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CROSS SECTIONAL STUDY OF BIOCHEMICAL PARAMETERS DURING FIRST AND SECOND WAVE OF COVID 19 PATIENTS ADMITTED IN RURAL TERTIARY CARE HOSPITAL CHENGALPET DISTRICT

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ABSTRACT

Introduction: The first case of COVID 19 emerged in city of Wuhan, China in December 2019, Till August 2020 World Health Organization (WHO) reported that 24.7 million cases were reported inclusive of 830,000 deaths. Many countries have suffered a two-wave pattern of COVID cases, called first wave and the second wave. This study was aimed to compare the levels of Biochemical markers (LDH, ferritin, D-dimer and CRP) from patients infected during the first wave and the second wave in a rural tertiary care hospital Chengalpet district. **Methodology**: A Cross sectional study was done between June to August 2020 and June to August 202. About 299 RT-PCR positive SARS COV-2 patients serum/plasma samples were collected from first and second wave of COVID-19 The inclusion criteria were individuals with age above 18years with RT-PCR positive for SARS COV-2 and the exclusion criteria was age below 18 years. **Result**: The median value of LDH for second wave is 611 and the first wave 473 which lies between the (425 – 804) and (385 - 625) as its 25th percentile and 75th percentile respectively, For ferritin, median value of second wave is 402 and the first wave is 254 which lies between the (217 - 707) and (112 - 422) at its 25th percentile and 75th percentile respectively, D-Dimer has its median value as 0.56 for second wave and 0.54 for first wave. CRP has its median value as 35 for second wave and 44 for first wave which lies between the (21 – 56) and (25 - 65) as its 25th percentile and 75th percentile respectively, Thus LDH, Ferritin and D-dimer serum levels are raised in second wave and CRP raised in First wave of COVID-19. **Conclusion**: The D-

dimer, CRP, LDH and ferritin were strongly associated with COVID-19 disease and these biomarkers have been shown to have the capacity to diagnose, predict severity and complication and have usefulness in monitoring treatment response

Keywords: COVID-19, LDH, Ferritin, D-dimer, CRP

INTRODUCTION

The first case of COVID 19 emerged in city of Wuhan, China in December 2019. Till August 2020 World Health Organization (WHO) reported that 24.7 million cases were reported inclusive of 830,000 deaths [1]. Many countries have suffered a two-wave pattern of COVID cases, called first wave and the second wave [2]. Outbreak of second wave of COVID-19 were reported in October 2020 by majority of countries with a significant rise in new cases recorded thus attaining their highest number of total cases [3, 4]. Japanese population suffered second wave of COVID-19 in late March and early May with sudden rise in new cases. With these outbreaks, the severity of the disease is still uncertainly projected. The clinical presentation of COVID-19 may vary from asymptomatic or mild symptoms to severe multi organ failure and even death. Symptoms get changed between first and second wave of COVID which includes fever, sore throat, loss of sense of smell and or taste, non-productive cough, shortness of breath, general fatigue, headache and myalgia. Some patients 15-20% may tend to develop acute respiratory distress syndrome (ARDS), kidney failure and heart failure [5-7]. COVID-19 had similar clinical and pathological findings with the Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) due to the genetic homologies between coronaviruses [8]. Severe form of COVID-19 cause a hyper inflammatory response, which leads to a pathological dysfunction of innate host defence mechanisms, causing complications like cytokine release syndrome (cytokine storm) and multiple organ failure [9]. Apart from circulating cytokines levels, there are certain inflammatory markers known to be associated with the severity of the disease such as lactate dehydrogenase (LDH), ferritin, D-dimer and C-reactive protein (CRP) [10]. Some of them are non-specific markers of sepsis and or inflammation while others are consistent with cytokine releasing syndrome (CRS). Thus been elevated with the severity of the disease [11]. The enzyme Lactate dehydrogenase (LDH) is involved in glycolysis which catalyses pyruvate to lactate conversion and present in all tissues. In viral infection LDH is released from cells upon damage of their cytoplasmic membrane [12]. Ferritin is a

storage protein of iron, it is one of the inflammatory marker. During infections due to virus or Bacteria, a decline in its transporting capacity resulting from spleen and liver damage increases ferritin. Levels also rise during infections due to iron release from the endoplasmic reticulum [13] D-dimers is one of the peptide fragments synthesized as a cross linked fibrin during degradation by plasmin. Its level gets increased in any process that involve breakdown of fibrin and production of fibrin, such as surgery, acute infections and acute or chronic inflammatory states [14]. C-reactive protein (CRP) is an acute-phase reactant protein. Liver synthesis CRP during inflammation, it has a plasma half-life of 19 hours [15]. This study was aimed to compare the levels of Biochemical markers (LDH, ferritin, D-dimer and CRP) from patients infected during the first wave and the second wave in rural tertiary care hospital Chengalpet district.

