

## Biochemical Parameters in Symptomatic and Asymptomatic COVID 19 patients- A comparative study

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### Abstract

**Background:** Covid-19 was first reported in Wuhan, China in the month of December 2019. Studies shows that different laboratory parameters are altered in Covid-19 patients with varied severity, and are useful as biomarkers to assess the progression of the disease. Certain biochemical parameters may predict the severity or the progression towards severity of the Covid-19 disease. Studies have stated that significant high value of LDH was noted in case of seriously ill patients. AST/ALT ratio a strong indicator of liver damage is used in analysing the severity of the disease. Elevation of ferritin is noted in case of inflammation. D-dimer has been identified as a potential indicator for its prognosis in COVID-19 patients. **Methods:** Total of 102 patients with RT-PCR test positive for COVID-19 were enrolled in the study. Study population is classified as Asymptomatic and symptomatic. Biochemical parameters like AST, ALT, Ferritin, D-dimer, LDH were analysed in serum samples obtained from the above patients. Fisher exact test and Chi-square test were used to find the significance of study parameters. **Results:** AST/ALT ratio was found to be moderately significant ( $p=0.044$ ) with an increased value in symptomatic patients. LDH, D-Dimer and ferritin values were found to be high in symptomatic patients compared to asymptomatic patients and found to be statistically significant. **Conclusion:** Routinely used biochemical parameters show promise as potential markers of severity and prognosis. However further studies are required to evaluate the statistical utility of these markers.

**Key words:** Aspartate Transaminase, Alanine Transaminase, Ferritin, D-Dimer

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### Background

COVID-19 (Coronavirus disease 2019) caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) has a severe effect on respiratory system. It was first reported in Wuhan, China in the month of December 2019. It was declared a pandemic globally by WHO (World health Organization) on 11<sup>th</sup> march 2020 due to its increased rate of infectivity, morbidity and mortality in a very short time line[1]. The inflammatory process due to SARS-CoV2 infection may play a main role in the pathogenesis of multiple organ damage and be responsible for the dramatic outcome of COVID-19 patients[2].

There is an urgent need to identify laboratory predictors of progression towards severity. Various studies till date shows that different laboratory parameters become altered in Covid-19 patients with varied severity, and are useful as biomarkers to assess the progression of the disease and categorize patients who may present a severe and/or fatal clinical condition[3]. Clinical Laboratory plays a crucial role in detecting the virus and aids in diagnosis of Covid-19 and other diseases[4]. Laboratory findings also helps in understanding the prognosis. Certain biochemical parameters may predict the severity or the progression towards severity of the Covid-19 disease such as LDH, AST/ALT ratio, D-Dimer, Ferritin. Elevated levels of LDH (Lactate dehydrogenase) indicated lung tissue damage. Many studies have stated that LDH were found to be with in normal range in less severe cases and a significant high value of the same were noted in case of seriously ill patients[5,6]. It is also stated that decline in levels of LDH is an indicator of good prognosis[7] AST (Aspartate Transaminase) and ALT (Alanine Transaminase) are frequently used

biochemical parameters to assess liver function. They are now being used in the covid-19 diagnosis panel. De Ritis ratio defined by Fernando De Ritis in the year 1957 is the ratio of AST and ALT which in turn is a strong indicator of liver damage[8]. Studies revealed that rates of De Ritis < 1.0 indicated moderate to severe liver damage, and rates higher than 1.0 indicated severe liver diseases[9,10]. Ferritin an iron containing protein, being a positive acute phase protein, whose serum level elevation is noted in case of inflammation. It is postulated that macrophages, which produce cytokines and account for the majority of the immune cells in the lung parenchyma, might be responsible of the secretion of serum ferritin[11]. D-dimer is a fibrin degradation product, widely used as a biomarker for thrombotic disorders. Increased D-dimer levels are noted with advanced age and pathologically its elevation is noted with increased severity of community-acquired pneumonia. D-dimer has been identified as a potential indicator for prognosis in COVID-19 patients[12,13].

This study aims to analyse and compare various biochemical parameters among symptomatic and asymptomatic Covid-19 patients.

### Materials and method

Total of 102 patients admitted in Dr Chandramma Dayananda Sagar Institute of Medical Education and Research, Harohalli, Ramanagara, Karnataka with RT-PCR test positive for COVID-19 were enrolled in the study after obtaining Institutional Ethical clearance and Written consent were obtained.

