"ASSESSMENT OF COAGULATION PARAMETERS IN COVID-19 PATIENTS."

By

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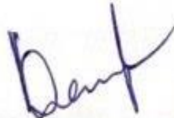

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LIST OF ABBREVIATIONS USED

ACE2	-	Angiotensin Converting Enzyme 2
ALC	-	Absolute Lymphocyte Count
aPTT	-	Activated Partial Thromboplastin Time
ARDS	-	Acute Respiratory Distress Syndrome
ATP	-	Adenosine Triphosphate
CBC	-	Complete Blood Count
CMET	-	COVID-19 Mediated Endothelialitis and Thrombosis
CRP	-	C-Reactive Protein
DAMP	-	Damage Associated Mollecular Patterns
DC	-	Dendritic Cells
DIC	-	Disseminated Intravascular Coagulopathy
DMV	-	Double Membrane Vesicle
E-Protein	-	Envelope Protein
EDTA	-	Ethylenediaminetetraacetic Acid
ELISA	-	Enzyme-linked Immunosorbent Assay
ER	-	Endoplasmic Reticulum
FPA	-	Fibrinopeptides A
FPB	-	Fibrinopeptides B
GA	-	Golgi Apparatus
G-CSF	-	Granulocyte Colony Stimulating Factor
HE	-	Hemagglutinin Esterase

HIV	-	Human Immunodeficiency Virus
ICTV	-	International Committee on Taxonomy of Viruses
IL	-	Interleukins
LDL	-	Low Density Lipoprotein
MERS CoV	-	Middle East Respiratory Syndrome Coronavirus
M-Protein	-	Membrane Protein
MSOF	-	Multi System Organ Failure
NETs	-	Neutrophil Extracellular Traps
NLR	-	Neutrophil Lymphocyte Ratio
N-protein	-	Nucleocapsid Protein
nRBC	-	Nucleated Red Blood Corpuscles
nsp	-	Non-Structural Proteins
ORFs	-	Open Reading Frames
PAI-1	-	Plasminogen Activator Inhibitor-1
PLR	-	Platelet Lymphocyte Ratio
PT	-	Prothrombin Time
RBD	-	Receptor Binding Domain
RdRp	-	RNA-dependent RNA polymerase
RNA	-	Ribose Nucleic Acid
ROS	-	Reactive Oxygen Species
RT- PCR	-	Reverse Transcription Polymerase Chain Reaction
SAA	-	Serum Amyloid A
SARS-COV2	-	Severe Acute Respiratory Syndrome Coronavirus-2

SIRS	-	Severe Inflammatory Response Syndrome
Sp	-	Structural Protein
SpO2	-	Oxygen Saturation
S-protein	-	Spike Protein
sTfR	-	Soluble Transferrin Receptor
TMPRSS	-	Transmembrane Protease serine Enzyme
TNFα	-	Tumor Necrosis Factor α
UTR	-	Untranslated Region
VTE	-	Venous Thromboembolism
VTM	-	Viral Transport Medium
vWF	-	Von Willebrand Factor
WBC	-	White Blood Cells
WHO	-	World Health Organisation

ABSTRACT

Title: Assessment of coagulation parameters in Covid-19 patients.

Background: The Corona Virus Disease-19 is the current pandemic affecting more than 200 countries and 25.3 million people worldwide. Covid-19 infection associated coagulopathy and abnormal levels in coagulation parameters are the most significant prognostic marker in COVID-19 patients. Coagulation parameters showed marked variation in Covid-19 infection such as increased D-Dimer and Fibrinogen levels along with mild to moderate thrombocytopenia. In critically ill patients disseminated intravascular coagulopathy (DIC) may develop and such patents may show increase PT and aPTT with normal or elevated fibrinogen levels.

Aims and Objective: To assess the various coagulation parameters in COVID-19 patients with correlation to severity of infection.

Methods: This prospective study was conducted among 200 covid- 19 patients admitted at Jawaharlal Nehru Medical College and KLEs Dr. Prabhakar Kore Hospital and MRC, Belagavi. The samples for coagulation test were collected on admission. D-Dimer, PT, aPTT, Fibrinogen and Platelet Count is determined using standard protocol and reagents. Relevant data is been extracted from electronic health records using a standardised form. Demographic, Medical history and outcome data were obtained from patients medical record. The clinical outcome was monitored from 1st January 2021 to 31st December 2021.

Results: In the present study coagulation parameter of 200 patients along with their baseline characteristics are statistically analysed. The mean age of study participants was 55.89 years. Hospital admission of patients with age less than 60 years (55.50%)

was more with predominance of male population (82.50%). Patients had marked hypercoagulability state characterized by significant D-Dimer elevated levels in 106/200(53.00%) with a median value of 770 ng/ml (mean +/- SD = 1332.16 +/- 1567.13), prolonged PT and aPTT and increased Fibrinogen levels in 95/200(47.50%) with a median value of 475 mg/dl (mean +/-SD = 521.62 +/- 248.84) along with low platelet count in 39% of study population.

Conclusion: COVID-19 associated coagulopathy is associated with high risk of morbidity and mortality and is a cause of concern especially in hospitalized patients. In this study, increased D-Dimer and Fibrinogen levels were found in maximum number of patients with COVID19 induced coagulopathy. Early assessment and dynamic monitoring of coagulation system parameters may be a benchmark to control the severity of COVID-19 infection and associated mortality by including these parameters to the criteria for hospitalization and preventing or stopping the occurrence of thrombus or DIC in COVID-19 patients.

Summary: Increase in coagulation parameter values with advancing age and male predominance was observed in the study. Most commonly exhibited symptoms in the study participants were fever, cough and breathlessness followed by less common symptoms such as myalgia, loss of smell and loss of taste. Thus these coagulation parameters on admission are of paramount importance in evaluating severity of COVID-19 patients especially those who require prompt management with anti-coagulants in order to reduce coagulation associated morbidity and mortality.

Keywords: Covid-19**,** coagulopathy, D-dimer, fibrinogen, platelet, PT, aPTT

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INTRODUCTION

The Corona Virus Disease-19 is the current pandemic affecting more than 200 countries and 25.3 million people worldwide. On 31 December 2019, the WHO was informed about cases of pneumonia of unknown origin spreading in Wuhan City, Hubei Province of China.[1] The causative agent behind the pandemic was a novel coronavirus of Coronaviridae family. The virus was named, Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).[2] The primary respiratory infection instigated by this virus was named as Coronavirus disease 2019 or COVID-19 by World Health Organisation.[3, 4]

The disease started by a zoonotic spread from the sea-food markets in Wuhan province of China. Soon after few weeks human to human transmission was recognised as the mode of spread of the disease.[5, 6] Majority of the patients in the absence of any comorbidities have good prognosis but some may develop acute respiratory distress condition, coagulation manifestations along with multiple organ failure which is more so in patients with comorbid conditions. The pathophysiology and extent of the disease pathology was unclear but coagulation abnormality along with multiple organ thrombi formation and cytokine storm were clearly understood in COVID-19 disease. [7, 8]

Covid-19 infection associated coagulopathy and abnormal levels in coagulation parameters are the most significant prognostic marker in COVID-19 patients.[9,10] Coagulation parameters showed marked variation in Covid-19 infection such as increased D-Dimer and Fibrinogen levels along with mild to moderate thrombocytopenia. Increased D-dimer levels are strongly associated with increased mortality rate in hospitalised patients. Such patients also show abnormal PT and aPTT values.[11, 12]

In critically ill patients Disseminated Intravascular Coagulopathy (DIC) may develop and such patents may show increase PT and aPTT with normal or elevated fibrinogen

levels.[13, 14] However, D-dimer values are much increased as compared to other coagulation parameters. All such findings are not seen in a classic case of DIC.[10, 11] The term "COVID-19-associated coagulopathy" is used to describe the spectrum of coagulation changes in the patient. It consists of three stages. Stage 1 presenting with elevated D-dimer levels. Stage 2 showing increased D-dimer levels along with increased aPTT, PT and fibrinogen levels and mild to moderate thrombocytopenia. Stage 3 presenting with severe illness and laboratory findings pointing towards classic DIC.[15, 16]

Coagulation abnormalities are distinctive findings in COVID-19 patients and are associated with poor clinical outcomes and death. The changes of coagulation function in these patients should be paid utmost attention to, especially for certain high-risk groups with thrombosis. As part of their treatment it may be possible to improve the patient's condition by early anticoagulation therapy and maintaining their normal physiological state.[17, 18] Hence in the present study, assessment of coagulation parameters in COVID-19 patients on hospital admission is emphasised. Most of patients have COVID-19 associated coagulopathy; evaluation of coagulation parameters holds upmost importance in order to decrease disease severity in such patients to reduce coagulation associated morbidity and mortality.[19]

OBJECTIVE OF THE STUDY

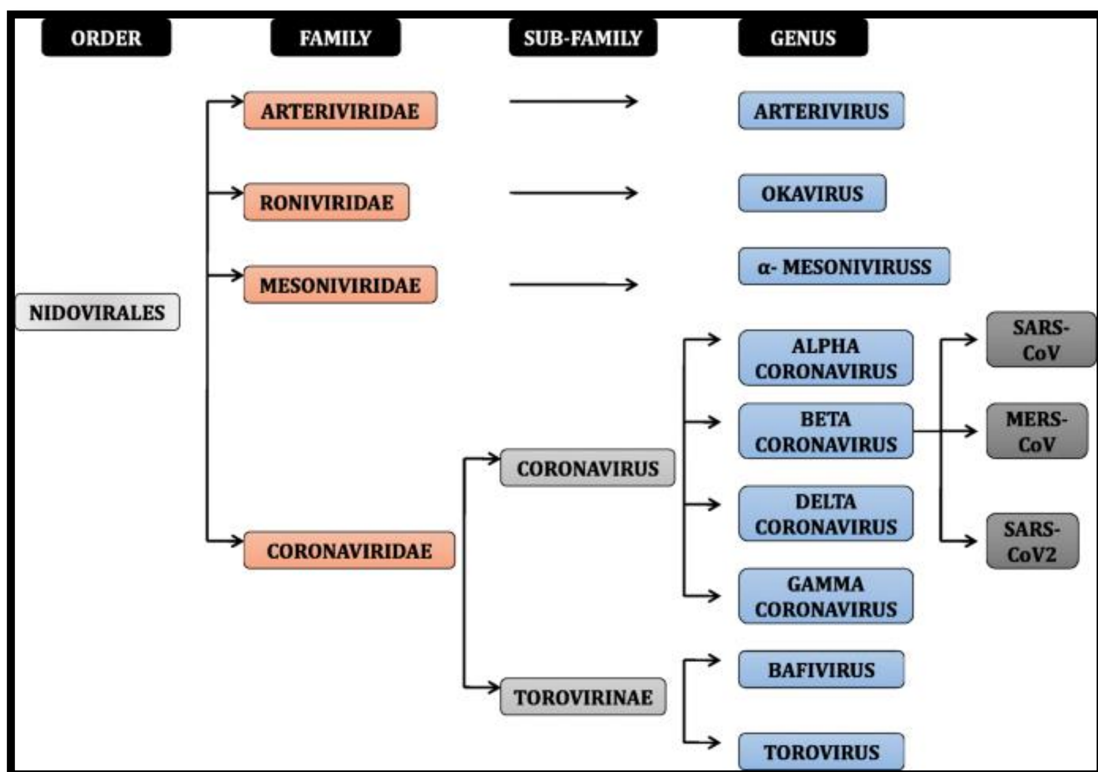
To assess the various coagulation parameters in COVID-19 patients with correlation to severity of infection.

REVIEW OF LITERATURE

HISTORY AND ORIGIN

Corona virus belong to the family Coronaviridae and the order Nidovirales. Nido in Latin means nest. The order nidovirales includes Arteriviridae, Roniviridae, Mesoniviridae and Coronaviridae families.[20]

CORONA VIRUS: ORDER, FAMILY, SUB-FAMILY AND GENUS



The Coronaviridae comprises of 2 subfamilies i.e. Coronavirinae and Torovirinae. The subfamily Coronavirinae is made up of of Alpha Coronavirus, Beta Coronavirus, Gamma Coronavirus and Delta Coronavirus Genus on the basis of genomic structure. SARS-CoV-2 comes under the Beta coronavirus genus.[21] Apart from SARS coronavirus-2, two more are known to be responsible for causing serious diseases like SARS-corona virus which was responsible for the SARS outbreak of

2002-2003 and MERS which caused the Middle East MERS Coronavirus outbreak of 2012.[21, 22]

Coronaviruses contain the largest known RNA genomes (26e32kilobases). The RNA genome of SARS-CoV-2 codes for 4 structural proteins (sp) and 16 non-structural proteins (nsp). The S, N, E and M proteins are the four structural proteins of the virus. The S (Spike) protein forms the distinctive protrusions from the surface of the virus and interacts with the plasma membrane receptor of the target cell to mediate the penetration of the virus into it. The N (Nucleocapsid) protein binds the RNA genome. The E (Envelope) and M(Membrane) proteins form the envelope and the membrane that coat the virus.[21, 23]

SARS-CoV-2, like any other RNA virus is susceptible to genetic advancement with the emergence of mutations over period resulting in various mutant forms. This is true even when SARS-CoV-2 adapts to its new human hosts. Many SARS-CoV-2 variants have been isolated throughout this epidemic but only a small number of these are regarded as variants of concern (VOC) by the World Health Organisation.[21, 22, 23]

Five variants of concern have been recognised so far.[23] They are alpha (B.1.1.7), first variant of concern initially found in the United Kingdom in december 2020. The second variants of concern beta (B.1.351), identified in South Africa in december 2020. Gamma (P.1) which was first testified in Brazil in january 2021. Delta (B.1.617.2), first identified and reported in India in december 2020 and Omicron (B.1.1.529) which was first reported in South Africa in november 2021.[24]

STRUCTURE

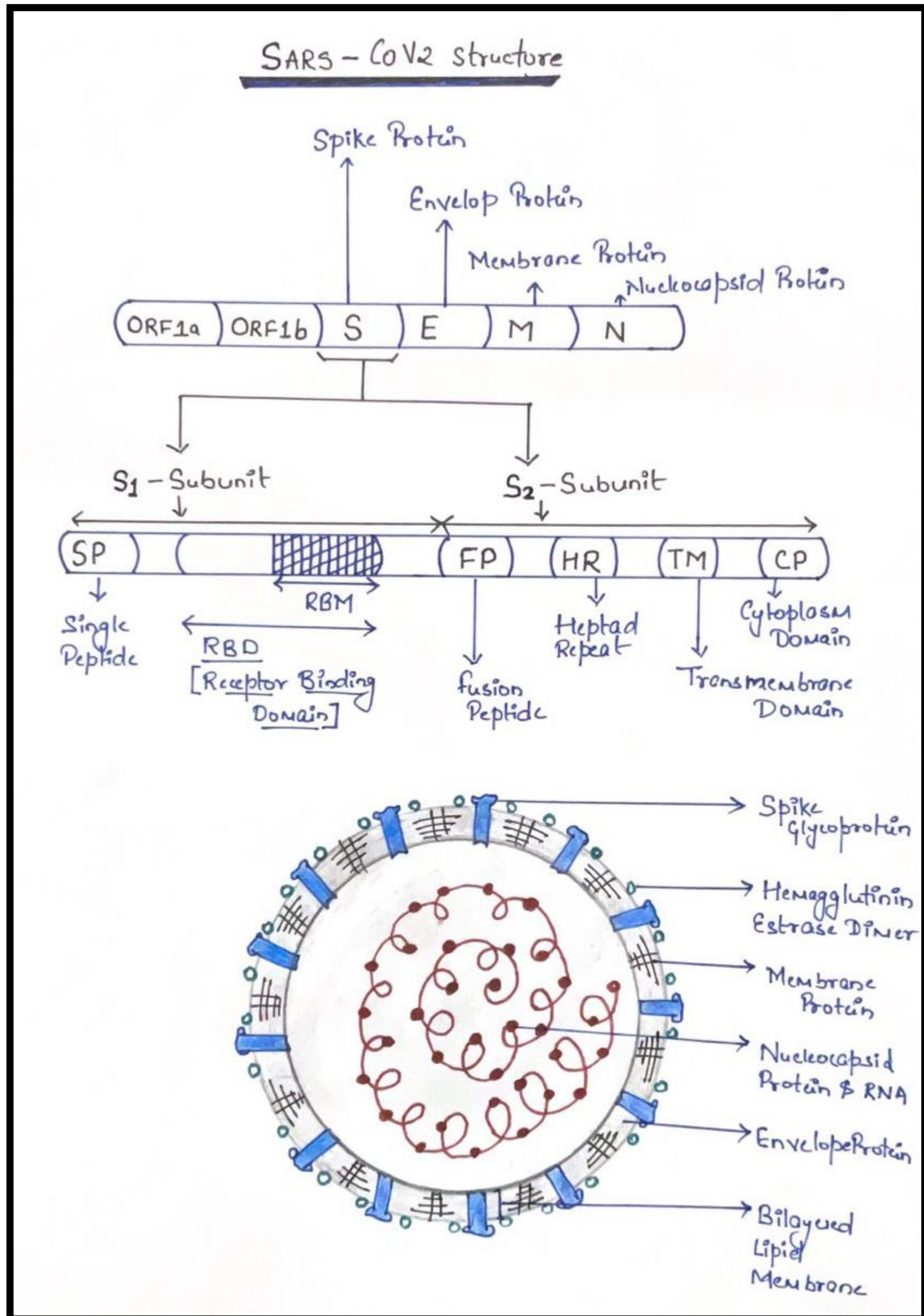
Coronavirus is a non-segmented, enveloped and single-stranded RNA virus. It measures 27 to 33 kb in largest dimension. It's genome is one of the largest genome among all RNA viruses. On electron microscopy SARS-CoV-2 are spherical in shape with diameter around 65–145 nm. They contain 9 to 12 nm long spikes in their outer membrane. Viral RNA is made up of 5′-capped and 3′-Polyadenylated untranslated regions (UTRs). It also have several Open reading frames (ORFs) that encrypt various functional proteins.[20, 21]

The viral genome is organized in the order with a noncoding 5′-UTR replicase genes (ORF1a and ORF1b) arranged first, structural proteins (S, E, M, and N) arrangement comes the next, followed by accessory proteins and noncoding 3′-UTR. ORF1a and ORF1b in the virus encode for 16 non-structural proteins. The structural genes of the virus code the structural proteins like spike (S) protein, envelope (E) protein, membrane (M) protein, and nucleocapsid (N) protein. [20, 21]

The 3′end contains 4 structural proteins responsible for virus and host cell receptor interaction, viral assembly and release of virus from the infected host cell. The S-protein present over the surface facilitates viral attachment to receptors and membrane fusions which allow the virus to enter the host cell. The E protein, smallest of all structural proteins is crucial for virus assembly, host cell membrane permeability and virus-host cell contact. The E protein helps in virus-like particle formation. M protein, the most abundant structural protein in the virus helps in viral assembly along with E and N proteins. The N protein helps in the formation of viral genomic structure.[22] On the viral surface, hemagglutinin-esterase dimers (HE) have

been discovered which helps in virus replication and may play a role in virus entry. The HE protein is crucial for infecting the natural host cell.

