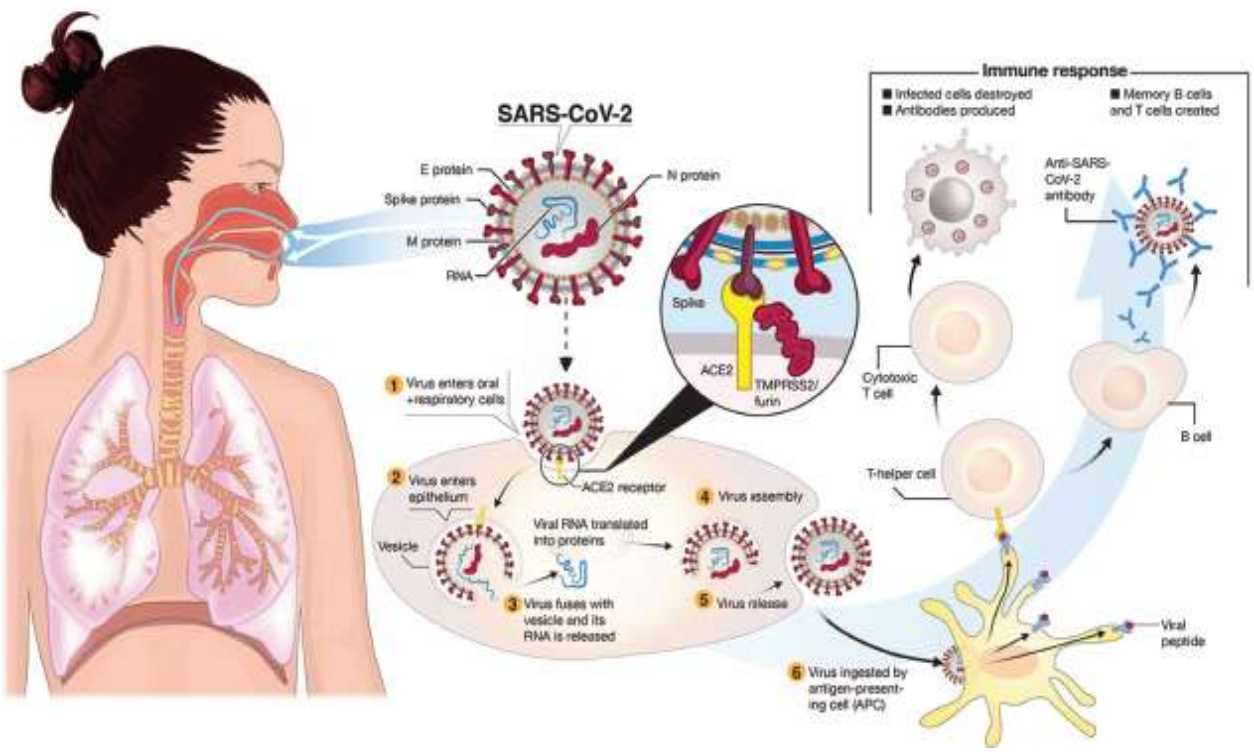
- Fever
- Cough
- Loss of taste
- Loss of smell
- Fatigue /generalised weakness
- Headache
- Myalgia
- Diarrhoea
- Sore throat
- Running nose /nasal congestion
- Loss of appetite /poor feeding
- Nausea / vomiting
- Altered mental status

THE LIFE CYCLE OF nCOVID-19 IN HUMAN CELLS

The COVID-19 infection and disease severity depends on virulence of infecting virus, and host factors. SARS-CoV-2 virus predilection to respiratory system, and produce pneumonic changes in lungs. A named protease - furin enhances viral entry. This protease level is elevated in diabetic patients. Spike proteins bind to

the ACE-2 receptor, after binding, conformational changes occur in the spike protein facilitating the fusion of the viral envelope with the host cell membrane.

After entering the host cell, the virus releases its RNA into the cell and the process of translation begins inside the cell. Acidic environment in the cytosol, presence of cathepsin favours the viral replication. Replicase polyproteins (pp1a and 1ab) are then cleaved by proteinases into smaller products. The viral genome RNA and the proteins assembled in the endoplasmic reticulum and Golgi complex as virions are then carried out through the vesicles and released out from the cells.



LIFE CYCLE OF nCOVID-19 IN HUMAN CELLS

IMMUNE DYSREGULATION AND COVID-19

In humans, two types of immunity play a role against pathogens - Natural (innate) and Specific (adaptive) immunity. Innate immunity is the first line of defence against pathogens, fast in response and has no antigen specificity. No long lasting immunity.

The human innate immune system consists of epithelial barriers on the surface of skin and mucous membrane. Cellular defences are neutrophils, macrophages, dendritic cells, natural killer cells, mast cells, lymphoid cells. Soluble mediators are kinins, C-reactive proteins, mannose binding lectin, surfactant coating the respiratory passages - Pattern recognition receptors, Toll-like receptors, NOD-like receptors, RIG-I-like receptors, and C-type lectin receptors.

The characteristic feature of COVID-19 is immune dysregulation in which there will be an increased cytokine release associated with reduced interferon response, lymph depletion and hyper activation of innate immunity.

RISK FACTORS FOR SEVERE COVID-19 INFECTION

- Type II Diabetes mellitus
- Serious cardiovascular disease
- Chronic obstructive pulmonary disease (COPD)
- Chronic kidney disease (CKD)
- Active malignancy

- Obesity
- Solid organ transplant history

FACTORS POSSIBLY INCREASE THE RISK FOR SEVERE COVID-19

- Type1 Diabetes mellitus
- Bronchial Asthma
- Cerebrovascular accident
- Pulmonary fibrosis
- Cystic fibrosis
- Current tobacco use
- Hypertension
- Immunocompromised state
- Liver disease
- Pregnancy

PATIENT CHARACTERISTICS WORSENING THE SEVERITY

- Obese
- Older age
- Frailty
- Uncontrolled and long diabetes duration
- Other comorbidities

OUTCOME WORSENING MEDIATORS

- Hyperglycemia
- Increased stress hormones
- Advanced glycation end products (AGEs)
- Impaired clotting
- Increased cytokines
- Oxidative stress
- Reduced lymphocytes
- Thromboembolic events
- Increased inflammatory markers
- Increased D-dimer
- High AST, ALT
- High Creatine phosphokinase
- High troponin

PATHOGENESIS OF COVID-19 INFECTION

COVID-19 infection is divided into three phases.

PHASE 1: INITIAL/EARLY INFECTIVE PHASE

Patient will have headache, fever,dry cough, laboratory findings suggestive of lymphopenia, elevated IL6, D-dimer and prothrombin with mild elevation of LDH.

PHASE2: PULMONARY PHASE

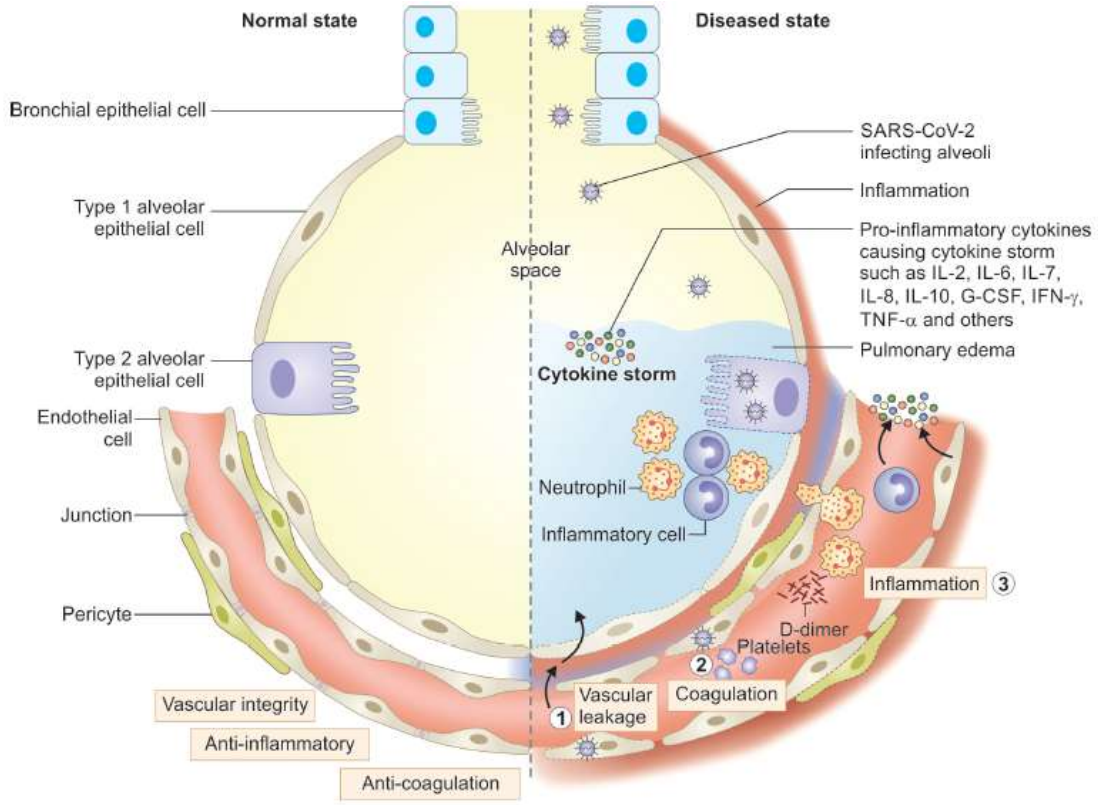
Patient with breathlessness and abnormal chest images, Elevated levels of serum transaminase levels. Some patients may go for serious cytokine storm, ultimately leads to shock, multi organ failure, ARDS, and death

PHASE 3: HYPERINFLAMMATION

In this phase, patient will have elevated levels of inflammatory biomarkers such as lactate dehydrogenase, C-reactive protein, serum ferritin, troponin, D-dimer, IL6.

In the respiratory system, inflammation occur with generation of multiple inflammatory cytokines and chemokine such as

- Tumour necrosis factor-alpha (TNF-α)
- Interleukin 1, 7-10
- Interferon gamma
- Granulocyte colony stimulating factors
- Granulocyte monocyte colony stimulating factors
- Fibroblast growth factor 2
- Monocyte chemo attractant protein 1
- Macrophages inflammatory protein 1alpha



The normal alveolus is shown on the left side. During acute phase of acute lung injury and ARDS, the injured alveolus is shown on the right side.

PATHOPHYSIOLOGY

The receptors involved in SARS-CoV-2 infection are ACE-2 and DPP4. They play a vital role in viral entry. Spike protein of the virus having high affinity for binding to ACE-2 receptor. In this process, TMPRSS2 also play role. Some studies reported that DPP4 is also a potential binding site for SARS-CoV-2. ACE-2 and TMPRSS2 are also expressed in renal, myocardial, neurologic, gastrointestinal tissues. So SARS-CoV-2 also has tropism to these tissues leading to direct viral tissue damage.

After entry, SARS-CoV-2 cause inflammation and endothelial damage and also create a prothrombotic state. Ultimately this result in increased thrombin production and inhibition of fibrinolysis. Activation of complement system leads to micro thrombi formation and deposition. There is activation of macrophages and cross talk between platelets and neutrophils play a role in pro-inflammatory effects, and formation of neutrophil extracellular traps (NETs), cytokine release and micro thrombi deposition. Acute lung injury can activate hypoxia inducible factor 1(HIF-1) signaling pathway through a mechanism related to hypoxia-induced hyper viscosity, which can increase the prothrombotic state.

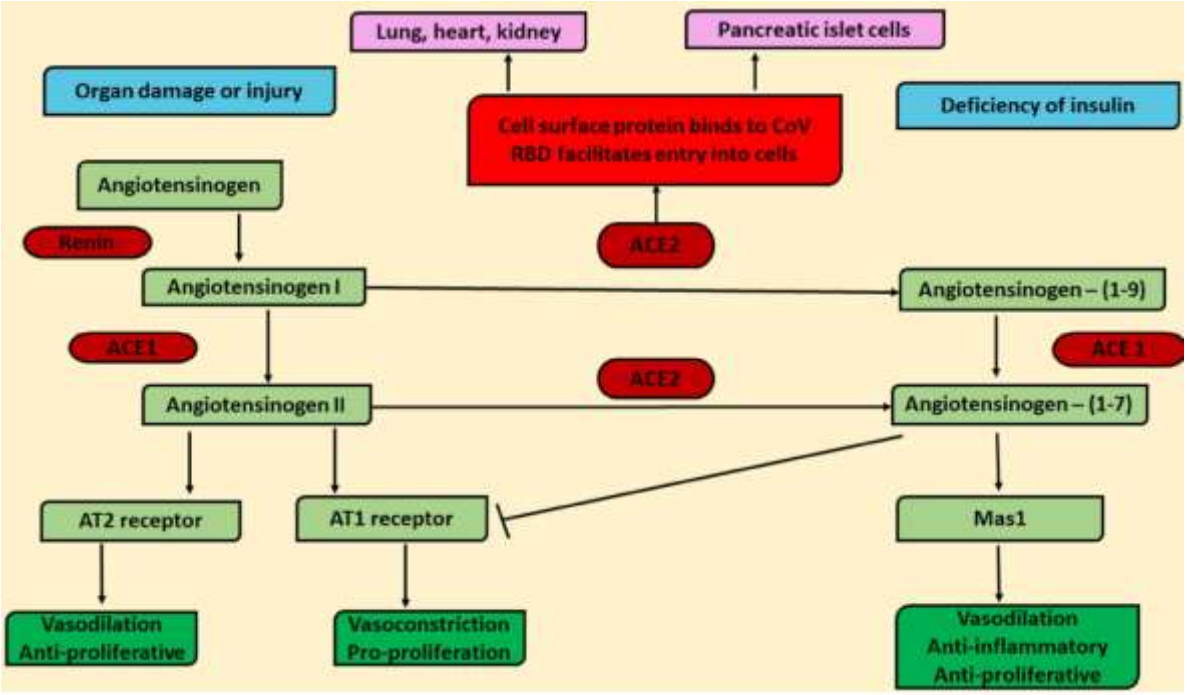
Two main pathophysiology involved in the COVID-19 infection are

1. Poor interferon response

2. Accelerated inflammatory response

RAAS (Renin angiotensin aldosterone system) DYSREGULATION:

RAAS system play role in many homeostatic processes such as regulation of blood pressure, fluid and electrolyte balance, tissue growth and vascular permeability. Angiotensin I is converted into angiotensin II by the enzyme Angiotensin converting enzyme (ACE). Angiotensin II causes vasoconstriction and proliferation. ACE2 cleaves Angiotensin I to inactive angiotensin 1-9, Angiotensin II to angiotensin 1-7, which has vasodilator and anti-fibrotic effects.



ACE2 ROLE IN COVID-19 PATHOGENESIS

DIAGNOSIS OF COVID-19

1. RT-PCR TEST

Real-time fluorescence based quantitative PCR is used as a standard test for COVID-19. Single stranded RNA of coronavirus is detected in nasal, nasopharyngeal swabs, sputum, broncho alveolar lavage secretion. Real-Time PCR is most widely used test for COVID-19 diagnosis. In this method, RNA is converted into cDNA by reverse transcriptase, which is quantified by different primer sets, using RNAse P as an internal control.

Primer which targets E gene, N gene, RNA replicase or RdRp. Number of multiplex assays also later developed, which can targets multiple genes together.

Sensitivity of multiplex assay is >95%.

False positive results obtained because of cross-reactivity of primer with other coronaviruses like SARS-CoV.

False negative results due to irregular sampling of samples, laboratory error, insufficient viral material in the specimen, contamination and technical problems, sometimes shortage of test kits, improper extraction of nucleic acid from specimen.

2. RAPID ANTIGEN DETECTION TEST

Qualitatively detect the COVID-19 antigen, and provide results in shorter period of time. ELISA method detect the antibodies in blood samples and respiratory secretions. IgM produced against virus as an initial humoral response. IgG is produced after 7 days of infection, stays thereafter as acquired immunoresponse.

3. CT CHEST

Chest Imaging methods play a vital role in early detection of COVID-19 infection and also useful for monitoring the course of disease. It is very sensitive to assess the nature and extent of lung involvement. The distribution, quantity, shape, pattern, density, concomitant signs also to be described.

The characteristic findings on CT chest are ground glass opacity. They are patchy, sub-segmental, or segmental, distributed in mid and lower lungs along the bronchovascular bundles. Located in peripheral and subpleural areas of the lungs.

In early stage, Single or multiple scattered patchy ground glass opacities seen. Main Pathology in early stage is dilatation and congestion of the alveolar septal capillary, exudation of fluid in the alveoli, Interlobular interstitial oedema.

In advanced stage, numerous new lesions that are similar to earlier lesions developed. Lesions increase in density, extent, along with new areas of disease. Areas of consolidation and mixed pattern ground glass opacities are seen. Main pathology occur in this stage, cell rich exudation in alveoli and interstitial space and vascular expansion.

In severe stage, as the severity of disease increases there will be a diffuse consolidation of the lungs with varying density in the CT chest it's due to exudate and dilated bronchi. If disease process affects the most of the lung, appearance of lung will be white out lung. Minimal pleural effusion and pleural thickening also noted.

In dissipation stage, gradual resolution of the ground glass opacity and consolidation.

DIFFERENTIAL DIAGNOSIS FOR COVID-19

The CT chest of COVID-19 appearance might share a similarity with other viral pneumonia, especially MERS, SARS-CoV, influenza, para influenza, adenovirus, respiratory syncytial virus, and human metapneumo virus. COVID-19

also to be differentiated from mycoplasma pneumonia and chlamydial and other bacterial pneumonia and pulmonary edema

SEVERITY OF COVID-19

As per Government of India (GOI) guidelines,

1. **MILD**

   Uncomplicated URI without shortness of breath (normal saturation)

2. **MODERATE**

   Pneumonia with no signs for severe disease, RR >24/min, SPO_2 90-94%

3. **SEVERE**

   Respiratory distress with RR >30/min, Spo2 <90%

4. **CRITICALLY ILL**

   Severe disease patients with need for mechanical ventilation due to respiratory failure or with shock or combined with multi organ failure requiring transfer to ICU.

Common features observed in critically ill COVID-19 patients are

- Severe illness/ICU admission/ARDS/mechanical ventilation
- Sudden worsening of disease after 1–2 weeks of onset

- High level of inflammatory biomarkers including CRP (C-reactive proteins) and serum ferritin, LDH, and interleukins.
- Damaged immune system, also reduction in the lymphocytes level
- Elevated levels of infiltrated immune cells like monocytes, macrophages
- Hypercoagulation, vasculitis and multiple organ damage also occur
- Septic shock
- Death

COMORBIDITIES AND COVID-19

Patients with comorbidities prone to develop severe disease of COVID-19, especially patients with diabetes, hypertension, cardiovascular disease, cancer, chronic renal failure patients with pre-existing lung disorders like Chronic obstructive pulmonary disease, bronchial asthma, cerebrovascular accident and chronic liver disease. Many studies reported that neurological complications more in COVID-19 than SARS-CoV and MERS-CoV.

DIABETES MELLITUS

Diabetes is the most common non communicable disease. Patients with diabetes have higher chance to get pneumonia and influenza. Many studies reported that patient with high blood glucose are prone to get MERS-CoV, H1N1, SARS-CoV leading to severe disease and increased risk of mortality.

The patients with diabetes and other cardiovascular risk disease patients are greater risk of serious and critical illness. Patients with diabetes and COVID-19 infection will have higher CRP. COVID-19 infection can trigger the stress hormones like catecholamine, glucocorticoids and leads to uncontrolled hyperglycemia which further worsens the illness. Insulin resistance and uncontrolled hyperglycemia increases oxidative stress and inhibits the production of glycosylation, pro-inflammatory cytokines and influence the synthesis of adhesion molecules, which increases the tissue inflammation.

Dysfunctional activation of complement and delayed hypersensitivity also observed in diabetic patients. Chronic low level inflammation in diabetic patients, promotes the accelerated activation of monocytes, macrophage, T cells, thereby further promote the inflammation, and causing damage to the lungs. Cytokine response activate the coagulation system. Uncontrolled hyperglycemia suppresses the antiviral response. Diabetic patients also have changes in the innate immunity. Some studies reported that COVID-19 patients had accumulation of viral particles and inflammatory cells in the blood vessels leading to pyroptosis and endothelial

inflammation. Endothelial damage and Dysfunction occur as a microvascular complication of patients with diabetes. Both SARS-CoV and SARS CoV-2 binds with ACE2 in the islet cells of pancreas to cause injury to these cells and increases the blood glucose levels and worsening the severity.

Many patients with severe COVID-19 infection had lot of preexisting comorbities, hence strict glycemic control linked to the reduced risk of severity, duration of hospitalisation and mortality. Inflammatory markers are high in diabetic patients. In patient with diabetes due to the altered glucose levels, insulin resistance and reduced immunity, they develop interstitial lung disease and alveolar capillary microangiopathy. Despite adequate treatment with insulin, antivirals, oxygen therapy, diabetes patients with COVID-19 infection have poor prognosis. Many patients with diabetes also had hypertension and dyslipidemia, obesity, so in addition to glycemic control, treatment for blood pressure and dyslipidemia was also adviced.

BIOCHEMICAL MARKERS

C- REACTIVE PROTEIN (CRP)

Plasma contains a pentameric protein called CRP, which is elevated in inflammatory conditions. During inflammatory process, macrophages and T cells produce IL-6, that time liver also synthesis CRP as an acute phase reactant. CRP belongs to a member of pentraxin family of proteins. It is the acute phase reactant first identified by pattern recognition receptor.

CRP is considered to be a native protein, gene situated in the chromosome 1. It has 224 amino acid, molecular weight is about 25106 Dalton. In the serum it assumes a shape of discoid. It was named as CRP because it react with somatic carbohydrate antibody of pneumococci capsule in a patient with acute inflammatory state. On the surface of dying cells, phosphatidyl choline was expressed, these CRP binds to phosphatidyl choline and activates complement system, thereby accelerating the phagocytic process by macrophages and remove the necrotic and apoptotic materials. It also increases the opsonin mediated phagocytosis by macrophages.

Elevated CRP levels are seen in inflammatory conditions due to bacterial, viral, fungal, malignancy, most of the rheumatological diseases and traumatic conditions. CRP is elevated in COVID-19.

Normal CRP level 0.8mg/L to 3mg/L

Half-life of CRP – 19 hours

Doubling time - 8 hours

About 36-50 hours of inflammation, CRP reaches its peak level.

Cut off values used in our institution was10mg/L, measured by spectrophotometry method.

Many studies reported that high levels of CRP associated with COVID-19 severity.

Jian-bo Xu et al (2020) found that the CRP level was highest in critically severe groups than lowest levels in moderate group and demonstrated that high CRP levels were associated with increased risk of mortality in severe group and older age group.

Ian Huang et al (2020) in a meta-analysis study reported that elevated CRP was associated with poor outcome of the disease by means of more severe the disease, increased risk mortality, ARDS, need of ICU care.

Some factors which affects the serum CRP levels are age, gender, smoking, weight, lipid levels, blood pressure and liver injury. Optimal serum CRP measurement in COVID-19 patient was useful to assess the severity of illness and used for prognostic significance. Recent evidence suggested that measurement of CRP levels in COVID-19 is useful in monitoring the progression and improvement of the disease.

LACTATE DEHYDROGENASE (LDH)

Lactate dehydrogenase is tetramer having 2 types of polypeptide units, H for heart, M for muscle. It has 5 isoenzymes. Liver and muscle produces mostly M subunits, myocardium and bone Marrow produces H subunits. Lung, brain, spleen produces both subunits. Increased LDH levels are seen in hemolytic anemia, hepatocellular damage, muscle dystrophies, leukemia, carcinoma, CVA, pancreatitis, kidney disease, infectious mononucleosis, megaloblastic anemia, intestinal and

pulmonary infarction. Elevated LDH levels reflect the multiple organ failure and play a role in influencing the prognosis of patients with COVID-19.

LDH is an intracellular enzyme. In case of cell damage, lactate dehydrogenase is released from cell and its concentration in the blood will increase. LDH is an important marker of various inflammatory states. LDH catalyses the conversion of pyruvate and lactate, with concomitant interconversion of NADH and NAD+.

Type	**Composition**	**Location**	**Diagnostic importance**
LDH1	HHHH	Heart, RBC	Myocardial infarction
LDH2	HHHM	Heart	Megaloblastic anemia, myocardial infarction
LDH3	HHMM	Brain	Leukemia, malignancy
LDH4	HMMM	Lung, muscle, spleen	Pulmonary infarction
LDH5	MMMM	Liver, muscle	Liver disease, muscle disease

Lactate dehydrogenase (LDH) is a hydrogen transfer enzyme. It catalyses the oxidation of L-lactate to pyruvate with the mediation of NAD+ as a hydrogen acceptor. LDH has a molecular weight of 134 kilo Dalton. LDH has been used as a marker of cardiac damage since 1960. Abnormal values can result from multiple organ injury and decreased oxygenation with up regulation of the glycolytic pathway. The acidic pH because of increased lactate from infection and tissue injury triggers the activation of metalloproteases and increases macrophage mediated angiogenesis

Severe infections may trigger the cytokine-mediated tissue damage and cause release of LDH. LDH is present in lung tissue. Patients with severe COVID-19 infections can be expected to release greater amounts of LDH in the circulation. This results in a severe form of interstitial pneumonia, evolving into ARDS, is the hallmark of the disease. However, the contribution of the different LDH isoenzymes and its elevation was not observed in COVID-19.