### Inclusion criteria

RT-PCR positive patients

### Exclusion criteria

Patients with pre-existing liver disease, chronic inflammatory disease, pre-existing disorders of coagulation.

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Study population is classified as Asymptomatic (RT-PCR positive for COVID-19 without any symptoms; n=17) and symptomatic (RT-PCR positive with symptoms; n=85). Blood sample were collected and serum analysis for the following biochemical investigations were performed

AST (Aspartate transaminase): Method- IFCC without P5P

ALT (Alanine transaminase): Method- IFCC without P5P

AST/ALT ratio: Method- Calculator method

D-Dimer: Method- Immunoturbidimetric

Ferritin: Method- Chemiluminescence

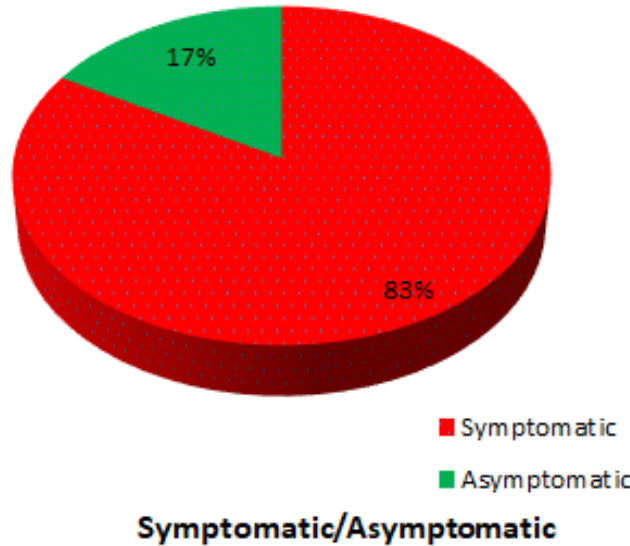
LDH (Lactate dehydrogenase): Method- Lactate to pyruvate.

All the above parameters are analysed using Beckman Coulter AU480 except Ferritin, it is analysed using Beckman Coulter Access 2.

**Statistical analysis**

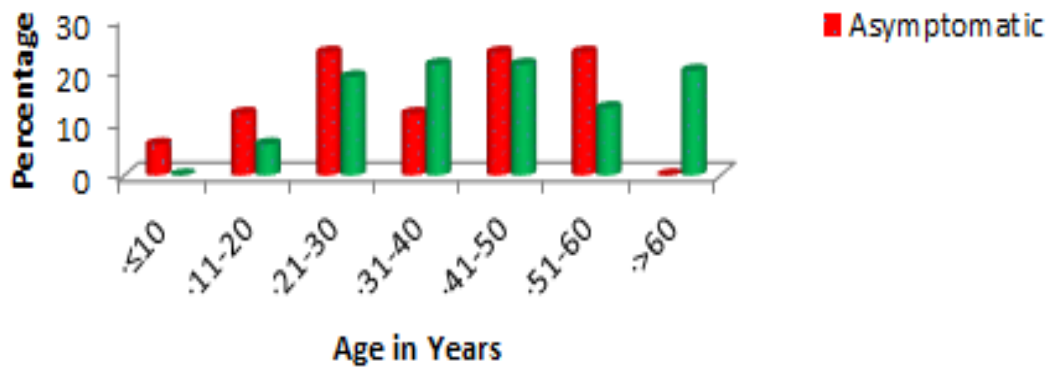
Pie chart to show the classification of the study subjects. Fisher exact test and Chi-square test is been used to find the significance of study parameters on categorical scale between two or more groups