METHODOLOGY

A cross sectional study was conducted to compare the levels of biochemical parameters in admitted COVID 19 patients during the first and second wave of COVID-19 in rural tertiary care hospital in Chengalpet district. Time duration of first wave and second wave taken for this study is between May 2020 to August 2020 and May 2021 to August 2021 respectively. About 299 RT-PCR positive SARS COV-2

patients serum/plasma samples were collected from first and second wave of COVID-19. The inclusion criteria's were individuals with age above 18years with RT-PCR positive for SARS COV-2 and the exclusion criteria was age below 18 years.

The primary variables included in this study were lactate dehydrogenase (LDH), ferritin D-dimer, C-reactive protein (CRP). In this study, Lactate dehydrogenase (LDH) analysed in Pyruvate method (BA 200), C-reactive protein (CRP)and Ferritin were analysed in Nephelometric method (Mispa-i2 Agapee) and D-dimer was anlysed in ELFA method in first wave (Minividas) and Nephelometric method (Mispa-i2 Agapee) in the second wave. Biological reference interval for LDH: 207-414 U/L, Ferritin: 30-220 ng/ml, CRP:0-6mg/l and cut off for D-dimer: <0.5 microgram/ml. After collecting the reports of biochemical parameters, a cross sectional study comparing Biochemical parameters was done among the admitted patients during first and second waves of COVID-19 pandemic.

RESULTS

The median value of LDH for second wave is 611 and the first wave 473 which lies between the (425 – 804) and (385 - 625) as its 25th percentile and 75th percentile respectively. LDH is higher in second wave with wide interval than first wave comparatively. For ferritin, median value of

second wave is 402 and the first wave is 254 which lies between the (217 - 707) and (112 - 422) at its 25th percentile and 75th percentile respectively. Ferritin is higher in second wave with wide interval than first wave comparatively. D-Dimer has its median value as 0.56 for second wave and 0.54 for first wave. Median D-Dimer was found to be higher in second wave than in first wave. CRP has its median value as 35 for second wave and 44 for first wave which lies between the (21 – 56) and (25 - 65) as its 25th percentile and 75th percentile respectively. Median CRP for first wave is higher than second wave **(Table 1, Figure 1-4)**.

