A cross sectional study to find out the lipid abnormalities and thyroid profile variations among SARS COVID-19 patients

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Abstract
Background: SARS-CoV-2 viruses are a group of viruses which are responsible for the present pandemic. The clinical presentation of this pandemic has been varied from simple flu like symptoms to severe pneumonia. It is also found to affect multiple organ systems in our body. The aim of this study was to find out the variations in the levels of ferritin, lipid profile and thyroid hormone status among SARS Covid- 19 patients. Materials & methods: This retrospective cross sectional study was done among 312 SARS Covid-19 patients admitted in Chettinad hospital and research Institute during the time period of July-August 2020. Ferritin values, TC (Total cholesterol),TGL(Triglycerides),HDL(High Density Lipoprotein), LDL(Low Density Lipoprotein) and thyroid hormone levels, TSH(Thyroid Stimulating Hormone) FT3(Free Thyroid Hormone)and FT4(FreeT4)were measured among SARS Covid-19 patients. Results: The patients were divided into those admitted in ICU (190) and ward(122). In this study we found out a statistically significant difference in the levels of ferritin,(ward-(439.22+/−380.5) and ICU -542+/−407.34) HDL(High Density Lipoprotein),(ward -33.8+/−15.74 and ICU- 31.04+/−11.78) and TSH(Thyroid Stimulating Hormone)(ward -2.7+/−8.83 and ICU-1.42+/−2.38) levels between patients admitted in ICU and ward. Pearson’s correlation analysis showed a significant positive correlation between ferritin with total cholesterol levels(r value-0.2067,P-value-0.0003),triglycerides(r value=0.336,p value=0.00001),and LDL levels (r value0.16 ,P-value-0.003). Conclusion: Lipid profile shows significant alterations in SARS Covid-19 patients.HDL
levels show a promising role in diagnosing the severity of SARS Covid-19 cases. TSH levels showed a significant difference in the levels between the patients admitted in ICU and ward showing the role of inflammation in the pathogenesis of thyroid dysfunction.

**Key words**: SARS Covid-19, High density lipoprotein, Thyroid profile


**Introduction**

SARS Covid-19 viruses are a family of viruses that can cause respiratory and intestinal diseases in animals and humans. These viruses tend to attack the cells of the upper respiratory tract. It can cause moderate to severe illnesses from cold to pneumonia. While most of the Covid-19 cases are found to be mild, some patients also present with respiratory failure, septic shock and/or multi organ failure and death. Corona virus has been declared as pandemic by the World Health Organization (WHO) having led to deaths and hospitalization of millions of people worldwide. Laboratory diagnostic tests especially biochemical blood tests play a pivotal role in the diagnosis and treatment monitoring of all diseases.

The target organ for corona virus is lungs and respiratory pathways. But it has been found to affect multiple organs in our body showing the systemic involvement of the virus. The pathophysiology behind multi organ involvement may be due to the immune response specific of each organ towards corona virus which in turn point towards the involvement of immunological system in the development of multi organ failure. SARS Covid 19 patients can present as totally asymptomatic, mildly symptomatic or develop severe form of the disease. The incubation period of this disease is approximately 4-7 days the death rate is 2.3%. Centre for disease control and prevention has suggested that elderly patients with associated risk factors such as hypertension, diabetes and cardiac problems had a higher chance of contracting SARS Covid infection. One pathogenic cofactor which is associated with all these risk factors is hypercholesterolemia. Studies on the abnormalities in lipid profile among SARS Covid-19 patients are very few. One study has shown a decrease in the levels of cholesterol among SARS Covid-19 patients when compared to healthy subjects. The status of thyroid profile changes in SARS Covid has not been deciphered still. A case study done by Ruggeri RMet al has shown the development of subacute thyroiditis among a patient infected with SARS Covid -19. The
aim of this study was planned to study the variations in the levels of thyroid hormone status and abnormalities in the lipid profile among SARS Covid-19 patients.

