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Study Significance of Low Plasma Homocysteine or Hypohomocysteinemia and Some Parameter to Syndrome Associated with COVID-19 in Basrah City, Iraq

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Abstract: The increasing interdependence between the countries of the world has led to an increase in the risks faced by societies in general. The COVID-19 pandemic, for example, has transcended national borders, affecting people regardless of nationality, level of education, income or gender. As for its consequences, it has affected the most vulnerable groups. In this study, we have considered the significance of low plasma homocysteine or hypohomocysteinemia and some parameters of the syndrome associated with COVID-19. Just as an increase in the level of homocysteine in plasma has a negative effect on the heart and blood vessels, its decrease may put the health of those who suffer from it at risk.

Homocysteine is known to be the natural mediator of the conversion of methionine to cysteine; hence, the danger, as the latter is necessary for the production of glutathione, taurine and sulphate. In this study, homocysteine and some indicators of COVID-19 syndrome were examined using ELISA kit and other methods. The homocysteine level in the serum of people who recovered from COVID-19 was found to be lower than in normal and healthy people. Thus, it indicates that people who have been cured may suffer from hypohomocystinemia. We also study some parameters, such as ALP, GOT, GPT, Glucose level and HDL, cholesterol. The results showed a significant decrease in the level of GOT enzyme and HDL level.

Key words: COVID-19, hypohomocysteinemia, ALP, GPT, GOT, HDL.

Introduction

According to the report of China-WHO Joint Mission (2020), severe acute respiratory syndrome (SARS-CoV-2) is an infectious disease caused by the COVID-19 coronavirus. The capital of China's Hubei Province is the first place where the disease was first discovered in 2019, and then began to spread globally as it became officially known as 2019-20 Corona virus pandemic (Hui et al., 2020). According to the Center for Disease Control and Preventio (2020), the common symptoms of COVID-19 are difficulty in breathing and dry cough, while the least common ones are muscle pain, phlegm production and sore throat.

Although most cases show mild symptoms, there have been development of some cases in which the infectious virus has also caused pneumonia as studies have shown, thereby leading to the emergence of multi-organ failure. In March 2020, the death rate for diagnosed cases was 4.4%. In general, the statistics indicate that it ranges from 0.2 percent to 15 percent, depending on the age group in addition to the health problems of each individual.

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Statistics indicate that the cases of COVID-19 have reached about 1010,000 in more than two hundred countries, and the reason is this deadly virus. The results also indicate that the deaths reached about 53,000 cases, with the recovery of nearly 211,000 individuals, at the beginning of April 2020 (Worldometer, 2020).

Respiratory droplets produced during coughing are the main method and reason for the spread of the virus from one person to another (Centre for Disease Control and Prevention, 2020). Touching contaminated surfaces and then touching one's face may be another cause of spread (Centre for Disease Control and Prevention, 2020). This virus can remain on surfaces effectively and actively for up to three days, as studies have shown the possibility of transmitting infection after a period of time (National Institutes of Health, 2020).

In general, and according to Centers for Disease Control and Prevention (2020), the time period that the disease takes between exposure and the appearance of symptoms extends from 2 to 14 days. The diagnosis is made by taking a nasopharyngeal swab for reverse transcription polymerase chain reaction (rRT-PCR), which is the standard method for diagnosing this infection. The infection can also be diagnosed from a combination of symptoms and factors, and a chest CT scan that shows features of pneumonia (Jin et al., 2020)

Although until mid-May 2020, the effects of the COVID-19 pandemic were not understood, however, the evidence indicates that compared to other events and diseases such as traffic accidents and AIDS caused by HIV and malaria, the death rate was higher. The virus could become the leading cause of death in countries with a high incidence of cancer and coronary artery disease due to the peak of the current wave of COVID-19 (Seom, 2020).

As for workers in the field of health and emergency services, the statistics indicate that an increase in the cases has negatively impacted them all over the world due to the momentum, and also because they are compelled to pay attention to the cases resulting from the pandemic instead of being preoccupied with their main work. Reports indicate that during April 2020 alone, COVID-19 caused nearly 200,000 deaths. The current crisis may be the cause of the death of more than 600 children per day in 118 low and middle-income countries and even in developed countries during the coming months due to the low rate of vaccinations for children, which is one of the health consequences of the pandemic (Santoli et al., 2020).