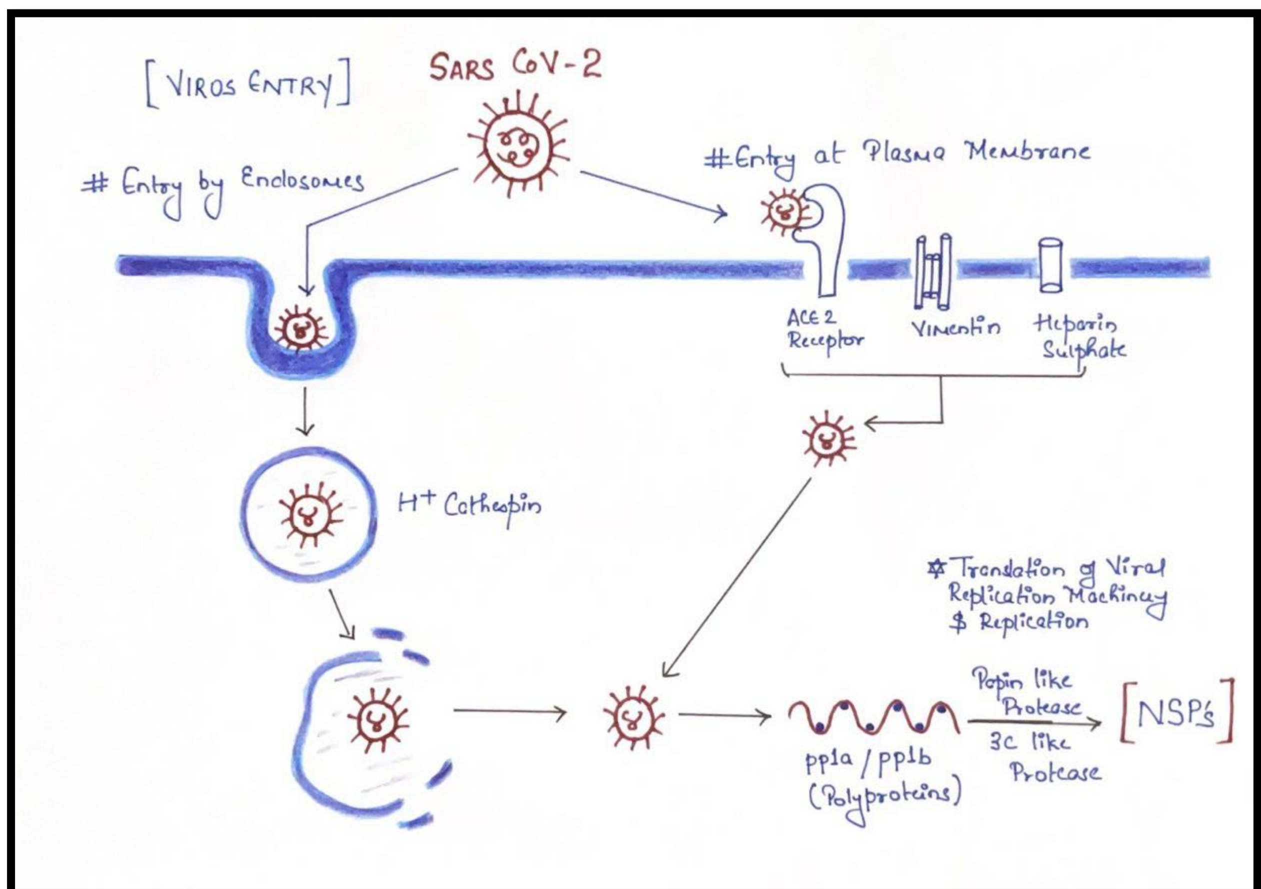
STRUCTURE OF CORONAVIRUS



LIFE CYCLE

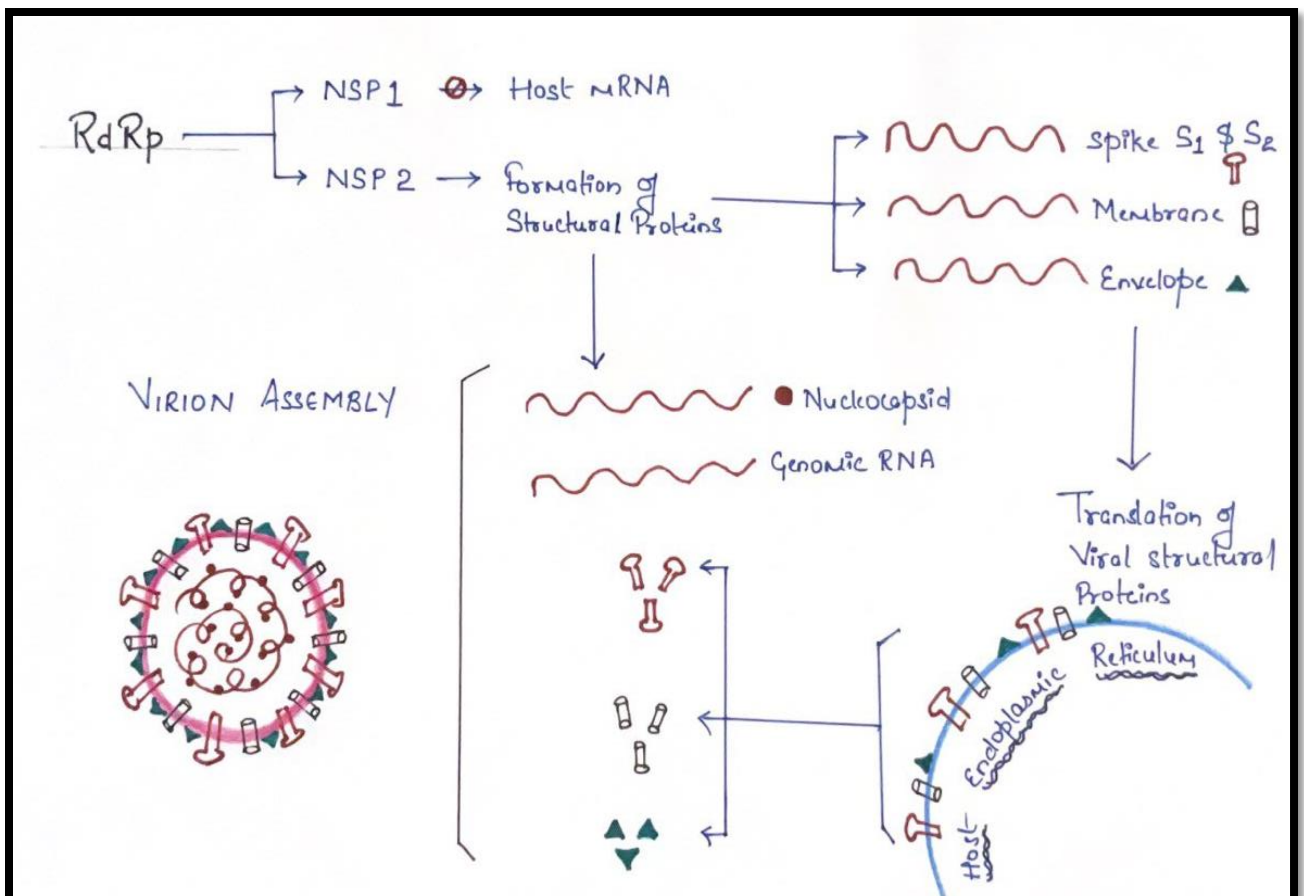
The enveloped Corona virus is a positive sense RNA virus. This virus with its club-like spikes on the surface has a unique method of replication. The attachment of the viral spike (S) proteins to host cell receptors along with priming of the Spike protein by host cell proteases enzyme are needed for the virus to enter the host cell.[17,18] Virus can enter the cell via fusion of the plasma membrane or endosomes. Spike proteins (S1, S2) of SARS-CoV-2 mediate adhesion to a host cell's membrane and activate ACE2 as the entrance receptor (in both directions). [19]

LIFE CYCLE OF CORONAVIRUS - I



Poly-proteins are translated after the viral RNA has been released into the host cell. Both structural proteins necessary for virion assembly and non-structural proteins (NSPs) essential for viral RNA synthesis are encoded by the coronavirus genomic RNA.[17, 19] The papain like protease and the 3C-like protease cleave the translated poly-proteins polypeptide1a and polypeptide1ab to produce functional NSPs like helicase or the RNA replicase-transcriptase complex (RdRp). The host shutoff factor Nsp1 is one of the earliest translated proteins. This viral protein slows down host mRNA translation and accelerates its degradation suppressing the host's innate immune response.[20]

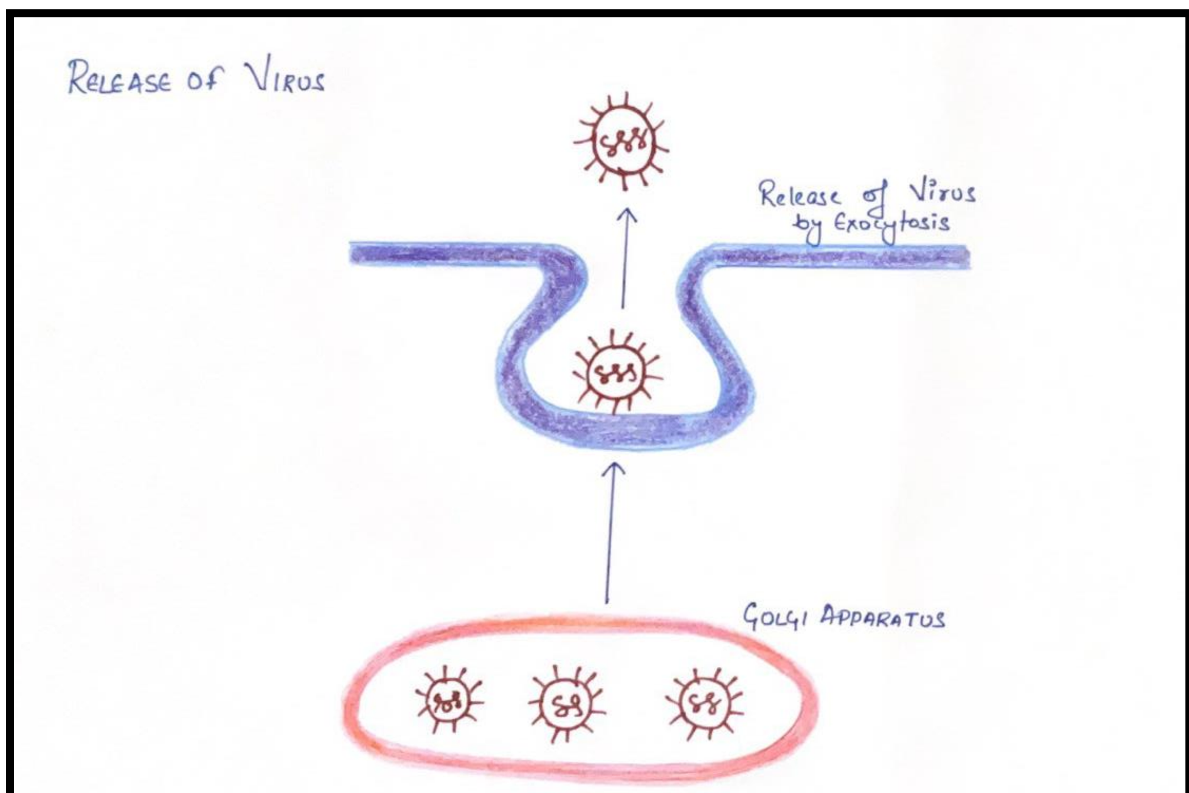
LIFE CYCLE OF CORONAVIRUS - II



Structural protein RNA replication is carried out by RdRp (Nsp12). Ribosomes attached to the endoplasmic reticulum(ER) translate the structural proteins (S), Envelope (E), and Membrane (M).[19, 21, 22] The viral RNA is copied and protected from the host's defence mechanism in a Double Membrane Vesicle (DMV), which are formed by Endoplasmic Reticulum (EM). The pathognomic viral RNA exits the DMVs through holes made by Nsp3 in preparation for virion assembly. The nucleocapsid proteins are put together from genomic RNA and remain in the cytoplasm.[21, 22]

Further they combine with the precursor of the virion, which is then carried to the cell surface by tiny vesicles from the ER through the Golgi apparatus (GA). Afterward, exocytosis allows the virus to leave the infected cell and move on to hunt for a new host cell.[23, 24]

LIFE CYCLE OF CORONAVIRUS - III



INCUBATION

The time interval between the viral entry into the body and the manifestation of first symptoms or signs in the form of persistent cough, high fever, fatigue on exertion and generalised myalgia is known as Incubation period of Covid-19 infection.[25] In COVID-19 infection incubation period is very important because all the asymptomatic individual with no signs or symptoms and symptomatic carriers with mild to moderate or even severe clinical manifestation, though on treatment, may spread the infection during this time interval.[26] Studies done by many virologists found that the incubation period of Covid-19 infection is of 14 days along with median time of 4-5 days.[27, 28]

TRANSMISSION

SARS-CoV-2 is mostly spread by close contact or droplet transmission of respiratory droplets carrying the infectious virus, transmission by air; fomite transmission from contamination of inanimate surfaces; viable virus was recovered from nonporous surfaces including glass and stainless steel for up to 28 days at 20 degrees celsius; spread through contact with infected surfaces however this is not the virus' primary method of transmission and the risk is low; potentially by feco-oral route and neonates from women who had COVID-19 demonstrated vertical transmission, however this is seen in minority of cases.[27, 28]

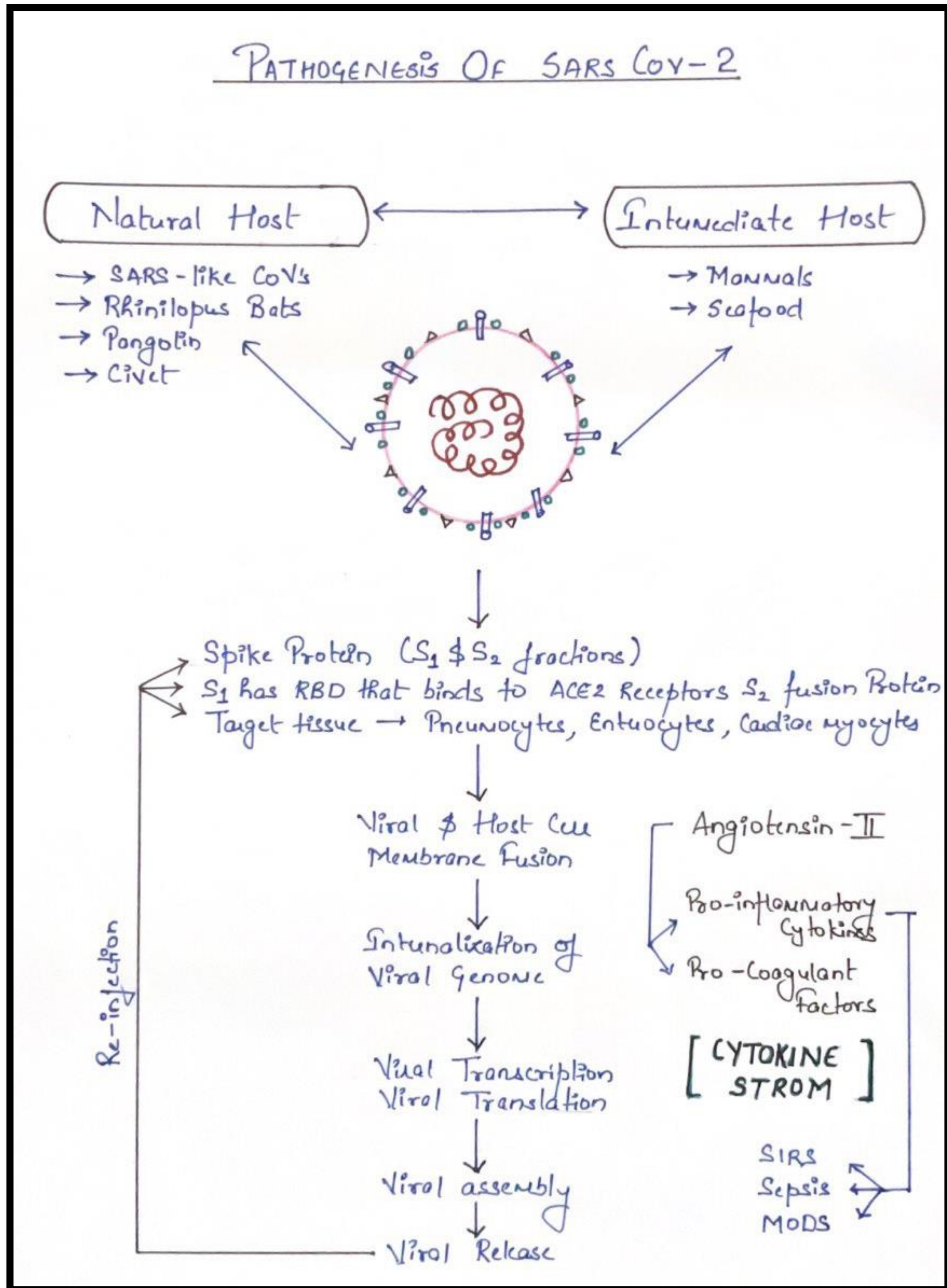
PATHOGENESIS

Respiratory alveolar epithelium contain abundant ACE-2 receptors, type II ACE-2 receptors more than type I ACE-2 receptors.[29] SARS CoV-2 binds with these receptors in order to enter the host cell with the help of spike (S) protein's S1 fraction with the help of Receptor binding domain (RBD).[30, 31] Transmembrane Protease Serine enzyme(TMPRSS)[31] along with S2 fraction of spike protein also plays an important role in viral entry and fusion of virus to host cell membranes.[32]

ACE-2 R and TMPRSSs[31] are also found in esophagus, intestine and lung alveolar type 2 pneumocytes. Hence the virus can not only invade lungs but also esophagus and the intestine causing multiple organ damage.[33] COVID-19 infection mainly manifest as a respiratory illness and coagulation disorder. The pathogenesis of Covid-19 infection can be sub-divided into two phases, Early phase and Late phase.[34,35] The Early phase represents viral replication and manifestations caused by viral associated tissue damage. Late phase represents host cell immune response to the viral attack in the form of release of various cytokines such as Tumor necrosis factor-α, Granulocyte macrophage colony stimulating factor, Interleukin-1 and Interleukin-6.[36, 37]

In severe form of Covid-19 infection the immune response to the viremic attack becomes significant and thus releasing large quantity of cytokines like IL-6 and TNF- α, resulting in a state of excess cytokine stimulation known as 'cytokine storm' which trigger both local and systemic inflammation. These factors contribute in the manifestation of sepsis like condition and resulting in multiple organ damage.[38,39]

