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Evaluation of Cardiovascular Risk in Post COVID-19 Infection Patients using Atherogenic Index

Divakar Elanchezhian¹; Dr. V.Jayachandran²; Dr. K.S. Premkumar³; Dr. S.Y.Jagannathan⁴

1. Third Year MBBS Student, Government Medical College, Thiruvallur, Chennai, Tamilnadu, India
2. Assistant Professor in Department of Pathology, Government Medical College, Thiruvallur
3. Professor and HOD of Department of Biochemistry, Government Medical College, Thiruvallur
4. Associate Professor of Pathology, Government Medical College Thiruvallur, Chennai, Tamilnadu, India

Corresponding author: Divakar Elanchezhian*

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ABSTRACT

The COVID-19 pandemic, caused by SARS-CoV-2, has not only led to acute health challenges but has also resulted in long-term effects in some individuals, termed "long COVID" or "Post COVID syndrome." This study focuses on evaluating cardiovascular risks in Post COVID-19 patients using the Atherogenic Index of Plasma (AIP), a measure of plasma atherogenicity and an important predictor of cardiovascular diseases.

Objective: To assess cardiovascular risks in Post COVID-19 patients through AIP and understand the impact of COVID-19 on cardiometabolic health.

Methodology: The study included 100 Post COVID-19 patients aged 18–45 years, meeting WHO criteria for Post COVID-19 condition. Blood samples were collected following 8-hour fasting, and lipid profiles were analyzed using automated biochemistry analyzers. AIP was calculated as $\log(\text{TG}/\text{HDL-C})$, and additional lipid parameters such as LDL, VLDL, and total cholesterol were also assessed. Data analysis involved descriptive and inferential statistics, with p-values <0.05 considered significant.

Results: Of the 100 patients, 56% were male and 44% female, all with normal BMI. AIP analysis revealed that 55% of patients had high cardiovascular risk ($\text{AIP} > 0.21$), 16% had intermediate risk ($\text{AIP} 0.11\text{--}0.21$), and 29% had low risk ($\text{AIP} < 0.11$). These findings indicate a significant impact of COVID-19 on cardiovascular health.

Discussion: The study highlights the correlation between COVID-19 pathogenesis and elevated AIP values in Long COVID patients. Comparable studies have demonstrated similar findings, suggesting that decreased HDL-C levels and increased triglycerides due to viral load and inflammation contribute to heightened cardiovascular risk.

Conclusion: This study underscores the importance of monitoring and managing cardiovascular health in Post COVID-19 patients. Identifying those at risk can inform targeted interventions to reduce long-term morbidity and mortality, emphasizing the need for continued evaluation of chronic effects in COVID-19 survivors.

Keywords: COVID-19, SARS-CoV-2, Atherogenic Index of Plasma (AIP), Triglycerides (TG), High-Density Lipoprotein Cholesterol (HDL-C), Cardiovascular disease (CVD)

INTRODUCTION

The COVID-19 pandemic is a global outbreak of coronavirus, an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. World Health Organization (WHO) to characterize the outbreak as a pandemic on 11 March 2020. Globally, as of 20 January 2023, there have been 663,640,386 confirmed cases of COVID-19, including 6,713,093 deaths, reported to WHO and documented in WHO Dashboard. A few of those who recovered from COVID-19 develop persistent or new Symptoms lasting weeks or months; this is called “long COVID”, “Long Haulers” or “Post COVID syndrome.” As per WHO the clinical case condition of Post COVID-19 condition occurs in individuals with **a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis.** Common symptoms include **fatigue, shortness of breath, cognitive dysfunction** but also others which generally have an **impact on everyday functioning.** Symptoms may be **new onset**, following initial recovery from an acute COVID-19 episode, or **persist** from the initial illness. Symptoms may also **fluctuate** or **relapse** over time. Atherogenic index of plasma (AIP) is an unconventional lipid ratio that shows the logarithm of the molar ratio of TGs to HDL-C. It is a measure of plasma atherogenicity due to a positive correlation with lipoprotein particle size, cholesterol esterification rates, and remnant lipoproteinemia. AIP not only accurately reflects the relationship between protective and atherogenic lipoproteins, but it is also a potent predictor of atherosclerosis and coronary heart disease. **Although Post COVID-19 infection patients are very susceptible to cardiovascular morbidity and mortality only very few studies have been conducted to evaluate the cardiovascular risk in them using Atherogenic Index.**