Increased homocysteine levels are the cause of many other clinical conditions, including neural tube defects, kidney failure, complications of diabetes, osteoporosis, rheumatoid arthritis, spontaneous abortion, alcoholism, placental abruption, neuropsychiatric disorders, and non-insulin-dependent diabetes mellitus (McCully, 2007).

Methionine is a non-protein amino acid that contains sulphur in its chemical structure, and homocysteine is one of its derivatives, which was discovered in the early 1930s by the scientist Du Vigneaud and was abbreviated as Hcy (McCully, 2007).

Hcy exists in different forms. It is present as the reduced form with a free sulphhydryl (SH) group, as homocysteine or the oxidised form with the disulphide (S-S) linkage, as Hcy thiolactone - a cyclic thioester, as a dimer with cysteine and as adducts (Latin for a product of 2 or more molecules). The adducts are formed by N-homocysteineylation, where Hcy thiolactone binds to lysine residues of proteins (Jakubowski, 2008; Satyanarayana, 2006).

The first pathway through which the Hcy acid enters depends on vitamin B6 and is called the trans-sulphur pathway and the result is cysteine, and the second is called remethylation and produces methionine, which depends on vitamin B12, which proves that methionine is the only source of homocysteine (Satyanarayana, 2006).

Kilmer McCully largely contributed to the present-day knowledge of the biomedical significance of Hcy. He described the history of the evolution of Hcy from being an innocuous amino acid to a causative factor of disease. Some important milestones in the history of Hcy in relation to the disease are briefly described (McCully, 2001).

A deficiency of homocysteine in the blood leads to a decrease in the availability of cysteine in the blood. This deficiency of cysteine leads to a reduction in the production of sulphate, taurine and glutathione, and this last compound (glutathione) is an antioxidant necessary to protect cells from oxidative stress (Vitvitsky, 2003). Alcohol consumption also leads to significant changes in homocysteine metabolism in addition to its role in decreasing cysteine availability and reducing glutathione synthesis by promoting non-reversible catabolism of cysteine to taurine via hypotaurine (Jung, 2003). Hypohomocysteinemia is exacerbated by conditions that cause an increased demand for any of the sulphur compounds produced by homocysteine, since many drugs and xenobiotics require more sulphur compounds for conjugation and disengagement in the body (Liu et al., 1996).

The disturbance in the levels of liver function enzymes shown by those infected with the emerging corona virus indicates that this virus does not affect only the respiratory system, but affects the various organs of the body, especially the liver, as it was reported in a study that at least half of the patients showed abnormalities in the levels of liver enzymes (Fan et al., 2020). Studies conducted in recent intervals are suggestive of ~15% to ~45% of sufferers who have reported encountering manifestations of liver damage during infection (Zhang et al., 2020)

Individuals with high blood pressure, diabetes mellitus (DM) and severe obesity (BMI 40 kg/m^2) are more likely to be infected and most vulnerable to complications and death from COVID-19 (Xu et al., 2020).

Methodolgy

The study was conducted on 37 people who had recovered from COVID-19 (17 men, 20 women) and 33 (15 women, 18 men) healthy adults of different ages enrolled in the study. Serum homocysteine levels were measured using Homocysteine ELISA technology with ELISA kit assay. All patients recovered from COVID-19 and control (volunteers) chosen from hospital staff. As for the other parameters, (GOT, GPT, ALP), they were measured by kinetic interaction method and (Glucose, CHOL, HDL) measured by end point enzymatic colorimetric method.

A strategy was used to describe all continuous variables as mean and standard deviation in addition to the mean and interquartile range after the data were normally distributed in some laboratory tests. The statistical analysis was performed by the Statistical Package for Social Sciences (SPSS version 25.0).

Results and Discussion

Total homocysteine in human plasma was first determined with ELISA kit assay. The obtained result listed in Table 1 show a highly significant decrease in homocysteine in people who had been cured from COVID-19 with a mean value of 10.98 compared with the control group 59.67. These findings explore a strong correlation between the reduction of homocysteine levels and recovery of COVID-19 patients.

It is very well known that a low level of homocysteine in blood hypohomocysteinemia causes cardiovascular disease Hypohomocysteinemia which is also found to cause the progression of atherosclerosis in cardiovascular diseases (Ganguly & Alam, 2015). Thus, this may reduce the hospitalisation and recovery period.