PATHOGENESIS OF SARS CoV 2



CLINICAL MANIFESTATIONS

The clinical range of COVID-19 includes asymptomatic, symptomatic and clinical sickness marked by multiple organ failure, septic shock and acute respiratory failure necessitating mechanical ventilation. 17.9% to 33.3% of infected patients are anticipated to show no symptoms. In symptomatic patients typically have fever, cough, shortness of breath, upper respiratory tract symptoms, loss of taste, loss of smell, nausea, generalised body pain and diarrhea. [40]

National Institutes of Health made the guidelines in order to classify COVID-19 induced clinical manifestations into 5 different types on the basis of presenting symptoms, pathological findings, radiological abnormalities.[41] Firstly, symptomatic or pre-symptomatic infection with positive SARS-CoV-2 RTPCR test without any presenting symptoms of typical infection. Secondly, mild disease in presence of clinical symptoms of COVID-19 but without any complains of shortness of breath and absence of any evidence of lung pathology in radiological findings. Thirdly, is moderate infection with clinical symptoms or presence of any radiologic evidence of lung pathology along with oxygen saturation (SpO2) more than and equal to 94% on room air. Fourth is severe illness with SpO2 less than and equal to 94% on room air along with ratio of partial pressure of arterial oxygen to fraction of inspired oxygen (PaO2/FiO2) is less than 300 with marked tachypnea with respiratory frequency more than 30 breaths/min or lung infiltrates more than 50%. Fifth and last is critical illness in which individuals have acute respiratory failure, septic shock or multiple organ dysfunctions. Patients with severe COVID-19 infection may become severely ill with the manifestation of acute respiratory distress syndrome (ARDS) which occur within one week after the onset of symptoms.[41, 42]

EVALUATION

A thorough medical history including history of travel, history of contact with other infected individual, history of presenting symptoms chronologically, associated comorbidities and history of on-going medical treatment should be obtained and properly documented.[43] Relevant history and typical presentation of symptoms should be considered for Molecular diagnostic testing to look for the presence of viral RNA in the individual.[44]

Molecular testing is done by real-time PCR assay using nasopharyngeal swab. Rapid antigen testing is another important modality of testing to find out antibodies present in the individual having Covid-19 infection. In order to see lung pathology associated with the viral infection chest x-ray, chest computed tomography or lung USG should be carried out.[45]

During the on-going pandemic, the Dutch Radiological Society gave standardised CO-RADS score based on radiological findings. CO-RADS measure the pulmonary association of infection on a scale from score 1 which denotes very low lung involvement to score 5 which is regarded as very high pulmonary pathology.[45, 46]

CO-RADS: LEVEL OF SUSPICION OF COVID-19 INFECTION

		CT findings
CO-RADS 1	No	normal or non-infectious abnormalities
CO-RADS 2	Low	abnormalities consistent with infections other than COVID-19
CO-RADS 3	Indeterminate	unclear whether COVID-19 is present
CO-RADS 4	High	abnormalities suspicious for COVID-19
CO-RADS 5	Very high	typical COVID-19
CO-RADS 6	PCR +	

PATHOPHYSIOLOGY OF COVID-19-ASSOCIATED COAGULOPATHY

Thromboembolic events are strongly related with SARS-COV-2 infection. However, a pathogen associated interaction between the host endothelium and activation of host's immune response and coagulation activation appears to be a major factor in the etiology of COVID-19-induced coagulopathy.[47] The vascular endothelium regulates the immune system to an extent along with inflammation and vasomotor tone via number of pathways in a basal state which is critical for maintaining homeostasis and contributing to COVID-19-mediated endothelialitis and thrombosis (CMET).[48]

All vascular beds' endothelium is varied and serves a variety of purposes. Individuals differ in their endothelium's state of health. There are several aspects of

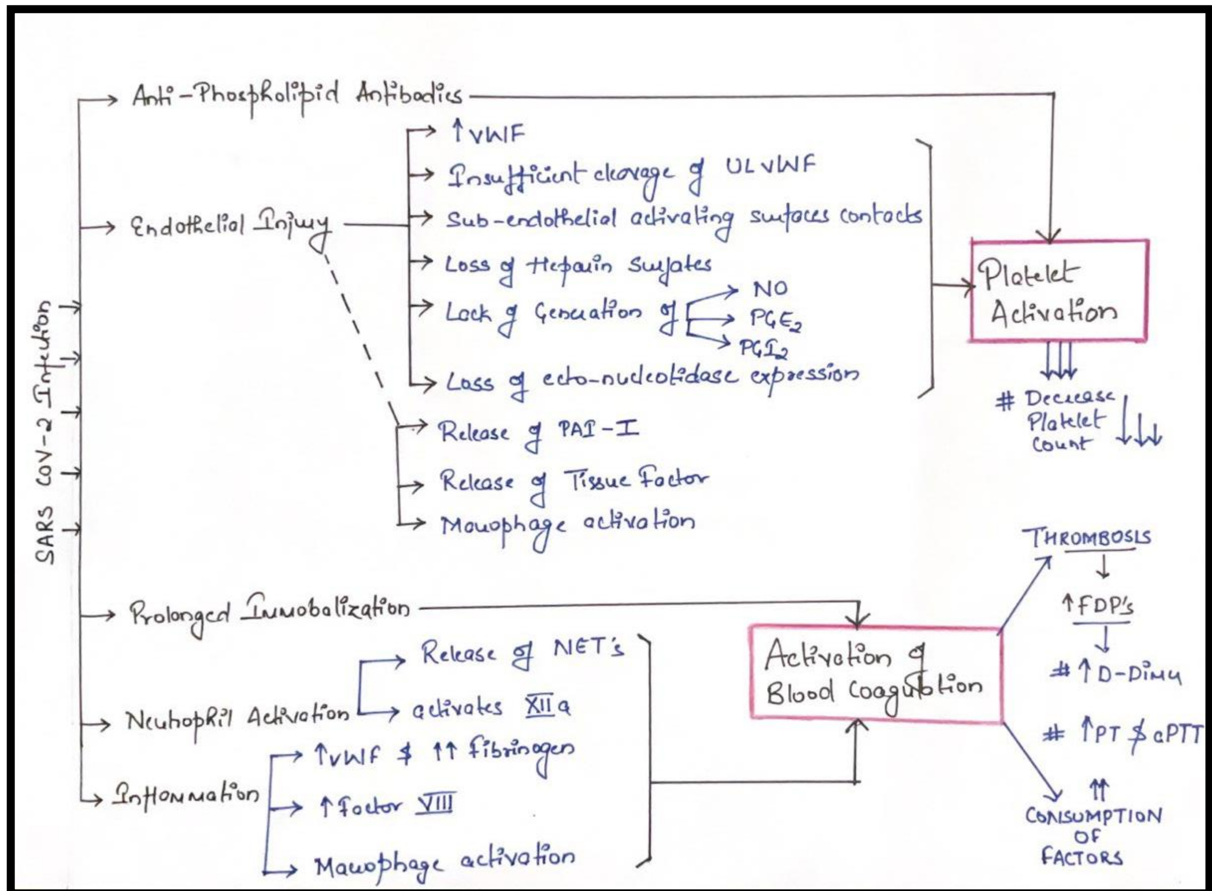
endothelial dysfunction including those related to coagulation. By supplying a non-thrombogenic inner surface to maintain an appropriate blood flow without causing systemic clotting or bleeding, endothelial cells regulate the coagulation system.[48]

The SARS-COV-2 virus once enters the body by expressing ACE2[49, 50] on endothelial cells they activate it to take part in host defence and to encourage localised inflammation. It makes the affected endothelial cell layer pro-coagulant and to an extent anti-fibrinolytic.[50] Von Willebrand factor (vWF) is released and thrombomodulin is also released into the blood stream when endothelial cells are activated. Critical illness and death are associated with greater blood levels of these biomarkers pointing to possible involvement of vW-Factor and thrombomodulin regulated coagulation pathways.[51, 52]

Impaired endothelial cells produce tissue factor which comes in contact to factor VII and activates it to initiate the clotting cascade mechanism. Thrombin is produced as an end product and a clot is formed. Further thrombus development is also made easier by the pro-inflammatory state causing deregulation of the anticoagulant mechanisms.[53, 54, 55]

Finally, the production of Plasminogen Activator Inhibitor-1(PAI-1) by endothelial cells during inflammation inhibits fibrinolysis. Sepsis may result in the inactivation of ADAMTS-13 which results in inadequate cleavage of vWF resulting in a prothrombotic condition. These systems aid in the elimination of the infection during a well-controlled immune response resulting in healing and the restoration of the homeostatic condition of the endothelial cell layer.[56, 57]

PATHOPHYSIOLOGY OF COVID-19-ASSOCIATED COAGULOPATHY - I



A typical inflammatory reaction occurs which consists of altered sequential stages, the recognition and recruitment of immune cells along with elimination of the threat and then back to normal stable homeostasis. With increased levels of additional pro-inflammatory mediators such as tumour necrosis factor α, IL-1β, IL-8 and IL6 causes an inflammatory cell response that leads to hypotension, vascular leakage, multi-organ failure, ARDS and mortality in this hyper-inflammatory response.[58, 59]

The pathogenesis of COVID-19-induced hyper-cytokinemia resembles that of influenza in that it is marked by an increase in neutrophils, macrophages and pro-inflammatory cytokines and a decrease in lymphocytes likely as a result of splenic and pulmonary apoptosis. Lower lymphocytes specifically CD4+ and CD8+ have

repeatedly been linked to worse outcomes in the individual affected with Covid-19 infection.[60, 61]

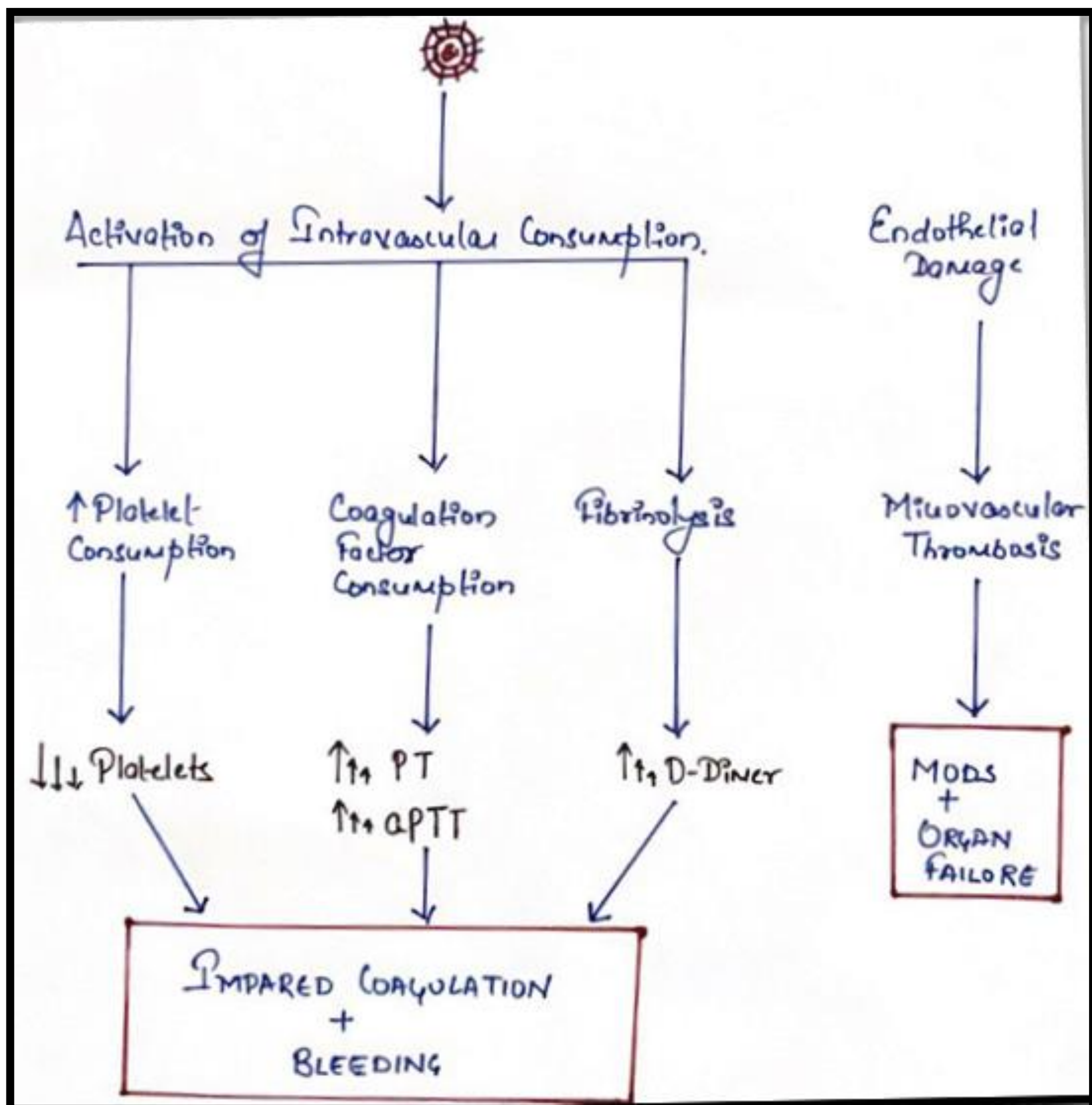
The majority of patients had pulmonary micro-thrombi at autopsy despite using anticoagulation which is a significant related finding. In certain cases pulmonary macroscopic thrombi were found during post-mortem examination. The term "immune-thrombosis" refers to this relationship between immunological activation and coagulation which has been hypothesised as a crucial cause of thrombus development in advance COVID-19 infection together with endothelial dysfunction.[62, 63]

Inflammatory cells are drawn to the site of infection or injury in reaction to a healthy immune response. As the initial line of innate defence neutrophils in particular are essential because they trigger pathogen killing and the development of Neutrophil extracellular traps (NETs). NETs is a type of immune defence in which controlled neutrophil death triggers the development of traps that capture microorganisms and stop their spread. In particular older neutrophils are more vulnerable to NETosis acting quickly at the infection site. The complement and coagulation systems interact with NETs which prevent fibrinolysis. The degree of NET production depends on the species and the stimulation. [64, 65]

Complement activation, which is brought on by activation of neutrophil and the recruitment of the contact system of coagulation intensifies immunothrombosis even further. Factor XIIa in this instance causes the development of bradykinin and kallikrein, two crucial immunological mediators and additional intrinsic coagulation system triggers. It's interesting to note that factor XIIa may start the traditional complement pathway by activating the C1 complex whereas the intrinsic coagulation

cascade starts the next step in the production of thrombin. Both the contact activation route and the complement pathway are significantly inhibited by the C1 esterase inhibitor.[64, 65, 66]

PATHOPHYSIOLOGY OF COVID-19-ASSOCIATED COAGULOPATHY - II



PLATELETS

Platelets are small and colourless fragments of cell formed in the bone marrow from progenitor cells known as Megakaryocytes. Their production is via cytokine mediator thrombopoietin. Thrombopoietin is produced in liver and kidneys and gets activated by inflammatory cytokines such as IL-6.[67] As platelets are the smallest component of the peripheral blood, they are moved to the walls of the vessels, helping plasma and other blood cells to flow in the center which aid platelets to reach quickly to the site of injury. Platelets have variety of intracellular materials which when released into circulation initiate inflammation. [67, 68]

Viral infection may result in decrease in platelet formation and its reduced function for a variety of reasons. The sudden decrease in platelet count is due to viral infection causing its destruction or its clearance from the blood stream.[68] Platelet activation is mediated to an extent via antigens which are present in the virus's outer surface and antigen-antibody complex activation when antigen comes in contact with antibody thus generated by the platelets. Direct viral injury to bone marrow and megakaryocyte may further lead to decrease platelet formation.[69]

Platelets have significant role in both, inflammation initiation and defence mechanism against the virus. Through its thrombotic effect and immune function platelet plays a vital role in disease pathology of the Covid-19 viral infection. Platelet helps in the recruitment as well as activation of leukocytes present in the blood stream to the site of endothelial injury caused by Covid-19 virus pathology.[69, 70]

Leukocyte recruitment along with its activation and interaction with platelets are important to reach pro-coagulant effect in the viral infection. Aggregation of platelets to the site of injury and their activation leads to a state of consumptive

coagulopathy. Platelets are also used up by the small to medium sized thrombi formed in various organs due to Covid-19 pathology; especially Lungs may further add to the process of platelet consumption.[67] In mild to severe cases of Covid-19, thrombocytopenia is well established component. Hence, in viral attacks like Covid-19 the platelet may show reduction in its level in blood stream which is proportional to the disease severity and amount of coagulation dysfunction.[69, 70]

D-DIMER

The D-dimer has changed throughout time since it was first introduced in the 1970s. The activation of the plasmin enzyme results in the formation of the D-dimer which is made up of two D fragments of fibrin.[71, 72] This suggests that a destroyed fibrin is present in the bloodstream. D-dimer is a sign that the coagulation and fibrinolysis systems are active.[73, 74] In circumstances when anticoagulants have been stopped it has more recently been utilised to forecast the probability of recurrent thrombosis

Nearly every patient with severe VTE has an increase in D-dimer levels.[104] The high level of D-dimer can be detected in physiological states like pregnancy and pathological conditions including cancer, inflammation and surgery. D-dimer kit sensitivity varies from maker to manufacturer and is said to be between 93 and 95 percent. [75, 76, 77]

In COVID-19, the significant prevalence of coagulopathy and venous thromboembolism (VTE) was demonstrated. It was believed that thrombosis and respiratory decline are related. Increased D-dimer along with increase lactate dehydrogenase levels and moderate to severe alterations in PT and aPTT were reported as signs of coagulopathy in the COVID-19 infection.[78, 79]

When the patient's D-dimer level is three times greater than the cut-off a VTE screening is triggered. Additionally a four-fold upsurge in D-dimer level in COVID-19 cases was proposed as a reliable indicator of mortality in COVID-19.[80, 81] Age-related increases in D-dimer levels are observed.

Patients with COVID-19 have higher D-dimer levels across the board. Higher amounts of D-dimer can occur in COVID-19 patients when there are concurrent diseases including diabetes, cancer, stroke, or physiological conditions like pregnancy.[82, 83] On the other hand the link between high D-dimer levels and coagulation abnormality emphasises the significance of detecting D-dimer in COVID-19 cases especially on hospital admission.[84, 85] These tests pave the door for better COVID-19 management. In managing the condition, it may be useful to comprehend the molecular basis for the D-dimer elevation seen in COVID-19 patients. These individuals' increased D-dimer values may be brought on by thrombin production-inducing endothelial cell malfunction or inflammatory reactions to viral infections. [83, 84, 85]

PT AND aPTT

Clotting is a plasma function brought up by orderly interaction of a group of plasma proteins which are sequentially activated after vascular endothelial injury with specific phospholipid present in damaged tissue along with platelet aggregation and activation in the presence of Ca++.[86, 87] In the later stage of sequential process of clot formation, thrombin is formed which then converts to fibrinogen, a soluble plasma protein and which in turn leads to the formation of fibrin which is insoluble.