**Materials and methods**

This is a single centre retrospective cross sectional study done over a period of one month from July to August 2020. Inclusion criteria: Details of 312 patients between the age group of 20-80 years of both sex who attended Chettinad Hospital and Research Institute from July 2020-August 2020 diagnosed as SARS Covid-19, were included in the study. The clinical criteria for diagnosis were as per the ICMR guidelines. All previously healthy individuals who were tested positive for SARS Covid-19 virus after examination of SARS-Covid RNA in the nasal swab of the patients by reverse transcriptase polymerase chain reaction by analyzing the E gene and the S gene, in the Microbiology Department of Chettinad Hospital and Research Institute, Chengalpattu were included in the study. Exclusion criteria: Patients admitted to our hospital due to diseases other than SARS Covid-19. SARS Covid-19 patients with previous H/O hemoglobinopathies, previous H/O diabetes, those on glucocorticoids, liver diseases, hematological disorders, HIV infection, pregnant women, patients less than 18 years of age, patients with cancer, were excluded from this study.

Institute ethical committee approval was obtained before commencement of the study. The medical records of all patients were collected and examined. The details of biochemical investigations, clinical, drug history and demographic details of the patients were collected. The patients in our hospital were grouped based on their admission in ICU or ward. The allocation into ICU/ward was based on the ICMR treatment guidelines for SARS Covid-19 patients. Details regarding patient’s age, gender, previous comorbidities, previous drug history, present clinical profile were collected. Data regarding biochemical investigations like ferritin, lipid profile and thyroid hormone levels were obtained from the Laboratory Information System (LIS) of our hospital. Ferritin was measured using the CLIA method in UNICEL-DXI machine, lipid profile was measured in the Seimens Dimensions X-Pand machine. Total cholesterol was measured using Cholesterol oxidase esterase peroxidase method, Triglyceride was measured using enzymatic method, HDL, using PEG method and LDL was calculated using Freidwalds equation. Thyroid hormones (TSH Thyroid Stimulating Hormone), FT3 (Free t3) and Free T4 (FT4) was measured using CLIA method in UNICEL DXI machine in Biochemistry laboratory. Any values above the normal reference interval were considered as abnormal. SPSS version 10 was used to analyze the data. Categorical variables were expressed as percentages and continuous variables as mean and standard deviation. Mean +/- SD was done for all parameters for
312 participants. The whole 312 patients were divided into two groups based on whether they were admitted in ward or ICU. All the parameters were the two groups were compared using independent sample t test. Pearson’s correlation analysis was done to find out the correlation between ferritin and lipid profile parameters. ROC curve was done to find out the diagnostic ability of the parameters. P value <0.05 was considered significant.

**Results:**

Among the 312 SARS Covid 19 patients participating in this study, 108 were females and 204 were males. Among them 190 were admitted in ICU and 122 were admitted in ward. Descriptive statistics showed that the levels of ferritin were higher than the normal reference range and the levels of HDL were found to be lower than the normal reference range. Independent sample t test done to compare the variables between those admitted in ICU and ward showed a significant difference in the levels of ferritin, HDL and TSH levels. Pearson’s correlation analysis showed a significant positive correlation between ferritin and TC, TGL and LDL and significant negative correlation between ferritin and HDL. Receiver operating curve was performed to find out the diagnostic ability of HDL in predicting the severity of SARS Covid. As shown in figure 1, the ROC curve for HDL showed an area under the curve of 0.563.

**Discussion:**

This study was conducted to find out the variations in the levels of ferritin, lipid profile, HbA1c levels and thyroid hormone levels among 312 SARS Covid 19 patients who were admitted in Chettinad Academy of research and education.