Yi Han et al (2020) reported that the LDH was an independent risk factor of severe COVID-19 patients. They concluded that LDH as a strong predictor for early recognition of lung injury and severe COVID-19.

PROCALCITONIN (PCT)

The 116-amino acid precursor of the hormone is calcitonin called as procalcitonin. It is normally synthesized by the parafollicular C cells of thyroid. Cut off value is about 0.5ng/ml. PCT production may be abruptly altered by an inflammatory stimuli, mainly mediated by increased concentrations of interleukin 6 (IL-6), tumour necrosis factor alpha (TNF-α) in turn triggered by lipopolysaccharide, the major component of Gram-negative bacteria. Calcitonin CALC-1 gene transcription occurs in many extra-thyroid tissues (e.g. liver, kidney, gut, lung and leukocytes), thus leading to increase procalcitonin concentration in blood.

Ze-Ming Liu et al (2021) reported the association of procalcitonin levels with the progression and prognosis of hospitalized patients with COVID-19. They

concluded that it was an independent risk factor for in hospital mortality. Patients with elevated levels likely to develop severe form of the disease.

D-DIMER

D-dimer is a fibrin degradation product, used as a biomarker for thrombotic disorders. D-dimer value < 0.5 mg/L is considered normal. In the COVID-19 pandemic, D-dimer has been identified as a potential indicator for prognosis of the disease. D-dimer measurement at hospital admission has role in predicting the disease severity in multiple studies. COVID-19 patients presenting with high D-dimer values were at increased risk of severe disease and mortality, and noted that no consistent cutoff value had been defined to predict adverse events.

Hui Long et al (2020) reported that the D-dimer and prothrombin time are the significant indicators of severe COVID-19 and associated with poor prognosis. Severely infected patients have significant coagulation dysfunction and leads to formation of microthrombi formation in lungs, heart, kidney and liver.

Ian Huang et al (2020) done a metaanalytic study and concluded that elevated levels of CRP, Procalcitonin, D-dimer and Serum ferritin were associated with poor outcome in the form of severe COVID-19 and increased mortality. COVID-19 infection associated with hemostatic system dysfunction leads to hypercoagulable state, increased thrombin production, occlusion and microthrombi formation. Patients with elevated D-dimer should be hospitalized, despite the severity of illness.

FERRITIN

Serum ferritin is one of the marker for predicting the severity in COVID-19. Elevated serum ferritin levels are associated with ARDS, need of ICU care, mechanical ventilatory support and mortality. Hemophagocytic lymphohistiocytosis is also reported in COVID-19. It is due to secondary process. Hemophagocytic lymphohistiocytosis characterised by hyperinflammation and cytokine storm leads to multi organ failure.

Ferritin is a protein, which is the storage form of iron inside the cells. The small amount of ferritin that circulates in the blood is a reflection of iron storage in the body. High ferritin levels are seen in patients with iron overload. Ferritin is an acute phase reactant and it can be elevated in acute illness, in such a condition total body iron content is normal only.

Ferritin was identified by Laufberger, a French scientist, who isolated a new protein from horse spleen. This protein contains 23% dry weight of iron. In 1972, using an immunoradiometric assay, Addison et al reported that increased serum ferritin seen in iron overload states, and decreased in iron deficiency patients.

Ferritin is a cytosolic protein in many cells, although a mitochondrial form is also present. Ferritin is a 24-subunit protein, H subunit is isolated from human heart, gene coding for this subunit is located in chromosome 11q, L subunit refers to ferritin

isolated from human liver and gene coding this subunit is located in chromosome 19q.

Normal ferritin concentrations vary by age and sex. Concentrations are high at birth, and continue to increase into adulthood. Males have higher values than females. Values of ferritin among men peak between 30–39 years of age. It tend to remain constant until about 70 years of age. Among women, serum ferritin values remains relatively low until menopause and then rise.

Ferritin is the most useful parameter to assess the prevalence of iron deficiency in a population, along with hemoglobin in all programme. Ferritin is measured in serum or plasma by enzyme-linked immune sorbent assays (ELISA) or enzyme immunoassay (EIA).

Ferritin as a signalling molecule

Patients with Hodgkin's disease and acute leukaemia exhibit elevated levels of serum ferritin and have impaired immunity. Serum ferritin is an acute phase reactant, so it is considered to be a marker of both acute and chronic inflammation, and is non-specifically elevated in chronic kidney disease, rheumatoid arthritis and many autoimmune disorders, acute infectious conditions.

Elevated serum ferritin levels are nonspecific marker of several illness, including infections and cancer, liver disease, renal disease, HIV, chronic transfusion, and sickle cell anemia.

Ferritin gives a clue in the evaluation of critically ill patients. **S**erum ferritin also predicts the risk of cirrhosis, the hemochromatosis. Elevated serum ferritin seen

in transfusion-associated iron overload states like myelodysplastic syndrome, thalassemia and hemoglobinopathies, predicts the end organ damage.

NEUTROPHIL-TO-LYMPHOCYTE RATIO (NLR)

Neutrophil-to-lymphocyte ratio is another independent risk factor for mortality. A meta analytic study reported that patient with severe disease had high NLR than patient with mild disease.

COMPLICATIONS OF COVID-19

- Pneumonia
- Acute kidney injury
- Sepsis
- Secondary infection
- Septic shock
- Thromboembolism
- ARDS
- Cardiomyopathy, arrhythmia, cardiac arrest
- Gastrointestinal bleeding

The need for vasopressors is variable, but a significant proportion need vasopressor support for hypotension (usually due to sedative agents or cardiac dysfunction). Data on the risk of secondary bacterial pneumonia are limited though it does not appear to be an important feature of COVID-19. Lung compliance is high compared to other ARDS aetiology, and the barotrauma rate appears to be low, with only 2 percent developing pneumothorax. Proinflammatory cytokines and reactive oxygen species (ROS) are produced from activated vascular endothelial cells. This contribute to the development of coagulopathy, systemic sepsis, a cytokine storm and ARDS. Another important source of proinflammatory cytokines and ROS is pulmonary activated platelets. Pulmonary activated platelets also exacerbate pulmonary neutrophil-mediated inflammatory responses and contribute to systemic sepsis by binding to neutrophils to form platelet-neutrophil complexes (PNCs). PNC formation increases neutrophil recruitment, activation priming and extraversion of these immune cells into inflamed pulmonary tissue, thereby contributing to ARDS. The sequestered PNCs cause the development of a procoagulant and proinflammatory environment.

DEFINITION OF ARDS

Berlin criteria: ARDS is defined as new or worsening respiratory distress that occurs within 1 week. The onset of ARDS in COVID-19 is mostly in second week. To prevent the risk of developing ARDS, crucial monitoring of the patients is needed in whose disease duration lasts for longer than one week. ARDS, which causes reduced lung compliance and severe hypoxemia.

Berlin Criteria in Diagnosis of ARDS

Criteria	Findings	
Timing	De novo or worsening respiratory distress that occurs within 1 week	
Pulmonary imaging	Bilateral opacity that cannot be explained by effusion, collapse or nodule	
Causes of edema	Evidence that respiratory distress is not due to heart failure or hypervolemia with objective measures such as echocardiography.	
Impairment of Oxygenation	Mild	200 mmHg ≤ PaO2/FiO2 < 300mmHg)
	Moderate	100 mmHg ≤ PaO2/FiO2 < 200mmHg)
	Severe	PaO2/FiO2 ≤ 100 mmHg) + PEEP ≥5cm H2O

TREATMENT

Most of the patients with COVID-19 presented with dyspnea, so hypoxia management is very important treatment modality.

For Non intubated patient

1. **Prone position**

Many studies reported that prone position of the patient improve the oxygenation in patients with COVID-19, regardless of whether they receive supplemental oxygen, HFNO or NIMV support alone. But it is still unclear whether pronation prevents intubation, accelerates recovery, or reduces mortality.

2. **Low flow oxygen delivery systems**

Oxygenation upto 6L/min given via Nasal cannula, O2 requirement upto 10-20L/min can be given via simple face mask, venturi face mask, and non-rebreathing mask. Disadvantage is risk of aerosolization increase.

3. **High-flow Nasal Oxygen (HFNO)**

Studies reported that HFNO reduces the need for mechanical ventilation in ARDS patients, when compared to usual oxygen therapy via face mask or non-rebreathing mask. HFNO can be advised if oxygen requirement is 20L/min. For NIV, a full face mask should be preferred, CPAP should start with 5-10 cm of H2O.

WHO recommends oxygen saturation to be maintained ≥ 94% during the first resuscitation and Spo2 > 90% for maintenance period. In the patient with severe or

critical COVID-19 pneumonia, oxygen saturation should be maintained between 90-96% at the lowest possible inspired oxygen fraction (FiO2). This target range may differ in patients with COPD and pregnancy.

Nebulizers are associated with increased aerosolization and potentially increase the risk of COVID-19 transmission. In suspected or documented COVID-19 patients, nebulized bronchodilator therapy should be reserved for patients with acute bronchospasm in case of asthma or COPD. Otherwise, nebulized therapy should generally be avoided.

For Intubated Patient

Most patients who develop ARDS in the course of COVID-19 will need mechanical ventilation. During early pandemic period, intubation was not advised. Later found that invasive ventilation might helpful in critical cases. Patients with oxygen support, should be re-evaluated with every 1 to 2 hours and blood gas control.

Indications for emergency endotracheal intubation:

- Rapid deterioration of the clinical status within hours
- No clinical improvement despite high flow O_2 at FiO2 > 0.6 and > 50 L/min
- Worsening dyspnea, development of hypercapnia
- Altered mental status
- Hemodynamic instability or multiple organ failure

DRUG THERAPY IN COVID-19

1. **Corticosteroids**

   Reduces the inflammation and fibrosis, used in the treatment of ARDS.

2. **NSAIDS**

   Paracetamol and other NSAIDS can be used for fever, pain and to relieve other signs of inflammation

3. **Antibiotic therapy**

   Empirical antibiotic therapy usually not recommended, unless associated secondary bacterial infection.

4. **Plasma therapy**

   Plasma obtained from donors who completely recovered from COVID-19, then administered to the patients. Efficacy expected to be good in patients treated in early stages disease.

5. **IL-6 receptor inhibitors**

   Tocilizumab is an IL-6 receptor inhibitors used in patients with severe disease. It is used in rheumatologic diseases and cytokine storm syndrome.

6. **Remdesivir**

   It is a nucleotide analogue that possess prominent activity against COVID-19. Common side effects are nausea, vomiting and elevated transaminase levels. IDSA and FDA gives conditional recommendation with moderate evidence dose 200mg if IV initial bolus followed by 100mg daily for 5 days.

7. Favipiravir

RNA polymerase inhibitor shows favourable result in COVID-19, is also used in influenza. Combined protease inhibitors Lopinavir- Ritonavir (400mg/100mg) twice daily for 14 days also be tried.

8. Hydroxychloroquine / chloroquine

This drug is believed to inhibit the ARDS progression by inhibiting TNF-alpha and IL-6. Used in initial part of COVID-19 pandemic. This drug can prolong the QTc interval, also affects the cardiac conduction, can cause retinopathy and cardiomyopathy. In June 2020, FDA cancelled the authorization for its use in severe COVID-19.

9. Azithromycin, Doxycycline, Vitamin C & D and Zinc

10.Monoclonal antibodies

11.COVID-19 vaccines

Name	Type	Doses	Interval
Pfizer/BioNtech Comirnaty	mRNA	2	21 days apart
Covishield	Adenoviral vector	2	12-16 weeks
AZD1222	Adenoviral vector	2	12-16 weeks
Janssen/ Ad26.COV 2.S	Viral vector	1	-
Moderna	mRNA	2	28 days apart
Covaxin	Whole-virion inactivated vero cell	2	28 days apart
Sputnik V	Adenoviral	2	21 days apart

MATERIALS AND METHODS

Study population

This study was carried out with the patients admitted and diagnosed with COVID-19 at Madurai Medical College and Government Rajaji Hospital, Madurai.

Sample size

50 randomly selected diabetic and 50 non diabetic patients with COVID-19 infections

Period of study: January 2021 to June 2021

Inclusion criteria

1. Both male and female patients of age above 40 years to 80 years
2. Nasal swab positive by RT-PCR method
3. Type II diabetes mellitus controlled and uncontrolled assessed with HbA1c levels
4. Patients with Type II diabetes mellitus along with other co-morbid association like cardiac and renal complications

Exclusion criteria

1. Age below 40 years & above 80 years
2. RT-PCR negative patients with radiological signs
3. Mixed secondary infections and sepsis
4. Type1 and secondary diabetes

Study design

Observational study

Methods of study

This is an observational & analytical study in patients admitted at Government Rajaji Hospital, Madurai and diagnosed to have COVID-19 infection by RT-PCR method. After approval from the institutional ethical committee, this prospective study will be conducted with oral and written informed consent form in patients aged above 40 years of both sex fulfilling the inclusion and exclusion criteria.

Data collection

Demographic data, time from onset of illness to hospital admission, Clinical, laboratory data, radiological imaging and treatment measures.

Demographic data: Age and sex

Clinical characteristics:

- Fever
- Cough
- Diarrhoea
- Dyspnea
- Myalgia
- Headache
- Vomiting

Pre-existing chronic comorbidities

- Cardiovascular disease
- Hypertension
- Cerebrovascular disease
- Malignancy
- Chronic pulmonary disease
- Chronic liver disease
- Severity on admission
- Oxygen support

Laboratory markers

- CRP
- LDH
- Ferritin
- D-dimer, PT, INR
- Procalcitonin
- WBC, Neutrophils, Lymphocytes, NLR, Platelets, Blood urea, Serum Creatinine, HbA1c, RBS, FBS, PPBS, ALT, AST and Bilirubin

Imaging – CT chest

Data was collected in the preferred proforma at the time of admission and during the hospitalization period and analysed for outcome.

Statistical methods

Chi-square test and Oneway ANOVA test is used to compare variables between diabetes and non-diabetes groups. All statistical analysis performed by using SPSS software. P values indicate difference between diabetes and non-diabetes patients. P value < 0.05 is considered statistically significant.

Collaborating departments

1. Department of Biochemistry
2. Department of Pathology
3. Department of Radiology

Ethical clearance: Obtained

Consent: Individual informed and written consent obtained

Conflict of interest: Nil

Financial support: Nil

RESULTS AND OBSERVATION

Table 1: Age distribution of study participants

Age	Frequency
40-50	51
51-60	36
>60	13
Total	100

Graph 1: Age distribution of study participants

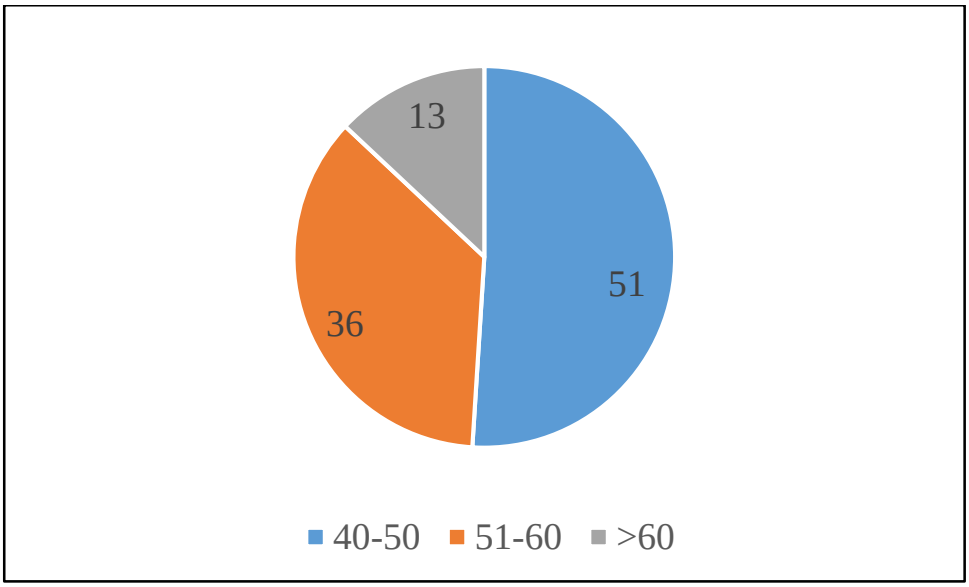


Table 1. Describes that about 51% are of age 40-50, 36% was age 51-60 and 13% were above age 60 (graph 1)

Table 2: Gender distribution of study participants

Gender	Frequency
Male	59
Female	41
Total	100

Graph 2: Gender distribution of study participants

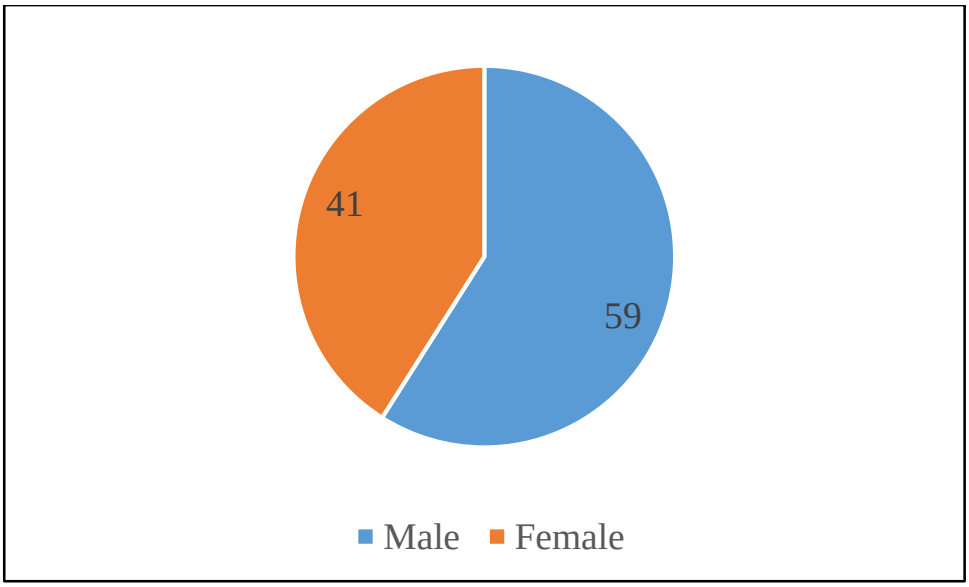


Table 2. Describes that about 59% were male and 41% were female (graph 2)

Table 3: Distribution of complaints among study participants

Complaints	Percentages
Fever	90
Cough	48
Diarrhoea	19
Dyspnea	46
Myalgia	73
Head ache	1
Vomiting	-
Others	10

Graph 3: Distribution of complaints among study participants

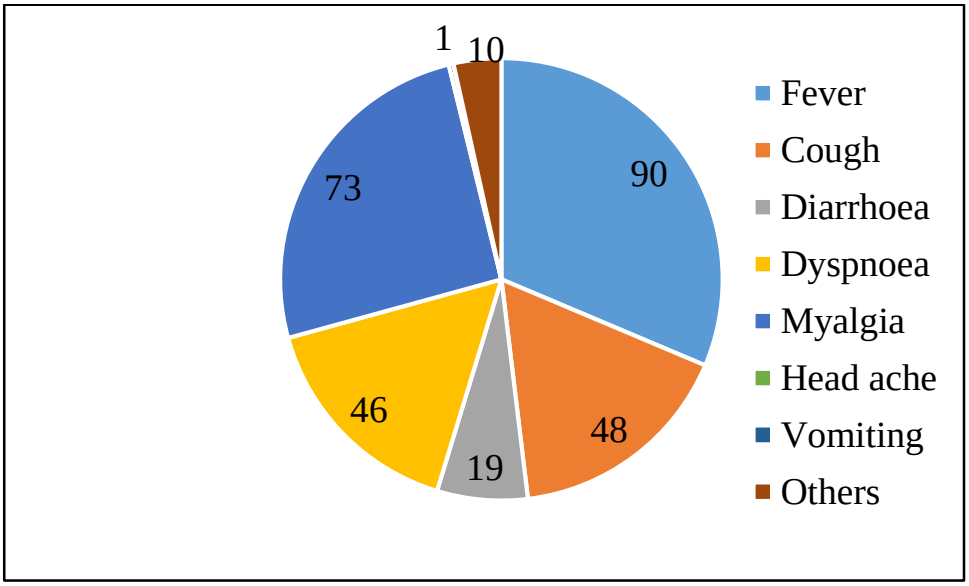


Table 3. Describes that 90% had fever, 73% Myalgia, 48% cough, 46% Dyspnea and 19% Diarrhoea. (Graph 3)

Table 4: Distribution of comorbidities among study participants (Excluding Diabetes)

Co Morbidities	Percentages
SHT	54
CAD	25
CVA	0
Malignancy	0
RS	10
CLD	0
CKD	4
Others	7

Graph 4: Distribution of comorbidities among study participants (Excluding Diabetes)

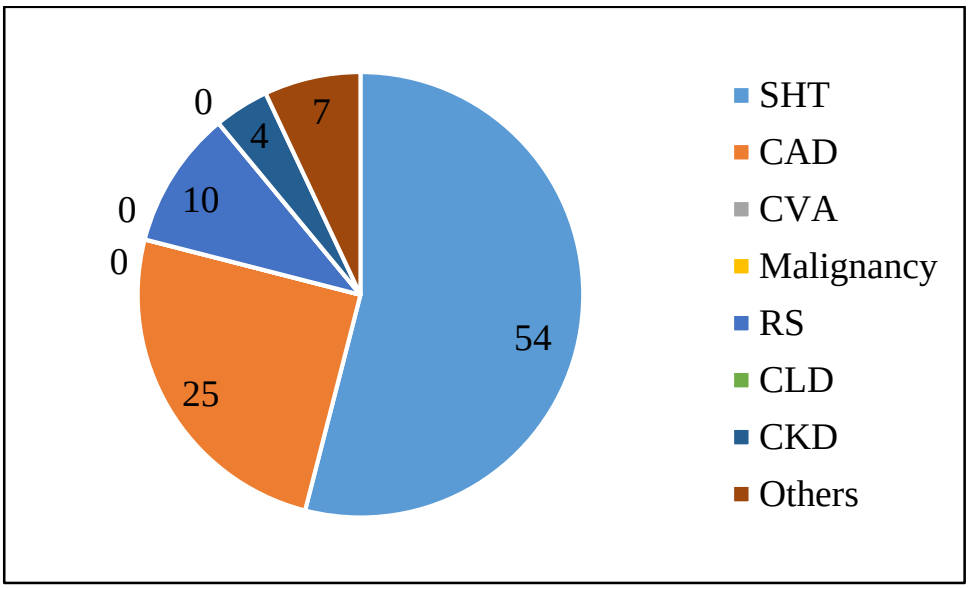


Table 4. Describe that among the patients with comorbidities other than 50 diabetic patients, majority were with hypertension (54%) and followed with 25% by CAD (Graph 4)

Table 5: Distribution of severity among study participants

Severity	Frequency
Mild	35
Moderate	34
Severe	20
Critically ill	11
Total	100

Graph 5: Distribution of severity among study participants

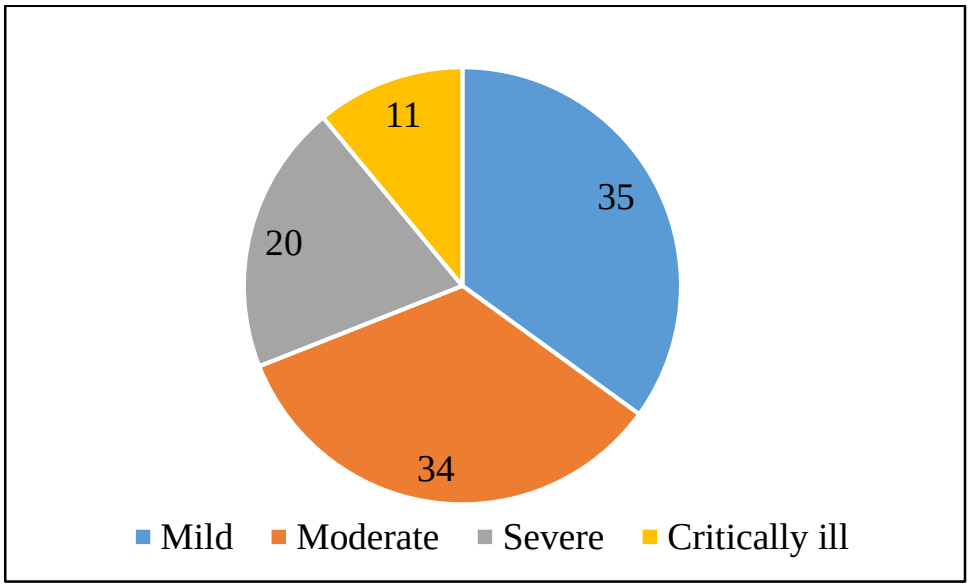


Table 5. Describes that majority were 35% mild and 34% were moderate, 20% were severe and 11% were critically ill. (Graph 5)

Table 6: Distribution of CT chest involvement among study participants

CT Chest involvement	Frequency
Nil	35
Bilateral (B/L)	48
Unilateral (U/L)	17
Total	100