Table 1

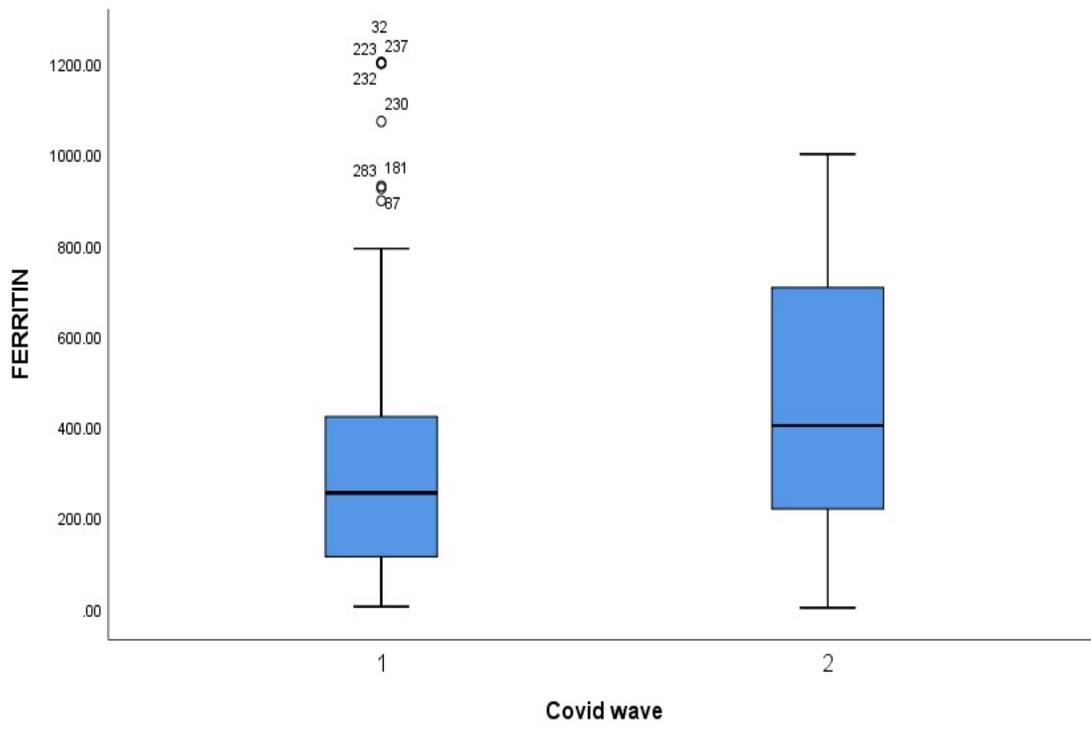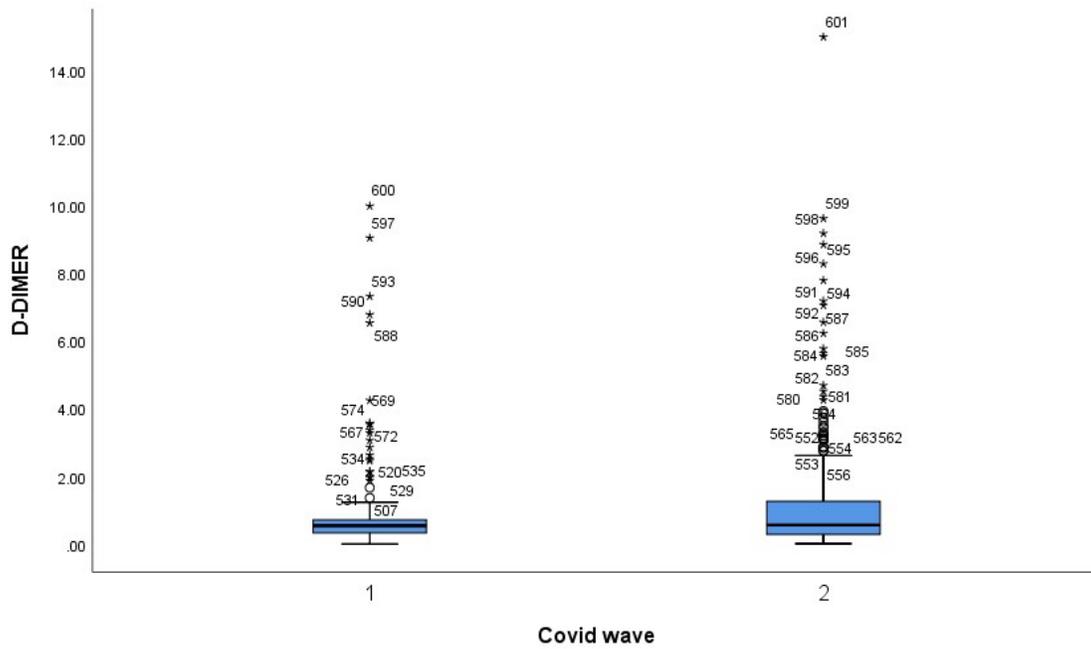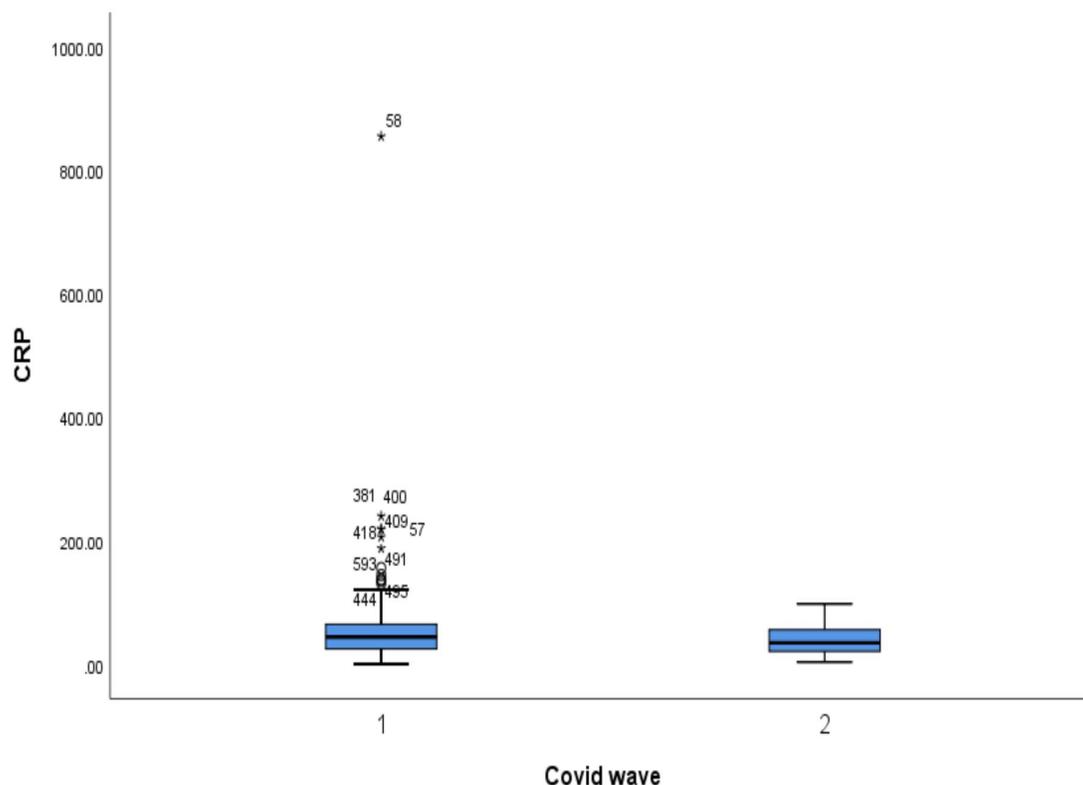| MEDIAN (INTER-QUARTILE RANGES)			
variables	**First wave**	**Variables**	**Second wave**
LDH (n = 299)	**473 (385 - 625)**	**LDH (n = 302)**	**611 (425 - 804)**