Several factors contribute to low levels of homocysteine, or hypohomocysteinemia. It could be the result of a metabolic insult that causes the body to produce more GSH than normal, a decreased level of MTHFR enzyme, a decreased intake of the amino acids methionine and cysteine and an increased intake of vitamins folate and B12, or increased detoxification of xenobiotics through the phase II liver reaction sulphation (Kalantar-Zadehetal., 2004).

In COVID-19 patients, most drugs used are antbiotics. This may lead to a variety of clinical disorders due to low levels of homocysteine.

The second phase of liver detoxification is one of the body's main uses for sulphate and taurine. The sulphur pathway is required for the removal of steroid hormones, phenolic compounds, and other compounds, while taurine is involved in the formation of bile acids.

When hypohomocysteinemia appears as a specific variable in some presentations, it is a major feature of the complex of malnutrition and inflammation, which indicates poor outcomes in patients on maintenance hemodialysis (Kalantar-Zadeh, 2005).

The link between homocysteine and cardiovascular disease was discovered in the late 1960s when Dr. Kilmer McCauley met two children with homocysteine (a rare genetic condition) who had advanced atherosclerosis, even though coronary plaques do not contain fat. Elevated levels of homocysteine, the intermediate substance for converting the amino acid methionine to cysteine, is an independent risk factor for coronary heart disease, stroke, and other vascular diseases.

The glucose level in human plasma was determined by the obtained result listed in Table 2, which shows that there is no significant relation in glucose level in people who had been cured of COVID-19.

Cholestrol and HDL levels in human plasma were determined from the obtained result listed in

Table 1: Level of homocysteine in serum control and recovery from COVID-19

	Group	*N*	*Mean*	*Std. Deviation*	*P-value*
Homocysteine	Total (recovery from COVID-19)	37	10.98651	16.299533	0.000
	Total (control)	33	59.67821	39.943840	

Table 2: Level of glucose in serum control and recovery from COVID-19

	Group	*N*	*Mean*	*Std. Deviation*	*P-value*
Glucose	Total (recovery from COVID-19)	44	100.77	20.446	0.090
	Total (control)	44	94.36	14.010	

Table 3: Level of cholestrol and HDL in serum control and recovery from COVID-19

	Group	*N*	*Mean*	*Std.Deviation*	*P-value*
CHOL	Total (recovery from COVID-19)	44	202.07	47.988	0.192
	Total(control)	44	189.82	38.944	
	Total (recovery from COVID-19)	44	57.070	13.6802	
HDL	Total(control)	44	49.789	15.8492	0.023

Table 4: Level of GPT, GOT, ALP in serum control and recovery from COVID-19

	Group	*N*	*Mean*	*Std. Deviation*	*P-value*
GPT	Total (recovery from COVID-19)	44	29.52	14.696	0.170
	Total(control)	44	25.36	13.449	
GOT	Total (recovery from COVID-19)	44	27.45	7.254	0.010
	Total(control)	44	22.50	10.055	
ALP	Total (recovery from COVID-19)	44	233.91	85.529	0.803
	Total(control)	44	229.68	72.615	

Table 3. Cholestrol shows no significance in the result but HDL show significance in the result in people who had been cured of COVID-19 with a mean value 57.070 compared with control group 49.78. According to research published in the journal *Arteriosclerosis, Thrombosis and Vascular Biology*, people who have high levels of C-reactive proteins after a heart attack may show negative result for high HDL, which leads to an increased risk of heart disease. The liver produces C-reactive proteins in response to high levels of inflammation in your body. Instead of acting as a preventative factor in heart health (Kalantar-Zadeh, 2005).

Enzyme level in human plasma was determined from the obtained result listed in Table 4. AST shows to be significant in results in people who had been cured of COVID-19 with a mean value of 27.45 compared with the control group at 22.50. High levels of AST enzyme can be caused by liver diseases, myocardial infarction (heart attack), acute pancreatitis, acute haemolytic anaemia, trauma (especially severe burns), acute kidney failure, diseases of the muscular and skeletal systems, and other causes. Sometimes the cause of the high AST result is obvious, e.g., if acute physical trauma is present. Many of the cases are asymptomatic, such as liver diseases. Unless the cause is obvious, more diagnostic work is called for.

The reason for the high level of the enzyme GOT can be attributed to the medicines that the person with COVID-19 takes, such as the antibiotic azithromycin, which has a defect in the work of the liver, in addition to taking any other medicines that are metabolized inside the liver.

According to outcomes detected in our study population, the *P* value of elevation of GOT was significant followed by ALP and ALT elevation and GPT.

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