Graph 6: Distribution of CT chest involvement among study participants

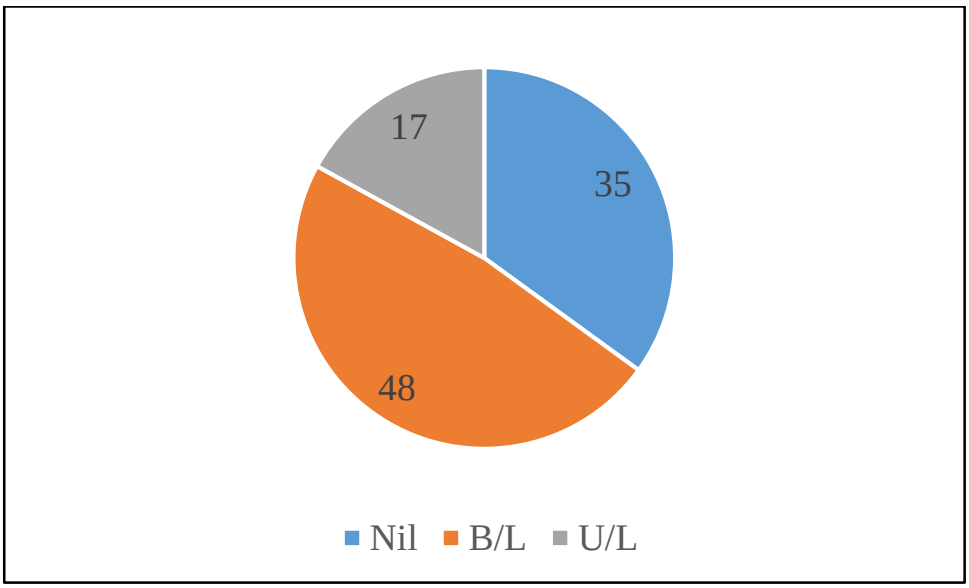


Table 6. describes that 48% were B/L and 17% were U/L. (Graph 6)

Table 7: Gender wise comparison of severity of COVID-19 patients

Gender	Mild	Moderate	Severe	Critically Ill	Total	Chi sq	p
Male	21	21	11	6	59	0.34	0.9
Female	14	13	9	5	41		
Total	35	34	20	11	100		

Graph 7: Gender wise comparison of severity of COVID-19 patients

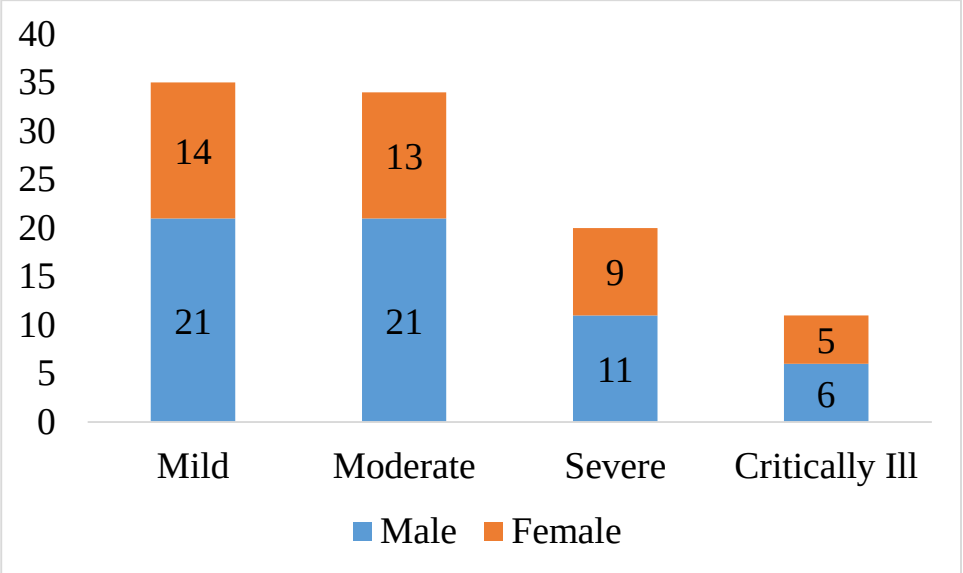


Table 7. Explains gender wise comparison of severity of COVID-19 patients by Chi square test. It was found there was no statistically significant difference exists between male and female patients with p= 0.9. (Graph 7)

Table 8: Age wise comparison of severity of COVID-19 patients

	Severity	N	Mean	SD	F	Sig.
Age	Mild	35	51	6.517	1.227	0.304
	Moderate	34	51.68	8.831		
	Severe	20	52.95	8.882		
	Critically Ill	11	56.09	8.24		
	Total	100	52.18	8.061		

Graph 8: Age wise comparison of severity of COVID-19 patients

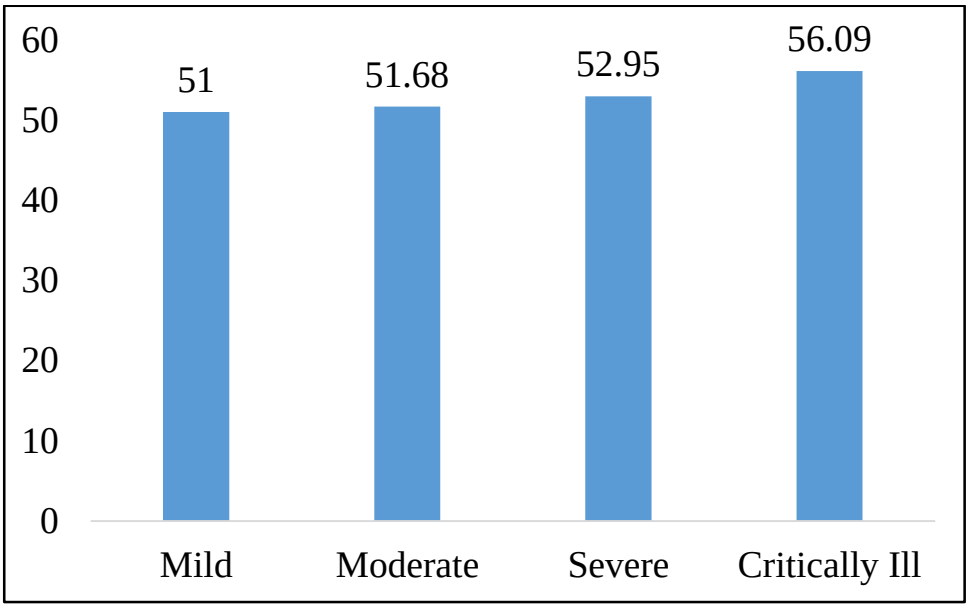


Table 8. Explains Agewise mean comparison of severity of COVID-19 patients by One way ANOVA test. It was found there was no statistically significant difference exists with p = 0.3. (Graph 8)

Table 9: Association of symptoms with severity of COVID-19 patients

Fever	**Mild**	**Moderate**	**Severe**	**Critically Ill**	**Total**	**Chi sq**	**p**
No	6	3	1	0	10	3.84	0.3
Yes	29	31	19	11	90		
Total	35	34	20	11	100		
Cough	Mild	Moderate	Severe	Critically Ill	Total	Chi sq	p
No	14	23	10	5	52	5.58	0.1
Yes	21	11	10	6	48		
Total	35	34	20	11	100		
Diarrhoea	Mild	Moderate	Severe	Critically Ill	Total	Chi sq	p
No	28	26	16	11	81	3.07	0.4
Yes	7	8	4	0	19		
Total	35	34	20	11	100		
Dyspnea	Mild	Moderate	Severe	Critically Ill	Total	Chi sq	p
No	35	17	1	1	54	58.3	**0.0001**
Yes	0	17	19	10	46		
Total	35	34	20	11	100		
Myalgia	Mild	Moderate	Severe	Critically Ill	Total	Chi sq	p
No	4	11	8	4	27	7	0.07
Yes	31	23	12	7	73		
Total	35	34	20	11	100		

Head ache	Mild	Moderate	Severe	Critically Ill	Total	Chi sq	p
No	35	33	20	11	99	1.96	0.6
Yes	0	1	0	0	1		
Total	35	34	20	11	100		
Others	Mild	Moderate	Severe	Critically Ill	Total	Chi sq	p
No	30	32	19	9	90	5.19	0.5
Anosmia	5	2	1	2	10		
Total	35	34	20	11	100		

Graph 9: Various symptoms with severity of COVID-19 patients

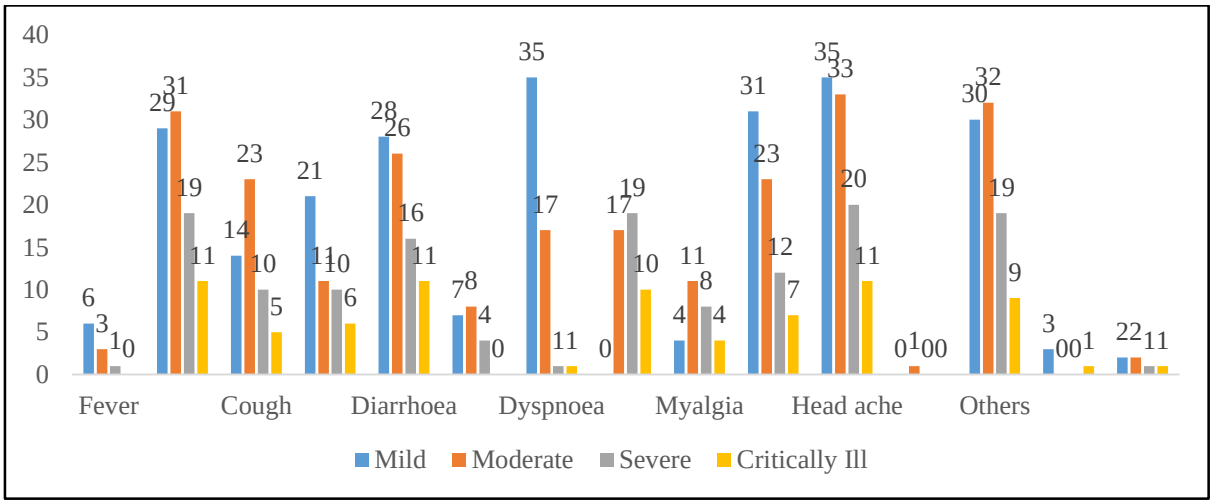


Table 9. Explains symptomwise comparison of severity of COVID-19 patients by Chi sq test.It was found there was no statistically significant difference exist between severity and fever (p= 0.3), cough (p=0.1), diarrhoea (p=0.4), myalgia (p=0.07), headache (p-0.6). but in dyspnea there was significant difference exists between the e of illness (p=0.0001). (Graph 9)

Table 10: Association of co morbidities with severity of COVID-19 patients

T2DM	**Mild**	**Moderate**	**Severe**	**Critically Ill**	**Total**	**Chi sq**	**p**
No	25	15	7	3	50	10.97	**0.01**
Yes	10	19	13	8	50		
Total	35	34	20	11	100		
SHT	Mild	Moderate	Severe	Critically Ill	Total	Chi sq	p
No	26	26	15	5	72	4.36	0.2
Yes	9	8	5	6	28		
Total	35	34	20	11	100		
CAD	Mild	Moderate	Severe	Critically Ill	Total	Chi sq	p
No	31	30	19	7	87	6.56	0.09
Yes	4	4	1	4	13		
Total	35	34	20	11	100		
RS	Mild	Moderate	Severe	Critically Ill	Total	Chi sq	p
No	33	33	18	11	95	1.97	0.6
Yes	2	1	2	0	5		
Total	35	34	20	11	100		
CKD	Mild	Moderate	Severe	Critically Ill	Total	Chi sq	p
No	35	33	19	11	98	2.01	0.6
Yes	0	1	1	0	2		
Total	35	34	20	11	100		

Others	Mild	Moderate	Severe	Critically Ill	Total	Chi sq	p
No	34	33	18	11	96	2.55	0.5
Yes	1	1	2	0	4		
Total	35	34	20	11	100		

Graph 10: Association of co morbidities with severity of COVID-19 patients

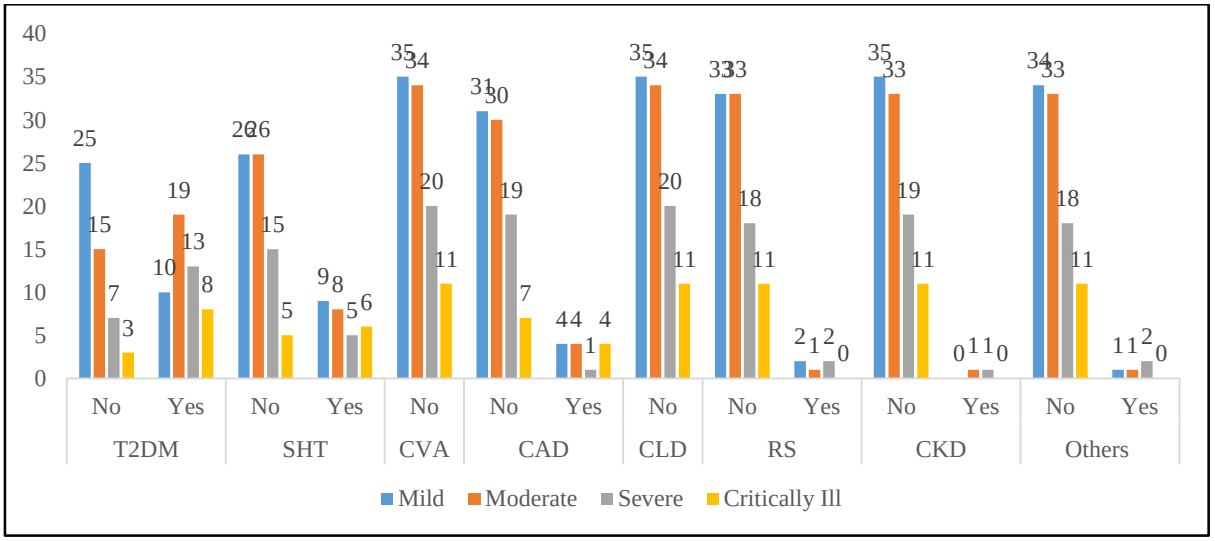


Table 10. Explains the association of comorbidity and severity of COVID-19 patients by Chi sq test. It was found that there was no statistically significant difference between severity and SHT (p= 0.2), CAD (p=0.09), RS (p=0.6), CKD (p=0.6) but in Type II DM, there exists significant difference between the severity of COVID-19. (p=0.01). (Graph 10)

Table 11: Mean comparison of blood pressures with severity of COVID-19

	Severity	N	Mean	SD		F	Sig.
SBP	Mild	35	121.14	12.312		0.646	0.588
	Moderate	34	124.12	14.167			
	Severe	20	121.5	9.881			
	Critically Ill	11	126.36	16.293			
	Total	100	122.8	12.955			
DBP	Mild	35	73.83	6.219		1.824	0.148
	Moderate	34	75.12	6.094			
	Severe	20	74	6.806			
	Critically Ill	11	78.73	6.467			
	Total	100	74.84	6.402			

Graph 11: Mean comparison of blood pressures with severity of COVID-19

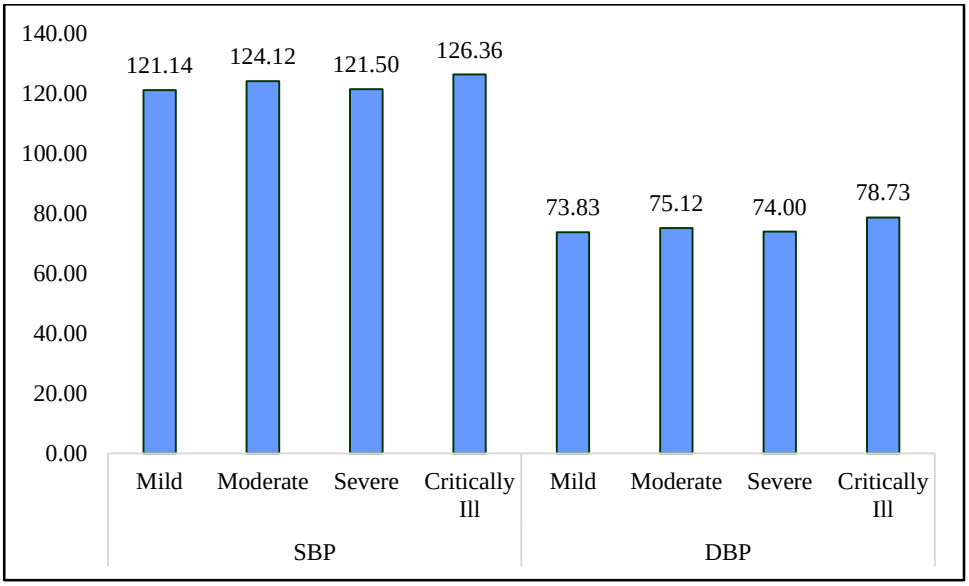


Table 11. Explains mean blood pressure comparison of severity of COVID-19 by One way ANOVA test. It was found that there was no statistically significant difference exists in systolic BP with p = 0.5 and diastolic BP with p = 0.1.(Graph 11)

Table 12: Mean comparison of PR and RR with severity of COVID-19 patients

	Severity	N	Mean	SD	F	Sig.
PR	Mild	35	78.63	5.462	19.548	**0.0001**
	Moderate	34	85.06	6.915		
	Severe	20	91.9	6.24		
	Critically Ill	11	91.27	11.217		
	Total	100	84.86	8.642		
RR	Mild	35	17.97	2.281	232.779	**0.0001**
	Moderate	34	24	2.296		
	Severe	20	32.15	2.56		
	Critically Ill	11	35.27	2.573		
	Total	100	24.76	6.729		

Graph 12: Mean comparison of PR and RR with severity of COVID-19

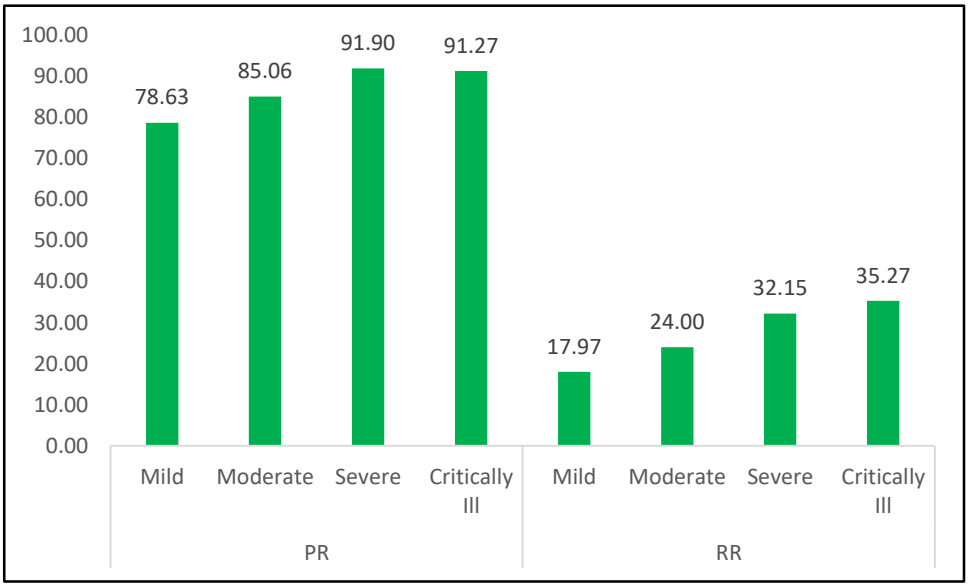


Table 12. explains mean Pulse rate and respiratory rate comparison of severity of COVID-19 patients by One way ANOVA test. It was found that there was statistically significant difference exists in PR with p = 0.0001 and RR with p = 0.0001. (Graph 12)

Table 13: Mean comparison of Spo2 with severity of COVID-19 patients

	Severity	N	Mean	SD	F	Sig.
ROOM AIR	Mild	35	96.74	1.559	126.482	**0.0001**
	Moderate	34	92.91	2.021		
	Severe	20	82.65	4.815		
	Critically Ill	11	74.45	8.733		
	Total	100	90.17	8.43		

Graph 13: Mean comparison of Spo2 with severity of COVID-19 patients

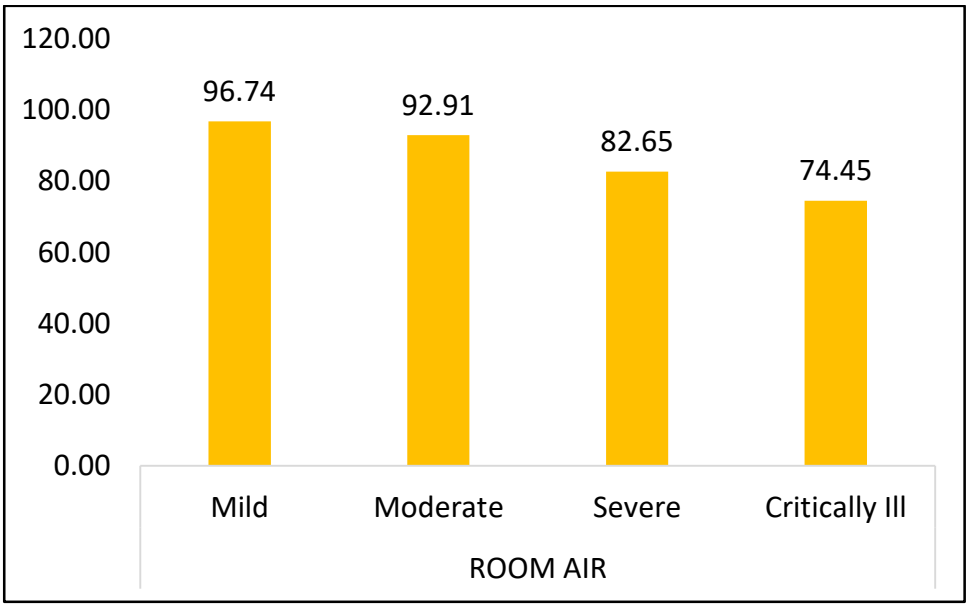


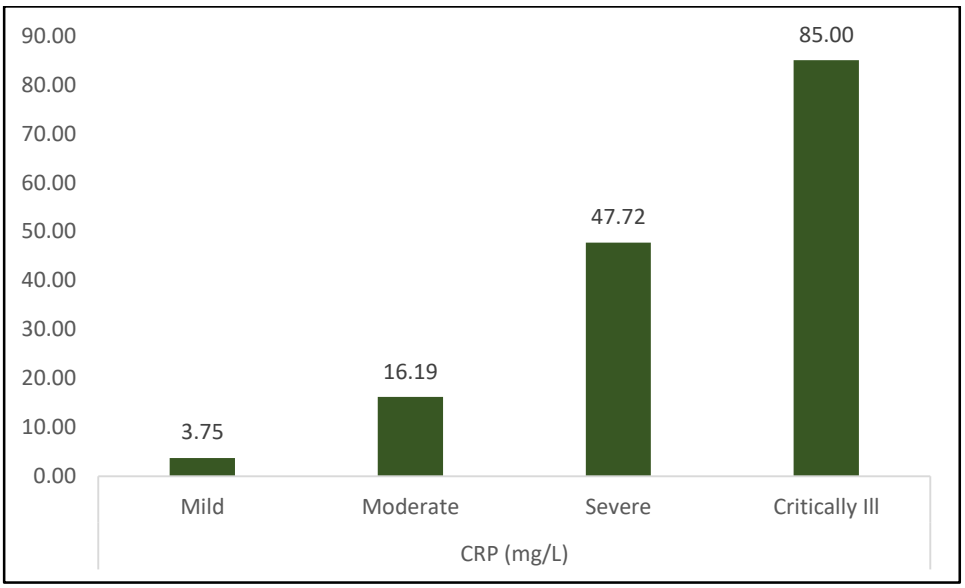
Table 13. Explains mean comparison of room air SpO2 with severity of COVID-19 patients by Oneway ANOVA test. It was found that there was statistically significant difference exists with p = 0.0001. (Graph 13)

Table 14: Mean comparison of CRP, LDH, Ferritin and D-dimer with severity

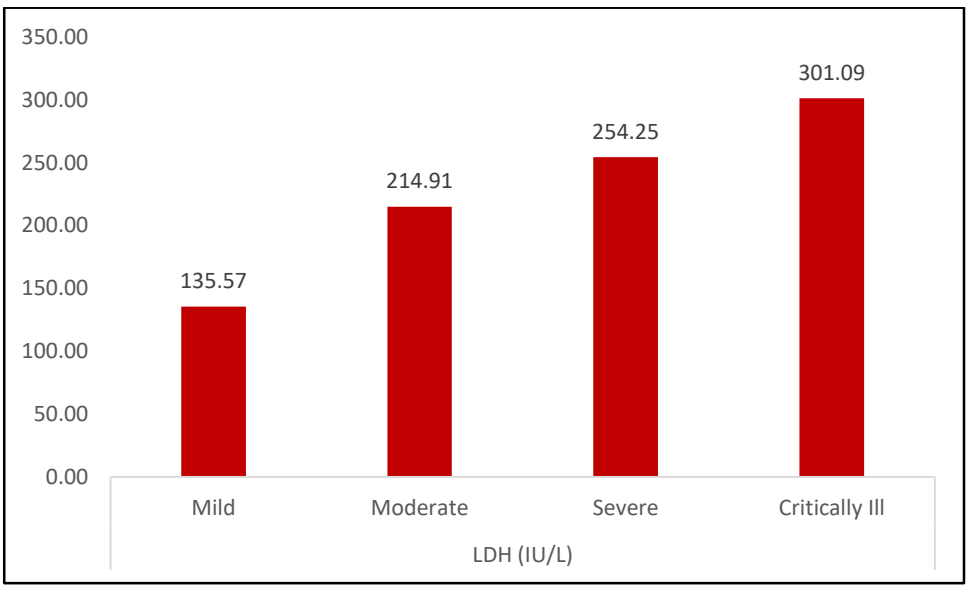
	Severity	N	Mean	SD	F	Sig.
CRP (mg/L)	Mild	35	3.749	1.8007	69.049	**0.0001**
	Moderate	34	16.194	14.7475		
	Severe	20	47.715	27.0132		
	Critically Ill	11	85	32.4142		
	Total	100	25.711	31.7775		
LDH (IU/L)	Mild	35	135.57	27.125	104.703	**0.0001**
	Moderate	34	214.91	35.73		
	Severe	20	254.25	26.487		
	Critically Ill	11	301.09	42.39		
	Total	100	204.49	65.176		
Ferritin (µg/L)	Mild	35	131.86	52.949	63.916	**0.0001**
	Moderate	34	223.88	57.381		
	Severe	20	285.45	55.68		
	Critically Ill	11	373.55	67.999		
	Total	100	220.45	96.742		
D-dimer (mg/L)	Mild	35	0.1374	0.02063	223.291	**0.0001**
	Moderate	34	0.2394	0.0257		
	Severe	20	0.323	0.04589		
	Critically Ill	11	0.4518	0.08171		
	Total	100	0.2438	0.10736		

Table 14. Explains mean comparison of CRP, LDH, Ferritin and D-dimer with severity of COVID-19 patients by One way ANOVA test. It was found that there was statistically significant difference exists with p = 0.0001 (Graph 14).