**Results**



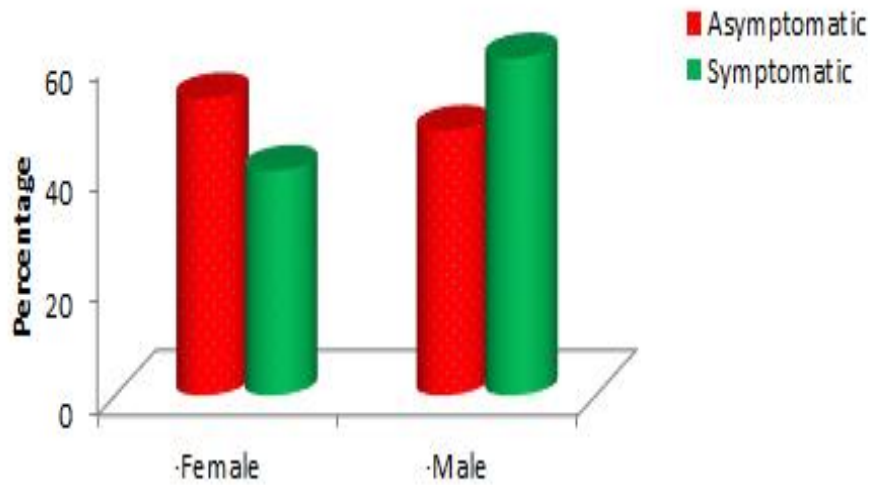
**Fig 1 Distribution of symptomatic and asymptomatic patient**

Total of 102 patients enrolled in our current study were divided into two groups i.e asymptomatic n=17 and symptomatic n=85 which is 17% and 83% of the total population respectively (Fig 1).



**Fig2: Age wise frequency distribution of patients**

Figure 2 represents age wise and gender wise frequency distribution of asymptomatic and symptomatic patients. It's evident from the graph that the number of cases distributed among different age groups were more in the asymptomatic category than symptomatic cases except for the age group > 60 where reverse of the above mentioned pattern is noted. Fisher exact test showed a suggestive correlation with p value of 0.087.



**Fig 3: Gender wise frequency distribution of patients**

Gender Wise frequency distribution shows that the number of females who were tested positive for COVID-19 were asymptomatic and the opposite pattern was noted in case of males i.e more were symptomatic (Fig 3).

**Table 1: AST, ALT, AST/ALT ratio- Frequency distribution of symptomatic and asymptomatic patients studied.**

Variables	Symptomatic/Asymptomatic		Total	P Value
	Asymptomatic	Symptomatic		
<b>AST</b>				
<5	0(0%)	0(0%)	0(0%)	<b>0.005**</b>
5-40	17(100%)	59(69.4%)	76(74.5%)	
>40	0(0%)	26(30.6%)	26(25.5%)	
<b>ALT</b>				
<7	0(0%)	2(2.4%)	2(2%)	0.550
7-56	17(100%)	74(87.1%)	91(89.2%)	
>56	0(0%)	9(10.6%)	9(8.8%)	
Total	17(100%)	85(100%)	102(100%)	
<b>AST/ALT ratio</b>				
<1	10(58.8%)	28(32.9%)	38(37.3%)	<b>p=0.044*</b>
≥1	7(41.2%)	57(67.1%)	64(62.7%)	
Total	17(100%)	85(100%)	102(100%)	

\*Moderately Significant, \*\*Strongly significant, Fisher Exact Test

Fisher exact test (table 1) was done to understand the frequency distribution of AST, ALT and AST/ALT ratio. AST and AST/ALT ratio was found to be more in symptomatic patients with p value 0.005(Strongly significant), 0.044 (Moderately significant) respectively. Although ALT was also found to be more in case of symptomatic group it was found to be statistically insignificant.

**Table 2: LDH, S.Ferritin and D-Dimer- Frequency distribution of patients studied.**

Variables	Symptomatic/Asymptomatic		Total	P Value
	Asymptomatic	Symptomatic		
<b>LDH</b>				
<140	2(11.8%)	6(7.1%)	8(7.8%)	<b>p=≤0.001**</b>
140-280	15(88.2%)	38(44.7%)	53(52%)	
>280	0(0%)	41(48.2%)	41(40.2%)	
Total	17(100%)	85(100%)	102(100%)	
<b>S. Ferritin</b>				
<12	4(23.5%)	5(5.9%)	9(8.8%)	<b>p=0.020*</b>
12-300	11(64.7%)	49(57.6%)	60(58.8%)	
>300	2(11.8%)	31(36.5%)	33(32.4%)	
Total	17(100%)	85(100%)	102(100%)	
<b>D-Dimer</b>				
≤250	0(0%)	33(38.8%)	33(32.4%)	<b>p=0.002**</b>
>250	17(100%)	52(61.2%)	69(67.6%)	
Total	17(100%)	85(100%)	102(100%)	