Clotting can be activated and progressed via two altered cascading pathways depending on the type of vascular damage or abnormality, the intrinsic pathway which is initiated by contact with an abnormal or foreign surface and the extrinsic pathway which is initiated by contact with an abnormal or foreign surface and is initiated by exposure to tissue factors.[86, 87] The two pathways converge so that the final steps are shared by both schemes which is known as common pathway. Clotting can be initiated via either the faster (15-20 secs) extrinsic or the slower (2-6 mins) intrinsic scheme.

Prothrombin Time Test:

The PT test is used to monitor patients who are taking certain medications and to help diagnose clotting disorders. A venepuncture is used to obtain a sample of the patient's blood. The blood is decalcified (by collecting it in a tube containing oxalate or citrate ions) to prevent clotting before the test. Centrifugation separates the blood cells from the liquid part of the blood (plasma).[88]

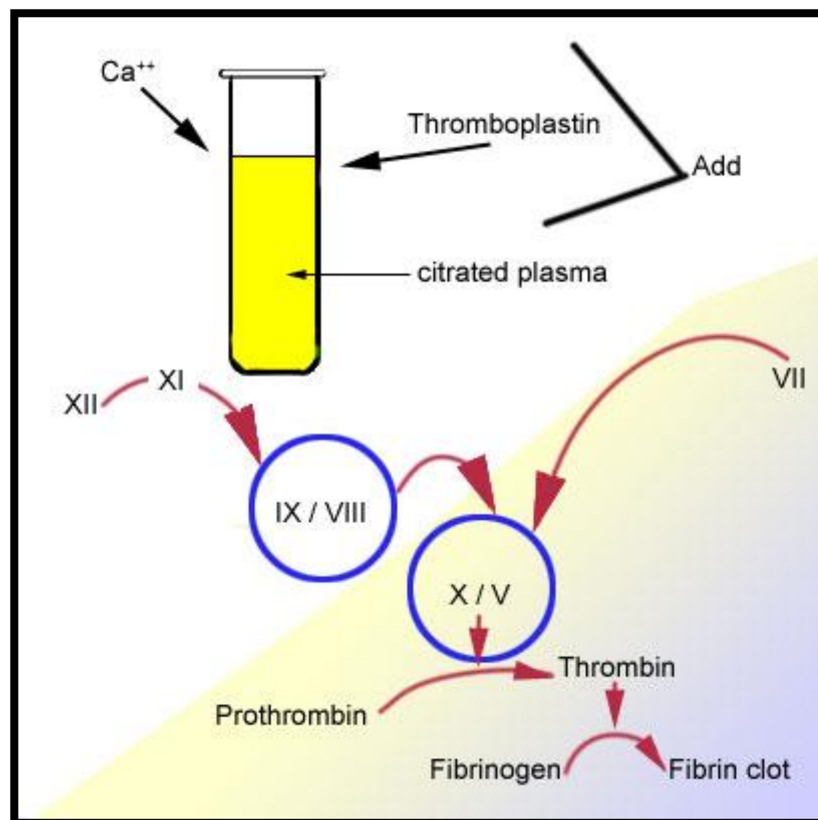
The PT test is performed by combining the patient's plasma with a Tissue Factor (e.g., thromboplastin, a protein derived from homogenised brain tissue) that converts prothrombin to thrombin. After that, the mixture is placed in a 37°C warm water bath for one to two minutes. To counteract the sodium citrate and allow clotting to begin, calcium chloride (excess ionised calcium) is added to the mixture. The test is timed from the time the calcium chloride is added until the plasma clots. This is known as the Prothrombin Time. [89, 90]

The prothrombin test specifically assesses the presence of factors VII, V, and X, as well as prothrombin and fibrinogen. A prothrombin time in the 11-15 second

range (depending on the source of thromboplastin used) indicates that the patient has normal levels of the clotting factors listed above.

Prothrombin time prolongation suggests deficiency of factors V, VII, X, prothrombin or fibrinogen.[91,92] It also indicates decrease in the levels of vitamin K (vitamin K is a cofactor in the synthesis of functional factors II, VII, IX, and X) or the person has some sort of Liver pathology because plasma protein factors are synthesised in the Liver).

PROTHROMBIN TIME TEST



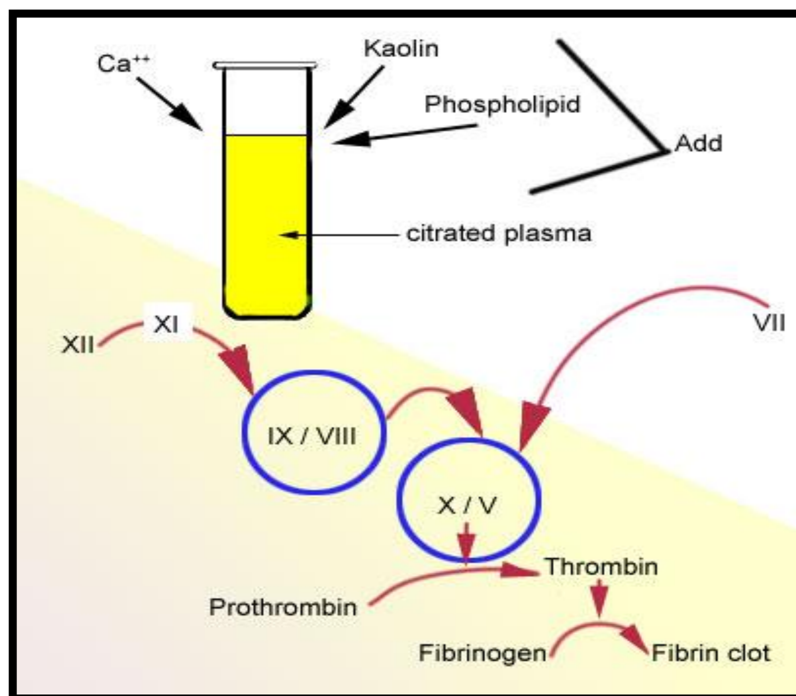
Activated Partial Thromboplastin Time Test :

The activated Partial Thromboplastin Time (aPTT) test is used to evaluate certain bleeding disorders.[93] The aPTT test uses decalcified blood because calcium causes activation of coagulation cascade. Centrifugation is used to separate the

plasma. To initiate the intrinsic pathway of the coagulation cascade, calcium (ionised) and activating substances are added to the plasma. Kaolin (hydrated aluminium silicate) and cephalin are the substances. Kaolin activates the Factor XII and cephalin replaces platelet phospholipids.[94, 95] The partial thromboplastin time, measured in seconds, is the time it takes for a clot to form. The sample will normally clot in 35 seconds. [95]

aPTT measures the factors of intrinsic system. Factors XII, XI, VIII, IX along with common clotting pathways integrity is altogether evaluated. Increased levels in a person suffering from a bleeding disorder indicate that a clotting factor is either missing or defective. Liver disease reduces factor production, raising the aPTT. [96, 97]

ACTIVATED PARTIAL THROMBOPLASTIN TIME TEST



Clotting mechanism and fibrinolytic activity forms coagulation system. The former checks excessive blood loss, whereas the latter is responsible to maintain blood circulation within the vasculature.[96, 97] Following any insult like viral injury both system gets activated in order to stabilise the normal blood haemostasis. There is sudden and acute activation of the blood coagulation system in Covid-19 patients causing generation and deposition of fibrin clots in small and medium sized blood vessels. This results in ischaemic necrosis of various organ systems like respiratory and renal, leading to organ failure.[97, 98]

The widespread inflammation and coagulation activation causes organ and vascular manifestations such as micro-thrombi in the lungs as well as systemic complications such as cytokine storm.[99, 100] As a result there is considerable fibrin formation and deposition. Fibrin deposition in the alveolar and interstitial lung spaces may play a role in acute respiratory failure. [99,100]

FIBRINOGEN

Fibrinogen (factor I), with a molecular weight of 340kD, is a hexameric plasma glycoprotein produced by the liver and circulated in the blood. Three major enzymes use fibrinogen as a substrate: thrombin, plasmin, and factor XIIIa. It is essential for hemostasis due to various functional interactions. Fibrinogen is a soluble precursor to insoluble fibrin that also helps platelets clump together.[101,1 02] The fibrin clot also activates the fibrinolytic system, so the clinical manifestations are determined by the balance of coagulation and fibrinolysis.[102]

When thrombin (factor IIa) binds to fibrinogen, it releases fibrinopeptides A and B (FPA and FPB) from the A alpha and B beta chains. The resulting molecule is a fibrin monomer, which polymerizes spontaneously to form a fibrin clot. Once

polymerized, factor XIIIa activates fibrin cross-linking, which strengthens the clot and protects it from mechanical or enzymatic disruption.[103, 104]

Fibrinogen, one of the acute phase proteins, is synthesised in large quantities by the liver in response to IL-1 and IL-6 stimulation. It is also involved in the formation of fibrin as the final step of a triggered coagulation activity. According to The International Society for Thrombosis and Haemostasis, fibrinogen estimation is one of the important parameter in scoring DIC.[105,106]

Severe covid-19 patients show features of DIC. Hence, fibrinogen estimation is one of the important investigations to grade disease progression. The dynamic changes in fibrinogen levels are strongly evident in Covid-19 severe patients.[101, 102] It has been discovered that the levels of fibrinogen and its degradation products are not only higher in Covid-19 patients than in healthy controls, but also higher in critical Covid-19 patients than in mild or moderate cases. Fibrinogen levels should be evaluated alongside D-dimer levels so that disease progression can be properly made out and prompt treatment can be given.[102, 106]

Covid-19 infection is thought to be multifactorial, manifesting with high D-dimer levels, elevated fibrinogen, occurrence of thrombocytopenia, mild to moderate prolongation of prothrombin time and activated partial thromboplastin time. In critically ill patients disseminated intravascular coagulopathy may develop and such patients may show further variation in coagulation parameters.

Hence there is a need to study such cases along with assessment of their coagulation parameters on hospital admission in order to decrease disease severity and to reduce coagulation associated morbidity and mortality. Early assessment and dynamic monitoring of coagulation system parameters may be a benchmark to control

the severity of COVID-19 infection and associated mortality by including these parameters to the criteria for hospitalization. This would also assist the concerned clinicians to develop anticoagulation therapeutic strategies at the earliest to prevent disease progression and mortality.

METHODOLOGY

Source of data: Jawaharlal Nehru Medical College and Research Centre and Hospital and KLE's Dr. Prabhakar Kore Hospital's free Haematology Laboratory and Hi-Tech Haematology Laboratory.

Ethical Consideration: Ethical clearance was given by Ethical Committee of Jawaharlal Nehru Medical College and Research Centre. Patients with confirmed COVID 19 Test with CO-RADS score of 4, 5 and 6 were studied.

Study Period: 1st January 2021 to 31st December 2021.

Study Population: Patients who were admitted to Covid Ward at KLE's Dr. Prabhakar Kore Hospital between the study period. The patients details were obtained from the requisition forms and the haematological parameters were obtained from the blood samples received over the period of 1st January 2021 to 31st December 2021.

Inclusion criteria:

1. CO-RADS 4 - abnormalities suspicious for covid-19
2. CO-RADS 5 - typical covid-19
3. CO-RADS 6 - Real time-RTPCR positive
4. 18 years and above

Exclusion criteria:

1. CO-RADS 1- normal or non-infectious abnormalities
2. CO-RADS 2 - abnormalities consistent with infections other than covid-19
3. CO-RADS 3 - unclear whether covid-19 is present

Sample size: 200 (two hundered).

Data collection: The present study is conducted by collecting the samples of COVID-19 confirmed cases admitted at Jawaharlal Nehru Medical College and KLEs Dr. Prabhakar Kore Hospital and MRC, Belagavi. The diagnosis of the patients CORADS Score is accordance to WHO interim guidelines and Covid working group of the Dutch Radiology Society and confirmed by positive results on Real Time RTPCR Assay of nasopharyngeal swab samples for SARS CoV2 or typical pattern on Chest CT scan in clinical laboratory of the Institute. The clinical outcome was monitored from 1st January 2021 to 31st December 2021.

The samples for coagulation test were collected on admission. D-Dimer, PT, aPTT, Fibrinogen and Platelet Count is determined using a standard coagulation analyser, blood parameter analyser and manual method of evaluation of parameters whenever required with standard protocol and reagents. Relevant data is been extracted from electronic health records using a standardised form. Demographic, Medical history and outcome data were obtained from patients medical record. After an overnight fast, venous blood samples were obtained from patients.

D-Dimer, PT, aPTT, Fibrinogen and Platelet Count Tests were performed within 2 hours of sample collection using a standard analyser in accordance to hospital laboratory policy. The institute laboratories follow the Quality Assurance system in India. The reference range of all the coagulation parameters is accordance with the normal reference values in Free Haematology Laboratory and Hi-Tech Laboratory Guidelines.

A) For Manual Coagulation Analysis :-

1. **MANUAL PREPARATION AND STAINING OF PERIPHERAL SMEAR FOR PLATELET COUNT**

Clinical significance: A stained blood smear helps to study abnormal morphology of platelets for diagnosis of different abnormalities and also to rule out Pseudo-thrombocytopenia (clusters of platelets in the blood smear).

Sample requirement:

- EDTA Blood– Sample
- Finger prick sample

Staining -Wright's stain

2. PROTHROMBIN TIME (PT) BY MANUAL METHOD

Normal Range: 11-16 seconds (The lab derives its own reference range with every lot and type of thromboplastin used)

Critical values: >3x control

3. ACTIVATED PARTIAL THROMBOPLASTIN TIME BY MANUAL METHOD

Normal Range: 25.3-32.1 seconds

Critical value: >78 sec

B) For Automated Coagulation Analysis :-

I. **Analyser used:** Mindray BC-6800 Automated Haematology Analyzer

MINDRAY AUTOMATED HAEMATOLOGY ANALYSER

Parameter : Platelet Count

Sample Requirement : EDTA blood

Sample Storage : 2-8 C

Reference range : 1,50,000-4,00,000

II.Analyser used : ACL TOP 500/550 coagulation system analyser

Parameters :

1. D-Dimer
2. PT

3. aPTT

4. Fibrinogen

ACLTOP 500

ACLTOP 500

Sample requirement: 3ml blood in 2.7 ml Sodium Citrate concentrate anti-coagulated tube.

Reagent used:

1. D-Dimer : Factor diluents, DD reaction Buffer, DD latex reagent
2. PT : Three Hemosil Prothrombin Reagent kits are available: Hemosil Recombiplastin, Recombiplastin and Recombiplastin Diluent
3. aPTT : Calcium Chloride 0.020M and Calcium Chloride 0.025M
4. Fibrinogen : Bovine Thrombin

Reference range:

1. D-Dimer : <200ng/ml
2. PT : 9.8-12.4 seconds

3. aPTT : 25.3-32.1 seconds
4. Fibrinogen : 180-360mg/dl

The coagulation parameters hence analysed, if within the normal range were considered normal along with increase or decrease from the normal range were considered Prolonged/High or Shortened/Low respectively. All the laboratory tests and interpretation were done following the manufactures recommendation and standard operating procedures set out by the Laboratories.

Data Analysis: The obtained data is coded and entered in Microsoft Excel. Analysis is done using SPSS 20 software. Descriptive statistics and chi-square test is used to evaluate the association between variables. The normal and abnormal distributive quantitative variable is compared using the students T-Test and the Mann-Whitney U test respectively. The results are given as the mean +/- Standard deviation, Median or Number percentage wherever appropriate. Data is analysed using Windows 10.

RESULTS

Baseline characteristics of patients: A total of 200 patients were studied during the study period from 1st January 2021 to 31st December 2021 who were admitted in COVID-19 Care ward in KLE's Dr. Prabhakar Kore Hospital who met the inclusion criteria for this study. The median age of the patients for coagulation parameter study is 57.50 year (mean +/- SD = 55.89 +/- 16.17) with minimum age of 20 years and maximum age of 90 years.

