Various Inflammatory Markers such as Fibrinogen , D-dimer and IL-6 levels in patients of COVID 19 ; and their co-relation with CT severity score and prognosis of COVID-19 disease.

Dr. Rabia Tinna[a] , Arpit Tinna [b] , Dr. Saurabh Singhal [c]

a Junior Resident, Department of Medicine, Chhatrapati Shivaji Subharti Hospital, Meerut, Uttar Pradesh,
b Researcher
c Professor and Head of department, Subharti Medical College, Meerut.

Abstract
Covid has proven its tremendous effect on entire planet with millions of cases and death so far. In our survey the clinical, democratic parameters were tested on 75 patients. Based on Real time and visual inspection tests were performed and CT severity scores were assigned out of 25 based on area covered by lung lobes. In our study level of lymphocytes and eoenophils levels were less in patients with critically ill patients. Moreover there was direct linear relation of d – dimer , IL 6, fibrinogen with CT severity score.
Keywords- *Covid, d-dimer, fibrinogen, IL-6, CT score*

I.   Introduction

A Number of cases of Pneumonia of an unknown etiology were detected in the city of Wuhan, China and first reported to WHO country office in December, 31st 2019 [1]. It was confirmed thereafter to be caused by SARS–COV 2, Severe Acute Respiratory Syndrome Coronavirus [2]. With its rapid spread, increasing number of cases have been reported worldwide. By February 2020 WHO had given the virus name , Novel Coronavirus 2019 or commonly used Covid -19. In early march shortly after the first cluster of cases was diagnosed in USA, WHO declared a pandemic [3].

In certain individuals, the disease progressed from Pneumonia and there were Severe Acute Respiratory Symptoms and patients developed ARDS, Respiratory Failure, Pulmonary Edema and various other complications leading to multi organ failure and death [4-6].

In a study done by Bilian Yu and Xin Li, it was found that D-dimer levels were significantly increased in covid-19 patients and abnormal levels are associated with poor prognosis[7]. Various Biological markers such as IL-6 levels and fibrinogen Levels are also associated with Poor Prognosis of the disease have been identified by previous studies. These markers can help clinicians identify patients who are at risk of deterioration.

The early identification of severe Covid 19 is significant in order to reduce mortality rates [8]. An important and effective method for diagnosing and evaluating the severity of Covid-19 is Computerized tomography [9][10]. At present, there is little known about the relationship between imaging results and presence of Systemic inflammatory mediators in Covid 19 patients. The study is aimed to analyze the severity of Covid 19 infection by quantifying Chest CT results and to determine relationship between CT severity scores and systemic inflammatory markers in effort to identify factors which can be used against Covid -19 pandemic.

II.   Materials And Methods

The retrospective study was carried out on patients at Chhatrapati Shivaji Subharti Hospital , Subharti University, Meerut, UP from September to December. A total 75 patients both males and females of age more than 18 were included in this study.
Place of Study - Post Graduate Department of Medicine , Chhatrapati Shivaji Subharti Hospital , Subharti University, Meerut, U.P
Study Design: This is a Retrospective Cross Sectional Study
Sample Size: 75 patients
Study Population: Patients tested positive for SARS CoV-2 (Severe Acute respiratory Syndrome Coronavirus 2) via RT-PCR technique
Study Duration: Three Months

Inclusion Criteria:
All Covid-19 positive Patients.
Age 18 years and above
Informed consent provided by patient/relatives
Exclusion Criteria:
All Covid 19 negative patients
Pregnant Females
Long Standing Chronic illness
Patients who have not given written informed consent

III. Methodology :

After written informed consent was obtained. All Patients with confirmed Covid 19 reports via real time RT-PCR technique were selected [11] based on there demographic data, clinical symptoms, signs , comorbidities (such as hypertension, diabetes, hypothyroidism) followed by collection of laboratory findings and chest CT.

The CT images were evaluated for ground-glass opacities (GGO), Consolidation, crazy paving pattern, air bronchogram, thoracic lymphadenopathy and pleural effusion as per Fleischner Society Recommendation [12][13].

CT DATA ANALYSIS : Five Lung Lobes , three on the right and two on the left are individually assessed and percentage involvement of the lobe will be noted. Based on visual assessment, individual scores will be assigned. Visual severity scoring of CT chest will be classified as :

Score 1 - <5%
Score 2 - 5-25%
Score 3 - 25-50%
Score 4 - 50-75%
Score 5 - >75%

CT severity score is defined by summing up the individual scores making a total of 25.
CT Score is assessed out of 25 based on percentage of area involved in each of 5 lobes.
Score of <8 - is Considered MILD
Score of 9-15- is MODERATE
Score of >15- is SEVERE
Various Inflammatory Markers IL-6, Fibrinogen and D-dimer levels will be co-related with Chest CT severity Score.

The study was initiated after obtaining the approval from institutional ethics committee. All potential participants were recruited only after written informed consent was obtained from them. A detailed explanation was given to all the participants regarding the study and their contribution to it .