\*Moderately Significant, \*\*Strongly significant, Chi-square test

Chi-square test in table 2 explains the frequency distribution of patients with respect to various biochemical parameters which includes LDH, S.Ferritin, D-Dimer. All the parameters mentioned earlier were found to be elevated in symptomatic patients more as compared to asymptomatic patients with p value being significant (LDH p value- ≤0.001; S.Ferritin p value- 0.020; D-Dimer p value- 0.002)

**Table 3: Comparison of clinical variables in patients with asymptomatic and symptomatic groups**

Variables	Symptomatic/Asymptomatic (COVID 19)		Total	P Value
	Asymptomatic	Symptomatic		
Age	35.47±15.86	44.53±17.26	43.02±17.29	<b>0.048*</b>
AST	23.47±5.58	40.07±29.52	37.3±27.72	<b>0.023*</b>
ALT	23.88±7.19	33.55±27.41	31.94±25.42	0.153
AST/ALT ratio	1.02±0.24	1.36±0.7	1.3±0.65	<b>0.049*</b>
LDH	184.88±33.64	305.04±160.62	285.01±153.82	<b>0.003**</b>
Serum Ferritin	85.36±26.77	346.52±87.19	302.99±69.86	<b>0.007**</b>

\*Moderately Significant, \*\*Strongly significant, Student t-test ( two tailed, independent)

Student t-test was done to compare various biochemical parameters among asymptomatic and symptomatic study groups. Mean±SD for age, AST, ALT, AST/ALT ratio, LDH, S.Ferritin was found to be more in symptomatic group in contrast with asymptomatic group of patients with p value significant for all the above mentioned variables except ALT. LDH and S.Ferritin showed strong significance with p value 0.003 and 0.007 respectively.

**Discussion**

Early diagnosis of Covid-19 and identifying its progress towards severity is an emergency round the globe due to its mortality and

morbidity. Hence in this study we tried to compare various biochemical parameters like AST, ALT, AST/ALT ratio, D-Dimer, Ferritin and LDH in symptomatic and asymptomatic patients to see if

the disease has an impact on the above parameters and the respective organs in a significant way. Our study showed a significant difference in the levels of liver enzymes; notably ALT, AST and AST/ALT ratio. The elevated liver enzymes can possibly be due to a systemic inflammatory response to COVID infection leading to damage to hepatocytes and bile duct epithelium[14]. De Ritis ratio is proven to be an indicator of liver damage. A ratio of < 1.0 has been universally considered as an indicator of moderate to severe damage to liver following several study findings. A ratio > 1 is considered an indicator of progression to cirrhosis of liver. In the current study a significant portion of symptomatic population were found to have De Ritis ratio of >1 which in turn indicated they are at risk of liver damage. D-dimer, a by-product of fibrin degradation, is used as a biomarker for thromboembolism and as a prognostic marker for critical patients. It is stated that hypoxia in patients with Covid-19 infection with underlying ARDS (acute respiratory distress syndrome) may lead to activation of extrinsic coagulation pathway and increase blood viscosity leading to hypercoagulable state in COVID-19 infection[15]. According to recent studies elevation of D-Dimer >2000 ng/ml is noted to be fatal[16]. Ferritin is a widely used acute phase protein, known to show marked elevations in inflammatory disease. COVID 19 associated with pneumonia and associated inflammatory response can elicit production of ferritin by the macrophages which serve as the prime immune cell in the lung parenchyma. Severe pneumonia with associated systemic inflammation can cause production of inflammatory mediators like IL – 6 which is known to induce ferritin synthesis. LDH sometimes used as an indicator of acute or chronic tissue damage and an inflammatory marker. Thus, the elevated levels of LDH indicates the inflammation that has occurred due to SARS Covid virus infection and its effect on tissues[17].

#### Limitations of this study

Confounding factors like age. Study with larger sample size and case control study design would help in minimizing confounders.

#### Conclusion

This study aimed to compare commonly used biochemical parameters among symptomatic and asymptomatic Covid patients. We found significant difference in the above-mentioned parameters in the two groups. Thus, these routinely used biochemical parameters show promise as potential markers of severity and prognosis. However further studies are required to evaluate the statistical utility of these markers with respect to disease classification and prognostic utility in a larger sample size.

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