TABLE 1: AGE (IN YEARS) DISTRIBUTION OF STUDY PARTICIPANTS

Mean	55.89
Median	57.50
Std. Deviation	16.17
Minimum	20.0
Maximum	90.0

GRAPH 1: AGE (IN YEARS) DISTRIBUTION OF STUDY PARTICIPANTS

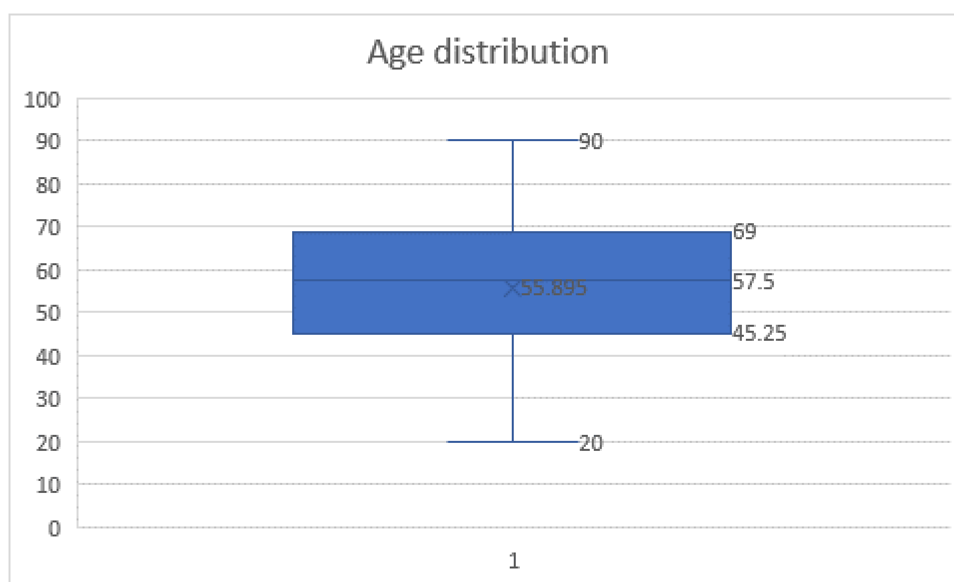
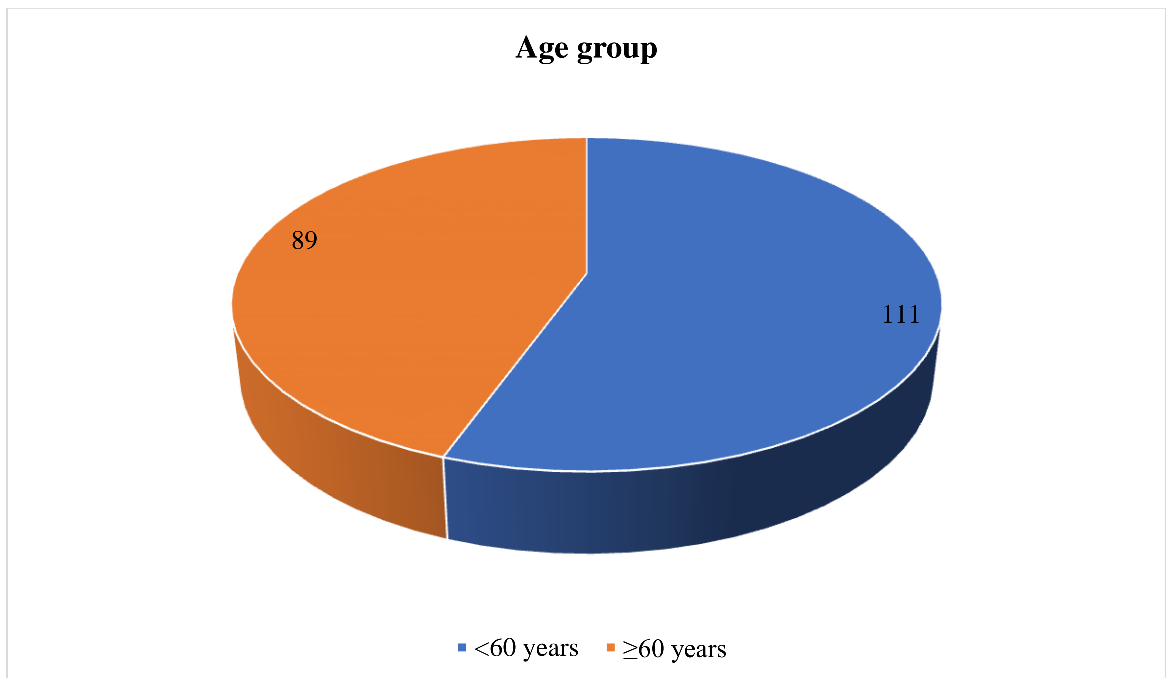


TABLE 2: DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO AGE GROUP

Age group	Frequency	Percentage
<60 years	111	55.5%
≥60 years	89	44.50%
Total	200	100.0%

GRAPH 2: DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO AGE GROUP

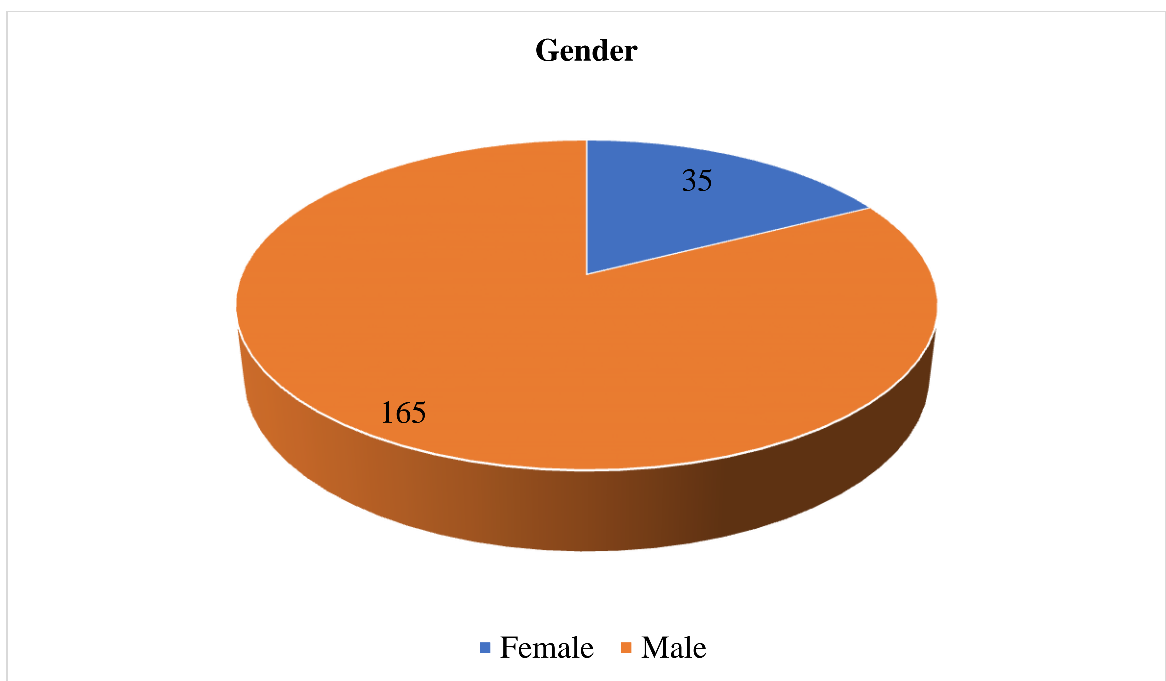


In the study population of 200 patients, distribution according to age group, cut off being <60 years and ≥60 years are 111(55.50%) and 89 (44.50%) respectively. Study results, hence shows more number of patients with coagulation abnormalities falling under the age group below 60 years.

TABLE 3 : DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO GENDER

Gender	Frequency	Percentage
Female	35	17.5%
Male	165	82.5%
Total	200	100.0%

GRAPH 3 : DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO GENDER



Out of the total 200 patients 35(17.50%) were females and 165(82.50%) were males. Hence in the study population there is predominance of Male population with variation in coagulation parameters as compared to Female population.

ANALYSIS OF ABNORMAL COAGULATION PARAMETERS AT THE TIME OF ADMISSION

TABLE 4: DISTRIBUTION OF COAGULATION PROFILE

	Mean	Median	SD	Minimum	Maximum
Platelets (X103/micro litre)	195.53	182	103.23	24	464
d-Dimer (ng/ml)	1332.16	770	1567.12	102	7028
PT (seconds)	20.27	14.5	12.50	10.9	76.10
APTT (seconds)	47.64	35.65	24.56	19.70	119.40
Fibrinogen (mg/dl)	521.62	475	248.83	124	998

In the population studied:-

- Platelet count showed a minimum value 24 x 103/micro litre of and a maximum value of 464 x 103/micro litre with median value of 182 x 103/micro litre (mean +/-SD = 195.53 +/- 103.23)
- D-Dimer showed a minimum value of 102 ng/ml and a maximum value of 7028ng/ml with median value of 770 ng/ml (mean +/- SD = 1332.16 +/- 1567.12)
- PT showed a minimum value of 10.9 seconds and a maximum value of 76.1 seconds with median value of 14.5 seconds (mean +/-20.27 SD = 12.50 +/-)

- aPTT showed a minimum value of 19.70 seconds and a maximum value of 119.4 seconds with median value of 35.65 seconds (mean +/-SD = 47.64 +/- 24.56)

- Fibrinogen showed a minimum value of 124 mg/dl and a maximum value of 998 mg/dl with median value of 475 mg/dl (mean +/-SD = 521.62 +/- 248.83)

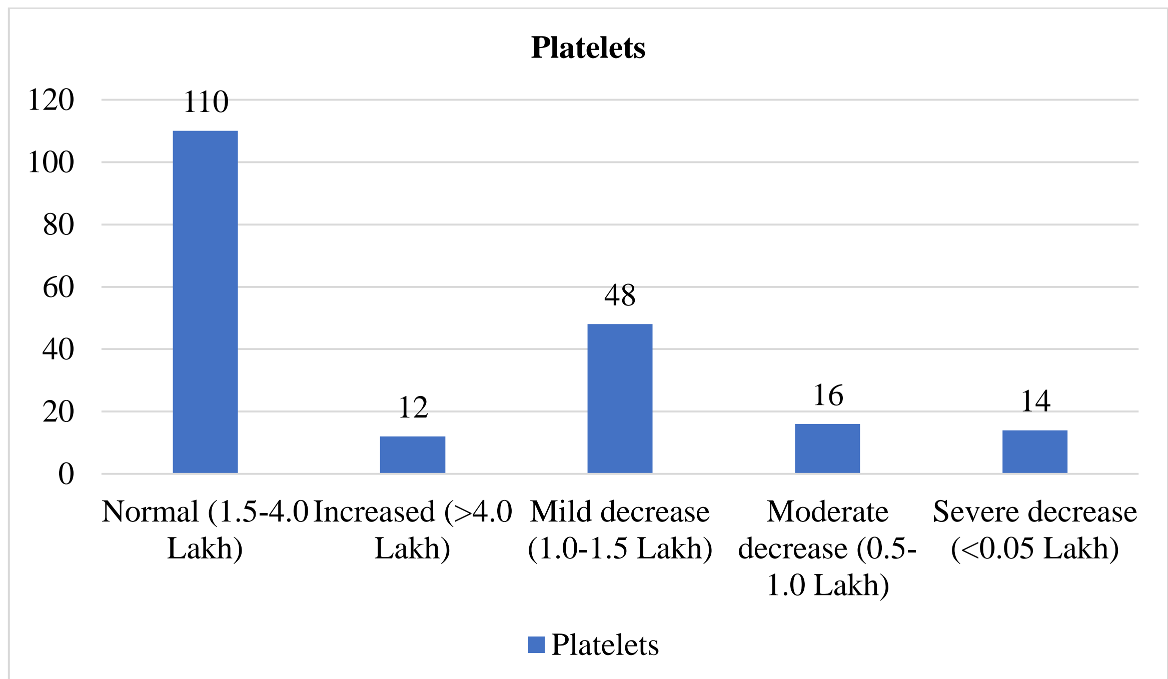
1. Platelet Count

Platelet count showed dispersed variation in values within the study population 200(100%). Normal Platelet count in healthy individual is 1.5 to 4.0 Lakh. Platelet count in majority of population 110/200(55.00%) were normal while platelet Count in other study population 90/200(45%) showed great variation in frequency with variables in both the dimension, i.e. Thrombocytosis (>4.0 Lakh) in 12/200(6%) and Thrombocytopenia (<1.5 Lakh) in 78/200(39%) and the latter being more significant and having more no of patient. Patients with mild thrombocytopenia (1.0-1.5 Lakh) were greater in number 48/200(24%) as compared to moderate thrombocytopenia (0.5-1.0 Lakh) and severe thrombocytopenia (<0.05 Lakh) i.e. 16/200(8%) and 14/200 (7%) respectively.

TABLE 5 : DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO PLATELETS

	Frequency	Percentage
Normal (1.5-4.0 Lakh)	110	55.0%
Thrombocytosis(>4.0 Lakh)	12	6.0%
Mild Thrombocytopenia(1.0-1.5 Lakh)	48	24.0%
Moderate Thrombocytopenia (0.5-1.0 Lakh)	16	8.0%
Severe Thrombocytopenia (<0.05 Lakh)	14	7.0%
Total	200	100.0%

GRAPH 4 : DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO PLATELETS



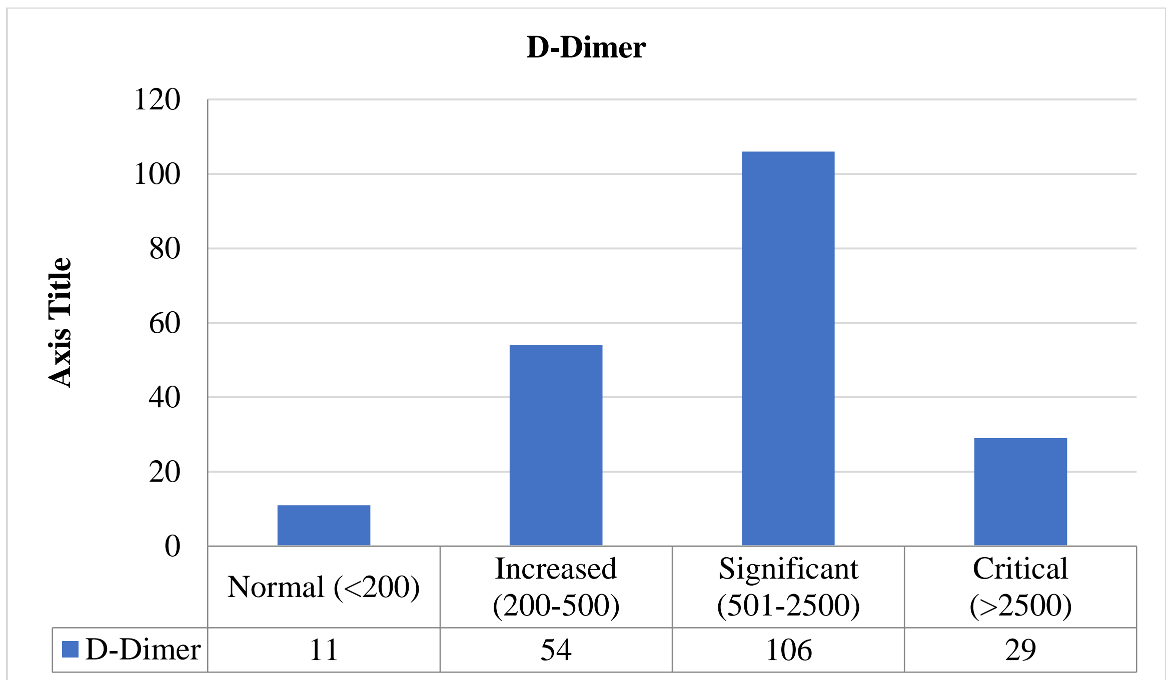
2. D-Dimer

The magnitude of D-dimer elevation on admission were found to be associated with increase in the values with advancing age (≥60 years) and predominantly more in males. D-dimer values evaluated in the study population of 200(100%) were in the broad range of 102ng/ml (minimum value) to 7028ng/ml (maximum value) with very few set of patients 11/200(5.50%) having normal (0-200ng/ml) D-Dimer value. Further analysis of D-Dimer showed highest number of patients 106/200(53.00%) with significant (501-2500ng/ml) change in the value followed by increase (200-500 ng/ml) in D-Dimer value 54/200(27.50%). The frequency under critical (>2500 ng/ml) value came out to be 29/200(14.500%). Hence, D-Dimer came out to be the most frequent abnormal coagulation parameter in accordance with the above findings.

TABLE 6 : DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO D-DIMER

D-Dimer (ng/ml)	Frequency	Percentage
Normal (0-200)	11	5.5%
Increased (200-500)	54	27.0%
Significant (501-2500)	106	53.0%
Critical (>2500)	29	14.5%
Total	200	100.0%

GRAPH 5 : DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO D-DIMER



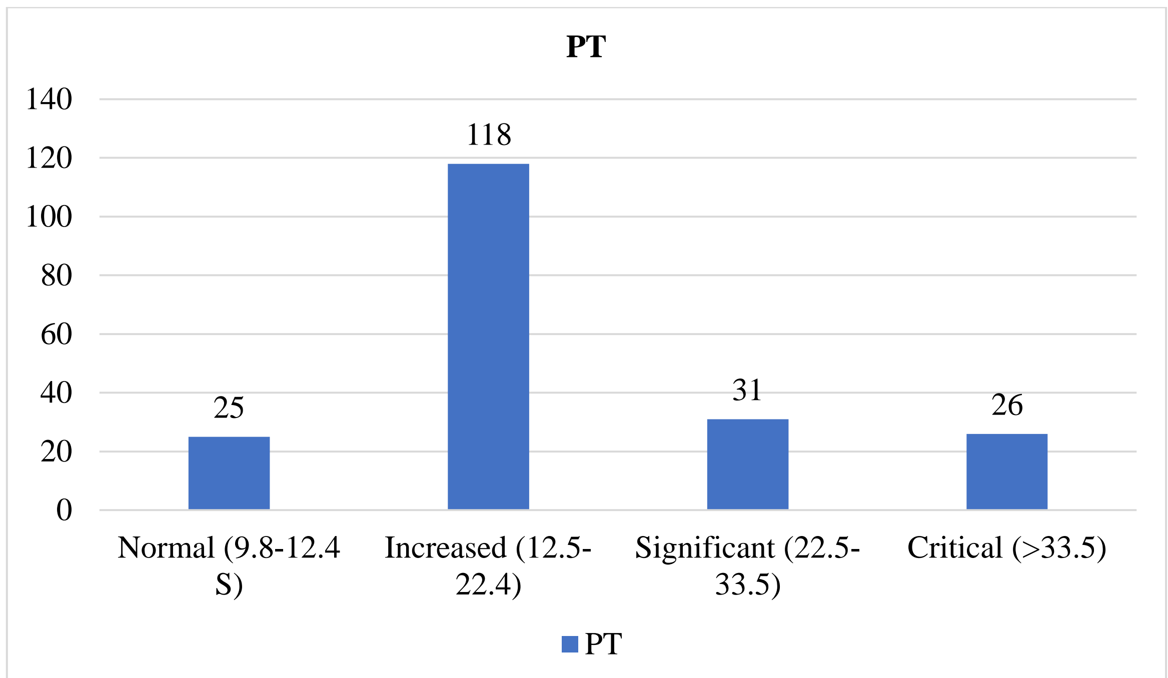
3.PT

Prothrombin time evaluated in the study population of 200(100%) patients on admission with normal reference range of 9.8 to 12.4 seconds, with a control of 11.20 seconds. Patients under normal range were found to be 25/200(12.5%), representing a very low set of patients as compared to a large group of patients 118/200(59%) with increased PT(12.5-22.4 seconds,) followed by patient group 26/200 with significant(22.5-33.5, 2xcontrol) and patient group26/200(13%) with critically(>33.5, 3xcontol) increased Prothrombin Time.

