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Review Article

Atherogenic index of plasma in COVID-19 infection

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Abstract

The atherogenic index of plasma (AIP) is calculated as the logarithmic conversion of the triglyceride to high density lipoprotein-cholesterol ratio [$\log_{10}$(Triglyceride/HDL-cholesterol)]. AIP values of <0.11 are considered lower risk, between 0.11 and 0.21 are considered medium risk, and >0.21 are considered higher risk. AIP produced by triglycerides and HDL-cholesterol, avoiding the inconsistent assessment of different lipid components and simplifies task of a marker in clinical application. It has been reported that AIP value is an important predictor for cardiovascular diseases and atherosclerosis. COVID-19 is a viral infection that started in 2019 and quickly caused a pandemic. And it continues to cause death, especially in people with pre-existing comorbidities. COVID-19 infection is associated with lipid levels and cardiovascular disease. Studies have shown that AIP levels are high in COVID-19 patients. In addition, studies have found that high AIP values are associated with prolonged hospital stay, poor prognosis, and increased disease severity. Reporting of AIP value in laboratory results may alarm clinicians for atherosclerosis and cardiovascular diseases.

Keywords: Atherogenic index of plasma, cardiak risk, COVID-19.

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INTRODUCTION

1. Atherogenic index of plasma (AIP)

AIP was first described by Dobiasova and Frohlich as a powerful and sensitive index reflecting the interaction between atherogenic and non-atherogenic lipoproteins. The AIP value is calculated as a base 10 logarithmic conversion of the triglyceride to high density lipoprotein-cholesterol ratio [AIP= $\log_{10}$ (Triglyceride/HDL-cholesterol)]. AIP values of <0.11 are considered lower risk, 0.11 and 0.21 are considered medium risk, and > 0.21 are considered higher risk (1). AIP is a powerful marker to predict the risk of atherosclerosis and cardiovascular disease (CVDs) (2-4). Compared with the routine lipid profile, AIP has been proven to be a better predictive indicator of atherosclerosis than low density lipoprotein-cholesterol (LDL-cholesterol) (1). AIP has also been associated with insulin resistance, diabetes mellitus (5), metabolic syndrome (6), and obesity (7). AIP avoids inconsistent evaluation of different lipid components and simplifies the routine estimation task (8).

2. Atherogenic index of plasma in cardiovascular diseases

One of the most important known risk factors for CVDs is dyslipidemia. It has been shown that both a decrease in HDL-cholesterol and an increase in total cholesterol and LDL-cholesterol levels contribute to the progression of atherosclerotic process (9). Due to the small particle size, small-density LDL particles (sdLDL) can penetrate artery walls, accumulate to be easily stored and oxidized to oxidized-LDL compared to LDL particles. When oxidized-LDL is phagocytosed by macrophages, macrophages transform into foam cells, causing atherosclerosis and CVD. The clinical use of sdLDL particles as a marker to predict atherosclerosis (10). But, measurement of sdLDL is limited in clinical routines due to the detection method and expensive costs (1). As noted in the their studies, the AIP value is inversely proportional to the circumference of the LDL particles and reflects the size of the sdLDL particles (1). It is also accepted that lipid ratios such as total cholesterol/HDL-cholesterol and LDL-cholesterol/HDL-cholesterol are predictive for CVD (9, 11). However, studies have revealed that the AIP value is a more reliable marker for CVD risk factors compared to traditional lipid parameters (12).

3. COVID-19 infection and lipids

SARS-CoV-2 was first detected in 2019 in China. COVID-19 infection, which is a coronavirus belonging to the zoonotic virus family and caused by an RNA virus, SARS-CoV-2, was declared a pandemic by the WHO on March 2020. COVID-19 is characterized by increased morbidity and mortality (13). In the COVID-19 process, there are different three stages that differ in the severity of the course as mild- moderate- severe, covering the period from early infection to recovery or death (14). Bae et al. evaluated the impact of CVD on the prognosis of patients with COVID-19, in a meta-analysis. They reported that the factors that worsen the prognosis of COVID-19 are arterial hypertension, diabetes and other CVDs (15). The results of these studies reported that the presence of CVDs significantly worsened the prognosis of COVID-19 patients (16).