Ferritin is considered as a promising marker to assess the severity progression of SARS Covid 19 patients. Ferritin, the storage form of iron has two subunits H & L. The concentration of these units is different from tissue to tissue. H is found to have inflammatory and immunomodulatory function. Ferritin has been found to increase the levels of inflammatory markers in the blood like interleukins. The increase in the levels of serum ferritin during inflammation may be due to its active secretion from the hepatocytes or by macrophages through a non-classical pathway.[9,10,11,] This study showed that the levels of ferritin among patients admitted in ICU(542+/−407.34) were significantly elevated when compared to the patients admitted in ward(439.22+/−380.5) and the difference was statistically significant.( p-value =0.026).(Table 2) Free iron levels alter the coagulation profile leading to vascular thrombosis in various organs of our body.
Lipid profile level alterations in SARS Covid patients has not been much studied. Patients with metabolic disorders are found to have more severe cases of SARS Covid than when compared to the patients with no metabolic disorders. In this study we found out that the levels of Total cholesterol were 138.12+/-43.5mg/dl, triglyceride levels were 137.56+/-64.64mg/dl, HDL cholesterol was 32.1 +/-13.5 mg/dl and LDL levels were 77.29+/-38.5 mg/dl. HDL levels among patients admitted in ICU and ward were 33.8+/-15.7mg/dl and 30.04+/-9.8 mg/dl and the difference was statistically significant.(p value=0.01)(Table:2)Total cholesterol, Triglycerides and Low density lipoproteins did not show much difference between the two groups. Pearson correlation analysis showed a significant positive correlation between ferritin and TC(p value=0.0003),TGL(p value =0.000) and LDL (0.003) and negative correlation was found out between ferritin and HDL levels but was not found to be statistically significant(p value=0.195).(Table 3) Receiver operating curve for HDL shows an area under the curve of 0.538 and is found to have significant ability in assessing the severity of SARS Covid infection (Fig-1)

Dyslipidemia has been associated with many viral diseases like HIV (Human Immunodeficiency virus) and HCV (Hepatitis virus C). Scavenger receptor type I protein acting as a receptor for HDL was affected in certain viral diseases. Cholesterol presents on the membrane of cell play a role in the entry of virus into the cell. [12,13] All these point towards a link between lipid profile alterations in the pathogenesis of viral diseases.

Studies done by Fan J et al; has shown that Total cholesterol, LDL and HDL levels decrease with the increase in the severity of the disease, but in our study the levels of TC and LDL did not show much significant difference between the patients admitted in ICU and ward [14].

HDL plays a role in reverse cholesterol transport process. Additionally it also has other functions like immunomodulatory, antithrombotic and antioxidant actions [15]. The exact mechanism about the decrease in HDL levels in inflammation is not clear. Inflammation has been found to alter the levels of apolipoprotein gene expression in the liver thereby reducing the levels of APO-A1, which is an integral part of HDL [16]. Decreased plasma levels of LCAT (Lecithin Cholesteryl acyl transferase) has also found to alter the HDL levels [17]. Another proposed mechanism is the oxidative modification of Apo-AI due to the inactivation of Paroxanase –I and antioxidant enzyme present in HDL [18,19]. These findings show the role of lipid profile alterations in the progression of this pandemic.

This is the first study to show a correlation between ferritin, a proved inflammatory marker in assessing the severity of SARS Covid 19 and TC, TGL, HDL and LDL levels. This study throws light into the crucial role played by lipids.
in the progression of SARS Covid 19 cases which has been overlooked so far.

TSH levels were found to have a significant difference between patients admitted in ICU (2.7 +/- 8.83) and ward (1.42 +/- 2.38) and the difference was found to be statistically significant. FT3 and FT4 levels did not show much difference among the two groups. A study done by Wei L, Sun S, Xu CH et al; has shown that SARS virus causes extensive injury to the follicular cell of thyroid[20]. Another study found out a significant difference in the levels of TT3 (Total T3), Total T4 and TSH levels between SARS Covid 19 patients and normal controls[21]. Some studies have also shown a decreased staining of the cells secreting TSH hormones in the pituitary gland[22]. The altered thyroid hormone levels may be due to the direct effect of the viral infection or due to the influence of treatment causing an alteration in the hypothalamo-pituitary-thyroid axis. Even though a positive correlation was present between ferritin levels and thyroid hormone values, it was not statistically significant.

**Conclusion:**

From this study we conclude that the lipid profile levels are altered due to SARS Covid infection. HDL values decrease with the increase in the severity of the disease and can be used as a promising maker for finding out the severity of the disease. There is no significant alterations in the levels of thyroid hormone levels among SARS Covid patients except for TSH which shows a significant difference between mildly affected and severely affected patients.

**Limitations:**

This study was a cross-sectional study, we couldn’t compare the data with a control group of normal healthy individuals.

**Acknowledgement:**

I would like to thank Chettinad Academy of research and education for giving us the opportunity to do this study.