TABLE 7 : DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO PT

	Frequency	Percent
Normal (9.8-12.4 S)	25	12.5%
Increased (12.5-22.4)	118	59.0%
Significant (22.5-33.5)	31	15.5%
Critical (>33.5)	26	13.0%
Total	200	100.0%

GRAPH 6 : DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO PT



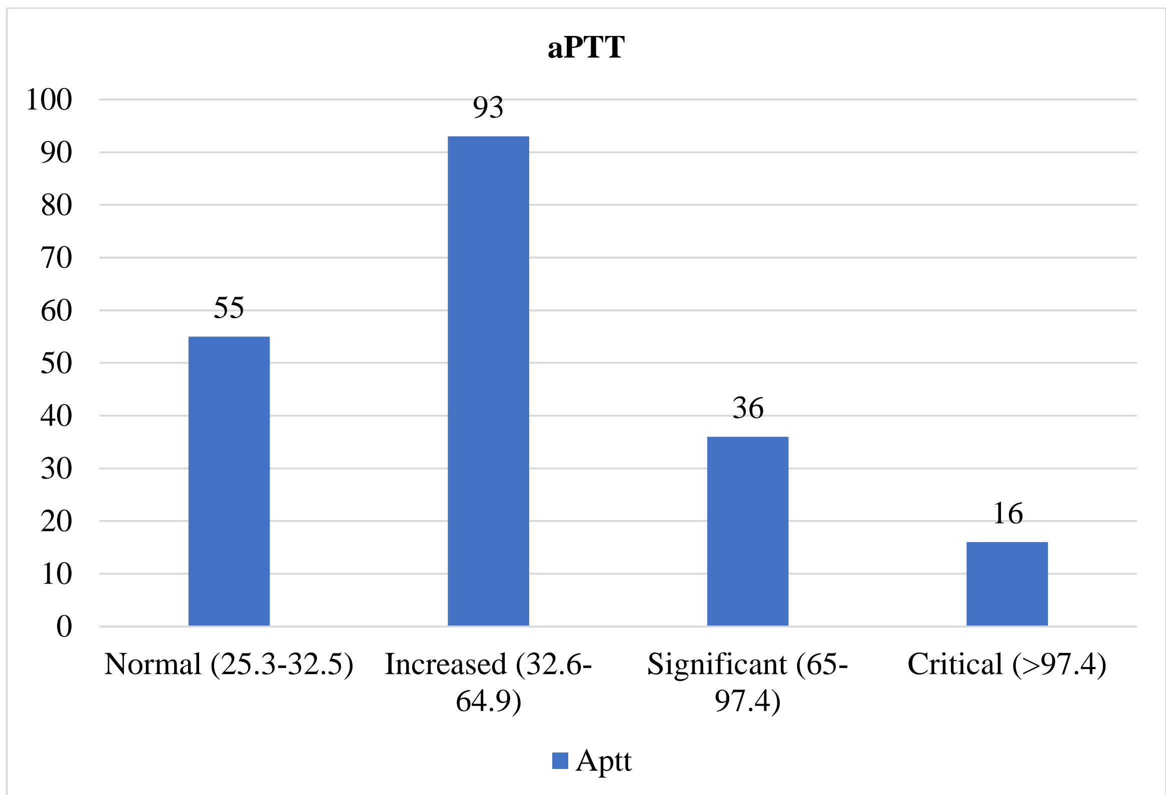
4.aPTT

Normal aPTT ranges from 25.3-32.5 seconds with control of 32.50 seconds. Number of patients showing normal aPTT level were 55/200 (27.50%). aPTT in the study population showed maximum number of patients 93/200(46.50%) with increased (32.6-64.9) aPTT followed by Significant (65-97.4) increase in aPTT in 36/200 (18.00 %) and Critical (>97.4) increase in aPTT values in 16/200 (8.00%) patients.

TABLE 8: DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO APTT

	Frequency	Percentage
Normal (25.3-32.5)	55	27.5%
Increased (32.6-64.9)	93	46.5%
Significant (65-97.4)	36	18.0%
Critical (>97.4)	16	8.0%
Total	200	100.0%

GRAPH 7: DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO APTT



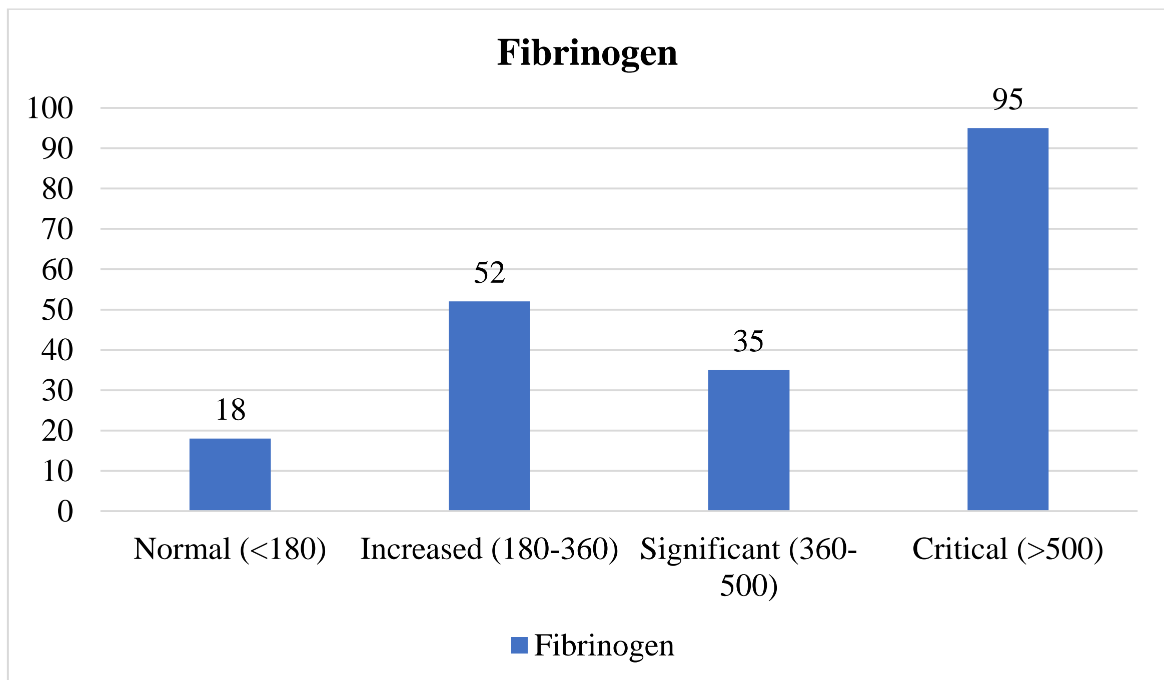
5.Fibrinogen

Fibrinogen values came out to be one of the important variables which were commonly increased in maximum number of patients after D-Dimer in the study population. Normal fibrinogen(180- 360 mg/dl) level were seen in less number of patients 18/200 (9.00 %) as compared to rest of the study population which showed marked rise in fibrinogen level accounting maximum number of patients 95/200(47.50%) showing significant value(>500 mg/dl) followed by increased fibrinogen levels(360-500 mg/dl)35/200 (17.50%).

TABLE 9: DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO FIBRINOGEN

	Frequency	Percentage
Decreased (<180)	18	9.0%
Normal (180-360)	52	26.0%
Increased (360-500)	35	17.5%
Significant (>500)	95	47.5%
Total	200	100.0%

GRAPG 8 : DISTRIBUTION OF STUDY PARTICIPANTS ACCORDING TO FIBRINOGEN



DISCUSSION

Coronavirus Disease 2019 also known as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) became a pandemic, affecting worldwide population with lung infection as a primary manifestation along with coagulation abnormality. The virus is susceptible to infect people of all age. Children were seen to be less affected by this virus whereas adult population with comorbidities were seen to be infected more with increase in severity of the disease. Major part of the infected population presented with less or no symptoms whereas some presented with mild to moderate form of the disease.

The virus came out to be highly transmissible which can transmit by air droplets, fomites or direct-transfer from the diseased person, especially caregiver. The RT-PCR to check for viral RNA is the current Gold standard test for the diagnosis of the disease. Rapid Antigen Testing is also one of the fast and important diagnostic tests in order to identify presence of viral antigen in the diseased individual. Respiratory infection was accompanied by haematological abnormalities in the form of reduced leukocytes, reduced lymphocytes and increase in neutrophil count along with low platelet count. Severe infection was marked by increase in Liver enzymes, C-reactive protein, Ferritin and various other pro-inflammatory cytokine. (like IL2, IL7, IL10, and TNFα).

As the disease progress, hosts defence system gets activated which results in an imbalance between the pro-coagulant and anticoagulant systems. The COVID-19 infection is been associated with a high rate of venous and arterial thrombotic complications including atypical thrombotic events as well as a derangement of coagulation parameters.

Coagulation parameters are significantly changed and haemostasis is extensively disrupted by the severe inflammatory condition brought on by COVID-19 infection. Coagulopathy is associated with worse outcome in COVID-19 patients. High D-dimer and

fibrinogen levels during hospitalisation are associated with a poor outcome. PT and aPTT are seen to be raised significantly in COVID-19 associated coagulopathy. Mild to moderate thrombocytopenia is another parameter which aid in the understanding of COVID-19 associated coagulopathy.

Covid-19 associated coagulopathy was first reported in China and the Netherland.[107, 108] 30 percent COVID-19 patients who were admitted in medical ICU showed coagulopathy and thromboembolic manifestations. [107, 108] Other consecutive studies conducted in different countries also found evidence of thrombosis and coagulopathy in critically ill COVID-19 patients.[109, 110] A number of studies found the occurrence of DVT and Pulmonary Embolism in ICU patients.[110,111,112] Study conducted in School of Medicine, University of Cattolica, Italy found incidence of DVT in non-ICU hospitalised patients is 11.9%. [113]

Many prospective and retrospective studies were conducted in several hospitals in Wuhan, China. Study results indicated development of thromboembolism in one-third of the study population. Study conducted in University Medical Center Amsterdam, Netherland by Middeldorp et al [114] found presence of DVT in 27% of ICU and 1.6% of non-ICU patients. A Dutch study on 184 ICU patients found 49% cumulative incidence of thrombotic complications.[115]

Many studies also found persistence of VTE even with medication in critically ill patients. Studies conducted in Netherland and France found, 25–35% of COVID-19 ICU patients with evidence of VTE and Thrombosis even with prophylaxis. Worldwide studies also found pneumonia, advancing age, comorbidities especially hypertension and diabetes, PT >3.5 seconds and aPTT >5.5 seconds were individual predictors of VTE. Khan et al.[116] found 20 patients out of 81 to develop VTE in lower limbs in the absence of any preventive medications on admission. Results were associated with advancing age with a mean age of 59.5 years.

In our study coagulation parameter of 200 patients along with their baseline characteristics are identified, observed, evaluated, documented and statistically analysed. The mean age of study participants was 55.89 years with minimum age of 20 years and maximum age of 90 years. Hospital admission of patients with age less than 60 years (55.50%) were more as compared to more than 60 years (44.50%) age group with predominance of male population(82.50%). We found that on admission, patients with SARS-CoV-2 infection had a marked hypercoagulability state. This was evident with elevated D-Dimer, PT, aPTT and Fibrinogen levels along with low platelet count.

1. Platelet Count-

The main function of platelets is to initiate a first cellular response to vascular injuries and thrombosis. With the new knowledge of platelet functions such as protein synthesis, autophagy and apoptosis, platelets are no more consider as a basic cell fragments, but now known as a major blood mediating elements.

Platelets play an important role, by activating inflammatory response due to viral insult. Platelets following viral infestation release various potent chemokines and cytokines. In many studies platelets along with their released products were found responsible for the favourable prognosis of the infection. The interactions between endothelial cells, platelets and leukocytes play a critical role in the procoagulant effect of viral infections. Thrombocytopenia, platelet secretion and interactions with leukocytes may have either injurious or protective immune consequences in viral infections like COVID-19.

In our study platelet count varied widely within the study population. Platelet count in majority of study population showed great variation in frequency with variation in both dimensions. Thrombocytopenia was common among 39% of the total study population. This

phenomenon can be explained by consumption of platelets and its released products in platelet aggregation and formation of thrombi.

Lippi Get et al.[117] and Yang X et al.[118] in their studies found strong association between thrombocytopenia and severity of the disease. They stated that death rate increase as platelet count decreases. In our study, thrombocytopenia was seen in maximum study population. We found correlation between decrease platelet level and increase in disease severity in the form of raised D-Dimer, PT, aPTT and fibrinogen levels along with male predominance and advancing age.

Comparable to our study, different other studies also reported majority of patient with normal platelet value on admission. Variation in platelet count on admission may be subjected to difference in time and state of infection and also may be regulated to an extent by drugs like antibiotics. Some patients on long term use of Aspirin were found to have low platelet count on admission.[124, 125] Another possible explanation for the disparity between studies can be thrombocytopenia caused by comorbidities or disease progression.[126, 127]

TABLE 10: PLATELET EVALUATION OF PATIENTS FROM 5 PUBLISHED STUDIES COMPARED TO OUR STUDY.

Study	Country	No. of Cases	Median Age (years)	Male %	Female%	Thrombocytopenia %
Our Study	**India**	**200**	**57**	**82.5**	**17.5**	**39**
Huang et al.[119]	China	41	49	72	28	15
Liu at al.[120]	China	12	54	67	33	41.7
Liang et al.[121]	China	173	47	58.1	41.9	36.2
Zhou et al.[122]	China	137	56	62	38	21
Young et al.[123]	Singapore	18	47	50	50	35

Platelet count varies with disease severity and course of anti-thrombotic drug treatment. On admission in absence of any prophylactic drug regime platelet count was found to be moderately to severely decrease. On the other hand, critically ill patients showed marked thrombocytopenia which indicates its strong association in disease severity. Platelet apoptosis and its consumption may result in disease-associated thrombocytopenia. Other contributing factors may be hypoxia, endothelial damage, pro-inflammatory cytokines activation, unwanted autoimmune reactions and activation of various autocrine pathways.

In COVID 19 pandemic, one of the important tasks is to identify the potential biomarkers which may indicate the severity of the infection and can also point toward the disease progression. Platelet count being a primary, simple, rapid, cheap and easily available

laboratory parameter with its potential to indicate disease severity can be used to assess the coagulation abnormality in COVID-19 patients.

2. D-Dimer

Many studies were conducted in the pandemic era to see the association between D-dimer and disease severity.[128, 129, 130] In almost all the studies, D-dimer was found to be strongly associated with disease severity and progression.[131, 132, 133] Also, many studies show increase levels of D-dimer in non-surviving patients which indicate presence of disease-associated coagulopathy in such patients.[134, 135, 136] Analyses of these previously conducted studies put forward the fact that critically ill patients are at higher risk of developing coagulopathy. Multistep process in development of hypercoagulability status of the patients, D-dimer plays a key role.[137, 138] As an important marker of coagulation and as a crucial component of DIC, increased D-dimer is strongly associated with disease severity. It also indicates presence of coagulation abnormality in the diseased person.[139, 140]

According to our study results, 94.50 % of COVID-19 patients presented with an increase in D-dimer level on hospital admission. The study revealed that the severity of D-dimer elevation on admission is correlated with an increase in values with advancing age (more than 60 years) and predominately higher in males. The 200 participants in the study showed D-dimer levels that ranged from 102ng/ml to 7028ng/ml with 5.50% patients having normal (0-200ng/dl) D-Dimer levels and 53.00% patients with critical (501-2500 ng/ml) D-Dimer levels. Also, 27.50% patients showed increased (200-500 ng/ml) D-Dimer levels and 14.50% patients presented with critically high D-Dimer levels on admission. Therefore, in accordance with the above findings, D-Dimer emerged as the most common abnormal coagulation parameter.

TABLE 11: D-DIMER EVALUATION OF PATIENTS FROM 7 PUBLISHED STUDIES COMPARED TO OUR STUDY.

S. no	Study	Country	No. of Cases	Median Age (years)	Male %	Female %	No of cases with increased D-Dimer value in %
1	**Our Study**	**India**	**200**	**57**	**82.5**	**17.5**	**67.5**
2	Liaeo et al.[141]	China	380	64	54	46	60.7
3	Bhadade et al.[142]	India	373	52	68.1	31.9	76.4
4	Yao et al.[143]	China	248	63	60	40	74.5
5	Pouder et al.[144]	Nepal	182	55	62.1	37.9	63.8
6	Guan et al.[145]	China	560	47	58.1	41.9	46.4
7	Zhang et al.[146]	China	343	55	52.5	47.5	77.8
8	Soni et al.[147]	India	483	61	69.9	30.1	80

Al-Samkari et al.[148] and Zhou et al[149]. in their study, illustrated association of inflammatory markers with coagulopathy. Higher D-dimer values indicate more risk for disease progression and thrombosis formation. Zhao et al.[136] suggested pulmonary rehabilitation in COVID-19 patients. Their study reported evidence of radiologic and physiologic damage to COVID-19 patients after treatment within 3 months of discharge. Hanif et al.[134] in their study found patients who were on anticoagulation prophylaxis or therapy showed no evidence of thrombosis and coagulation complication. Early detection of D-dimer value and prompt treatment with anticoagulation therapy showed good results in critical COVID-19 patients. Varikasuvu et al.[140] in their study article with meta-analysis of 100

studies clearly mention association of D-dimer with disease severity, hypercoagulability state and disease progression. Cui S et. Al[133] in their study found high D-dimer value in critically ill patients. Value more than 2.5 g/mL of D-Dimer were common in non-survival patients.

TABLE 12: D-DIMER CUT-OFF VALUE OF 4 PUBLISHED STUDIES COMPARED TO OUR STUDY.

S. no	Study	Country	D-Dimer (ng/ml) cut off value for evaluation
1	Our study	India	Normal - 0 to 200, Increased- 200 to 500, Significant- 500 to 2500 Critical - >2500
2	Cui S et al.[133]	China	>2500
3	Yao et al.[143]	China	>2000
4	Soni et al.[147]	India	>1500
5	Shah et al.[150]	India	No cutoff value to define D-Dimer sevrity

Critically ill patient may land up into organ damage due to formation of thrombus and coagulopathy. Hence, D-Dimer monitoring plays an important role for such patients in early assessment of the disease condition and its associated severity in different organ system. A higher level of D dimer is indicative of presence of clot which is regarded as a dangerous sign in patients with COVID-19.[151, 152] D-dimer in combination with other markers can also assist in the treatment of these patients, since higher D-dimer levels are related with more number of clots in the lungs and higher chances of respiratory failure. Thus D-

Dimer test can be used to indirectly measure the severity of COVID-19 disease and assess its complications at an early stage.

3. PT and aPTT

Studies done by Huang C et al.[153], Tang N et al.[154] and Tarik et al.[155] reported increase in the value of prothrombin time and activated partial thromboplastin time in the ICU patients. Study done by Wang et al.[156] on 213 study population in Renmin Hospital of Wuhan University found that prolonged PT and aPTT at admission shows a strong association between disease severity and its poor outcome in critically ill patients.

Studies done by Hong et al.[157], Iba et al.[158] , Martinelli et al.[159] and Long et al.[160] found that critical patients had significantly increased PT and aPTT than non-critical patients. In our study we also found significant changes in the PT and aPTT values. PT was measured in the study population with a control of 11.20 seconds (normal reference range of 9.8 to 12.4 seconds) and 59% patients showed increase PT (12.5-22.4 seconds). Also, aPTT with a control of 32.50 seconds (normal reference range of 25.3-32.5 seconds) was evaluated. A total of 46.50 % patient showed increased (32.6-64.9) aPTT levels.

PT and aPTT being the primary and most important biomarker of coagulation pathway can help in early assessment of coagulopathy and associated complication in Covid-19 patients. These tests are quick, cost effective and accurate to evaluate extrinsic and intrinsic pathways of the coagulation system. These tests can also be used to evaluate the disease condition, its severity and associated complications. Hence, critically ill patients may get early clinical supervision and prompt treatment.

TABLE 13: PT AND aPTT FINDINGS FROM DIFFERENT PUBLISHED STUDIES COMPARED TO OUR STUDY.