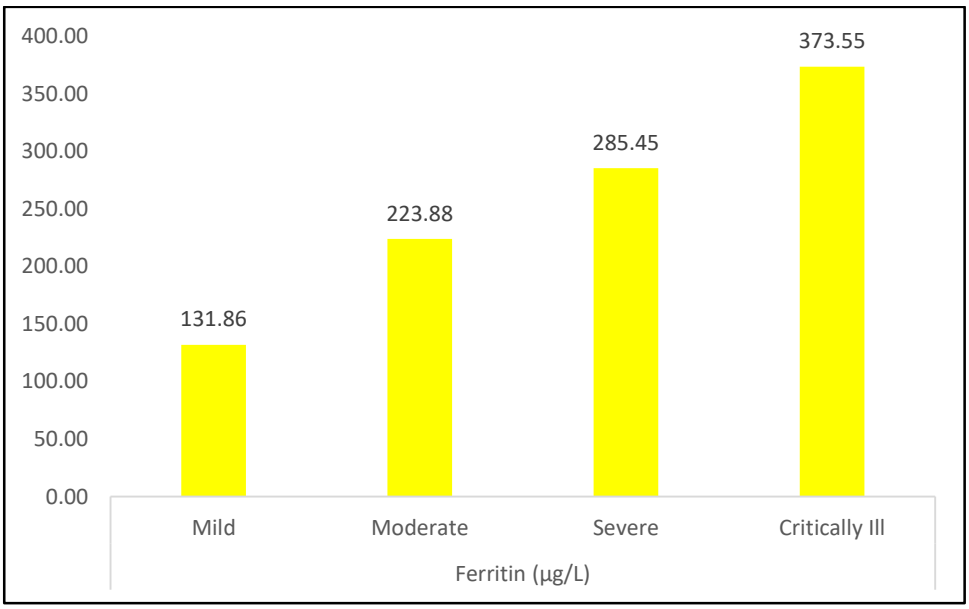
Graph 14: Mean comparison of CRP, LDH, Ferritin and D-dimer with severity



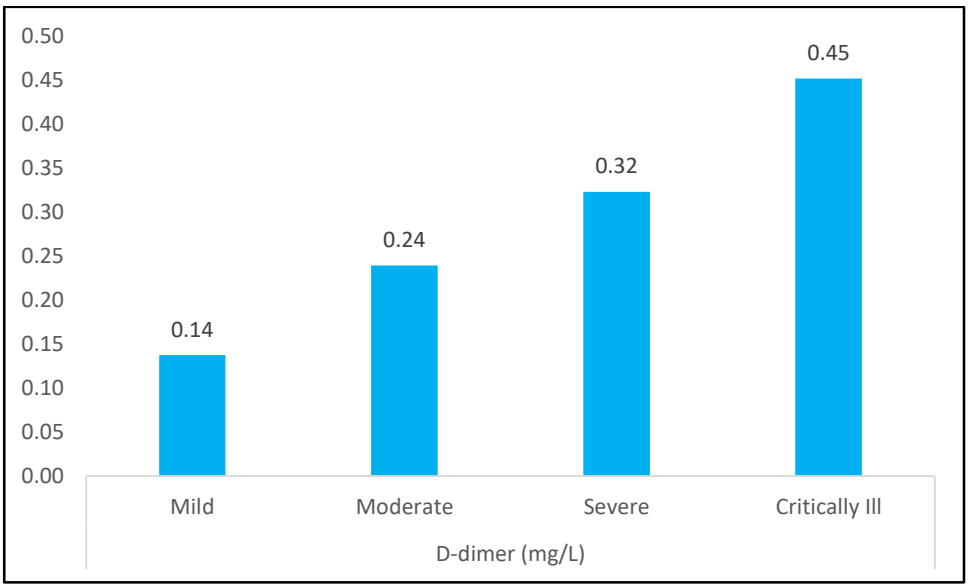
CRP Vs Severity



LDH Vs Severity



Ferritin Vs Severity



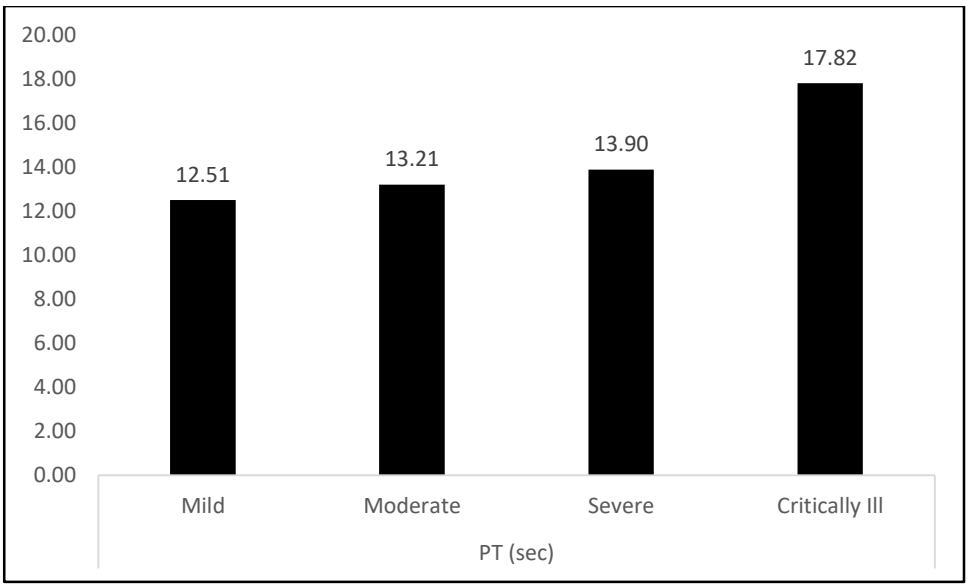
D-Dimer Vs Severity

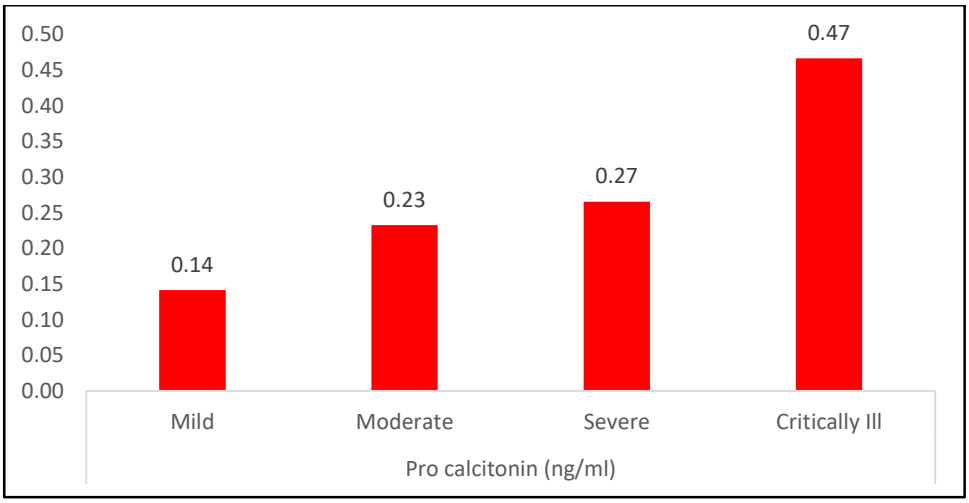
Table 15: Mean comparison of PT, Procalcitonin and WBC with severity

	Severity	N	Mean	SD	F	Sig.
PT (sec)	Mild	35	12.51	1.011	40.31	**0.0001**
	Moderate	34	13.21	1.647		
	Severe	20	13.9	1.373		
	Critically Ill	11	17.82	1.834		
	Total	100	13.61	2.103		
Procalcitonin (ng/ml)	Mild	35	0.1414	0.02144	123.656	**0.0001**
	Moderate	34	0.2326	0.03306		
	Severe	20	0.2655	0.06637		
	Critically Ill	11	0.4664	0.10053		
	Total	100	0.233	0.10778		
WBC (in thousands)	Mild	35	7.269	2.1277	3.055	**0.032**
	Moderate	34	7.088	2.4058		
	Severe	20	9.235	3.6803		
	Critically Ill	11	7.975	3.1791		
	Total	100	7.678	2.7897		

Table 15. Explains mean comparison of PT, Procalcitonin with severity of COVID-19 patients by Oneway ANOVA test. It was found that there was statistically significant difference exists with p=0.0001 and WBC with severity had significant difference with p = 0.03. (Graph 15).

Graph 15: Mean comparison of PT, Procalcitonin and WBC with severity





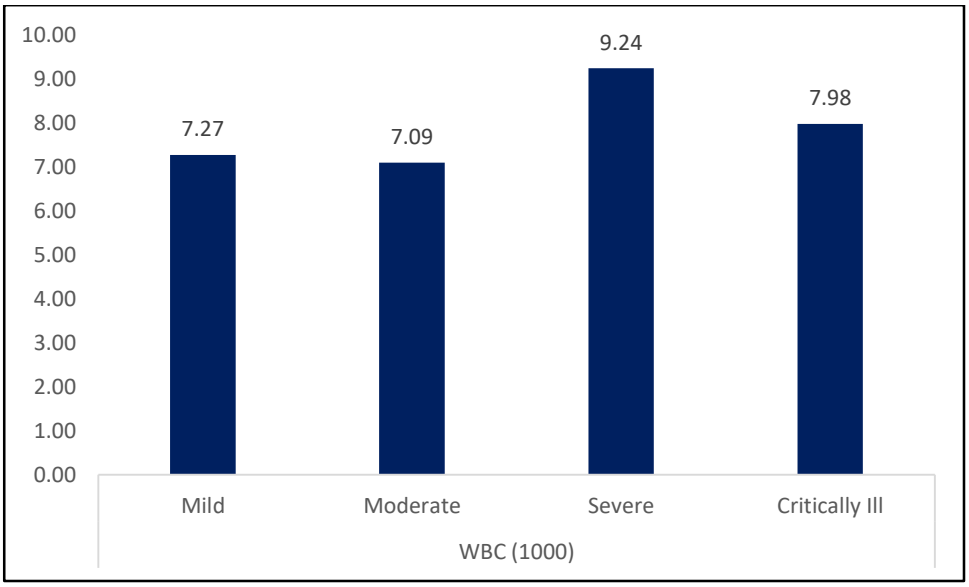
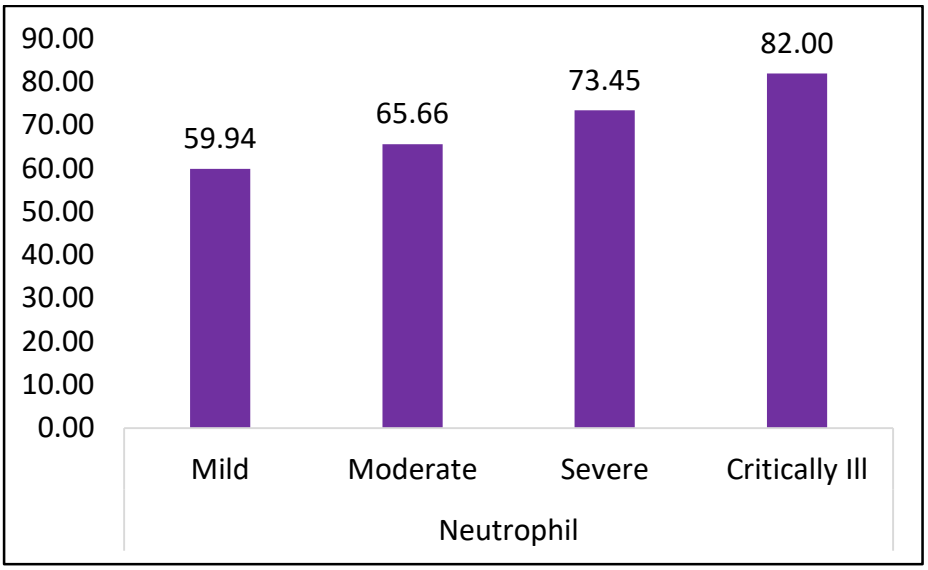


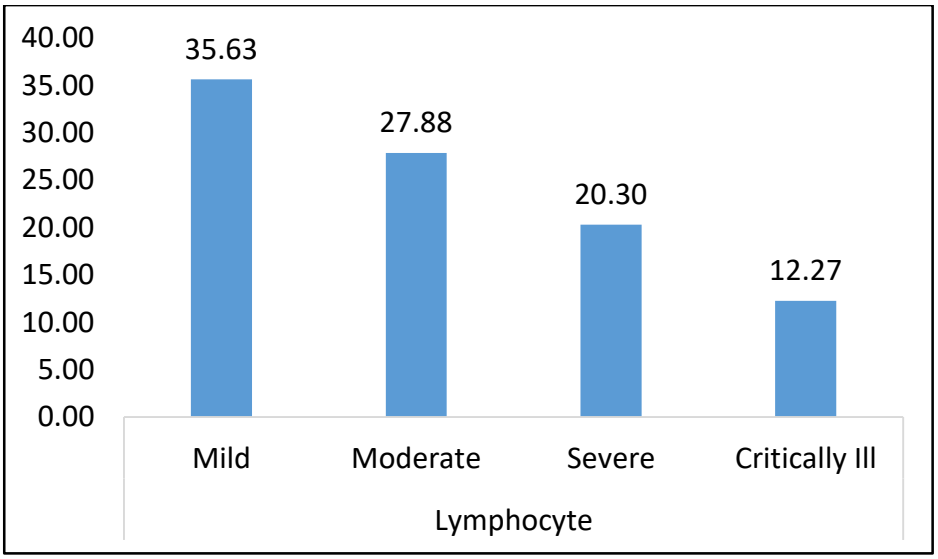
Table 16: Mean comparison of Neutrophil, Lymphocyte and NLR with severity

	Severity	N	Mean	SD	F	Sig.
Neutrophil	Mild	35	59.94	6.804	23.236	**0.0001**
	Moderate	34	65.66	10.903		
	Severe	20	73.45	7.857		
	Critically Ill	11	82	6.083		
	Total	100	67.01	11.079		
Lymphocyte	Mild	35	35.63	7.57	22.057	**0.0001**
	Moderate	34	27.88	12.072		
	Severe	20	20.3	9.28		
	Critically Ill	11	12.27	4.125		
	Total	100	27.36	12.088		
NLR	Mild	35	1.788	0.5338	22.744	**0.0001**
	Moderate	34	3.256	2.7229		
	Severe	20	4.478	2.2046		
	Critically Ill	11	7.387	2.4662		
	Total	100	3.441	2.6537		

Table 16. Explains mean comparison of Neutrophil, Lymphocyte and NLR with severity of COVID-19 patients by One way ANOVA test. It was found there was statistically significant difference exists with p=0.0001. (Graph 16).

Graph 16: Mean comparison of Neutrophil, Lymphocyte and NLR with severity





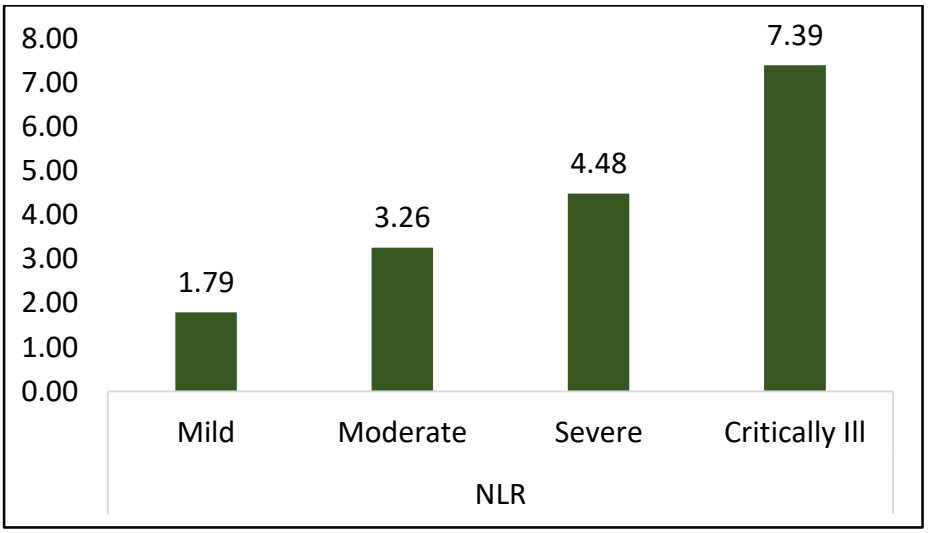
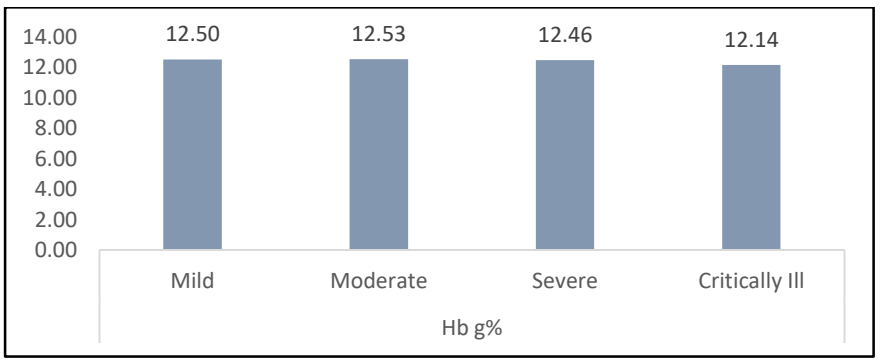


Table 17: Mean comparison of Hb and platelets with severity

	Severity	N	Mean	SD	F	Sig.
Hb g%	Mild	35	12.5	1.363	0.17	0.917
	Moderate	34	12.529	1.856		
	Severe	20	12.455	1.7727		
	Critically Ill	11	12.136	1.4928		
	Total	100	12.461	1.6212		
Platelets (lakh)	Mild	35	2.4114	0.63558	1.267	0.29
	Moderate	34	2.6997	0.93516		
	Severe	20	2.2905	0.7811		
	Critically Ill	11	2.3918	1.08037		
	Total	100	2.4831	0.83162		

Graph 17: Mean comparison of Hb and platelets with severity



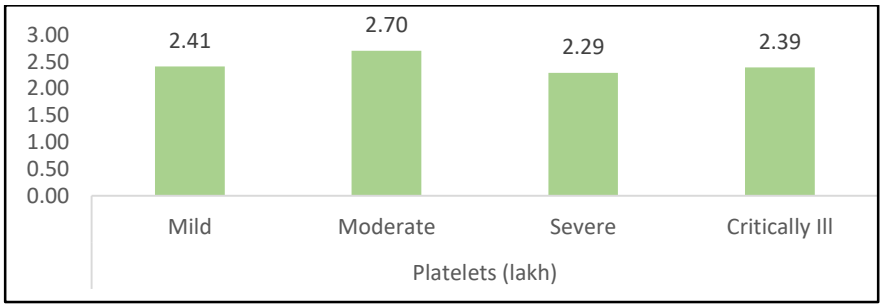


Table 17. Explains mean comparison of Hb and platelet counts with severity of COVID-19 patients by One way ANOVA test. It was found there was no statistically significant difference exists with $p>0.05$.. (Graph 17).

Table 18: Mean comparison of blood urea and serum creatinine with severity

	Severity	N	Mean	SD	F	Sig.
B.Urea	Mild	35	26.89	10.203	1.851	0.143
	Moderate	34	33.15	16.63		
	Severe	20	32.15	16.959		
	Critically Ill	11	36.55	10.482		
	Total	100	31.13	14.334		
Sr.Creatinine	Mild	35	0.834	0.2388	2.567	0.059
	Moderate	34	0.991	0.3621		
	Severe	20	1.11	0.5505		
	Critically Ill	11	0.964	0.2976		
	Total	100	0.957	0.3753		

Graph 18: Mean comparison of blood urea and serum creatinine with severity

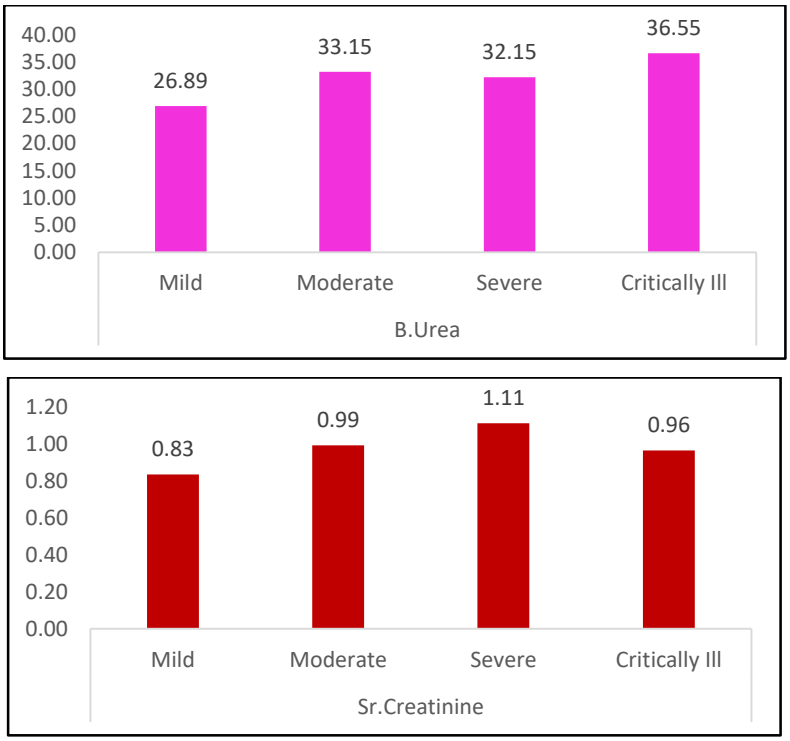


Table 18. Explains mean comparison of blood urea and Serum creatinine with severity of COVID-19 patients by One way ANOVA test. It was found there was no statistically significant difference exists with $p>0.05$. (Graph 18).

Table 19: Mean comparison of blood RBS, FBS and PPBS with severity

	Severity	N	Mean	SD	F	Sig.
RBS	Mild	35	137.97	42.767	8.861	**0.0001**
	Moderate	34	168.21	55.709		
	Severe	20	202	91.053		
	Critically Ill	11	235.36	71.057		
	Total	100	171.77	69.325		
FBS	Mild	35	98.6	29.848	10.364	**0.0001**
	Moderate	34	124.41	40.994		
	Severe	20	137.7	49.828		
	Critically Ill	11	166.73	31.433		
	Total	100	122.69	43.699		
PPBS	Mild	35	155.54	36.699	11.378	**0.0001**
	Moderate	34	186.47	60.045		
	Severe	20	224	71.78		
	Critically Ill	11	249.27	53.965		
	Total	100	190.06	63.208		

Graph 19: Mean comparison of blood RBS, FBS and PPBS with severity

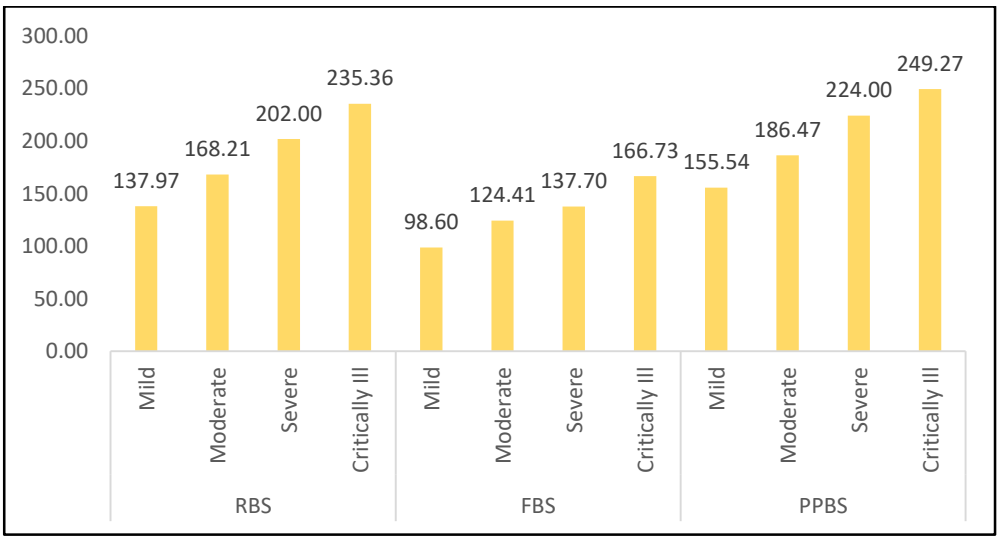


Table 19. Explains mean comparison of RBS, FBS and PPBS with severity of COVID-19 patients by One way ANOVA test. It was found there was statistically significant difference exists with p=0.000I. (Graph 19).