FERRITIN (n=299)	**254 (112 - 422)**	**FERRITIN (n=302)**	**402 (217 - 707)**
D-DIMER (n=298)	**0.54 (0.33 -0.72)**	**D-DIMER (n=295)**	**0.56 (0.28 - 1.26)**
CRP (n=299)	**44 (25 - 65)**	**CRP (n=301)**	**35 (21 - 56)**
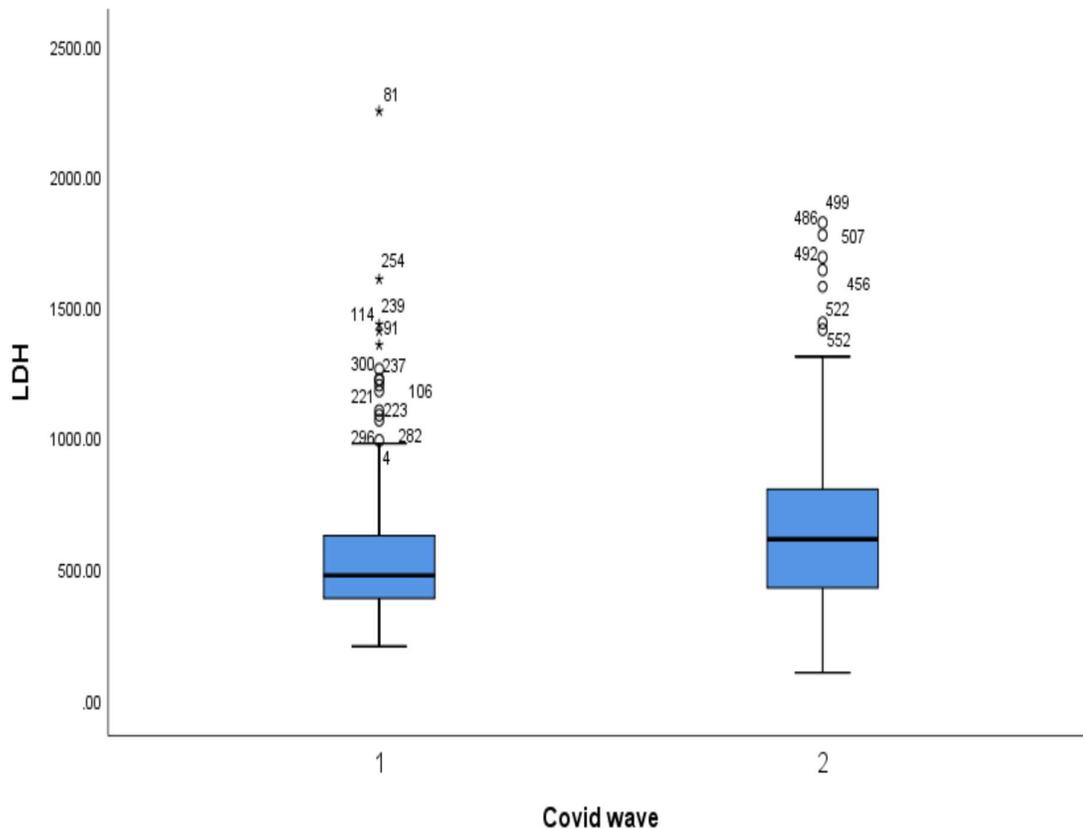
Figure 1