Study	Findings and Comments
Our study	• Prolonged PT and aPTT at admission in association with advanced age and male predominance. • PT and aPTT as important predictive dynamics for clinical outcomes of COVID-19 patients.
Huang C et al., Tang N et al. and Tarik et al.	• Prolonged PT and aPTT at admission is an indicator of ICU care.
Hong et al., Iba et al., Martinelli et al. and Long et al.	• Critical patients had significantly increased PT and aPTT than non-critical patients. • Prolonged PT and aPTT on hospitalization is indicator of severe disease and increase mortality.
Tang et al	• Overall mortality was 11.5% in COVID 19 patients • On admission non-survivors had increased PT and aPTT compared with survivors.
Cui et al	• Incidence of VTE in COVID 19 patients is 25% without prophylactic anticoagulation.
Lang Wang et al.	• Prolonged PT and aPTT were more common in critically ill patients.
Huang et al	• PT and D-dimer level on admission were higher in ICU patients than in non-ICU patients in COVID 19.

4. Fibrinogen

Fibrinogen is an important coagulating protein found in blood. It is synthesised in liver and megakaryocytes. Its high concentration in the blood reflects an acute insult in the form of inflammation activated by the viremic action activated by the virus in the body. Fibrinogen is directly related to consumption coagulopathy. Fibrinogen estimation is one of the important investigations in evaluating the disease condition and severity. Its value is found to be constantly high in severe patients and show variation in mild to moderate cases also. High Fibrinogen level is an effective predictor of severe illness present in the body due to COVID-19 infection. Fibrinogen estimation with its quick results and interpretation makes it an effective biomarker for severity prediction and treatment. Its dynamic monitoring can also provide information about treatment effectiveness and disease prognosis in COVID-19 patients.

Li et al.[161] in their study found Fibrinogen levels to be constantly high in severe and non-survival patients. Gao et al.[162] and Liao et al.[163] in their studies found fibrinogen levels to be raised in patients on hospitalisation. It was also associated with poor clinical outcome. Sui J et al.[164] in their study population mentioned fibrinogen values to be raised with poor outcome and ICU admission of such patients. Tohet al.[165] and Han et al.[166] in their studies mentioned about increase in the value of fibrinogen in acute stages of the disease and gradual decrease in the value as DIC sets in.

TABLE 14: FIBRINOGEN FINDINGS FROM DIFFERENT PUBLISHED STUDIES COMPARED TO OUR STUDY.

Study	Findings and Comments
Our study	• Fibrinogen levels found to be one of the most relevant parameter. • Found to be increased in maximum number of patients on admission.
Li et al	• Fibrinogen levels are increased in both study population i.e. survival group and non-survival group.
Gao et al. and Liao et al.	• Fibrinogen levels to be raised in patients on hospitalisation
Sui J et al.	• Fibrinogen levels are raised with poor outcome on ICU admission.
Tohet al. and Han et al.	• Increase in the value of fibrinogen in acute stages of the disease and gradual decrease in the value as DIC sets in.

Fibrinogen levels were shown to be one of the most relevant variables in our study population which was found to be increased in maximum number of patients. Normal fibrinogen levels were seen in less number of patients (9.00 %) as compared to rest of our study population which showed marked rise in fibrinogen level accounting to maximum number of patients (47.50%) showing significant rise in Fibrinogen (>500 mg/dl). Hence, the value of Fibrinogen has been considered as one of the important parameter in COVID19 induced DIC and Coagulopathy.

With the data of our study, we consider that coagulation parameters (such as D-dimer, PT, aPTT, fibrinogen and Platelet count) are important biomarkers to be evaluated on

admission. These parameters may reliably predict the outcome of COVID-19 patient. Their quick assessment and dynamic monitoring may help in assessing the disease associated complications during their treatment. Assessing coagulation parameters at the time of admission has the benefit of providing essential information and appropriate treatment for the patient in the early stages of disease.

CONCLUSION

- In this study, most common coagulation parameter with maximum variation was found to be D-dimer.
- Fibrinogen levels were also found to be increased in maximum number of patients with COVID-19 induced coagulopathy.
- Thrombocytopenia, prolonged PT and aPTT were significant in COV1D-19 patients older than 65 years and predominantly in males.
- Thus, on admission prompt investigation and management of severe cases should be done and more emphasis to be given for monitoring of D-Dimer, Fibrinogen, PT, aPTT and platelet count in hospitalized COVID-19 patients.
- Early assessment and dynamic monitoring of coagulation parameters may be a benchmark to control the severity of COVID-19 infection and associated mortality by including these parameters to the criteria for hospitalization.
- This may limit the disease severity and prevent disease progression. This may also help in effective patient management.

SUMMARY

- Coronavirus disease 19 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) affects the coagulation cascade.
- A total of 200 RT-PCR positive patients with SARS-CoV-2 having CO-RADS score of 4, 5 or 6 were included in the study.
- Patients D-dimer, fibrinogen, PT, aPTT and platelet count values on admission were evaluated and association of the coagulation parameters with disease severity was analysed.
- Increase in coagulation parameter values with advancing age and male predominance was observed in the study. Most commonly exhibited symptoms in the study participants were fever, cough and breathlessness followed by less common symptoms such as myalgia, loss of smell and loss of taste.
- COVID-19 patients showed significantly higher levels of D-dimer and fibrinogen in maximum number of population. Prolongation of PT and aPTT along with dispersed variation in platelet count were commonly seen in the study population. Higher levels of D-dimer and fibrinogen are predictive of increased disease severity among COVID-19 patients, with additional prognostic value aided by PT, aPTT and platelet count that make this study relevant in terms of COVID19 associated coagulopathy evaluation and disease progression at hospital admission.
- Selection bias due to the hospital-based population and absence of serial assessments of D-dimer, fibrinogen, PT, aPTT and platelet count were limitations of this study.
- Thus these coagulation parameters on admission are of paramount importance in evaluating severity of COVID-19 patients especially those who require prompt

management with anti-coagulants in order to reduce coagulation associated morbidity and mortality.

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ANNEXURE – I - PREPARATION AND STAINING OF PERIPHERAL SMEAR

Purpose: To make good peripheral smear

Clinical significance: A stained blood smear helps to study abnormal morphology of RBCs WBCs and platelets thus enabling the diagnosis of different anaemias, leukemias, platelet abnormalities etc.

Sample requirement:

- EDTA Blood– Sample
- Finger prick sample

Requirements:

- Leishman's stain
- Buffer(pH 7)
- Glass slide
- Spreader

Reagents preparation:

Leishman's stain:

Powdered stain - 0.2g

Methyl alcohol - 100ml

Buffer (pH 7):

Sodium dihydrogen phosphate - 3.76g

Potassium dihydrogen phosphate - 2.10g

Distilled water- 1000ml

Store at room temperature

Principle: The polychromatic staining solution (Wright's stain) contains methylene blue and eosin. Methanol acts as a fixative and also as a solvent. The basic and acidic dyes induce multiple colours when applied to cells. The basic dye colours the acidic component of cells i.e the nucleus blue, whereas the acidic dye colours basic component of cells i.e cytoplasm pink. The neutral components are stained by both dyes.

Procedure:

I. Smear preparation: (Two slide or Wedge method):

1. Place a clean, dust free slide on firm flat surface. Put a small drop of blood (2-3 mm) 1cm from one end of the slide.
2. Take a second glass slide of width 4mm less than the total slide width (spreader).
3. Place the edge of the spreader against the surface of the first slide at an angle of 30^0.
4. Draw it backwards till it touches the blood drop. Allow blood to spread along the spreading edge.
5. Push the spreader forward with uniform motion at a moderate speed, forming a thin smear.
6. Air dry the smear and label with a diamond pencil the unique identification number

Note: A well made smear is tongue-shaped, smooth at the end, contains no lines extending across or down through the film and it should show no spaces or holes in the smear.

II. Staining (Wright's stain):

Place the air dried smear on a staining rack (2 parallel glass rods 5 cm apart).

1. Using a marked Pasteur pipette, cover the entire smear with 10-15 drops of undiluted Wright's stain.
2. Allow to stain for one minute.
3. Add equal volume of buffer until a metallic scum appears on the surface.
4. Allow to stain for 10 minutes.
5. Wash off the stain with gentle stream of tap water.
6. Air dry.

Note: Poor staining makes the blood film blue, pink or too dark

III. Examination of the film:

Examine first under low power. In an ideal smear, three zones will appear:

a) thick area (head)
b) b)body
c) c)thin area(tail)

ANNEXURE – II – CONSENT FORM

FROM,

Date: 27.09.2020

Post Graduate,

Department of Pathology,

JNMC Belagavi

TO,

DR. HARSHA HEGDE,

Chairperson, JNMC, IEC

& Scientist D,

ICMR, National Institute of

Traditional Medicine,

Belagavi -9480422500

Subject: Request for waiver of individual consent for study of coagulation parameters in Covid-19 positive patients.

Respected Madam,

This is to inform you that we would like to conduct a one year prospective and six months retrospective study for the study of blood parameters of covid 19 positive patients and their inflammatory markers. We request you to provide the Ethical clearance with waiver of individual consent for the same. The synopsis is attached with the application.

Kindly do the needful.

Your's faithfully

Guide,

Professor,

Department of Pathology,

JNMC Belagavi.

Post graduate,

Department of Pathology

S.No	Name	IP No	Date of Admission	Age	Sex	Symptoms (C=cough; F=Fever; B=breathlessness; M=Myalgia, Loss of smell=LS; Loss of taste=LT)	Time to hospital from symptom onset (Days)	DATE OF INV	d-Dimer (ng/ml)	PT (seconds)	APTT (seconds)	Fibrinogen (mg/dl)	Platelets ($X10^3$/micro litre)
1	Nangawa Kochargi	1020455	07-Aug-2021	60	M	C,F, B	2	08-Jul-2021	282	12.3	34.5	358	119
2	Suresh Bhate	1019426	23-Jul-2021	65	M	C, F	5	23-Jul-2021	746	14.3	46.25	458	134
3	Shankar Rao	1023326	16-Sep-2021	85	M	FC	2	16-Sep-2021	661	13.5	38.1	654	203
4	Parwati Sangannavar	1024174	28-Sep-2021	60	F	F	5	28-Sep-2021	472	11.2	22.4	421	25
5	Tabrez Khan	1021407	28-Aug-2021	20	M	CFM	1	28-Aug-2021	250	12.3	30.2	180	191
6	Gulab Mulani	1022906	10-Sep-2021	78	M	CB	5	09-Nov-2021	6702	11.4	28.6	996	87
7	Shankar Patil	1025516	15-Oct-2021	82	M	B	1	15-Oct-2021	864	21.1	37.8	654	156
8	Vaman Rao	1020680	10-Aug-2021	70	M	CB	3	08-Oct-2021	400	15.2	35.5	495	260
9	Dhanamma Shetty	1024333	29-Sep-2021	26	F	CBM	2	29-Sep-2021	140	13.3	28.4	135	229
10	Shubash Nandgauda	1023878	23-Sep-2021	72	F	BF	2	23-Sep-2021	1451	12.2	26.6	496	117
11	Shiva Linga	1024370	30-Sep-2021	54	M	CF	1	30-Sep-2021	386	16.1	28.7	304	222
12	Ramachandra Patil	1023727	21-Sep-2021	60	M	CF	5	21-Sep-2021	6675	13.5	22.5	658	227
13	Ashoak Korishetti	1020944	14-Aug-2021	39	M	FB	8	14-Aug-2021	437	12.6	33.3	342	340
14	Anand Basappa	1021397	20-Aug-2021	56	M	B	5	21-Aug-2021	1519	12.2	38.5	778	131
15	Murli Dhar	1023886	23-Sep-2021	59	M	MB	3	23-Sep-2021	605	13.5	33.8	335	200
16	Mruti Gurav	1023858	23-Sep-2021	66	M	CFMB	4	23-Sep-2021	588	13.6	25.9	322	203
17	Shivappa Melavanki	1024081	26-Sep-2021	70	M	FB	3	26-Sep-2021	1617	12.7	29.8	455	111
18	Ashwani Patil	1024337	29-Sep-2021	30	M	CB	3	29-Sep-2021	162	13.3	25.6	155	214
19	Shantilal Vohra	1022372	04-Sep-2021	70	M	F	2	09-Apr-2021	785	15.5	39.5	455	236
20	Kalappa Rajenewar	1023275	15-Sep-2021	75	M	F	3	15-Sep-2021	>5000	59.2	39.1	998	124
21	Ganga Bai	1023734	21-Sep-2021	58	F	M	2	21-Sep-2021	260	12.3	33.2	354	229
22	Hema Morkar	1019966	30-Jul-2021	36	F	F	4	30-Jul-2021	856	13.5	32.4	789	348
23	Pruthvi Raj	1019037	17-Jul-2021	32	M	FM	5	17-Jul-2021	102	12.5	34.2	124	183
24	Smita Kutre	1023978	25-Sep-2021	45	M	CB	4	25-Sep-2022	478	14.1	38.5	365	235
25	Mahantesh	1022559	09-Jun-2021	49	M	CB	3	09-Jun-2021	996	11.6	21.9	887	129
26	Namita Prakash	1019554	24-Jul-2021	28	M	CMF	3	24-Jul-2021	546	13.5	33.4	456	387
27	Ruhikesh Deshpandey	1018960	16-Jul-2021	30	M	CMF	4	17-Jul-2021	260	11.8	32.3	189	439
28	Sudakar Khobri	1019276	21-Jul-2021	36	M	CBF	7	21-Jul-2021	242	12.1	33.6	231	248
29	Rupa Kamble	1019504	23-Jul-2021	22	F	FM	3	23-Jul-2021	390	13.4	34.4	304	210
30	Akawwa Desurkar	1019491	23-Jul-2021	23	M	CFM	5	23-Jul-2021	203	14.2	33.2	178	319
31	Mahantesh Hiremath	1019294	21-Jul-2021	57	M	FB	2	21-Jul-2021	288	14.1	36.7	188	166
32	Somshekhar Hoti	1019830	29-Jul-2021	35	M	CFB	2	29-Jul-2021	412	12.2	33.2	355	147
33	Chandrahas Virnekar	1019960	30-Jul-2021	70	M	MF	3	30-Jul-2021	250	13.2	33.4	201	398
34	Saira Bainu	1025257	12-Oct-2021	46	F	MFC	2	10-Dec-2021	789	12.5	46.7	655	345
35	Kondawal Shiwamani	1020431	06-Aug-2021	27	M	CMB	3	08-Jul-2021	265	12.7	31.9	187	287
36	Nagesh Desai	1019553	24-Jul-2021	35	M	CF	5	24-Jul-2021	335	14.6	35.5	354	232
37	Vijay Yadav	1019545	24-Jul-2021	52	M	BM	5	24-Jul-2022	725	15.2	39.5	247	187
38	Anil Shindey	1019047	18-Jul-2021	65	M	CB	10	18-Jul-2022	362	13.4	34.2	756	285
39	Dyanesh Morkar	1019822	29-Jul-2021	50	M	CB	3	29-Jul-2021	321	14.6	39.5	341	147
40	Niruthi Morkar	1019822	24-Aug-2021	74	M	FB	7	24-Aug-2022	948	13.2	16.5	812	127

41	Rudrappa Tanvashi	1019401	22-Jul-2021	69	M	FBC	6	22-Jul-2022	572	15.5	38.4	475	191
42	Mangala Shetti	1019733	27-Jul-2021	72	F	CB	3	28-Jul-2022	562	76.1	48.7	475	160
43	Jayashree Tipanawar	1013634	05-Jun-2021	51	M	CFM	4	06-May-2021	4589	45.5	50.6	987	63
44	Shaikh aftulla	1019721	27-Jul-2021	64	M	CFMB	10	28-Jul-2021	>5000	40.2	69.4	936	115
45	Iragouda Patil	1021469	21-Aug-2021	85	M	B	3	21-Aug-2021	4521	11.6	22.4	564	115
46	Vijayalaxmi Pramaj	1022318	03-Sep-2021	66	F	FMB	7	03-Sep-2021	1346	12.1	25.9	624	107
47	Sarojni Khot	1022362	03-Sep-2021	58	M	FB	3	03-Sep-2021	400	12.2	24.4	321	115
48	Vishwanath Hatapaki	1021169	17-Aug-2021	70	M	M	3	17-Aug-2021	280	13.5	33.5	178	192
49	Hamichand Chavan	1021530	22-Aug-2021	57	M	CB	5	23-Aug-2021	>5000	18.6	44.7	933	109
50	Sangeeta Deshpande	1023272	15-Sep-2021	52	M	CFB	2	15-Sep-2022	1217	15.2	21.1	649	140
51	Nanda Jangale	1021459	21-Aug-2021	56	M	M	4	21-Aug-2022	765	12.7	31.2	672	234
52	Jaganath Hanmathgad	1021997	29-Aug-2021	71	M	CFB	7	29-Aug-2022	660	16.9	29.5	562	132
53	Indumati Jirankali	1021081	16-Aug-2021	66	F	CFB	2	16-Aug-2022	328	14	26.2	220	130
54	Vishwanath Karachi	1021843	27-Aug-2021	84	M	B	11	28-Aug-2022	898	14.3	26.7	743	236
55	Vishwanath Bellad	1021421	21-Aug-2021	64	M	CB	5	21-Aug-2022	7028	15	29	991	108
56	Irshad Naik	1021050	15-Aug-2021	32	M	CFB	20	15-Aug-2022	871	15.2	39.5	365	419
57	Adiveppa Kadamani	1022051	31-Aug-2021	65	M	CFB	5	31-Aug-2022	346	13.4	34.2	155	107
58	Anil Chougale	1021386	20-Aug-2021	36	M	MB	2	20-Aug-2022	2789	14.6	39.5	658	135
59	Manohar Munagi	1020930	13-Aug-2021	68	M	FB	3	13-Aug-2022	3214	13.2	16.5	647	140
60	Basaveshawar Channavar	1020766	11-Aug-2021	56	M	BM	5	08-Nov-2021	187	15.5	38.4	165	179
61	Tammanna Kore	1019711	27-Jul-2021	77	M	CFMB	4	27-Jul-2022	431	76.1	48.7	354	121
62	Mahadevi Patanshetti	1021514	22-Aug-2021	65	F	CB	3	23-Aug-2022	1528	11.7	36.2	887	157
63	Jaysingh Desai	1021972	29-Aug-2021	69	M	CB	5	29-Aug-2022	509	11.4	33.6	389	203
64	Mallikarjun Puthane	1021262	18-Aug-2021	68	M	FB	3	19-Aug-2022	>5000	13.9	45.6	948	108
65	Mahadev Minache	1020855	13-Aug-2021	81	M	CFB	4	13-Aug-2022	4568	13.2	36.1	874	267
66	Annasaheb Bagewadi	1021636	24-Aug-2021	61	M	CFB	3	25-Aug-2021	350	13.2	27	354	203
67	Ishwar Kankanwadi	1021950	29-Aug-2021	58	M	CFB	3	30-Aug-2022	1327	13.1	26.8	879	248
68	Arunkumar Katti	1021326	19-Aug-2021	57	M	CMB	5	20-Aug-2021	4258	15.2	21.1	654	205
69	Appasaheb Kolaki	1022949	11-Sep-2021	84	M	CFB	3	11-Sep-2021	1580	12.7	31.2	784	292
70	Sangeeta Kurale	1021523	22-Aug-2021	52	M	CB	7	22-Aug-2022	4500	16.9	29.5	684	428
71	Shantavva Patil	1023099	13-Sep-2021	81	F	FBM	2	14-Sep-2021	1245	14	26.2	624	206
72	Indarchand Oswal	1020115	08-Feb-2021	78	M	B	3	02-Aug-2021	899	15.5	39.4	452	131
73	Padmavati Ranavath	1020763	11-Aug-2021	60	F	CB	4	08-Nov-2021	2568	14.5	40.2	874	100
74	Raghoba Malik	1023505	19-Sep-2021	90	M	B	3	19-Sep-2021	>5000	14.5	50.6	987	116
75	Sanjay Ginde	1022988	11-Sep-2021	60	M	FB	5	09-Nov-2021	1193	13.9	30.1	511	99
76	Shekargouda Patil	1022752	09-Aug-2021	38	M	CFB	6	09-Sep-2021	1258	13.2	28.6	654	447
77	Altaf Hussain	1020910	13-Aug-2021	59	M	CFB	6	13-Aug-2022	2587	15.2	39.5	984	60
78	Shidagouda Patil	1021528	22-Aug-2021	70	M	CFB	3	23-Aug-2022	968	13.4	34.2	844	139
79	Appasaheb Naik	1023093	13-Sep-2021	70	M	CF	4	13-Sep-2022	781	17.8	37.4	637	402
80	Sharada Mahajan	1022908	09-Oct-2021	55	F	FB	7	09-Oct-2021	666	16.9	32.4	475	217
81	Laxman Anagolkar	1020525	08-Aug-2021	50	M	B	4	08-Aug-2021	2879	17.6	39.4	644	135