Table 20: Mean comparison of HbA1C with severity

	Severity	N	Mean	SD	F	Sig.
HbA1c	Mild	35	5.763	0.4187	13.901	**0.0001**
	Moderate	34	6.279	0.9425		
	Severe	20	7.025	1.1539		
	Critically Ill	11	7.3	1.0677		
	Total	100	6.36	1.0212		

Graph 20: Mean comparison of HbA1C with severity

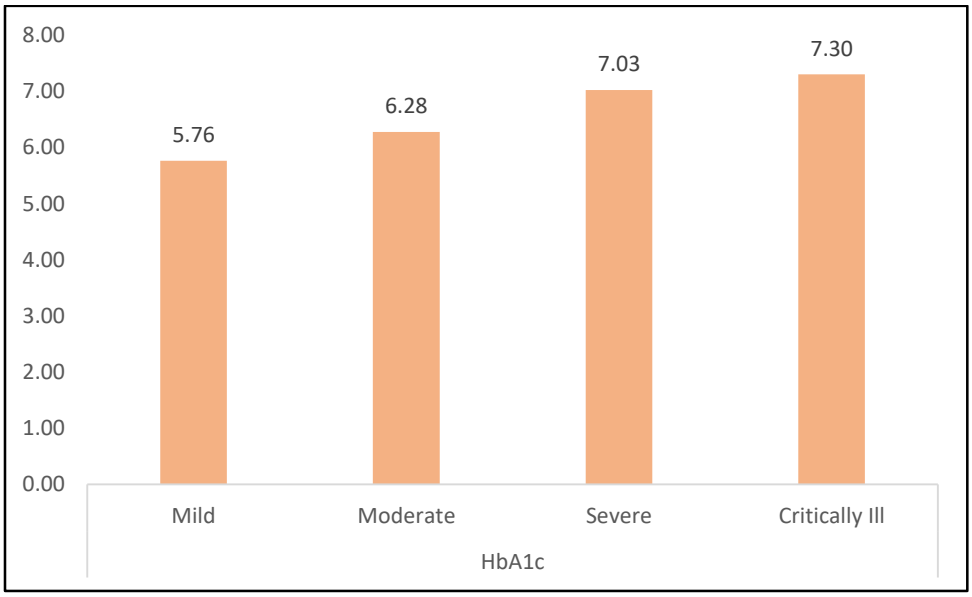


Table 20. Explains mean comparison of HbA1C with severity of COVID-19 patients by One way ANOVA test. It was found there was statistically significant difference exists with p=0.0001. (Graph 20).

Table 21: Mean comparison of SGOT and SGPT with severity

	Severity	N	Mean	SD	F	Sig.
SGOT	Mild	35	37.14	14.781	3.886	**0.011**
	Moderate	34	34.85	13.994		
	Severe	20	43.8	18.702		
	Critically Ill	11	51.55	18.057		
	Total	100	39.28	16.418		
SGPT	Mild	35	38.94	13.211	3.436	**0.02**
	Moderate	34	36.85	18.697		
	Severe	20	48.1	18.442		
	Critically Ill	11	51	15.44		
	Total	100	41.39	17.157		

Graph 21: Mean comparison of SGOT and SGPT with severity

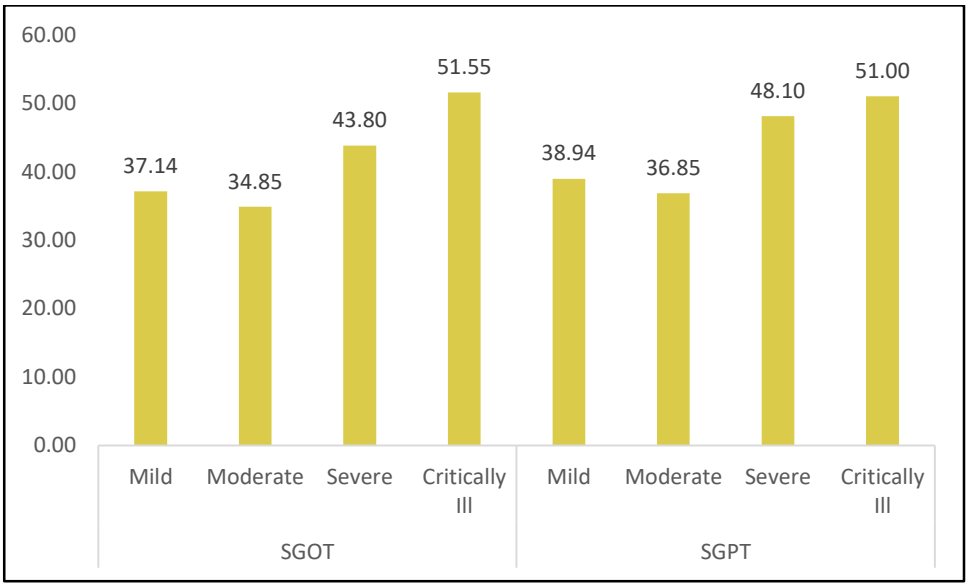


Table 21. Explains mean comparison of SGOT and SGPT with severity of COVID-19 patients by One way ANOVA test. It was found there was statistically significant difference exists with $p<0.05$. (Graph 21).

Table 22: Mean comparison of bilirubin counts with severity

	Severity	N	Mean	SD	F	Sig.
Total. Bilirubin	Mild	35	0.849	0.3776	4.491	**0.005**
	Moderate	34	0.844	0.3395		
	Severe	20	1.145	0.4729		
	Critically Ill	11	1.236	0.65		
	Total	100	0.949	0.4442		
Direct Bilirubin	Mild	35	0.534	0.3143	2.155	0.098
	Moderate	34	0.471	0.3234		
	Severe	20	0.64	0.3662		
	Critically Ill	11	0.745	0.5027		
	Total	100	0.557	0.358		
Indirect Bilirubin	Mild	35	0.314	0.17	3.185	**0.027**
	Moderate	34	0.374	0.2327		
	Severe	20	0.505	0.2911		
	Critically Ill	11	0.491	0.3885		
	Total	100	0.392	0.2557		

Graph 22: Mean comparison of bilirubin counts with severity

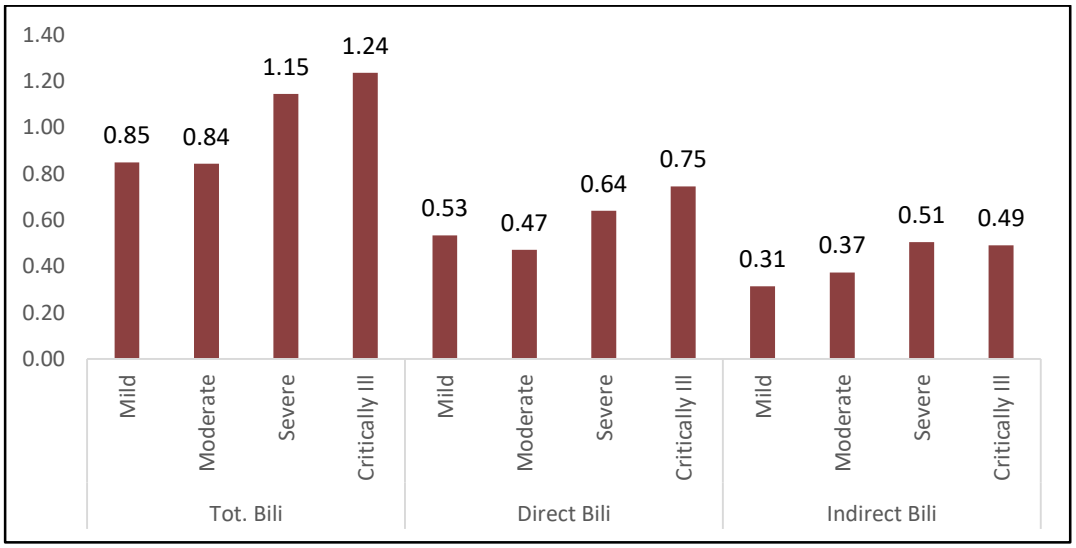


Table 22. Explains mean comparison of bilirubin counts with severity of COVID-19 patients by One way ANOVA test. It was found there was statistically significant difference exists in total bilirubin (p=0.005) and indirect bilirubin (p=0.02). but there was no difference exists in direct bilirubin (p=0.09). (Graph 22).

Table 23: Mean comparison of ALP with severity

	Severity	N	Mean	SD	F	Sig.
ALP	Mild	35	74.6	17.508	3.039	**0.033**
	Moderate	34	70.74	18.878		
	Severe	20	81.85	20.861		
	Critically Ill	11	87.45	16.046		
	Total	100	76.15	19.112		

Graph 23: Mean comparison of ALP with severity

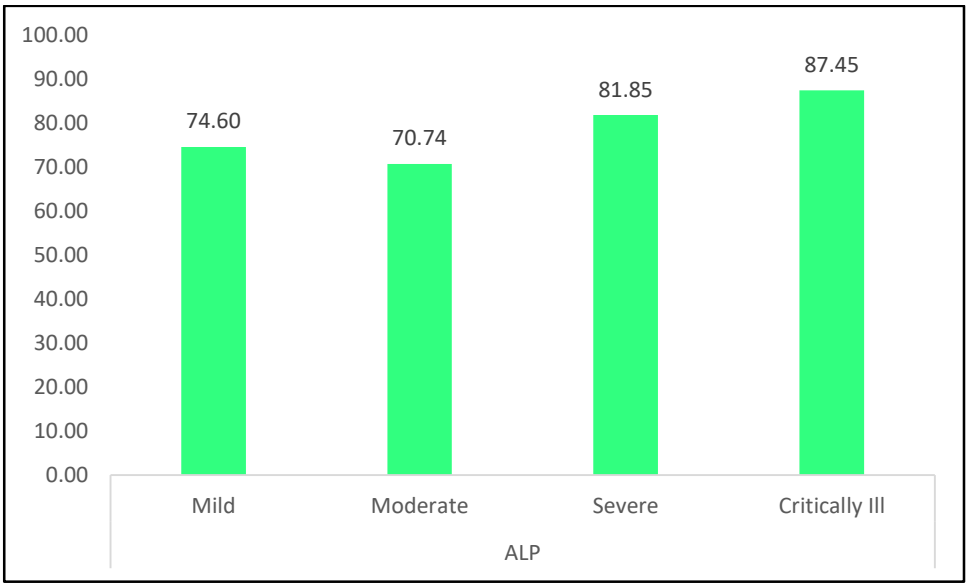


Table 23. Explains mean comparison of ALP with severity of COVID-19 patients by One way ANOVA test. It was found there was statistically significant difference exists with p=0.03. (Graph 23).

Table 24: Mean comparison of Stay with severity

	Severity	N	Mean	SD	F	Sig.
Duration of stay	Mild	35	6.69	1.451	19.489	**0.0001**
	Moderate	34	10	3.542		
	Severe	20	14.35	7.103		
	Critically Ill	11	14.36	3.828		
	Total	100	10.19	5.085		

Graph 24: Mean comparison of Stay with severity

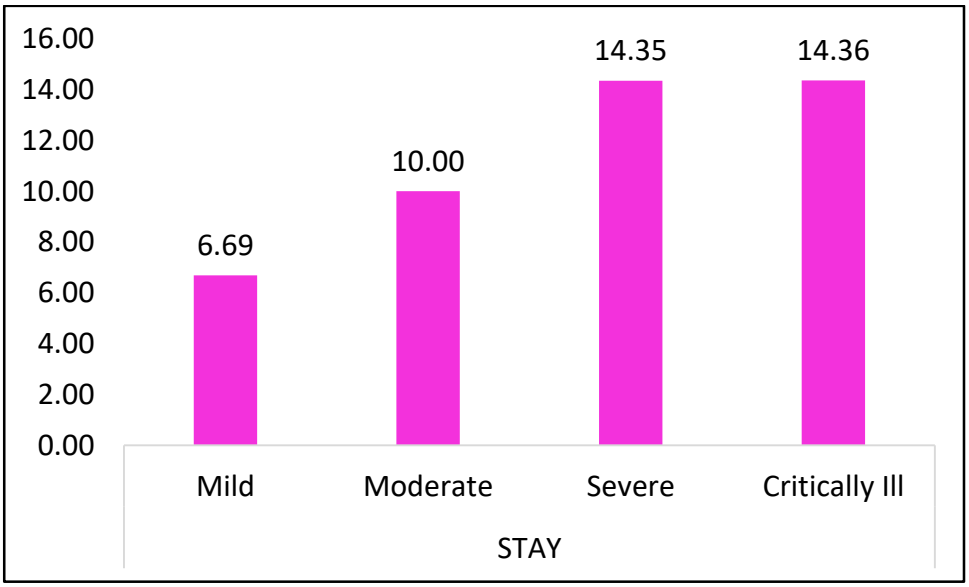


Table 24. Explains mean comparison of hospital stay with severity of COVID-19 patients by One way ANOVA test. It was found there was statistically significant difference exists with p=0.0001. these mean comparison were shown as simple bar diagram. (Graph 24).

Table 25: Association of CT chest involvement with Diabetic status

CT Chest involvement	No DM	DM	Total	Chi sq	p
Nil	25	10	35	13.71	**0.001**
B/L	15	33	48		
U/L	10	7	17		
Total	50	50	100		

Graph 25: Association of CT chest involvement with Diabetic status

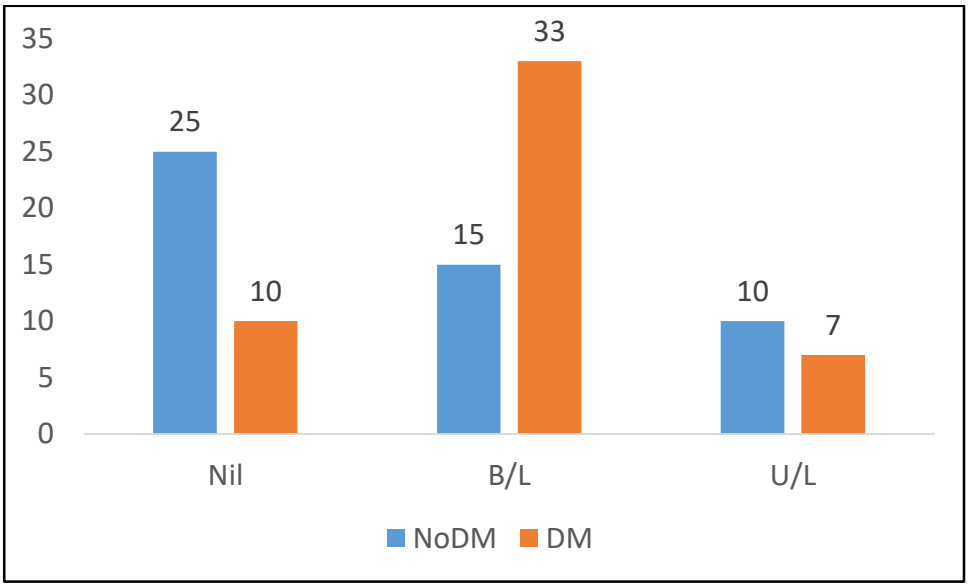


Table 25. Explains that there was significant association with CT chest involvement and diabetic status by chi square test with p =0.001. (Graph 25)

Table 26: Association of dyspnea with Diabetic status

Dyspnea	No DM	DM	Total	Chi sq	p
No	35	19	54	10.3	**0.001**
Yes	15	31	46		
Total	50	50	100		

Graph 26: Association of dyspnea with Diabetic status

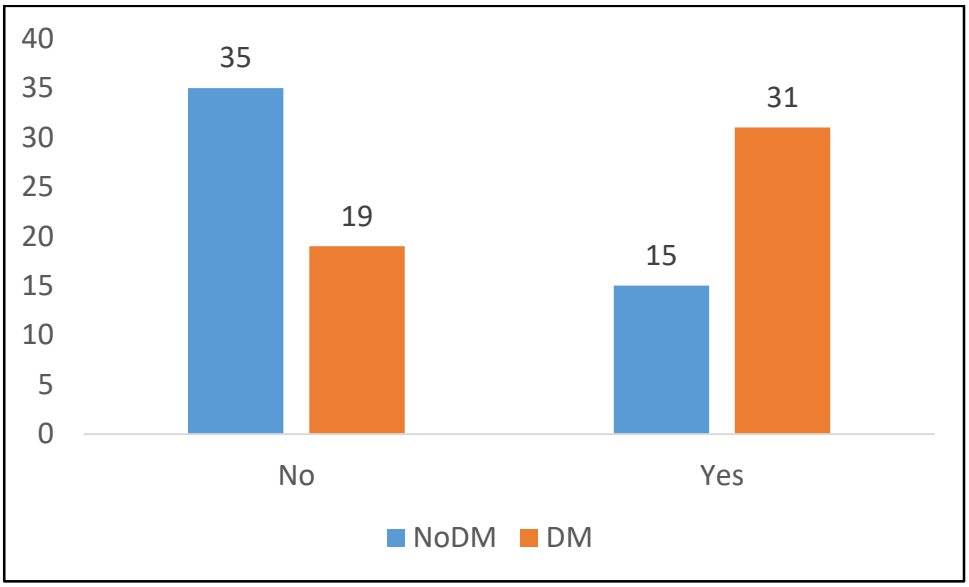


Table 26. Explains that there was significant association with dyspnea and diabetic status by chi square test with p = 0.001; where all other symptoms variables were not significant (Graph 26)

Table 27: Comparison of mean CRP with Diabetic status and covid severity

T2DM vs CRP	Severity	Mean	SD	N	F	Sig.
No DM	Mild	4.004	1.884	25	7.96	**0.0001**
	Moderate	7.193	5.9381	15		
	Severe	34.986	9.3417	7		
	Critically Ill	57.967	2.0108	3		
	Total	12.536	16.3372	50		
DM	Mild	3.11	1.4662	10		
	Moderate	23.3	15.827	19		
	Severe	54.569	31.0859	13		
	Critically Ill	95.138	32.6981	8		
	Total	38.886	37.6706	50		

Graph 27: Comparison of mean CRP with Diabetic status and covid severity

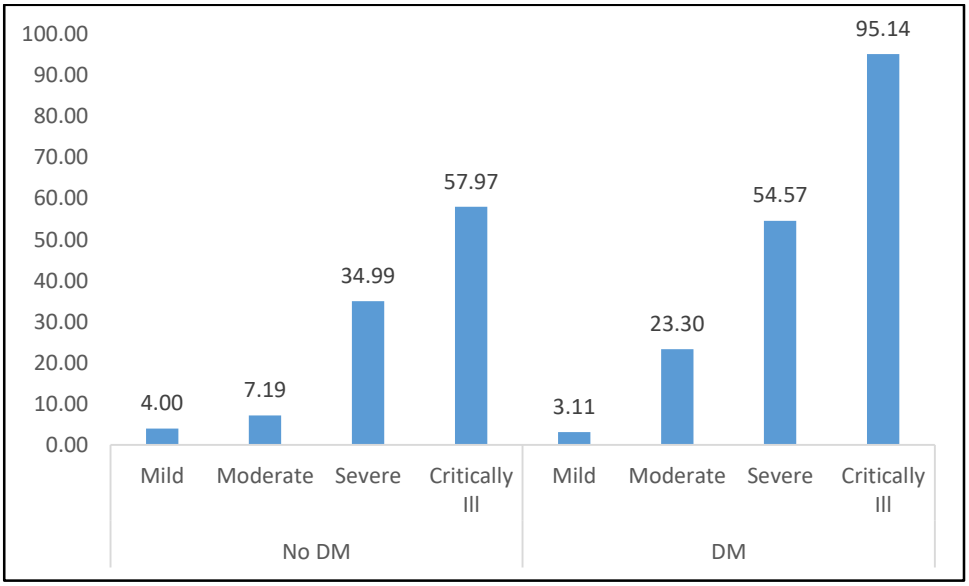


Table 27. Explains the diabetic status along with severity of COVID-19 status for mean CRP levels by generalized linear models. It shows that there were significant difference exists in the subcategories of severity among DM status with p = 0.0001 (Graph 27)

Table 28: Comparison of mean LDH with Diabetic status and covid severity

T2DM vs LDH	Severity	Mean	Std. Deviation	N	F	Sig.
No DM	Mild	121.04	14.345	25	2.788	**0.011**
	Moderate	176.27	7.851	15		
	Severe	220.43	6.852	7		
	Critically Ill	237.67	7.024	3		
	Total	158.52	43.247	50		
DM	Mild	171.9	13.337	10		
	Moderate	245.42	8.092	19		
	Severe	272.46	7.795	13		
	Critically Ill	324.88	13.506	8		
	Total	250.46	48.985	50		

Graph 28: Comparison of mean LDH with Diabetic status and covid severity

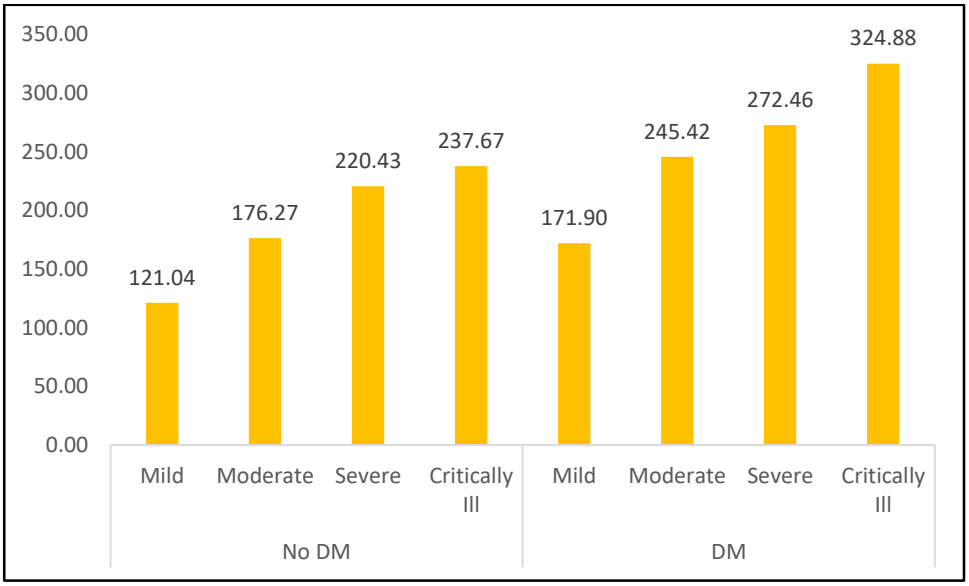


Table 28. Explains the diabetic status along with severity of COVID-19 status for mean LDH levels by generalized linear models. It shows that there were significant difference exists in the subcategories of severity among DM status with p = 0.01 (Graph 28)

Table 29: Comparison of mean Ferritin with Diabetic status and covid severity

T2DM vs Ferritin	Severity	Mean	Std. Deviation	N	F	Sig.
No DM	Mild	110.48	33.453	25	5.764	**0.0001**
	Moderate	179.67	28.477	15		
	Severe	231.43	14.774	7		
	Critically Ill	327.67	46.199	3		
	Total	161.2	68.642	50		
DM	Mild	185.3	56.252	10		
	Moderate	258.79	49.902	19		
	Severe	314.54	46.697	13		
	Critically Ill	390.75	68.959	8		
	Total	279.7	83.862	50		

Graph 29: Comparison of mean Ferritin with Diabetic status and covid severity

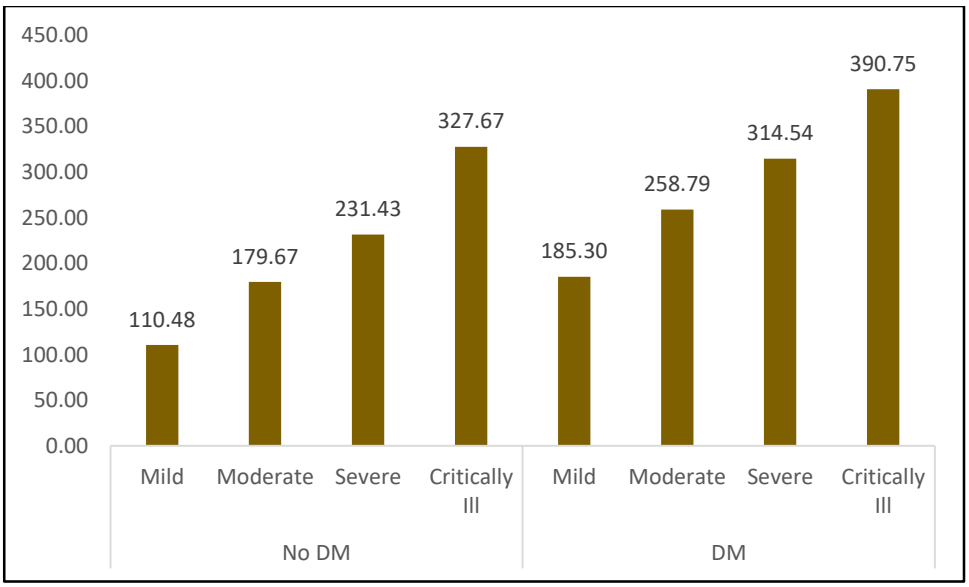


Table 29. Explains the diabetic status along with severity of COVID-19 status for mean ferritin levels by generalized linear models. It shows that there were significant difference exists in the subcategories of severity among DM status with p = 0.0001 (Graph 29)