Figure 2

Figure 3

Figure 4

DISCUSSION

COVID 19 has become one of the major global problem for the past few years and it is characterized with increased mortality, higher rate of complications and even it has created major impact on global economy. Thus there is a need for cost effective early diagnosis for the management of COVID-19. Various studies have found that there is an increased level of biochemical parameters in COVID-19 patients and also pro inflammatory cytokines were elevated in severe cases when compared to mild or moderate cases. In our study comparison of biochemical parameters (LDH, CRP, D-dimer and Ferritin)was done between first and second wave of COVID19. Our findings of CRP, LDH, ferritin and D-dimer levels shows significant raise in RT-PCR positive COVID-19 patients. A study in Italy stated that LDH and CRP are markedly rise in COVID-19 patients and this finds to be alternative for RT-PCR [16]. Further studies reported that LDH, ferritin, D-dimer and CRP were used to evaluate the severity of the disease and a high level are associated with mortality and poor outcome [17, 18]. Results of the various analysis have shown that LDH, ferritin D-dimer and CRP are associated with increased risk of COVID-19 infection. A recent study [19] revealed that high

levels of ferritin, D-dimer and CRP are associated with poor outcome in COVID-19. In every tissue LDH is present and is a cytoplasmic glycolytic enzyme. In general, increased levels of LDH indicate tissue damage and common in patients infected with MERS-CoV [20-22], H7N9 [23, 24] and H5N1 [25]. Study stated that LDH is an independent factor of mortality in patients with H1N1 infection [26] and severe acute respiratory syndrome [27-29]. Increased LDH in early phase of COVID-19 severe cases suggest that there is a possible subclinical tissue damage. The virus binds to ACE2(human angiotensin converting enzyme 2) receptor in the lung [30, 31], so the lungs are the first organ to get affected, but on disease progression, various cytokine abnormalities and multiple organs dysfunction can be seen in severe COVID 19 patients, resulting systemic organ damage due to excessive activation of immune system. Further LDH isoenzymes test can help to locate the damaged tissues or organs. Ferritin acts as a marker for serious illness, liver damage, and treatment course in COVID 19. From destroyed hepatocytes the acute phase protein Ferritin gets released [32, 33]. Impaired liver activity or a metabolic syndrome results in Ferritinemia [34]. Abnormal ferritin levels in Covid-19 patients have more risk of liver injury and severe illness and studies found that liver

injury is common in covid-19 patients. The early analysis of ferritin can efficiently have recognized catastrophic disease, liver damage and prognosis of covid-19 patients. The D-dimer is a degradation product of fibrin and is a small protein fragment formed by fibrinolysis. The identification of circulating D-dimer concentrations in blood is found to be a sensitive marker in diagnosing thrombotic states like pulmonary embolism and Disseminated intravascular coagulation [35]. Increased D-dimer levels in COVID-19 patients might be helpful to identify in patients with pulmonary complications, high disease severity and risk of venous thromboembolism. This would assist with risk stratification and the early introduction of therapeutic measures that might reduce COVID19 related morbidity and mortality. COVID-19 patients with elevated D-dimer levels may require hospitalization, despite the clinical presentation severity. CRP levels are in association with the level of inflammation, and its concentration level is not affected by age, sex and physical condition. CRP levels can activate the complementary pathway and enhance phagocytosis and clearing the pathogenic microorganisms invading the body. CRP levels found to be useful in the early phase of pneumonia diagnosis. It is an important biomarker for the evaluation and diagnosis of severe pulmonary infectious diseases. A

study shows increased value of CRP levels in severe pneumonia. CRP levels were also correlating with the lung lesions and disease severity. In the early phase of COVID-19, CRP levels found to be associated with lung lesions and disease severity and also to monitor the disease improvement. Thus, the Biomarkers D-dimer, CRP, LDH and ferritin is simple, convenient, cost effective and useful in predicting the severity and diagnosis of COVID-19 before proceeding to the high cost techniques like RT-PCR and CT imaging.

CONCLUSION

In this study on comparing the levels of Biochemical parameters between first and second wave of COVID-19 the LDH, ferritin and D-dimer raised in second wave and CRP raised in first wave of COVID-19, Thus the D-dimer, CRP, LDH and ferritin were strongly associated with COVID-19 disease and these biomarkers have been shown to have the capacity to diagnose, predict severity and complication and have usefulness in monitoring treatment response. This will help in early isolation and treatment and decreases the rate of morbidity and mortality in COVID-19.

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