82	Uday Fadipatil	1020446	06-Aug-2021	46	M	MB	4	06-Aug-2021	4568	18.6	39.4	547	408
83	Shivanand Sannaik	1021029	15-Aug-2021	75	M	CFB	3	15-Aug-2022	>5000	17.8	67.5	974	102
84	Amar Tibile	1023170	14-Sep-2021	47	M	CF	3	14-Sep-2022	1141	19.5	39.4	657	184
85	Smita Naragund	1051379	13-Sep-2021	41	F	B	2	24-Aug-2022	280	14.1	36.7	154	147
86	V. Prakash Babu	1050982	08-Feb-2021	41	M	CB	4	22-Jul-2022	1099	12.2	33.2	566	195
87	Raghunath Belgaonkar	1051829	11-Aug-2021	48	M	CFB	5	28-Jul-2022	729	13.2	33.4	664	60
88	Vinod Uppin	1051878	19-Sep-2021	64	M	CFB	3	06-May-2021	281	12.5	46.7	240	164
89	Sandhya Yallur	1051391	11-Sep-2021	36	F	MB	1	28-Jul-2021	165	12.7	31.9	147	214
90	Shivbasappa Murod	1051885	09-Aug-2021	33	M	FB	7	15-Oct-2021	411	14.6	35.5	325	378
91	Bhimappa Nagai	1051132	13-Aug-2021	65	M	BM	4	08-Oct-2021	574	15.2	39.5	357	38
92	Mahantesh Somashekar	1051448	16-Aug-2021	32	M	CFMB	3	29-Sep-2021	228	13.4	34.2	124	225
93	Praveen Badami	1051394	27-Aug-2021	33	M	CB	4	23-Sep-2021	370	14.6	39.5	322	238
94	Chinnamma Bogur	1051219	21-Aug-2021	43	M	CB	3	30-Sep-2021	1402	13.2	16.5	874	69
95	Kumarswamy Mahalingappa	1051877	15-Aug-2021	57	M	FB	2	21-Sep-2021	1308	15.5	38.4	669	459
96	Gurupad Shivannavar	1051251	09-Jun-2021	47	M	CFB	2	14-Aug-2021	1045	76.1	48.7	655	102
97	Narmada Jadhav	1051879	24-Jul-2021	59	F	CFB	3	21-Aug-2021	956	45.5	50.6	455	184
98	Pundalik Patil	1051627	16-Jul-2021	46	M	FB	5	23-Sep-2021	1015	13.1	22.4	865	47
99	Madhusudan Choudary	1050964	21-Jul-2021	51	M	FBC	4	23-Sep-2021	1020	11.6	22.4	985	95
100	Shivakka Pagashetti	1052021	23-Jul-2021	52	F	CB	3	26-Sep-2021	750	12.1	25.9	655	131
101	Rajaram Yadav	1051867	23-Jul-2021	53	M	CFM	5	29-Sep-2021	752	12.2	24.4	358	464
102	Sujata Jathar	1051852	21-Jul-2021	53	F	CFMB	3	09-Apr-2021	1001	13.5	33.5	327	347
103	Kallavva Kamble	1051428	29-Jul-2021	64	M	B	4	15-Sep-2021	5200	11.1	21.2	666	464
104	Ishwar Padennavar	1051430	30-Jul-2021	43	M	FMB	3	21-Sep-2021	1026	13.2	37.9	654	347
105	Sanjay Karguppikar	1051956	29-Sep-2021	57	M	FB	3	30-Jul-2021	1008	15.5	39.4	645	246
106	Veeraktayya Salimath	1051881	23-Sep-2021	69	M	M	5	17-Jul-2021	1035	14.5	40.2	785	278
107	Sheela Hipparagi	1051817	30-Sep-2021	48	F	CB	3	25-Sep-2022	1484	22.2	43.6	667	133
108	Manjula Ganesh Patil	1051886	21-Sep-2021	37	F	CFB	7	09-Jun-2021	700	17.5	45.2	457	78
109	Doddakallappa	1036826	14-Aug-2021	78	M	CFM	2	24-Jul-2021	850	13.4	34.2	354	185
110	Mudakappa Itagi	6078015	20-Aug-2021	65	M	BF	3	17-Jul-2021	827	14.6	39.5	485	202
111	Shantavva Madar	1052167	23-Sep-2021	35	M	CB	3	21-Jul-2021	1010	13.2	16.5	687	376
112	Vinay Bankar	1051954	23-Sep-2021	48	M	FB	3	09-Jul-2021	300	15.5	38.4	665	147
113	Mallikarjun Gaddikeri	1051793	23-Jul-2021	41	M	CMB	7	09-Sep-2021	4705	67.5	48.7	669	195
114	Mahadev Dundappa	6082182	23-Jul-2021	65	M	CF	4	14-Jul-2021	790	35.1	50.6	432	200
115	Mallikarjun Basavant	1051793	21-Jul-2021	41	M	B	4	09-Aug-2021	1398	13.1	22.4	687	164
116	Mallikarjun Shilasangi	1024932	07-Oct-2021	49	M	C,F	5	10-Jul-2021	>5000	15.1	27.3	955	103
117	Chinnappa Kabbaligar	1023058	13-Sep-2021	74	M	CFMB	5	13-Sep-2021	938	13.4	20.8	550	174
118	Rajashri Bali	1021470	21-Aug-2021	48	F	FB	4	21-Aug-2021	344	12.2	33.2	250	289
119	Sardar Mulla	1024346	30-Sep-2021	78	M	CFMB	2	30-Sep-2021	590	17.7	34.8	412	174
120	Vijay Manjrekar	1024283	29-Sep-2021	72	M	FB	1	29-Sep-2021	150	13.5	34.6	223	274
121	Anand Sogalad	1023950	24-Sep-2021	55	M	CFB	5	24-Sep-2021	872	12.1	39.3	412	353
122	Sagar Desai	1021418	21-Aug-2021	42	M	CB	2	21-Aug-2021	924	13.7	33.2	542	295

123	Ashoak Sawadatti	1023907	24-Sep-2021	67	M	CFB	2	24-Sep-2021	517	14.2	27.5	640	135
124	Shivaputtra Biradar	1024635	04-Oct-2021	52	M	CFB	4	10-Apr-2021	346	14.4	36.3	244	143
125	Rayappa Katti	1020024	31-Jul-2021	60	M	CF	5	31-Jul-2021	363	12.6	34.2	278	289
126	Gaurav Deshpande	1022622	07-Sep-2021	39	M	C	3	09-Jul-2021	147	11.4	27.5	189	168
127	Mahadevi Sadalagi	1022763	09-Sep-2021	70	M	CMF	1	09-Sep-2021	897	12.7	28.9	356	251
128	Umesh Dandur	1024049	25-Sep-2021	50	M	F	7	25-Sep-2021	248	12.6	33.3	150	246
129	Sanjay	1021264	18-Aug-2021	43	M	FM	4	19-Aug-2021	498	11.1	36.6	378	385
130	Apporva Deshpande	1022375	04-Sep-2021	30	M	CFB	3	09-Apr-2021	531	14.8	38.5	361	337
131	Meenakshi Patil	1021495	22-Aug-2021	75	M	CFBM	4	22-Aug-2021	181	10.9	21.1	128	227
132	Rudraappa Patil	1022667	07-Sep-2021	59	M	CFB	3	09-Jul-2021	>5000	23.5	60.4	647	88
133	Rajashekara Hiremath	1022797	09-Sep-2021	64	M	CM	2	09-Sep-2021	120	12.1	29.6	157	250
134	Sashwat Porwal	1018721	14-Jul-2021	25	M	CFMB	2	14-Jul-2021	205	13.6	29.6	214	235
135	Shaila Raddi	1022636	07-Sep-2021	54	M	CFB	5	09-Aug-2021	308	12.1	28.1	321	418
136	Nazir Ahmad	1018431	10-Jul-2021	74	M	CFMB	2	10-Jul-2021	456	14.5	30.5	514	169
137	Laxman Nimbergi	1021041	15-Aug-2021	33	M	CFMB	4	15-Aug-2022	996	13.5	30.6	841	178
138	Arjun Bhumereddy	1019405	22-Jul-2021	24	M	CFB	3	22-Jul-2021	125	13.8	29.8	165	268
139	Yuvaraj Marad	1023483	18-Sep-2021	57	M	CFB	5	18-Sep-2021	570	11.9	27.9	341	436
140	Jayashree Iyer	1021292	19-Aug-2021	23	F	CF	3	19-Aug-2021	660	15.2	38.8	475	288
141	Kishan Rao	1024867	07-Oct-2021	60	M	CM	3	10-Jul-2021	390	12.2	36.7	465	202
142	Chinmay CS	1019869	29-Jul-2021	26	F	CB	3	29-Jul-2021	1247	13.6	35.2	941	119
143	Preema Hubbali	1021570	24-Aug-2021	56	F	CFB	8	24-Aug-2021	759	13.7	25.6	465	245
144	Ashna Singh	1019413	22-Jul-2021	27	F	CMB	3	22-Jul-2021	250	12.2	29.6	189	252
145	Mahesh Yaradal	1020943	14-Aug-2021	48	M	CMB	3	14-Aug-2021	503	13.4	32.6	325	151
146	Venkanna Katti	1021531	23-Aug-2021	54	M	B	1	23-Aug-2021	487	12.6	28.6	235	223
147	Shankar Laxman	1025361	13-Oct-2021	61	M	CMF	2	13-Oct-2021	250	12.6	31.7	324	261
148	Sujata Madiwal	1020424	06-Aug-2021	45	F	CF	4	08-Jun-2021	319	12.8	32.6	312	186
149	Bhairu Patil	1024956	08-Oct-2021	60	M	CBF	2	10-Aug-2021	502	13.7	37.1	359	216
150	Nutan Chavan	1020649	16-Aug-2021	54	F	CB	3	16-Aug-2021	250	12.8	29.4	169	197
151	Padmawati Rangan	1021443	21-Aug-2021	27	F	CMF	3	21-Aug-2021	702	13.9	32.3	658	392
152	Amol Khankachan	1023840	29-Sep-2021	26	M	CB	3	29-Sep-2021	500	12.7	34.6	456	182
153	Mahadevi Savanur	1020811	12-Aug-2021	41	M	CF	3	08-Dec-2021	217	12.3	29.1	176	229
154	Meghna Shrma	1019609	25-Jul-2021	24	M	CB	3	25-Jul-2021	250	13.1	33.4	188	260
155	Amit Motawani	1022727	08-Sep-2021	25	M	CBF	3	08-Sep-2021	401	13.9	34.5	256	250
156	Bhuwaneshwari Math	1024639	04-Oct-2021	44	F	F	7	04-Oct-2021	448	13.2	31.4	321	235
157	Sandeep Sangoram	1017707	05-Jul-2021	45	M	BFM	7	07-May-2021	548	12.5	31.5	465	259
158	Prakash Mote	1023711	21-Sep-2021	71	F	CB	5	21-Sep-2021	338	11.8	34.4	358	178
159	Vijay Patil	1021836	27-Aug-2021	59	M	CFB	4	27-Aug-2021	1532	16.4	40.2	887	122
160	Shandayala Toroji	1021845	27-Aug-2021	52	M	B	5	28-Aug-2021	>5000	18.8	45.2	987	115
161	Rao Sahab	1023488	18-Sep-2021	64	M	CF	3	19-Sep-2021	775	14.4	34.3	456	164
162	Sheetal Neelagouder	1023297	15-Sep-2021	49	M	CFB	5	16-Sep-2022	2147	22.4	34.2	587	47
163	Udaykumar Desai	1021203	18-Aug-2021	60	M	CB	4	18-Aug-2022	1301	18.9	25.6	547	195

164	Sidharaya Patil	1021494	22-Aug-2021	81	M	MFB	3	22-Aug-2022	2145	14.1	28.4	687	131
165	Yallappa Madagannavar	1023059	13-Sep-2021	77	M	MB	4	13-Sep-2022	999	13.1	25.2	947	464
166	Subhash Hooli	1020214	03-Aug-2021	74	M	FB	3	08-Mar-2021	517	13.1	25.2	347	347
167	Balaram Dhangawade	1020620	09-Aug-2021	54	M	B	3	08-Sep-2021	1608	14.2	27.3	874	246
168	Laxman Hongekar	1020695	10-Aug-2021	70	M	CB	2	08-Oct-2021	2314	14.6	30.1	846	134
169	Prabhavati Kale	1023607	20-Sep-2021	63	M	M	3	20-Sep-2021	881	19.6	19.7	475	133
170	Balagouda Patil	1024541	02-Oct-2021	80	M	B	4	10-Feb-2021	>5000	19.5	46.5	887	78
171	Bhupal Badachi	1023176	14-Sep-2021	70	M	CFB	4	14-Sep-2022	4987	15.1	33.3	687	185
172	Shantadevi Kore	1024729	05-Oct-2021	80	F	CB	3	10-Jun-2021	655	15.4	25.6	688	202
173	Annappa Patanshetti	1024059	26-Sep-2021	79	M	CFBM	4	26-Sep-2022	1458	18.6	25.9	624	348
174	Manohar Gawade	1022971	11-Sep-2021	57	M	CFB	5	09-Nov-2021	673	13.4	29.8	357	96
175	Krishna Kutre	1019824	28-Jul-2021	58	M	CFB	2	28-Jul-2022	1237	13.5	33.4	475	285
176	Vinaykumar Kumbar	1052184	29-Aug-2021	52	M	CFB	2	24-Jul-2021	644	11.8	32.3	325	120
177	Basavraj Avaradi	1051865	19-Aug-2021	48	M	M	1	24-Jul-2022	685	12.1	33.6	541	112
178	Pundalik Dongare	1051608	11-Sep-2021	50	F	CFB	5	18-Jul-2022	790	13.4	34.4	472	180
179	Madhuja Nathbuwa	1051286	22-Aug-2021	29	M	CFB	2	29-Jul-2021	780	14.2	33.2	244	176
180	Naseen Mulgani	1019598	25-Jul-2021	60	M	CFB	3	25-Jul-2021	854	13.2	37.9	741	182
181	Basavani Hanji	1020782	08-Dec-2021	82	M	CFM	5	08-Dec-2021	725	15.5	39.4	654	166
182	Nanda Ghasati	1021922	28-Aug-2021	58	F	BF	2	28-Aug-2022	723	14.5	40.2	632	145
183	Patreppa Munoli	1020039	31-Jul-2021	73	M	CB	3	31-Jul-2022	1023	22.2	43.6	658	95
184	Dannamma Kavali	1022367	03-Sep-2021	75	M	FB	3	09-Mar-2021	676	17.5	45.2	425	120
185	Basavraj Tummarguddi	1020295	04-Aug-2021	59	M	CMB	2	08-May-2021	1254	22.5	78.5	741	112
186	Vithal Naik	1020750	11-Aug-2021	64	M	CF	5	08-Nov-2021	>5000	33.8	65.2	945	180
187	Savitri Naik	1022733	08-Sep-2021	70	M	B	4	09-Sep-2021	103	13.2	33.2	155	376
188	Suresh Rao	1020523	08-Aug-2021	71	M	CFB	2	08-Aug-2021	290	12.3	31.2	178	147
189	Jayant Chougle	1019616	25-Jul-2021	83	M	FB	4	25-Jul-2021	1043	13.5	37.4	654	195
190	Jagdeesh Khot	1022407	09-Apr-2021	67	M	CBM	3	09-Apr-2021	1320	12.1	22.6	945	200
191	Mahananda Katti	1021629	24-Aug-2021	73	F	CFB	3	24-Aug-2022	360	12.5	32.1	278	164
192	Shrishail Uppin	1023926	24-Sep-2021	72	M	FB	7	24-Sep-2022	419	14.4	35.8	369	214
193	Shankar Chougle	1022264	02-Sep-2021	60	M	CFB	4	02-Sep-2021	1352	12.1	22.6	482	378
194	Naganath Kodakany	1022671	07-Sep-2021	39	M	CB	4	07-Sep-2021	2145	34.9	39.7	645	38
195	Uday Revankar	1023965	24-Sep-2021	70	M	CFB	3	24-Sep-2022	644	13.9	35.1	374	225
196	Mahadev Maruti	1022916	11-Sep-2021	50	M	CB	3	11-Sep-2021	1392	13.2	36.1	654	138
197	Mahadev Mageppa	1022462	05-Sep-2021	51	M	CBF	4	05-Sep-2021	1349	13.2	32.1	745	69
198	Shanaka Balikai	1022738	08-Sep-2021	63	M	CFMB	2	08-Sep-2021	1482	22.5	78.5	783	459
199	Noorjahan	1019602	25-Jul-2021	68	M	CFB	3	25-Jul-2021	>5000	48.5	65.2	965	88
200	Chandrakant Mali	1020598	08-Aug-2021	49	M	FM	8	08-Sep-2021	937	13.2	33.2	749	147
201	Ramappa Kagawade	1022740	08-Sep-2021	74	M	B	1	08-Sep-2021	>5000	78.6	98.4	975	98
202	Dadu Shetti	5783029	25-Jul-2021	73	M	CFB	4	26-Jul-2022	1205	13.5	37.4	782	184
203	Govind Salunkhe	1023296	15-Sep-2021	66	M	CFB	7	16-Sep-2022	573	13.2	31.5	437	169