Table 30: Comparison of mean D-dimer with Diabetic status and covid severity

T2DM vs D-dimer	Severity	Mean	SD	N	F	Sig.
No DM	Mild	0.1352	0.0196	25	3.203	**0.004**
	Moderate	0.2233	0.01759	15		
	Severe	0.2714	0.01676	7		
	Critically Ill	0.34	0.02646	3		
	Total	0.193	0.06729	50		
DM	Mild	0.143	0.02312	10		
	Moderate	0.2521	0.02417	19		
	Severe	0.3508	0.02842	13		
	Critically Ill	0.4938	0.04438	8		
	Total	0.2946	0.11617	50		

Graph 30: Comparison of mean D-dimer with Diabetic status and covid severity

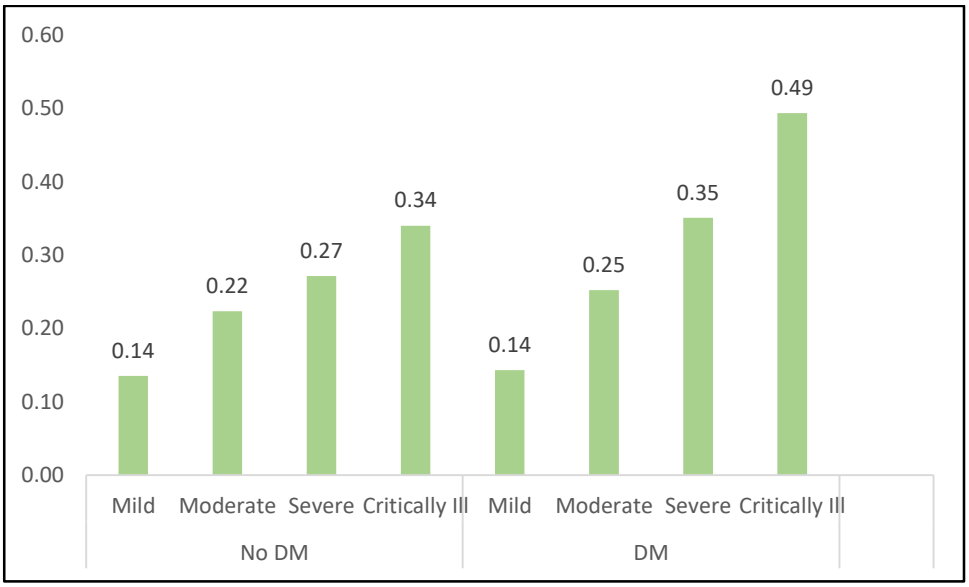


Table 30. Explains the diabetic status along with severity of COVID-19 status for mean D-dimer levels by generalized linear models. It shows that there were significant difference exists in the subcategories of severity among DM status with p = 0.004 (Graph 30)

Table 31: Comparison of mean Procalcitonin with Diabetic status and covid severity

T2DM vs Procalcitonin	Severity	Mean	SD	N	F	Sig.
No DM	Mild	0.1392	0.01913	25	7.215	**0.0001**
	Moderate	0.2367	0.02193	15		
	Severe	0.2557	0.03823	7		
	Critically Ill	0.52	0.08888	3		
	Total	0.2076	0.09884	50		
DM	Mild	0.147	0.02669	10		
	Moderate	0.2295	0.04007	19		
	Severe	0.2708	0.07847	13		
	Critically Ill	0.4462	0.10239	8		
	Total	0.2584	0.11129	50		

Graph 31: Comparison of mean Procalcitonin with Diabetic status and covid severity

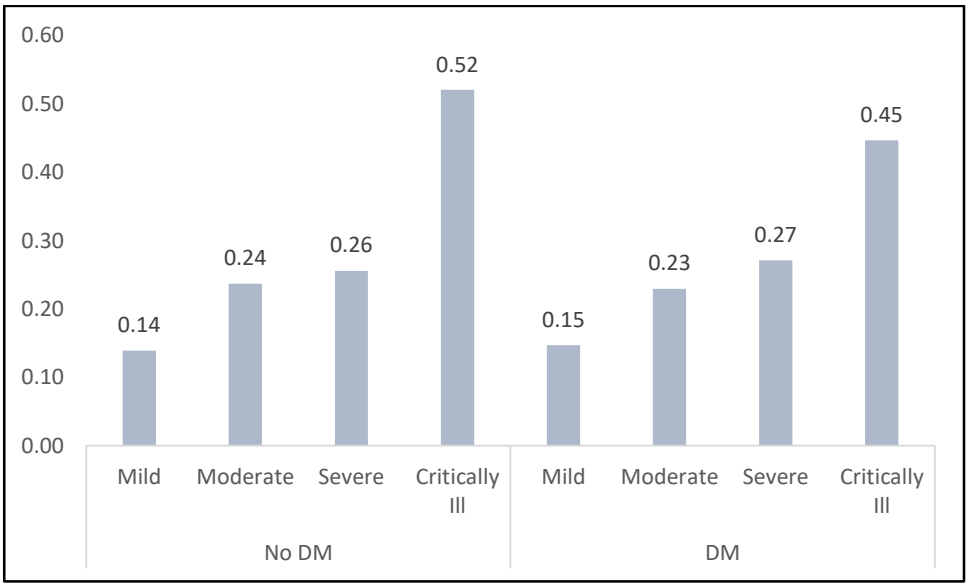


Table 31. Explains the diabetic status along with severity of COVID-19 status for mean procalcitonin levels by generalized linear models. It shows that there were significant difference exists in the subcategories of severity among DM status with p = 0.0001 (Graph 31)

Table 32: Comparison of mean WBC with Diabetic status and covid severity

T2DM vs WBC	Severity	Mean	SD	N	F	Sig.
No DM	Mild	7.34	2.3502	25	3.284	**0.004**
	Moderate	6.9	2.2469	15		
	Severe	8.514	3.0667	7		
	Critically Ill	9.7	0.8	3		
	Total	7.514	2.4273	50		
DM	Mild	7.09	1.5242	10		
	Moderate	7.237	2.5751	19		
	Severe	9.623	4.0345	13		
	Critically Ill	7.328	3.5357	8		
	Total	7.842	3.1268	50		

Graph 32: Comparison of mean WBC with Diabetic status and covid severity

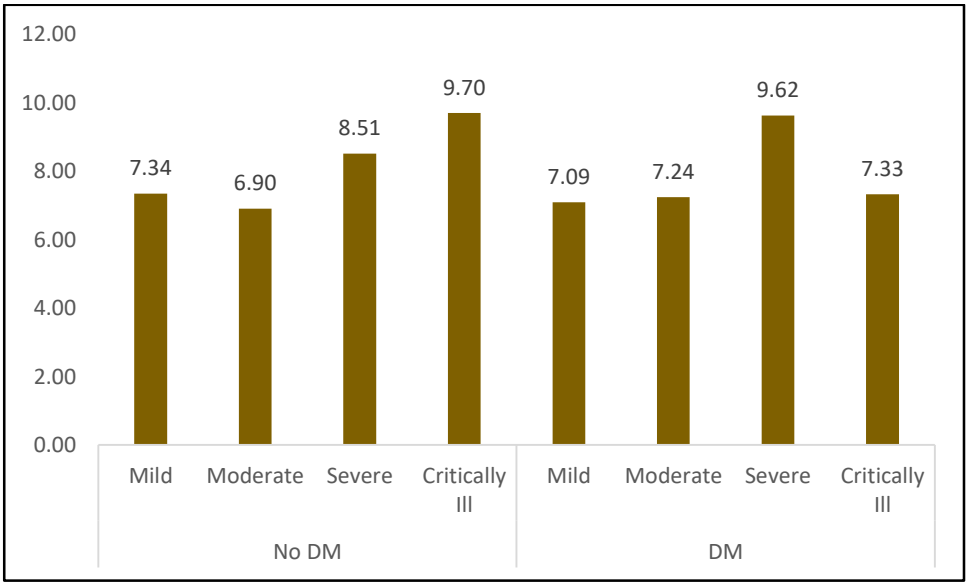


Table 32. Explains the diabetic status along with severity of COVID-19 status for mean WBC counts by generalized linear models. It shows that there were significant difference exists in the subcategories of severity among DM status with p = 0.0001 (Graph 32)

Table 33: Comparison of mean neutrophils with Diabetic status and covid severity

T2DM vs Neutrophil	Severity	Mean	SD	N	F	Sig.
No DM	Mild	59.56	7.5	25	2.452	**0.024**
	Moderate	60.2	8.099	15		
	Severe	68.86	9.227	7		
	Critically Ill	84.33	4.041	3		
	Total	62.54	9.918	50		
DM	Mild	60.9	4.841	10		
	Moderate	69.96	11.069	19		
	Severe	75.92	6.02	13		
	Critically Ill	81.12	6.707	8		
	Total	71.49	10.429	50		

Graph 33: Comparison of mean neutrophils with Diabetic status and covid severity

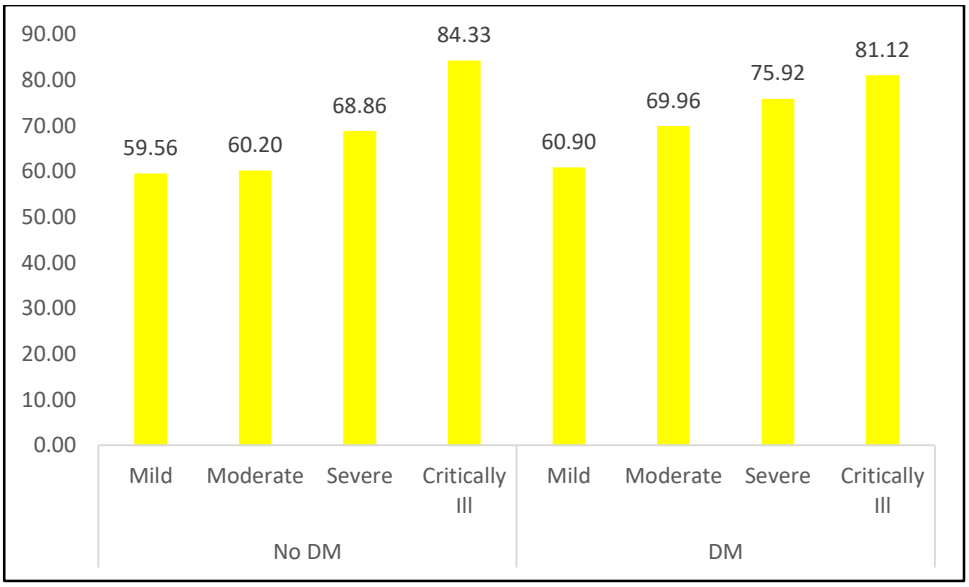


Table 33. Explains the diabetic status along with severity of COVID-19 status for mean neutrophils by generalized linear models. It shows that there were significant difference exists in the subcategories of severity among DM status with p = 0.02 (Graph 33)

Table 34 : Comparison of mean NLR with Diabetic status and covid severity

T2DM vs NLR	Severity	Mean	SD	N	F	Sig.
No DM	Mild	1.762	0.5827	25	4.73	**0.0001**
	Moderate	1.784	0.7211	15		
	Severe	2.834	1.3272	7		
	Critically Ill	7.982	2.0247	3		
	Total	2.292	1.7159	50		
DM	Mild	1.853	0.4054	10		
	Moderate	4.418	3.1558	19		
	Severe	5.364	2.0945	13		
	Critically Ill	7.164	2.7035	8		
	Total	4.59	2.9306	50		

Graph 34: Comparison of mean NLR with Diabetic status and covid severity

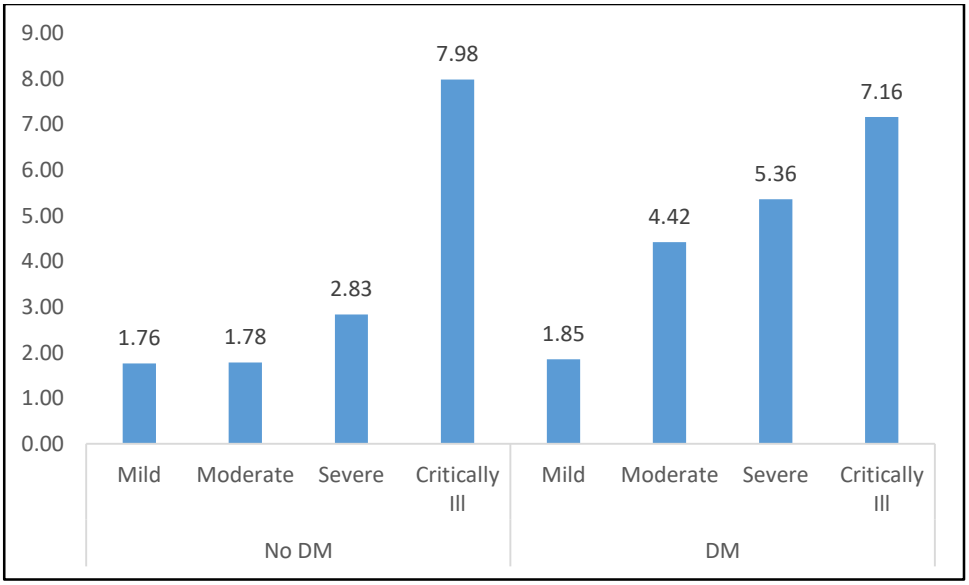


Table 34. Explains the diabetic status along with severity of COVID-19 status for mean NLR by generalized linear models. It shows that there were significant difference exists in the subcategories of severity among DM status with p = 0.0001 (Graph 34)

Table 35: Comparison of mean HbA1C with Diabetic status and covid severity

T2DM vs HbA1C	Severity	Mean	SD	N	F	Sig.
No DM	Mild	5.632	0.4007	25	5.157	**0.0001**
	Moderate	5.567	0.383	15		
	Severe	5.786	0.418	7		
	Critically Ill	6.167	0.1155	3		
	Total	5.666	0.4044	50		
DM	Mild	6.09	0.2601	10		
	Moderate	6.842	0.8701	19		
	Severe	7.692	0.8015	13		
	Critically Ill	7.725	0.9316	8		
	Total	7.054	0.98	50		

Graph 35: Comparison of mean HbA1C with Diabetic status and covid severity

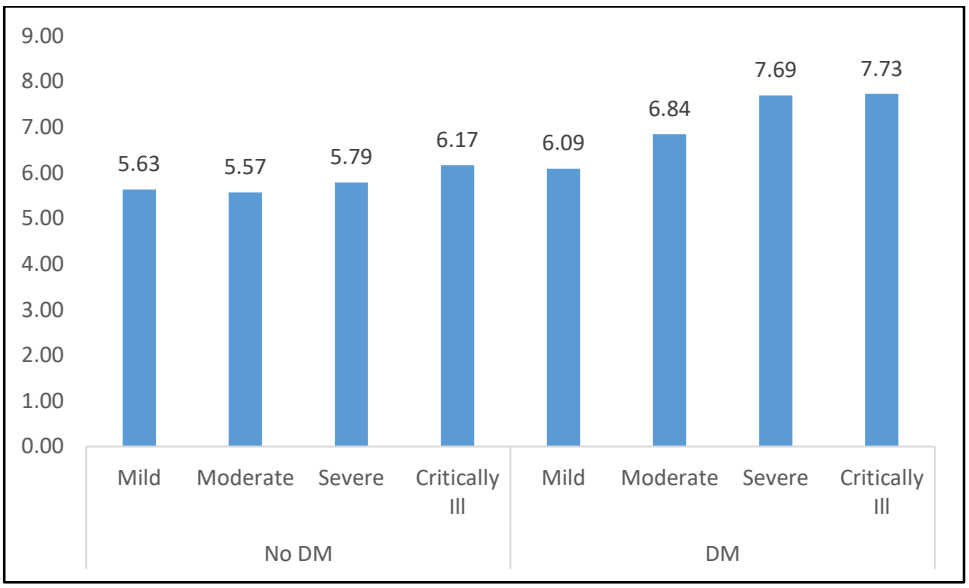


Table 35. Explains the diabetic status along with severity of COVID-19 status for mean HbA1C levels by generalized linear models. It shows that there were significant difference exists in the subcategories of severity among DM status with p = 0.0001 (Graph 35)

Table 36: Comparison of mean RBS, FBS and PPBS with Diabetic status and covid severity

T2DM vs RBS	Severity	Mean	SD	N	F	Sig.
No DM	Mild	122.6	37.768	25	5.393	**0.0001**
	Moderate	137.8	22.431	15		
	Severe	126.71	41.411	7		
	Critically Ill	160.33	6.658	3		
	Total	130	34.039	50		
DM	Mild	176.4	28.438	10		
	Moderate	192.21	62.607	19		
	Severe	242.54	84.751	13		
	Critically Ill	263.5	62.313	8		
	Total	213.54	70.645	50		

T2DM vs FBS	Severity	Mean	SD	N	F	Sig.
No DM	Mild	85.6	20.185	25	2.671	**0.015**
	Moderate	90	19.986	15		
	Severe	85.43	14.627	7		
	Critically Ill	124	14	3		
	Total	89.2	20.757	50		
DM	Mild	131.1	25.221	10		
	Moderate	151.58	31.692	19		
	Severe	165.85	37.042	13		
	Critically Ill	182.75	16.723	8		
	Total	156.18	33.74	50		

T2DM vs PPBS	Severity	Mean	Std. Deviation	N	F	Sig.
No DM	Mild	136.68	21.416	25	6.056	**0.0001**
	Moderate	131.2	26.611	15		
	Severe	144.43	10.706	7		
	Critically Ill	170	14.107	3		
	Total	138.12	23.082	50		
DM	Mild	202.7	20.144	10		
	Moderate	230.11	38.776	19		
	Severe	266.85	49.178	13		
	Critically Ill	279	20.007	8		
	Total	242	45.096	50		

Graph 36: Comparison of mean RBS, FBS and PPBS with Diabetic status and covid severity

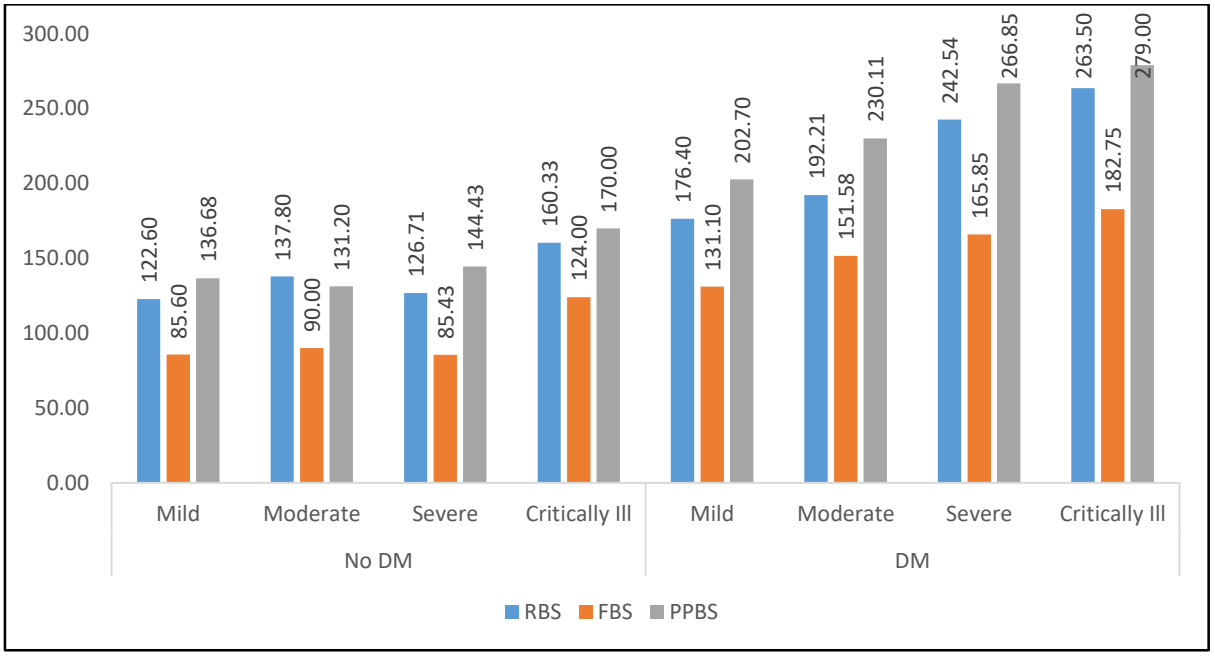


Table 36. Explains the diabetic status along with severity of COVID-19 status for mean blood sugar levels by generalized linear models. It shows that there were significant difference exists in the subcategories of severity among DM status with p = 0.0001 for RBS and PPBS; FBS with p = 0.01. (Graph 36)

Table 37: Comparison of mean bilirubin with Diabetes and covid severity

T2DM vs total bilirubin	Severity	Mean	SD	N	F	Sig.
No DM	Mild	0.868	0.3761	25	4.134	**0.001**
	Moderate	0.967	0.2795	15		
	Severe	1.214	0.2545	7		
	Critically Ill	1.3	0.2646	3		
	Total	0.972	0.3505	50		
DM	Mild	0.8	0.3972	10		
	Moderate	0.747	0.358	19		
	Severe	1.108	0.5634	13		
	Critically Ill	1.212	0.7624	8		
	Total	0.926	0.524	50		

T2DM vs direct bilirubin	Severity	Mean	SD	N	F	Sig.
No DM	Mild	0.516	0.3197	25	2.572	**0.018**
	Moderate	0.587	0.3461	15		
	Severe	0.643	0.4392	7		
	Critically Ill	0.733	0.1528	3		
	Total	0.568	0.3359	50		
DM	Mild	0.58	0.312	10		
	Moderate	0.379	0.28	19		
	Severe	0.638	0.3404	13		
	Critically Ill	0.75	0.5952	8		
	Total	0.546	0.3818	50		

T2DM indirect bilirubin	Severity	Mean	SD	N	F	Sig.
No DM	Mild	0.352	0.1735	25	2.014	0.062
	Moderate	0.38	0.2274	15		
	Severe	0.571	0.2928	7		
	Critically Ill	0.567	0.3786	3		
	Total	0.404	0.2303	50		
DM	Mild	0.22	0.1229	10		
	Moderate	0.368	0.2428	19		
	Severe	0.469	0.2955	13		
	Critically Ill	0.462	0.4138	8		
	Total	0.38	0.2807	50		

Graph 37: Comparison of mean bilirubin with Diabetes and covid severity

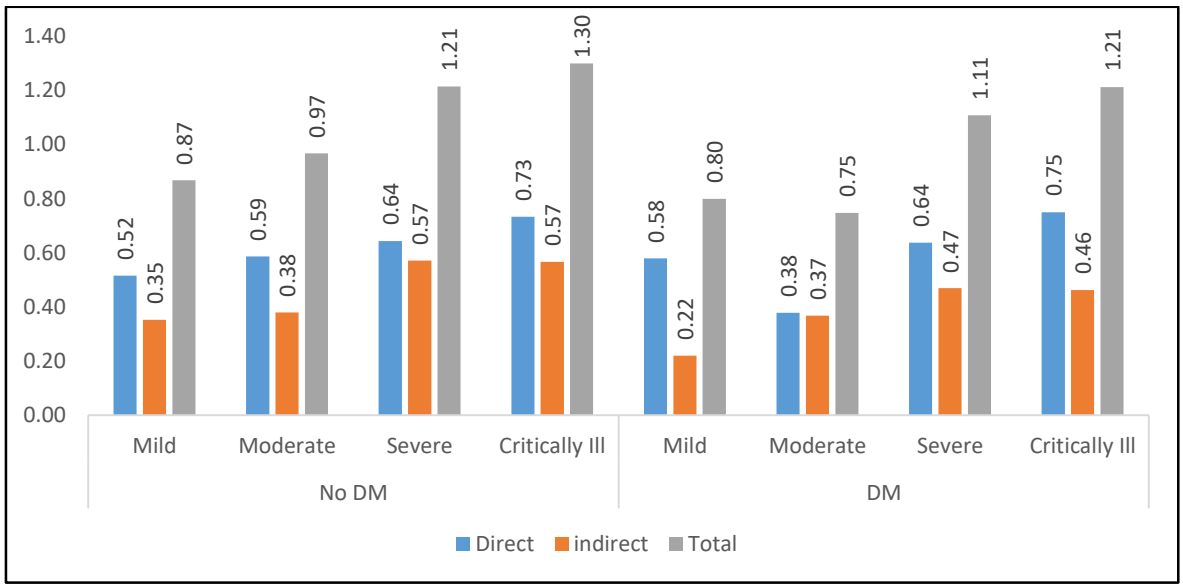


Table 37. Explains the diabetic status along with severity of COVID-19 status for mean bilirubin counts by generalized linear models. It shows that there were significant difference exists in the subcategories of severity among DM status with $p < 0.01$ for direct and total bilirubin counts but it was not significant for indirect bilirubin counts $P>0.05$. (Graph 37)

Table 38: Comparison of mean stay with Diabetic and covid severity

T2DM vs Stay	Severity	Mean	SD	N	F	p
No DM	Mild	6.88	1.453	25	5.642	**0.0001**
	Moderate	8.87	1.598	15		
	Severe	14.14	1.952	7		
	Critically Ill	11.67	2.082	3		
	Total	8.78	2.978	50		
DM	Mild	6.2	1.398	10		
	Moderate	10.89	4.37	19		
	Severe	14.46	8.828	13		
	Critically Ill	15.38	3.926	8		
	Total	11.6	6.269	50		

Graph 38: Comparison of mean stay with Diabetic and covid severity

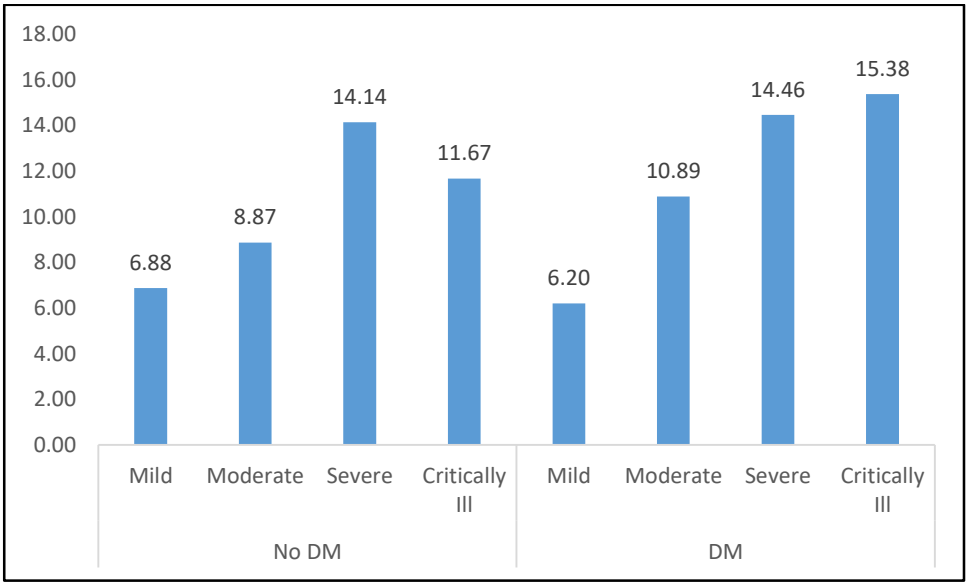


Table 38. Explains the diabetic status along with severity of COVID-19 status for mean stay of participants by generalized linear models. It shows that there were significant difference exists in the subcategories of severity among DM status with p = 0.0001 (Graph 38)

DISCUSSION

A novel virus causing pneumonia found in Wuhan, China, during the end of year 2019, later identified as a SARS-CoV-2, also known as COVID-19. Later this virus spreads rapidly into many countries and produced a pandemic disease. COVID-19 infection leads to severe pneumonia and ARDS, increased mortality. Patients with comorbidities more likely to develop severe disease.