**Research Quality and ethical statement:**

The authors of this manuscript declare that this scientific work complies with reporting quality, formatting, and reproducibility guidelines set forth by the EQUATOR Network. This study was approved by the Chettinad Academy of Research and Education human ethical committee.

**Funding:** No funding was received

**Conflict of interest:**

There are no conflict of interests.
Ethical conduct of research:
Institute human ethical committee approval was received before the commencement of the study. The authors followed the EQUATOR network guidelines while conducting this study.

References:


Table: 1 Descriptive statistics of the variables among SARS Covid 19 patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(Yrs)</td>
<td>59.46</td>
<td>11.8</td>
</tr>
<tr>
<td>Ferritin(ng/ml)</td>
<td>501.224</td>
<td>398.12</td>
</tr>
<tr>
<td>Total cholesterol(TC) (mg/dl)</td>
<td>138.12</td>
<td>43.5</td>
</tr>
<tr>
<td>Triglycerides(TGL) (mg/dl)</td>
<td>137.56</td>
<td>64.64</td>
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<tr>
<td>High Density cholesterol(HDL) (mg/dl)</td>
<td>32.1</td>
<td>13.5</td>
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<tr>
<td>LDL(Low density cholesterol) (mg/dl)</td>
<td>77.29</td>
<td>38.5</td>
</tr>
<tr>
<td>HbA1c(Glycated hemoglobin)</td>
<td>7.7</td>
<td>2.15</td>
</tr>
<tr>
<td>FT$_3$ (Free T3) (pg/ml)</td>
<td>2.62</td>
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<tr>
<td>FT$_4$(Free T4) (ng/dl)</td>
<td>1.23</td>
<td>0.44</td>
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<td>TSH(Thyroid stimulating Hormone) (uIU/ml)</td>
<td>1.94</td>
<td>5.84</td>
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</table>

SD-Standard deviation

Table: 2 Independent sample t test for variables done among patients admitted in ICU and ward
<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients admitted in ward</th>
<th>Patients admitted in ICU</th>
<th>P value</th>
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</thead>
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<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
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<tr>
<td>Ferritin (ng/ml)</td>
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<td>542</td>
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<tr>
<td>Total cholesterol (TC) (mg/dl)</td>
<td>135.9</td>
<td>42.8</td>
<td>139.7</td>
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<tr>
<td>Triglycerides (TGL) (mg/dl)</td>
<td>134.6</td>
<td>72.7</td>
<td>139</td>
</tr>
<tr>
<td>High Density cholesterol (HDL) (mg/dl)</td>
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<td>LDL (Low density cholesterol) (mg/dl)</td>
<td>74.57</td>
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<td>79</td>
</tr>
<tr>
<td>FT₃ (free T3) (PG/ML)</td>
<td>2.7</td>
<td>0.53</td>
<td>2.58</td>
</tr>
<tr>
<td>FT₄ (Free T4) (ng/dl)</td>
<td>1.2</td>
<td>0.36</td>
<td>1.24</td>
</tr>
<tr>
<td>TSH (Thyroid stimulating Hormone) (uIU/ml)</td>
<td>2.7</td>
<td>8.83</td>
<td>1.42</td>
</tr>
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</table>

SD: Standard deviation
Table 3  Pearson’s correlation analysis between ferritin, lipid profile and HbA1c

<table>
<thead>
<tr>
<th></th>
<th>Total Cholesterol</th>
<th>Triglycerides</th>
<th>High density lipoprotein</th>
<th>Low density lipoprotein</th>
<th>TSH</th>
<th>FT3</th>
<th>Ft4</th>
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<tbody>
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<td>Ferritin</td>
<td>r value</td>
<td>P value</td>
<td>r value</td>
<td>P value</td>
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<td>P value</td>
<td>r value</td>
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<tr>
<td></td>
<td>0.2067</td>
<td>0.0003</td>
<td>0.336</td>
<td>0.000</td>
<td>-</td>
<td>0.133</td>
<td>0.003</td>
</tr>
</tbody>
</table>

P value <0.05 was considered to be statistically significant, r value – correlation coefficient

Figure 1  Receiver operating curve shows the value of HDL in the prediction of severity of SARS Covid