Cholesterol plays an important role in the entry of the SARS-CoV-2 virus into host cells (17). In a study, it was shown that the depletion of membrane-bound cholesterol, in cells expressing Angiotensin Converting Enzyme-2 (ACE-2), caused a decrease in the infectivity of SARS-CoV-2, because of the binding of spike protein was reduced by 50% (18). Systemic total cholesterol concentration is increased in patients with dyslipidemia, which may result in an increased number of ACE-2 receptors in the lipid rafts of cells and facilitate their penetration by SARS-CoV-2 (17). Some studies have reported a relationship between reductions in HDL-cholesterol levels and the severity of COVID-19 (19, 20). Zaki et al. (21), in their study, total cholesterol, HDL-cholesterol and LDL-cholesterol levels were found to be consistently lower in the group infected with COVID-19 compared to the control group, and they showed that HDL-cholesterol was significantly lower in patients with increased disease severity. Fan et al. (22) and Wei et al. (23) reported same findings in their studies. In studies of 21 and 597 patients, COVID-19 patients had lower total cholesterol and LDL-cholesterol than healthy subjects. They found lower levels of lipids levels in severe cases. Their results could be explained by changes in cholesterol metabolism due to COVID-19, changes in lipids due to hyperinflammation, LDL-cholesterol leakage due to increased vascular permeability, and accelerated lipid degradation (24).

4. Studies on COVID-19 infection and AIP

The relationship between the AIP value and COVID-19 was examined by the researchers, and the studies found relationships between these two (25-29) (Table 1).

Table 1: Study finding of the related articles in the literature

Authors (References)	Year	Study findings
Karaseva et al. (25)	2022	Severe COVID-19 patients had significantly increased levels of triglyceride and AIP compared with patients with moderate and mild course.
Sastrawan et al. (26)	2022	AIP is associated with prolonged hospital stay in COVID-19 patients with type 2 DM.
Taha et al. (27)	2022	AIP was found to be high in COVID-19 patients.
Evdokimova et al. (28)	2021	AIP was higher in subjects with severe course compared to subjects with moderate and mild course
Turgay Yıldırım et al. (29)	2021	AIP values are statistically higher than the surviving group. >0.6285 AIP can predict mortality for COVID-19. AIP is emerging as a candidate to predict the need for pneumonia, intubation, and intensive care.

In the study conducted by Karaseva et al. (25); they found that severe COVID-19 patients had increased AIP and triglyceride levels and lower HD-cholesterol levels. In this cross-sectional study, 270 patients aged 26-84 years who had COVID-19 in the previous two months were included. They found significantly higher triglyceride and AIP levels in patients with severe COVID-19 compared to patients with moderate and mild course.

In the study by Sastrawan et al. (26) an analytical observational study was conducted among COVID-19 subjects with comorbid type 2 DM. They reported that AIP is associated with prolonged hospital stay in COVID-19 patients with type 2 DM. And they noted a strong correlation between AIP and prolonged hospital stay in these patients.

In the study conducted by Taha et al. (27); they showed that total cholesterol and HDL-cholesterol levels in COVID-19 subjects were significantly reduced than in control subjects. Triglyceride, VLDL-cholesterol and AIP were found to be significantly higher in COVID-19 patients compared to control subjects. In their study, they showed that risk factors such as AIP are increased for CVD in patients with COVID-19 infection. Therefore, they stated that lipids can fulfill a vital physiological function in patients infected with COVID-19.

In another study, patients were divided into three subgroups as mild, moderate and severe. In their study, they reported that patients in the group with moderate and severe course of novel Coronavirus infection had higher AIP and HDL-cholesterol values. A moderate chance of a COVID-19 course is associated with a severe course with an increased AIP ≥ 0.11 and HDL-cholesterol level <40 mg/dL. They stated that the chance of a severe course of COVID-19 is associated with AIP ≥ 0.11 and HDL-cholesterol level <40 mg/dL (28). Turgay Yıldırım et al. (29) found in their study that the total cholesterol, HDL-cholesterol and LDL-cholesterol levels of the patients in the surviving group were higher than those of the deceased group. They found that the AIP and triglyceride levels of the patients in the deceased group were statistically higher than those who survived. They showed that AIP levels greater than 0.6285 could predict in-hospital mortality for COVID-19 subjects. In addition, AIP; indicated that it emerged as a good candidate to be used as an early marker to predict the need for pneumonia, intubation, and intensive care. Therefore, they found high AIP levels to be associated with poor prognosis. They stated that regular control of AIP in COVID-19 could improve the management of these subjects and prevent the worsening of the disease.

CONCLUSION

COVID-19 infection is associated with altered lipid levels and cardiovascular disease. Studies have shown that AIP is high in COVID-19. In addition, studies have shown that high AIP values are associated with prolonged hospital stay, poor prognosis and increased disease severity. Reporting of AIP value in laboratory results may alarm clinicians for atherosclerosis and cardiovascular diseases.

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