In this study, we analysed the age distribution of patients, in which 51% were in 40-50 years, 36% were in 51-60 years, 13% were in above 60 years. The distribution of patients admitted in the tertiary care centre decreases with increase in age. The severity of COVID-19 showed no statistically significant difference among different ages of patients admitted in this tertiary centre with p=0.3.

In this study, gender analysis showed that the patients admitted were more in number of males with 59% and female with 41%. The severity analyses showed no statistically significant difference between male and female patients with p = 0.9.

Analysing the symptoms, most patients had fever (90%) followed by myalgia (73%), cough (48%), dyspnea (46%) and diarrhoea (19%). The severity of disease was found to be significant with the dyspnea (p=0.0001) and was not associated with other symptoms included in this study. We found that dyspnea had significant association with diabetic patients (p=0.001) compared with non-diabetic patients.

Regarding the presence of associated comorbidities other than 50 diabetes among the participants, hypertension and coronary artery diseases were present in majority of patients (79%). The severity of patients irrespective of diabetes were about 69% with mild and moderate disease, followed by severe in 20% and critically ill in 11% of patients. We found that among the comorbidities, diabetes was found to be significantly associated with severity of COVID-19 (p=0.01).

Among the study participants, the lung involvement in Computed tomography were found to be bilateral in 48%, no lung involvement in 35% and unilateral in 17%. CT chest showed that diabetic patients had extensive and bilateral lung involvement than non-diabetic patients (p=0.001). Most of non-diabetic had normal to unilateral involvement.

On analysing the pulse rate, respiratory rate and SpO_2 with the severity of COVID-19 by one way ANOVA test, we found that a significant difference exists with p=0.0001, p=0.0001, p=0.0001 respectively. But we found no significant association with the blood pressure of the patients admitted in this centre.

In this study, we found the significant association of biochemical markers like CRP, LDH, ferritin and D-dimer with the severity of COVID-19 (each with p value = 0.0001). All these biochemical markers also showed significant association with the severity in diabetic patients compared to non-diabetic patients. This is because of higher inflammatory cytokine storm, leads to higher biomarkers levels.

There was also significant association of prothrombin time, procalcitonin and white blood cells count with the severity of COVID-19 with p value of 0.0001, 0.0001 and 0.032 respectively. The mean procalcitonin and white blood cells count showed significant association with the diabetic patients compared to non-diabetic patients.

In this study, Mean comparison of neutrophils, lymphocytes, NLR with severity of COVID-19 showed significant association with p=0.0001.

This study showed no association of haemoglobin, platelets, blood urea and serum creatinine with the severity of COVID-19. The mean neutrophils count and neutrophil lymphocyte ratio showed significant association with the diabetic patients compared to non-diabetic patients.

The values of RBS, FBS, PPBS to the severity of COVID-19 showed statistically significant difference with p=0.0001. Most patients with uncontrolled hyperglycaemia had severe disease than patients with controlled glycaemic levels. Patients with diabetes had higher HbA1c levels than those without diabetes. Patients with high HbA1c levels had higher glycaemic levels, leading to high cytokine storm, and severity of the disease (p=0.0001).

The blood levels of SGOT, SGPT, ALP, Total and indirect bilirubin are found to be having significant association with the severity of the disease with p values 0.011, 0.02, 0.033, 0.005, 0.027 respectively. The mean SGOT, SGPT, ALP, Total and indirect bilirubin values showed significant association with the diabetic patients

compared to non-diabetic patients. The direct bilirubin level showed no significant association with the severity of COVID-19.

Out of 100 patients admitted, the duration of hospital stay varies with disease severity and it shows a significant difference exist with p=0.0001. Patients with severe and critically ill disease stayed in hospital for longer duration than patients with mild to moderate disease. The mean duration of hospital stay showed significant association with the diabetic patients compared to non-diabetic patients.

SUMMARY

This observational study was done with laboratory confirmed 100 COVID-19 patients were admitted in Government Rajaji hospital, Madurai. From this study, we found that there was an association of biochemical markers like CRP, ferritin, LDH and the radiological lung involvement with the severity of COVID-19 infection in diabetic patients.

CONCLUSION

From this observational study, we found that diabetic patients had higher biochemical markers than compared to non-diabetic patients like CRP, LDH, ferritin, D-dimer and procalcitonin because of the cytokine storm. Diabetic patients, also had more lung involvement and its correlation with severity of COVID-19 than those without diabetes. The other blood tests along with associated symptoms also helps in assessing the severity of the COVID-19 in patients admitted in the tertiary care centre. We are concluding that the patients with elevated markers and extensive lung involvement are to be monitored crucially to prevent the severe nature of the illness, reduces the duration of hospitalisation and prevent the mortality of the disease. More particularly the diabetic patients need strict glycaemic control and more care in view of severe cytokine storm in them than compared to non-diabetic patients.

LIMITATION

4. This study was conducted in a single centre. Large multicentre study may needed for better correlation of severity.
5. Time interval between onset of illness to hospital admission vary which further increases the severe nature of illness.
6. Other co-morbid conditions also included in this study which may also increases the severity.

ஆராய்ச்சி ஒப்புதல் படிவம்

பெயர்: தேதி:

வயது : நோயாளி எண்:

ஆராய்ச்சி சேர்க்கை எண்:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு விளக்கபட்டது.

எனக்கு விளக்கபட்ட விஷயங்களை நான் புரிந்து கொண்டு எனது முழுமனதுடன் சம்மதிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில்தான் பங்குபெறுகிறேன் மற்றும் நான் இந்த ஆராய்ச்சியில் இருந்து எந்த நேரமும் பின்வாங்கலாம் என்றும் அதனால் எந்த பாதிப்பும் எனக்கு ஏற்படாது என்பதையும் புரிந்து கொண்டேன்.

நான் என்னுடைய சுயநினைவுடன் மற்றும் முழு சுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் பங்குகொள்ள சம்மதிக்கிறேன்.

BIBLIOGRAPHY

1. **Yang JK, Feng Y, Yuan MY, Yuan SY, Fu HJ, Wu BY.** Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. Diabet Med 2006;23(6):623e8.
2. **Al-Tawfiq JA, Hinedi K, Ghandour J, Khairalla H, Musleh S, Ujayli A.** Middle East respiratory syndrome coronavirus: a case econtrol study of hospitalized patients. Clin Infect Dis 2014;59:160e5.
3. **Kulcsar KA, Coleman CM, Beck SE, Frieman MB.** Comorbid diabetes results in immune dysregulation and enhanced disease severity following MERS-CoV infection. JCI Insight 2019;4(20):131774.
4. **Gupta R, Ghosh A, Singh AK, Misra A.** Clinical considerations for patients with diabetes in times of COVID-19 epidemic. Diabetes Metab Syndr 2020 Mar 10;14(3):211e2.
5. **Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J.** Clinical characteristics of hospitalized patients with 2019 novel corona virus infected pneumonia in Wuhan, China. J Am Med Assoc 2020;323(11):1061e9.
6. **Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ**. Clinical characteristics of 140 patients infected with SARSCoV-2 in Wuhan, China. Allergy 2020 Feb 19.
7. **Yang X, Yu Y, Shu H, Xia J, Liu H, Wu Y.** Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single centered, retrospective, observational study. Lancet Respir Med 2020.
8. **Vaduganathan M, Vardeny O, Michel T, McMurray JJV, Pfeffer MA, Solomon SD.** Renin angiotensin aldosterone system inhibitors in patients with COVID-19. NEJM March 30, 2020.
9. **Maddaloni E, Buzzetti R.** COVID-19 and diabetes mellitus: unveiling the interaction of two pandemics. Diabetes Metab Res Rev 2020 Mar 31.

10. **Iacobellis G.** COVID-19 and Diabetes: can DPP4 inhibition play a role? Diabetes Res Clin Pract 2020 Mar 26:108125.
11. **Yang JK, Feng Y, Yuan MY, Yuan SY.** Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. Diabet Med 2006 Jun;23(6):623e8.
12. **Chen W, Zhen W, Cai M, Penninger JM, Jiang C, Wang X.** Angiotensin-converting enzyme 2 (ACE2) mediates influenza H7N9 virus-induced acute lung injury. Sci Rep 2014;4:7027.
13. **Fang L, Karakiulakis G, Roth M.** Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med 2020.
14. **Rubino F, Amiel SA, Zimmet P.** New-onset diabetes in COVID-19. N Engl J Med. 2020;383(8):789-790.
15. **Pal R, Banerjee M, Yadav U, Bhattacharjee S.** Clinical profile and outcomes in COVID-19 patients with diabetic ketoacidosis: a systematic review of literature. Diabetes Metab Syndr. 2020;14(6):1563-1569.
16. **Zhu L, She ZG, Cheng X.** Association of blood glucose control and out-comes in patients with COVID-19 and pre-existing type 2 diabetes. Cell Metab.2020;31(6):1068e1077.e3.
17. **Bode B, Garrett V, Messler J.** Glycemic characteristics and clinical outcomes of COVID-19 patients hospitalized in the United States. J Diabetes Sci Technol. 2020;14(4):813e821.
18. **Cariou B, Hadjadj S, Wargny M.** Phenotypic characteristics and prognosis of inpatients with COVID-19 and diabetes: the CORONADO study. Diabetologia. 2020;63(8):1500e1515.
19. **Agarwal S, Schechter C, Southern W, Crandall JP, Tomer Y.** Preadmission diabetes-specific risk factors for mortality in hospitalized patients with diabetes and coronavirus disease 2019. Diabetes Care. 2020;43(10):2339e2344.

20. **Muniyappa R, Gubbi S.** COVID-19 pandemic, coronaviruses, and diabetes mellitus. Am J Physiol Endocrinol Metab. 2020;318(5): E736–E741.
21. **Katulanda P, Dissanayake HA, Ranathunga I.** Prevention and management of COVID-19 among patients with diabetes: an appraisal of the literature. Diabetologia. 2020;63(8):1440–1452.
22. **Singh AK, Gupta R, Ghosh A, Misra A.** Diabetes in COVID-19: prevalence, pathophysiology, prognosis and practical considerations. Diabetes Metab Syndr. 2020;14(4):303–310.
23. **Roncon L, Zuin M, Rigatelli G.** Diabetic patients with COVID-19 infection are at higher risk of ICU admission and poor short-term outcome. J Clin Virol. 2020;127:104354.
24. **Conway J, Gould A, Westley R.** Characteristics of patients with diabetes hospitalised for COVID-19 infection-a brief case series report. Diabetes Res Clin Pract. 2020;169:108460.
25. **Yan Y, Yang Y, Wang F.** Clinical characteristics and outcomes of patients with severe COVID-19 with diabetes. BMJ Open Diab Res Care. 2020;8:e001343.
26. **Wang F, Yang Y, Dong K.** Clinical characteristics of 28 patients with diabetes and COVID-19 in Wuhan, China. Endocr Pract. 2020;26:668-674
27. **Zhang Y, Cui Y, Shen M.** Comorbid diabetes mellitus was associated with poorer prognosis in patients with COVID-19: a retrospective cohort study. Medrxiv. 2020.
28. **Huang I, Lim MA, Pranata R.** Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia –a systematic review, meta-analysis, and meta-regression. Diabetes Metab Syndr. 2020;14:395-403.
29. **Abdi A, Jalilian M, Sarbarzeh PA, Vlaisavljevic Z.** Diabetes and COVID-19: a systematic review on the current evidences. Diabetes Res Clin Pract. 2020;166:108347.
30. **Zhang Y, Li H, Zhang J.** The clinical characteristics and outcomes of patients with diabetes mellitus and secondary hyperglycaemia with coronavirus disease 2019: a single-

center, retrospective, observational study in Wuhan. Diabetes Obes Metab. 2020;22:1443-1454.

31. **Li H, Tian S, Chen T.** Newly diagnosed diabetes is associated with a higher risk of mortality than known diabetes in hospitalized patients with COVID-19. Diabetes Obes Metab. 2020;22:1897-1906.
32. **Apicella M, Campopiano MC, Mantuano M.** COVID-19 in people with diabetes: understanding the reasons for worse outcomes. Lancet Diabetes Endocrinol. 2020;8(9):782-792.
33. **Muniyappa R, Gubbi S.** COVID-19 pandemic, coronaviruses, and diabetes mellitus. Am J Physiol Endocrinol Metab. 2020;318(5):E736-E741.
34. **Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y.** Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. (2020) 395:497–506.
35. **Guan W, Ni Z, Hu Y, Liang W, Ou C, He J.** Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. (2020) 382:1708– 20.
36. **Li G, Deng Q, Feng J, Li F, Xiong N, He Q.** Clinical characteristics of diabetic patients with COVID-19. Journal of diabetes research. 2020 Jul 16;2020.
37. **Abdullah Alshukry, Mohammad Bu Abbas, Yaseen Ali.** Clinical characteristics and outcomes of COVID-19 patients with diabetes mellitus in Kuwait. Heliyon 7 (2021) e06706
38. **Pandita A, Gillani FS, Shi Y, Hardesty A, McCarthy M, Aridi J.** (2021) Predictors of severity and mortality among patients hospitalized with COVID-19 in Rhode Island. PLoS ONE 16(6): e0252411
39. **Awadhesh Kumar Singh, Ritesh Gupta, Amerta Ghosh, Anoop Misra.** Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 14 (2020) 303-310

40. **Yan Y, Yang Y, Wang F.** Clinical characteristics and outcomes of patients with severe covid-19 with diabetes. BMJ Open Diab Res Care 2020;8:e001343.
41. **Soo Lim, Jae Hyun Bae, Hyuk- Sang Kwon.** COVID-19 and diabetes mellitus: from pathophysiology to clinical management. Nature reviews. volume 1,January 2021.
42. **Varikasuvu S, Dutt N, Thangappazham B, Varshney S.** Diabetes and COVID-19: A pooled analysis related to disease severity and mortality. Primary Care Diabetes. 2021;15(1):24-27.
43. **Gangadharan C, Ahluwalia R, Sigamani A.** Diabetes and COVID-19: Role of insulin resistance as a risk factor for COVID-19 severity. World Journal of Diabetes. 2021;12(9):1550-1562.
44. **Wan zhou.** Clinical features of COVID-19 patients with diabetes and secondary hyperglycemia. Jour. Of Diabetes Res. Volume 2020
45. **Poon J, Ho K, Herrera Y, Jean R.** Clinical outcomes in diabetic vs non-diabetic patients with severe covid-19. Chest. 2020;158(4):A688.
46. **S.Mahalakshmi.** "Comparison of Inflammatory Markers and Lung Involvement Between Diabetic And Non Diabetic Covid-19 Patients." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), 20(03), 2021, pp. 01-06.
47. **Varikasuvu S, Varshney S, Dutt N.** Markers of coagulation dysfunction and inflammation in diabetic and non-diabetic COVID-19. Journal of Thrombosis and Thrombolysis. 2020;51(4):941-946.
48. **Lopez-Castaneda S, García-Larragoiti N, Cano-Mendez A, Blancas-Ayala K, Damian-Vázquez G, Perez-Medina A.** Inflammatory and Prothrombotic Biomarkers Associated With the Severity of COVID-19 Infection. Clinical and Applied Thrombosis/Hemostasis. 2021;27:107602962199909.

49. **D. Pitocco, L. Viti, L. Tartaglione, M. Di Leo, G.E. Rizzo, A. Manto, A. Rizzi, S.Caputo, A. Pontecorvi.** Diabetes and severity of COVID-19: what is the link?, Medical Hypotheses (2020),
50. **Kristan M, Kim Y, Nelson T, Moxley M, Yip T, Munir K.** Predictors of Severe COVID-19 in Patients With Diabetes: A Multicenter Review. Endocrine Practice. 2021;27(8):842-849.
51. **Malik S, Chowdhury P, Hakim A, Islam M, Alam M, Azad A.** Blood biochemical parameters for assessment of COVID-19 in diabetic and non-diabetic subjects: a cross-sectional study. International Journal of Environmental Health Research. 2021;:1-14.
52. **Gregory.** COVID-19 Severity Is Tripled in the Diabetes Community: A Prospective Analysis of the Pandemic's Impact in Type 1 and Type 2 Diabetes. Diabetes Care 2021;44:526–532. Diabetes Care. 2021;44(5):e102-e102.
53. **Koh H, Moh AMC, Yeoh E.** Diabetes predicts severity of COVID-19 infection in a retrospective cohort: A mediatory role of the inflammatory biomarker C-reactive protein. J Med Virol. 2021;93: 3023–3032
54. **Rastad H, Karim H, Ejtahed H, Tajbakhsh R, Noorisepehr M, Babaei M.** Risk and predictors of in-hospital mortality from COVID-19 in patients with diabetes and cardiovascular disease. Diabetology & Metabolic Syndrome. 2020;12(1).
55. **Guo W, Li M, Dong Y.** Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev. 2020;e3319.
56. **Merzon E, Green I, Shpigelman M, Vinker S, Raz I, Golan-Cohen A.** Haemoglobin A1c is a predictor of COVID-19 severity in patients with diabetes. Diabetes/Metabolism Research and Reviews. 2020;37(5).
57. **Landstra CP and de Koning EJP (2021)** COVID-19 and Diabetes: Understanding the Interrelationship and Risks for a Severe Course. Front. Endocrinol. 12:649525.

58. **Pandita A, Gillani FS, Shi Y, Hardesty A, McCarthy M, Aridi J.** (2021) Predictors of severity and mortality among patients hospitalized with COVID-19 in Rhode Island. PLoS ONE 16(6): e0252411.
59. **Moin ASM, Al-Qaissi A, Sathyapalan T, Atkin SL and Butler AE (2021).** Type 2 Diabetes Coagulopathy Proteins May Conflict With Biomarkers Reflective of COVID-19 Severity. Front. Endocrinol. 12:658304.
60. **Rawshani A, Kjölhede E, Rawshani A, Sattar N, Eeg-Olofsson K, Adiels M.** Severe COVID-19 in people with type 1 and type 2 diabetes in Sweden: A nationwide retrospective cohort study. The Lancet Regional Health - Europe. 2021;4:100105.
61. **Shukla A, Tchang B, Lam T, Steller I, Touhamy S, Askin G.** Preadmission predictors of severe COVID-19 in patients with diabetes mellitus. Journal of Diabetes and its Complications. 2021;107967.
62. **Verma A, Beg M, Bhatt D, Dev K, Alsahli M, Rahmani A**. Assessment and Management of Diabetic Patients During the COVID-19 Pandemic. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2021;Volume 14:3131-3146.
63. **Laurenzi, A.; Caretto, A.; Molinari, C.; Bazzigaluppi, E.; Brigatti, C.; Marzinotto, I.; Mercalli, A.; Melzi, R.; Nano, R.; Tresoldi, C..** Pre-Existing Diabetes and COVID-Associated Hyperglycaemia in Patients with COVID-19 Pneumonia. Biology 2021, 10, 754.
64. **Kumar A, Arora A, Sharma P, Anikhindi S, Bansal N, Singla V.** Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(4):535-545.