REVIEW OF LITERATURE

The COVID-19,2 pandemic has brought attention to its impact on various physiological systems, including the cardiovascular system. One notable effect is the alteration of plasma lipid levels, which are crucial indicators of cardiovascular health. Evaluation of long term effects of COVID – 19 in Long COVID patients is the major motto of this study^{3,4}. Studies have shown that COVID-19 can lead to dyslipidemia, characterized by elevated levels of total cholesterol, lowdensity lipoprotein cholesterol (LDL-C), and triglycerides, along with decreased levels of high-density lipoprotein cholesterol (HDL-C)^{5,6}. These changes are believed to result from the inflammatory response triggered by the virus, as well as the effects of certain medications used in COVID-19 treatment^{7,8,9}. The dyslipidemia observed in COVID-19 patients may contribute to an increased risk of cardiovascular events, highlighting the importance of monitoring lipid levels in these individuals and implementing appropriate management strategies. Studies show that those patients who have severe COVID infection had lower HDL cholesterol levels and higher triglyceride levels. Basically, factors such as age, body mass index greatly influence the lipid profile in Post – COVID patients. The measure that will be evaluated in this study is atherogenic index, which is a significant evaluation parameter in the case of lipid profile analysis and cardiometabolic health and the extent of formation of atheromas. The frequency of major adverse cardiovascular events (MACEs) can be evaluated⁷. Very few studies have been conducted in correlation with atherogenic index in general populations. As journals indicate the significant rise of triglycerides and reduction in HDL – cholesterol in Post – COVID, this study will be evaluating the atherogenic index in Post COVID population rather than the general population to extensively know about the ill – effects of the SARS – CoV – 2 viruses on the cardiovascular health^{8,9}.

AIMS AND OBJECTIVES

To evaluate the cardiovascular risk in Post COVID-19 condition Patients using Atherogenic Index of Plasma.

METHODOLOGY

In the undertaken study 100 individuals with Post COVID 19 Conditions satisfying the WHO criteria - 4 details were interpreted. The cases will be taken from laboratory - the blood samples from the cases. The inclusion criteria includes individuals of both male and female genders within the age group 18 to 45 years and must satisfy the WHO criteria - 4 of Post COVID – 19 infection (Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARSCoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others and generally have an impact on everyday functioning. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms may also fluctuate or relapse over time). The study excludes individuals not satisfying the WHO criteria, patients with COPD, pulmonary thromboembolism, chronic renal failure, pregnancy, myocardial infarction, atrial fibrillation, cerebrovascular disease. It also excludes patients who are known smokers/alcoholics/on statin therapy and obese individuals whose BMI exceeds 30 Kg/m².

The patients attending the Post COVID OPD and fulfilling the inclusion criteria will be included in the study. The blood samples will be collected from the patients with 8 hours fasting. A fully automated biochemistry analyser will be used to calculate whole blood counts e AIP was calculated with the formula;

AIP= log [triglyceride (TG) /high-density lipoprotein (HDL-C)].

Estimation of HDL-C:

From the sample obtained, HDL-C was estimated using Direct HDL method using an automated analyzer. The major principle is based on the assay that is based on a modified polyvinyl sulfonic acid (PVS) and polyethylene glycol-methyl ether (PEGME) coupled classic precipitation method with the improvements in using optimized quantities of PVS/PEGME and selected detergents. LDL, VLDL and chylomicron (CM) react with PVS and PEGME and the reaction results in inaccessibility of LDL, VLDL and CM by cholesterol oxidase (CHOD) and cholesterol esterase (CHER). The enzymes selectively react with HDL to produce H₂O₂ which is detected through a Trinder reaction.

HDL + LDL +VLDL +CM ----- HDL + (LDL + VLDL + CM)

PVS/PEGME

CHOD, CHER

HDL ----- Fatty acid + H₂O₂

2H₂O₂ + 4-AA + TODB ----- Quinone + 5H₂O

The expected values are about 30 – 60 mg/dl in adult males and 35 – 75 mg/dl in adult females. The principle of estimation of triglycerides is that triglycerides are first hydrolyzed by lipoprotein lipase to glycerol and free fatty acids. Glycerol is then phosphorylated by adenosine triphosphate (ATP) forming glycerol-3-phosphate (G-1-P) and adenosine-5'-diphosphate (ADP) in the reaction catalyzed by glycerol kinase (GK). The normal range of triglycerides is less than 150 mg/dl. The parameters analysed in this study are majorly age, BMI, Atherogenic Index (log TG/HDL), VLDL, LDL-C, HDL-C, TG levels.