IV. Relation between CT Severity Score and Fibrinogen

Fibrinogen is a glycoprotein molecule consisting of peptide chains. It is a protein content present in plasma of blood which results in the formation of fibrin generated by the enzyme mainly thrombin[14]. In our study fibrinogen is the prognostic factor in patients suffering from Covid 19 . The CT severity score of patients is measured using radiographic testing [15] and is compared with the fibrinogen content present in patients suffering from Covid 19 . The measurement of fibrinogen content in patients was performed with different samples to drive the relation between the level of fibrin content with CT score as shown in fig 1. The graph predicts the linear outcome of fibrinogen level and CT Score with root mean score value of 0.9343.
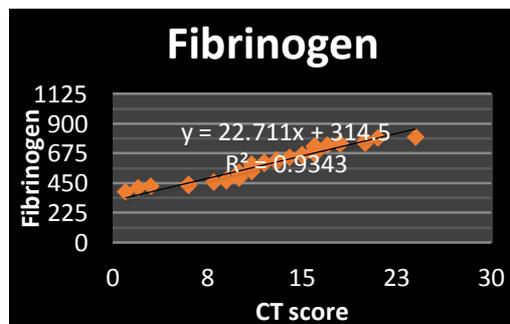

Fig 1 Relation between fibrinogen and CT Score of Covid-19 patients

V.   Relation between CT severity and D dimer

D dimer is process of breakdown of fibrin and use of that fibrin as a biomarker of its degradation and formation [16]. Various papers have been reviewed and being concluded that d dimer is a valuable tool for activation of fibrinolysis[17] In our survey between effect on d dimer level in patients with Covid 19 . It can be better understood that the abnormal elevated d dimer (> 0.5) and lack of anticoagulated therapy in Covid 19 patients with major sign of severity. D dimer was diagnosed in 75 patients and its correlation with CT score was performed as shown in fig 2. The proposed result shows the exponential relation between CT score and d dimer content in patients.
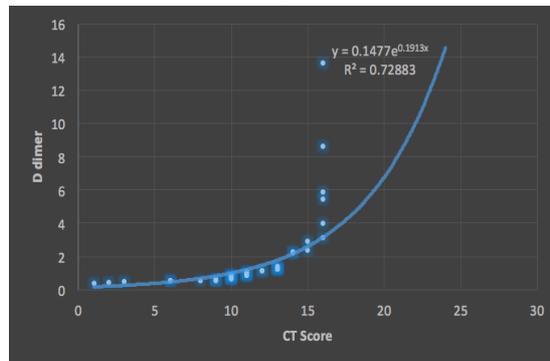

Fig 2 Relation between d dimer and CT Score of Covid-19 patients

VI.   Relation between IL 6 with CT Score

In our study the demographic investigation and imaging features of 75 patients were performed and IL 6 was one such clinical characteristic. The normal range of IL 6 content in human body is 4.4 pg/ml. But in our study there was elevated il 6 in human body. Higher IL 6 level results in presence of inflammatory state hyper immune with increased mortality and morbidity. There was a direct logarithmic relation between the IL 6 content and CT score with root mean square value of 0.92386.
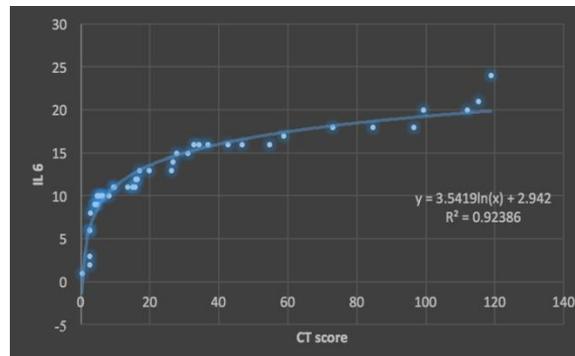

Fig 3 Relation between IL-6 and CT Score of Covid-19 patients

VII. Results And Discussion

The effect of various human constituents like IL 6 , d dimer and fibrinogen with CT score has been surveyed. The measurement of these constituents was performed with different test samples to derive the relation between the surveyed fibrinogen, d dimer and IL 6 values with CT severity score. The corresponding fibrinogen value was computed using equation 1 that is 22.711x+314.5 as shown in figure 1. In order to find the relation between the CT severity score with blood samples were initially taken and obtained samples were analysed using PLX DAQ software. Moreover mean value of all the fibrin content, IL 6 and d dimer values with corresponding CT severity score were determined. Figure 2 depicts the relation between d dimer and CT severity with $y = 0.1477e^{0.1913x}$. Figure 3 depicts the relation between IL 6 and CT score with $y = 3.5419\ln(x)+2.942$. The raised inflammatory biomarkers were significantly related to more lung involvement thus helpful in diagnostic and prognostic marker of the disease.

VIII.   Conclusion

It is thus concluded from this study that inflammatory markers have strong linear relationship with CT severity score and presents promising efficacy in prediction of critical illness and need for ICU admission.

Credit authorship contribution statement
Rabia Tinna: Conceptualization, Writing – original draft. **Arpit Tinna**: Resources, Writing – review & editing.
Declaration of Competing Interest
The author declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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