MASTER CHART

S.No	Age/Sex	Co-morbidities									CT Chest	%	Vitals		SPO2 %				Sev
		T_2DM	SHT	CAD	CVA	Malignancy	RS	CLD	CKD	Others			PR	RR	ROOOM AIR	FACE MASK	NRM	CPAP/HFNO	Mild/ Mod/ Sev/ C.ill
1	59/M	Y	Y	N	N	N	N	N	N	N	B/L	40	98	34	74	-	98	-	Sev
2	58/M	Y	Y	N	N	N	N	N	N	N	B/L	30	96	26	90	-	95	-	Mod
3	60/M	Y	Y	N	N	N	N	N	N	N	B/L	35	84	32	89	-	99	-	Sev
4	40/F	Y	N	N	N	N	N	N	N	N	U/L	30	94	24	97	-	-	-	Mod
5	43/M	Y	N	N	N	N	N	N	N	N	B/L	25	90	16	98	-	-	-	Mod
6	46/M	Y	Y	N	N	N	N	N	N	N	B/L	50	98	34	74	-	94	96	C.ill
7	58/M	Y	Y	N	N	N	N	N	N	N	U/L	15	92	24	92	96	-	-	Mod
8	58/F	Y	N	N	N	N	N	N	N	N	-	-	92	18	98	-	-	-	Mild
9	49/F	Y	N	N	N	N	N	N	N	N	B/L	40	102	32	86	95	-	-	Sev
10	58/M	Y	Y	Y	N	N	N	N	N	N	B/L	40	90	40	55	-	-	95	C.ill
11	42/M	Y	Y	N	N	N	N	N	N	N	B/L	30	84	25	93	-	-	-	Mod
12	47/M	Y	N	N	N	N	N	N	N	N	B/L	28	94	32	79	95	-	-	Sev
13	46/F	Y	N	N	N	N	N	N	N	N	B/L	27	82	27	92	95	-	-	Mod
14	43/M	Y	N	N	N	N	N	N	N	N	U/L	12	96	24	93	-	-	-	Mod
15	64/F	Y	N	N	N	N	BA	N	N	N	B/L	38	88	32	82	-	93	-	Sev
16	53/M	Y	N	N	N	N	N	N	N	N	B/L	27	96	30	88	95	-	-	Sev
17	44/F	Y	N	N	N	N	N	N	N	N	B/L	35	104	32	79	-	90	-	Sev
18	50/F	Y	Y	N	N	N	N	N	N	Hypo thyr	B/L	45	90	36	86	-	95	-	Sev
19	52/M	Y	N	N	N	N	N	N	N	N	B/L	13	82	24	93	-	-	-	Mod
20	60/M	Y	Y	Y	N	N	N	N	N	N	B/L	75	96	38	86	-	97	-	Sev
21	55/M	Y	N	N	N	N	N	N	N	N	U/L	12	80	23	94	-	-	-	Mod
22	50/M	Y	N	N	N	N	N	N	N	N	B/L	30	84	26	93	-	-	-	Mod
23	45/F	Y	N	N	N	N	N	N	N	N	-	-	76	20	97	-	-	-	Mild
24	46/M	Y	N	N	N	N	N	N	N	N	-	-	74	16	98	-	-	-	Mild
25	41/F	Y	Y	N	N	N	Y	N	N	N	-	-	70	20	97	-	-	-	Mild
26	48/M	Y	N	Y	N	N	N	N	N	N	B/L	15	86	26	93	-	-	-	Mod
27	45/F	Y	N	N	N	N	N	N	N	N	-	-	80	18	98	-	-	-	Mild
28	47/M	Y	N	N	N	N	N	N	N	N	-	-	84	18	97	-	-	-	Mild
29	55/F	Y	N	N	N	N	N	N	N	N	-	-	78	20	98	-	-	-	Mild
30	57/M	Y	Y	Y	N	N	N	N	N	N	B/L	20	90	26	90	95	-	-	Mod
31	80/M	Y	N	N	N	N	N	N	Y	N	B/L	52	92	32	76	-	96	-	Sev
32	43/M	Y	N	N	N	N	N	N	N	N	-	-	76	16	97	-	-	-	Mild
33	60/M	Y	N	N	N	N	Y	N	N	N	B/L	35	90	34	86	-	95	-	Sev
34	79/F	Y	N	N	N	N	N	N	Y	N	B/L	30	94	22	91	-	-	-	Mod
35	53/F	Y	N	N	N	N	N	N	N	N	B/L	35	98	32	82	-	95	-	Sev

S.No	Age/Sex	Co-morbidities									CT Chest involvement	%	Vitals		SPO2 %				Sev
		T_2DM	SHT	CAD	CVA	Malignancy	RS	CLD	CKD	Others			PR	RR	ROOOM AIR	FACE MASK	NRM	CPAP/HFNO	Mild/ Mod/ Sev/ C.ill
36	70/M	Y	N	Y	N	N	N	N	N	N	B/L	56	106	36	78	-	90	95	C.ill
37	64/F	Y	N	N	N	N	N	N	N	N	U/L	15	92	22	93	-	-	-	Mod
38	53/M	Y	N	N	N	N	N	N	N	N	U/L	10	96	24	91	-	-	-	Mod
39	49/M	Y	N	N	N	N	N	N	N	N	-	-	82	16	95	-	-	-	Mild
40	61/M	Y	N	N	N	N	N	N	N	N	-	-	78	22	98	-	-	-	Mild
41	52/M	Y	Y	N	N	N	N	N	N	N	B/L	60	92	36	69	-	-	97	C.ill
42	50/F	Y	N	N	N	N	N	N	N	N	B/L	35	94	32	82	93	-	-	Sev
43	47/M	Y	N	N	N	N	N	N	N	N	B/L	25	86	24	96	-	-	-	Mod
44	58/F	Y	N	N	N	N	N	N	N	N	B/L	30	84	26	91	-	-	-	Mod
45	70/F	Y	N	N	N	N	N	N	N	N	B/L	15	88	22	93	-	-	-	Mod
46	45/F	Y	N	N	N	N	N	N	N	N	U/L	9	84	24	92	-	-	-	Mod
47	61/F	Y	N	N	N	N	N	N	N	N	B/L	56	98	32	78	-	-	94	C.ill
48	61/F	Y	N	N	N	N	N	N	N	N	B/L	45	86	36	69	-	-	94	C.ill
49	65/F	Y	Y	Y	N	N	N	N	N	N	B/L	42	64	32	87	-	-	95	C.ill
50	58/F	Y	N	N	N	N	N	N	N	N	B/L	50	98	38	70	-	-	98	C.ill
51	54/M	N	Y	N	N	N	N	N	N	N	-	-	82	16	95	-	-	-	mild
52	46/M	N	N	N	N	N	N	N	N	N	-	-	78	18	98	-	-	-	mild
53	45/M	N	N	N	N	N	N	N	N	N	-	-	70	14	97	-	-	-	mild
54	61/M	N	N	Y	N	N	N	N	N	N	-	-	82	14	95	-	-	-	mild
55	60/M	N	Y	Y	N	N	N	N	N	N	-	-	68	17	99	-	-	-	mild
56	47/M	N	N	N	N	N	N	N	N	N	-	-	74	18	98	-	-	-	mild
57	42/M	N	N	N	N	N	N	N	N	N	-	-	88	20	97	-	-	-	mild
58	56/M	N	Y	N	N	N	N	N	N	N	-	-	82	16	95	-	-	-	mild
59	52/M	N	Y	Y	N	N	N	N	N	N	-	-	74	18	97	-	-	-	mild
60	56/M	N	N	N	N	N	N	N	N	N	-	-	82	14	94	-	-	-	mild
61	41/M	N	N	N	N	N	N	N	N	N	-	-	76	20	97	-	-	-	mild
62	52/M	N	Y	N	N	N	COPD	N	N	N	-	-	90	22	98	-	-	-	mild
63	48/M	N	N	N	N	N	N	N	N	N	-	-	76	16	95	-	-	-	mild
64	50/M	N	N	N	N	N	N	N	N	N	-	-	84	15	94	-	-	-	mild
65	64/M	N	Y	N	N	N	N	N	N	N	-	-	78	17	95	-	-	-	mild
66	58/M	N	Y	N	N	N	N	N	N	N	-	-	70	20	96	-	-	-	mild
67	59/F	N	Y	Y	N	N	N	N	N	Hypo thyr	-	-	80	21	97	-	-	-	mild
68	59/F	N	N	N	N	N	N	N	N	N	-	-	82	17	95	-	-	-	mild
69	46/F	N	N	N	N	N	N	N	N	N	-	-	74	16	98	-	-	-	mild
70	50/F	N	N	N	N	N	N	N	N	N	-	-	78	18	97	-	-	-	mild

S.No	Age/Sex	Co-morbidities									CT Chest invlovement	%	Vitals		SPO2 %				Sev
		T_2DM	SHT	CAD	CVA	Malignancy	RS	CLD	CKD	Others			PR	RR	ROOOM AIR	FACE MASK	NRM	CPAP/HFNO	Mild/ Mod/ Sev/ C.ill
71	57/F	N	N	N	N	N	N	N	N	N	-	-	82	21	95	-	-	-	mild
72	49/F	N	N	N	N	N	N	N	N	N	-	-	80	19	94	-	-	-	mild
73	45/F	N	N	N	N	N	N	N	N	N	-	-	78	17	99	-	-	-	mild
74	53/F	N	N	N	N	N	N	N	N	N	-	-	74	20	99	-	-	-	mild
75	45/F	N	N	N	N	N	N	N	N	N	-	-	80	21	99	-	-	-	mild
76	49/M	N	Y	Y	N	N	N	N	N	N	B/L	10	68	26	92	-	-	-	Mod
77	45/M	N	N	N	N	N	N	N	N	N	B/L	13	74	25	90	96	-	-	Mod
78	49/M	N	Y	N	N	N	N	N	N	N	B/L	18	78	26	94	-	-	-	Mod
79	60/M	N	N	N	N	N	N	N	N	N	U/L	5	86	24	93	-	-	-	Mod
80	56/M	N		N	N	N	BA	N	N	N	U/L	5	82	22	90	-	-	-	Mod
81	51/M	N	Y	N	N	N	N	N	N	N	U/L	10	90	20	95	-	-	-	Mod
82	48/M	N	N	N	N	N	N	N	N	N	U/L	7	88	22	93	-	-	-	Mod
83	43/M	N	N	N	N	N	N	N	N	N	U/L	5	76	24	95	-	-	-	Mod
84	45/M	N	N	N	N	N	N	N	N	N	U/L	12	90	24	95	-	-	-	Mod
85	62/F	N	Y	Y	N	N	N	N	N	Hypo thyr	B/L	25	84	26	90	-	-	-	Mod
86	55/F	N	N	N	N	N	N	N	N	N	B/L	17	74	28	91	-	-	-	Mod
87	43/F	N	N	N	N	N	N	N	N	N	U/L	7	82	24	93	-	-	-	Mod
88	58/F	N	N	N	N	N	N	N	N	N	U/L	5	84	26	94	-	-	-	Mod
89	42/F	N	N	N	N	N	N	N	N	N	U/L	25	80	23	95	-	-	-	Mod
90	43/F	N	N	N	N	N	N	N	N	N	U/L	12	76	21	94	-	-	-	Mod
91	45/M	N	N	N	N	N	N	N	N	N	B/L	30	86	28	82	-	96	-	Sev
92	49/M	N	Y	N	N	N	N	N	N	N	B/L	26	92	30	89	-	98	-	Sev
93	49/M	N	N	N	N	N	N	N	N	N	B/L	35	96	34	78	-	94	-	Sev
94	40/M	N	N	N	N	N	N	N	N	N	B/L	30	84	28	88	-	93	-	Sev
95	50/F	N	N	N	N	N	N	N	N	BA	B/L	40	88	33	74	-	96	-	Sev
96	48/F	N	N	N	N	N	N	N	N	N	B/L	33	82	28	86	98	-	-	Sev
97	49/F	N	N	N	N	N	N	N	N	N	B/L	40	84	34	81	-	96	-	Sev
98	52/M	N	Y	Y	N	N	N	N	N	N	B/L	60	92	36	75	-	-	96	C.ill
99	42/M	N	N	N	N	N	N	N	N	N	B/L	45	98	32	80	-	-	95	C.ill
100	52/F	N	Y	N	N	N	N	N	N	N	B/L	53	82	36	84	-	-	98	C.ill

S.No	Laborartory markers																				
	CRP (mg/L)	LDH (IU/L)	Ferritin (µg/L)	D-dimer (mg/L)	PT (sec)	INR	Pro calcitonin (ng/ml)	WBC (1000)	Neutro	Lymp	NLR	RBS	FBS	PPBS	HbA1c	Tot. Bili	Direct Bili	Indirect Bili	SGOT	SGPT	ALP
1	87.0	276	386	0.35	16	1	0.3	12.3	82	9	9.1	312	160	240	7.2	0.5	0.3	0.2	29	37	53
2	42.0	254	276	0.26	12	0.7	0.2	6.5	77	22	3.5	117	141	270	8.2	0.6	0.3	0.3	26	22	77
3	34.0	267	327	0.38	14	0.8	0.3	3.5	75	14	5.4	234	196	274	8	0.3	0.1	0.2	31	37	84
4	11.9	237	201	0.24	11	0.6	0.3	5.4	65	23	2.8	103	92	138	5.3	0.5	0.3	0.2	29	30	47
5	52.4	254	265	0.28	12	0.8	0.1	5.1	59	34	1.7	263	163	243	6.6	0.4	0.2	0.2	22	13	78
6	88.3	342	428	0.54	19	1.1	0.3	9.6	84	12	7.0	339	202	276	8.6	0.5	0.2	0.3	29	26	85
7	26.9	256	345	0.27	14	1	0.1	4.9	57	16	3.6	190	144	272	8.1	0.4	0.2	0.2	21	15	84
8	2.0	176	143	0.18	12	0.7	0.1	9.0	58	33	1.8	182	102	224	6.4	0.3	0.2	0.1	29	32	119
9	30.4	275	276	0.32	13	0.8	0.2	6.5	79	12	6.6	262	112	243	8.2	0.2	0.1	0.1	17	28	80
10	87.0	332	456	0.53	21	1.1	0.4	11.5	83	7	11.9	317	182	294	8.6	0.3	0.1	0.2	31	37	80
11	24.0	238	267	0.25	13	0.9	0.2	6.5	60	14	4.3	186	132	220	6.9	0.6	0.3	0.3	26	22	77
12	22.4	264	323	0.39	12	0.7	0.3	7.8	72	11	6.5	130	128	198	6.8	0.8	0.4	0.4	18	20	66
13	18.4	241	198	0.27	16	0.7	0.3	4.5	68	19	3.6	166	192	216	6.1	0.6	0.5	0.1	22	46	42
14	10.1	238	262	0.24	18	0.8	0.2	5.4	74	14	5.3	260	132	210	6.7	0.9	0.3	0.6	43	66	122
15	36.8	265	275	0.33	17	1	0.2	4.3	72	18	4.0	176	156	218	6.9	1.3	0.4	0.9	55	45	98
16	42.2	262	387	0.38	15	0.9	0.3	6.2	67	32	2.1	126	112	198	6.2	0.8	0.6	0.2	61	57	72
17	36.4	287	283	0.31	13	0.9	0.3	13.9	72	11	6.5	139	206	333	7.8	1.2	0.9	0.3	72	92	121
18	70.0	279	265	0.35	14	1	0.3	8.1	67	23	2.9	402	216	306	9.2	1.3	0.9	0.4	80	62	78
19	24.7	238	304	0.29	13	0.7	0.3	7.6	68	25	2.7	119	198	204	6.1	0.6	0.2	0.4	32	42	74
20	61.0	273	384	0.33	16	1.1	0.4	14.4	88	10	8.8	236	132	256	8.2	1.4	0.9	0.5	60	46	112
21	3.1	251	264	0.22	15	1	0.3	7.4	60	32	1.9	142	108	210	6.6	0.7	0.3	0.4	34	21	76
22	28.8	259	276	0.28	14	0.9	0.3	8.1	68	14	4.9	192	152	242	7.1	1.5	0.3	1.2	55	17	38
23	1.6	183	143	0.11	13	0.7	0.2	8.6	66	28	2.4	182	136	198	6.6	0.9	0.7	0.2	18	22	76
24	2.6	165	243	0.16	14	0.6	0.1	7.2	56	38	1.5	136	116	204	5.8	1.1	0.9	0.2	20	24	60
25	2.3	158	127	0.13	12	0.7	0.2	5.6	62	34	1.8	176	152	192	6.1	1.2	0.9	0.3	55	46	102
26	26.4	245	347	0.26	12	0.6	0.2	8.8	86	6	14.3	266	188	272	6.9	0.6	0.1	0.5	55	46	76
27	6.2	176	129	0.16	15	0.7	0.1	5.2	66	32	2.1	184	165	220	5.9	1.1	0.9	0.2	56	32	78
28	2.2	164	221	0.15	11	0.7	0.2	8.9	58	36	1.6	138	136	196	5.8	0.4	0.3	0.1	22	31	108
29	3.1	157	127	0.13	13	0.8	0.2	7.8	65	26	2.5	204	170	232	6.1	1.4	0.9	0.5	38	45	78
30	12.6	247	275	0.25	12	0.8	0.2	4.9	59	32	1.8	232	179	278	6.8	1.6	1.1	0.5	35	55	102
31	76.0	275	324	0.37	14	0.8	0.2	15.5	80	20	4.0	236	165	306	7.8	2.2	1.1	1.1	56	47	92
32	5.2	164	254	0.14	12	0.7	0.2	6.7	54	46	1.2	156	106	204	5.9	0.6	0.3	0.3	43	38	80
33	36.2	282	320	0.38	12	0.7	0.3	8.6	79	16	4.9	306	202	342	8.4	1.4	0.9	0.5	56	58	63
34	10.2	237	216	0.23	12	0.6	0.3	12.5	81	17	4.8	316	196	276	8.3	1.1	0.9	0.2	62	70	73
35	135.0	274	276	0.31	13	0.8	0.3	10.1	79	19	4.2	342	206	312	8.1	1.4	0.8	0.6	34	52	70

S.No	Laborartory markers																				
	CRP (mg/L)	LDH (IU/L)	Ferritin (µg/L)	D-dimer (mg/L)	PT (sec)	INR	Pro calcitonin (ng/ml)	WBC (1000)	Neutro	Lymp	NLR	RBS	FBS	PPBS	HbA1c	Tot. Bili	Direct Bili	Indirect Bili	SGOT	SGPT	ALP
36	172.0	325	480	0.49	16	1.1	0.4	1.1	70	10	7.0	213	179	296	7.6	1.1	0.9	0.2	40	38	57
37	22.4	232	187	0.25	13	0.7	0.2	12.2	89	9	9.9	156	161	262	7.8	0.5	0.1	0.4	30	20	56
38	12.6	254	274	0.28	12	0.6	0.2	7.4	65	23	2.8	276	149	217	6.7	0.7	0.4	0.3	45	41	60
39	3.2	175	256	0.11	12	0.7	0.1	7.1	57	34	1.7	230	126	197	6.1	0.3	0.2	0.1	37	51	78
40	2.7	201	210	0.16	13	0.8	0.1	4.8	67	32	2.1	176	102	160	6.2	0.7	0.5	0.2	38	41	62
41	98.0	342	445	0.54	18	1.3	0.4	4.1	88	10	8.8	310	202	302	9.1	2.1	1.5	0.6	72	68	98
42	42.0	263	263	0.36	14	0.7	0.1	13.9	75	16	4.7	252	165	243	7.2	1.6	0.9	0.7	42	34	72
43	28.4	254	330	0.22	13	0.7	0.3	12.1	78	19	4.1	229	149	263	7.9	1.2	0.9	0.3	82	68	81
44	65.6	243	212	0.21	15	0.8	0.2	6.5	88	12	7.3	148	124	210	5.9	0.5	0.3	0.2	32	18	37
45	9.3	239	216	0.27	12	0.7	0.3	7.4	75	23	3.3	159	176	193	6.1	0.8	0.3	0.5	26	34	60
46	12.9	246	202	0.22	14	0.7	0.2	4.3	52	39	1.3	132	104	176	5.9	0.4	0.2	0.2	32	46	72
47	86.4	325	325	0.42	20	1.3	0.6	10.7	90	10	9.0	173	156	278	6.5	0.4	0.3	0.1	43	36	86
48	76.8	316	363	0.45	18	1.2	0.4	7.0	76	20	3.8	249	163	247	6.9	1.3	0.8	0.5	55	48	78
49	63.4	305	317	0.51	16	1.1	0.4	5.8	82	14	5.9	305	192	286	7.2	2.1	1.7	0.4	80	66	120
50	89.2	312	312	0.47	17	1.2	0.6	8.8	76	19	4.0	202	186	253	7.3	1.9	0.5	1.4	76	54	92
51	3.4	101	126	0.11	12	0.6	0.1	8.4	57	32	1.8	103	76	144	5.3	0.7	0.3	0.4	34	52	70
52	1.7	128	132	0.14	14	0.7	0.2	6.1	70	28	2.5	146	103	158	5.7	0.5	0.4	0.1	36	52	80
53	2.4	95	117	0.12	12	0.7	0.1	3.4	59	32	1.8	86	124	132	6.1	1.5	0.9	0.6	32	40	60
54	6.2	124	142	0.15	11	0.7	0.2	7.4	68	32	2.1	162	93	152	6	1.2	0.7	0.5	40	52	84
55	4.2	143	147	0.11	12	0.8	0.2	5.0	65	28	2.3	76	65	106	5.4	0.9	0.3	0.6	45	38	66
56	3.2	138	135	0.15	13	0.7	0.1	4.2	61	39	1.6	90	72	138	5.1	1.0	0.9	0.1	38	55	72
57	6.6	125	127	0.15	12	0.6	0.2	7.6	63	33	1.9	153	102	162	5.8	1.2	0.9	0.3	55	33	86
58	7.4	129	138	0.14	14	0.8	0.1	8.5	53	46	1.2	132	58	142	6	1.4	0.9	0.5	35	42	72
59	3.2	116	126	0.16	13	0.7	0.1	9.5	56	43	1.3	176	88	132	5.9	0.5	0.1	0.4	31	55	82
60	2.1	104	151	0.11	12	0.7	0.2	8.3	59	39	1.5	75	62	101	5.4	0.6	0.3	0.3	26	16	55
61	6.8	97	144	0.18	15	0.8	0.1	5.5	55	36	1.5	136	98	132	6.1	0.5	0.3	0.2	28	31	84
62	3.4	113	132	0.14	12	0.7	0.1	9.7	64	34	1.9	115	80	104	5.3	0.6	0.3	0.3	85	78	111
63	5.2	105	126	0.12	12	0.8	0.2	9.6	70	28	2.5	106	72	142	5.9	0.5	0.4	0.1	43	55	76
64	3.1	109	143	0.17	12	0.8	0.1	4.6	55	41	1.3	75	65	153	6.1	0.8	0.2	0.6	65	38	73
65	1.9	116	128	0.13	13	0.8	0.2	10.8	70	26	2.7	186	102	163	6	1.3	1.1	0.2	23	34	64
66	3.9	134	133	0.15	12	0.7	0.2	11.7	55	42	1.3	156	92	138	6.5	1.4	0.9	0.5	32	40	77
67	6.4	128	64	0.12	11	0.7	0.1	9.7	46	52	0.9	153	116	182	5.4	0.3	0.1	0.2	15	28	55
68	5.6	142	72	0.12	12	0.7	0.1	6.0	68	25	2.7	178	136	158	5.9	1.4	0.9	0.5	38	32	86
69	7.4	124	51	0.14	12	0.7	0.2	4.4	70	28	2.5	132	76	151	5.1	0.4	0.1	0.3	36	48	72
70	2.0	129	75	0.14	14	0.8	0.2	5.6	46	53	0.9	166	71	130	5.3	0.6	0.4	0.2	38	24	60

S.No	Laborartory markers																				
	CRP (mg/L)	LDH (IU/L)	Ferritin (µg/L)	D-dimer (mg/L)	PT (sec)	INR	Pro calcitonin (ng/ml)	WBC (1000)	Neutro	Lymp	NLR	RBS	FBS	PPBS	HbA1c	Tot. Bili	Direct Bili	Indirect Bili	SGOT	SGPT	ALP
71	3.2	115	81	0.11	12	0.9	0.1	9.7	66	26	2.5	126	82	143	5.6	1.1	0.8	0.3	40	36	43
72	2.0	117	69	0.13	12	0.7	0.1	4.6	50	50	1.0	90	78	108	5.4	0.6	0.1	0.5	32	18	60
73	4.1	114	73	0.11	13	0.7	0.1	5.6	55	36	1.5	78	72	123	5.1	0.8	0.4	0.4	16	22	36
74	2.2	143	64	0.15	12	0.7	0.1	8.6	54	41	1.3	109	93	121	5.3	1.3	0.7	0.6	60	54	82
75	2.5	137	66	0.13	12	0.8	0.1	9.0	54	38	1.4	60	64	102	5.1	0.6	0.5	0.1	21	28	64
76	16.2	165	226	0.21	12	0.7	0.2	8.6	65	33	2.0	146	112	172	5.6	1.0	0.9	0.1	38	16	77
77	7.5	169	176	0.20	13	0.8	0.2	4.9	52	48	1.1	152	75	102	5.1	0.8	0.5	0.3	16	32	80
78	12.2	183	192	0.24	12	0.7	0.3	5.3	60	34	1.8	97	102	152	5.6	1.1	0.9	0.2	22	30	64
79	5.9	179	217	0.21	15	1	0.3	10.7	58	38	1.5	129	65	109	6.1	1.3	1.1	0.2	30	18	86
80	2.1	167	209	0.23	14	0.8	0.2	3.5	51	49	1.0	163	102	107	5	0.8	0.3	0.5	22	16	36
81	10.1	183	192	0.22	12	0.7	0.2	8.6	61	36	1.7	168	76	96	5.3	1.2	0.3	0.9	36	55	82
82	2.3	175	173	0.21	16	1	0.2	6.0	65	34	1.9	112	82	142	5.1	0.7	0.2	0.5	40	85	102
83	3.7	163	194	0.25	14	0.8	0.3	5.2	52	48	1.1	136	130	172	5.8	1.4	0.9	0.5	32	36	84
84	4.2	173	205	0.23	12	0.6	0.2	10.4	75	23	3.3	152	102	128	6	1.0	0.8	0.2	30	40	55
85	20.6	182	142	0.21	13	0.7	0.2	7.9	64	28	2.3	149	109	153	5.8	1.2	0.7	0.5	32	18	62
86	13.2	177	137	0.26	12	0.8	0.2	7.7	63	33	1.9	136	86	106	5.3	0.9	0.2	0.7	38	40	63
87	1.9	192	158	0.21	10	0.7	0.3	6.9	75	23	3.3	158	73	132	5.8	0.5	0.3	0.2	20	30	80
88	2.5	179	139	0.22	14	0.8	0.2	3.8	54	42	1.3	132	102	162	5.9	0.6	0.1	0.5	24	32	55
89	2.1	181	174	0.24	12	0.7	0.3	5.4	48	52	0.9	144	74	132	6	1.3	1.1	0.2	38	55	74
90	3.4	176	161	0.21	15	1	0.2	8.6	60	34	1.8	93	60	103	5.1	0.7	0.5	0.2	58	58	73
91	38.6	231	237	0.26	12	0.9	0.2	4.3	78	21	3.7	134	84	142	5.9	0.9	0.6	0.3	23	42	67
92	23.2	217	232	0.25	14	1	0.3	11.3	82	16	5.1	190	102	163	6	1.3	0.5	0.8	30	54	70
93	43.2	224	251	0.30	13	1	0.2	6.4	58	42	1.4	54	72	136	5.1	1.0	0.2	0.8	38	76	128
94	31.4	212	248	0.27	15	1.1	0.3	8.6	60	38	1.6	150	101	152	5.9	1.6	1.3	0.3	60	78	102
95	40.6	219	217	0.26	14	0.9	0.3	13.0	66	26	2.5	110	65	138	5.3	1.3	1.1	0.2	58	34	76
96	22.6	226	221	0.28	13	0.7	0.3	9.7	64	30	2.1	117	78	148	6.1	1.0	0.1	0.9	22	31	78
97	45.3	214	214	0.28	14	0.8	0.3	6.3	74	22	3.4	132	96	132	6.2	1.4	0.7	0.7	34	32	55
98	60.2	245	365	0.36	19	1.4	0.5	10.5	89	9	9.9	162	114	172	6.3	1.6	0.6	1.0	55	72	102
99	57.4	237	342	0.35	17	1.2	0.6	9.7	82	10	8.2	166	118	183	6.1	1.1	0.7	0.4	51	65	86
100	56.3	231	276	0.31	15	1.1	0.5	8.9	82	14	5.9	153	140	155	6.1	1.2	0.9	0.3	35	51	78