The collected study data was entered in Microsoft Office Excel 2013 and analyzed using SPSS software version 26. The descriptive statistics include continuous variables that are expressed as mean and standard deviation. Description of categorical variables are expressed as frequency and proportion. The test of significance is CHI SQUARE TEST will be used in order to compare two categorical variables. Unpaired t test will be used to compare two means. If a continuous variable is

measured in several time period in two groups REPEATED MEASURES ANOVA will be used. All tests are two – tailed, with results considered statistically significantly if the p – value was less than 0.05.

RESULTS:

On evaluation of 100 samples, the following are the results:

PARAMETER	MEAN (95% CI)	Standard Deviation
Age	35.38 (34.1 - 36.7)	6.7
Height (m)	1.62 (1.43 – 1.81)	0.099
Weight (kg)	64.27 (62.82 – 65.72)	7.42
Body Mass Index	24.57 (24.23 – 24.91)	1.73
Triglycerides (mg/dl)	217 (205.83 – 228.17)	57
HDL – C (mg/dl)	54.4 (52.42 – 56.38)	10.1
LDL – C (mg/dl)	153.3 (147.34 – 159.26)	30.4
VLDL (mg/dl)	42.5 (39.87 – 45.13)	13.4
Total Cholesterol (mg/dl)	251.96 (243.04 – 260.88)	45.5
AIP	0.234 (0.207 – 0.261)	0.14

Over the period of September 2023 till November 2023, 100 samples were analysed from the laboratory of those patients who satisfied the Post COVID – 19 criteria as per WHO and satisfied the inclusion and exclusion criteria of the study. Of the total patients, 44% were females and the remaining 56% were of males satisfying the criteria. The patient selection had a proper normal BMI range such that no other external factors such as obesity influence the study parameters. On analysing their total lipid profile, the atherogenic index of plasma (AIP) was calculated using the above formula and we can interpret that 55% of the patients have increased risk of cardiovascular disease with AIP values ranging more than 0.21. 16% of the individuals have intermediate cardiovascular risk with AIP values ranging from 0.11 to 0.21. The remaining 29% of patients have their AIP values below 0.11 thereby having a low cardiovascular risk. This signifies the presence of impact caused by COVID -19 on the cardiometabolic health of the individual.

DISCUSSION

In the study undertaken, the relationship between the pathogenesis of COVID – 19 and the impact on the cardiovascular risk due to the same is investigated in Long COVID patients. The results depict significantly higher values of atherogenic index of plasma in the Long COVID patients without any external factors that can influence the cardiovascular health. As COVID – 19 had created a worldwide deadly pandemic it is important to evaluate not only the acute effects but also the long-term chronic effects of COVID – 19 on various organ systems. In our study, not only parameters required for AIP are alone calculated (TG and HDL – C), but also VLDL, LDL and total cholesterol values are also evaluated to get a better prognosis in the results. A similar study was conducted by Masana et al. which depicted the baseline values of AIP in hospitalized patients due to COVID – 19. That study also added that hypoxemia could also be a reason for increased sympathetic discharges increasing the viral load and thereby decreasing the HDL cholesterol levels but this study had a comparatively worse prognosis. The values evaluated in our study suggests that AIP values that are increased indicate the increased risk of cardiovascular diseases due to the viral load of COVID – 19.

CONCLUSION

Our data not only evaluates the cardiovascular risk in Post COVID patients but also helps to identify the Long COVID patients amongst the COVID – 19 survivors and also helps to improve the treatment options and also prevention techniques to treat the co – morbidities that can occur due to

the persistent viral load of SARS-CoV-2 virus and can also significantly help in reducing the mortality of COVID – 19 survivors. Not only the acute effects of COVID – 19 are lethal, even certain long-term effects of the viral load can cause high levels of morbidity and mortality in patients which can be highly prevented with the use of our study and similar such studies.

SUMMARY

COVID Pandemic has caused severe morbidity and mortality in the world. Very few research studies have been conducted in Post COVID condition patients. These individuals suffer with the symptoms even after many months of the disease onset which affects their daily lifestyle. Due to the disease pathogenesis Post COVID-19 Condition patients are susceptible to cardiovascular morbidity. Atherogenic Index (AIP) is a simple lab parameter to assess the cardiovascular risk due to atherogenicity. **Significant elevated AIP levels in Post COVID-19 Condition cases will signify the importance of periodic cardiac monitoring in Post COVID-19 Condition patients and reduce the cardiovascular mortality.**

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