DOI: 10.7860/JCDR/2022/55477.16744

Original Article

Biochemistry Section

Correlation of Lipid Profile with Inflammatory Markers among COVID-19 Positive Patients: A Retrospective Study

ASHA KUMARI[1], YUTHIKA AGARWAL[2], SANGEETA BHATTACHARYA SINGH[3], SHIKHAA MAHAJAN[4], VIVEK SHARMA[5]

ABSTRACT

Introduction: Lipids are fundamental biomolecules of the body. Infections like Coronavirus Disease-2019 (COVID-19) with intricate immune response in some patient's leads to acute complications by affecting metabolic pathways at multiple levels. Metabolism of cholesterol, triglyceride and High Density Lipoprotein-Cholesterol (HDL-C) is deranged by cytokines and multiple inflammatory mediators. The sex differences in lipid metabolism may contribute in susceptibility, severity and outcome COVID-19. Performing lipid profile in COVID-19 patient may help in assessing severity and prognosis of disease.

Aim: To assess the relationship between lipid profile and inflammatory markers in COVID-19 patients and also to evaluate the gender-wise differences in lipid parameters and their correlations with inflammatory markers.

Materials and Methods: This retrospective study was conducted in Department of Biochemistry at SHKM, GMC, Mewat, Haryana, India (tertiary care health centre) on COVID-19 positive patients attending Outpatient Department (OPD) and Inpatient Department (IPD), from October 2020 to December 2020. The data of 85 patients with COVID-19 positive, confirmed by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and who were prescribed for lipid profile along with C-Reactive Protein (CRP) and serum ferritin were included in the study. Serum total cholesterol, triglyceride, HDL-C, CRP and ferritin were measured in the subjects. Data was statistically analysed using Student's t-test and Pearson's correlation coefficient.

Results: Total 85 (46 males and 39 females) COVID-19 patients were included in the study. Mean age in male and female patients were 43.02±15.52 years and 42.02±15.25 years, respectively with a range of 5-82 years. Mean value of Serum triglycerides, HDL-C and total cholesterol was 204.94±141.27 mg/dL, 42.97±13.38 mg/dL and 187.058±45.75 mg/dL, respectively. Serum triglycerides were statistically significantly higher in males than females (p-value=0.0413). The HDL-C, however, was significantly higher in females than males (p-value=0.0006). In male patients, r-value between cholesterol and CRP was -0.3538, and p-value was 0.016. Ferritin had a significant negative correlation with HDL-C (r-value=-0.3578, p-value=0.00079). Weakly positive correlation was noted between triglyceride and ferritin (r-value=0.2285, p-value=0.035).

Conclusion: High levels of serum triglycerides, low total cholesterol, and low HDL-C correlates with inflammatory markers like CRP and ferritin in COVID-19 patients. Lipid profile may be used as a potential marker in all COVID-19 patients in assessing prognosis of disease.

Keywords: Cholesterol, Coronavirus disease 2019, Ferritin, Triglyceride

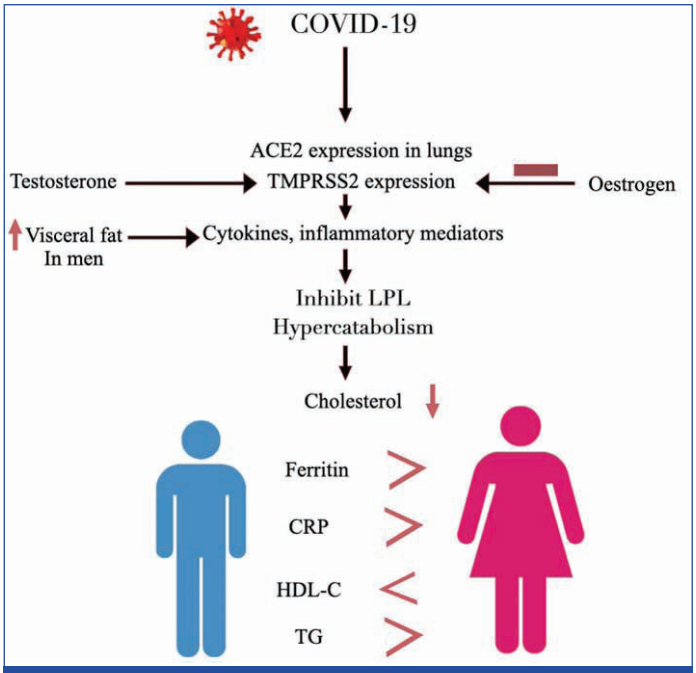
INTRODUCTION

It has been almost two years since the outbreak of COVID-19 from Wuhan, China. The world seems to be struggling in the claws of this pandemic [1]. The clinical spectrum of COVID-19 ranged from mild asymptomatic cases to severe pneumonia which along with intense systemic inflammation, resulted in acute respiratory distress syndrome, organ failures and death [2]. Other causes of fatalities implicated were acute cardiac injury, venous thromboembolism, acute kidney injury, coagulopathy and shock [3].

Major pathophysiological pathways have been hypothesised which can predict varied clinical presentation but other potential factors needs to be identified for better patient care [4]. Severity of COVID-19 increases with age, male gender and co-morbidities like diabetes mellitus and hypertension. The associations are multifactorial. Scavenger Receptor class B type 1 (SRB1), an important protein for High Density Lipoprotein (HDL) cholestrol trafficking helps in binding for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) proteins [4].

Lipids are fundamental structural components of bio membranes and participate in various processes of infection. The binding of SARS-CoV-2 to host cell membrane, activation, cell entry and spread to other cells is affected by lipid composition of membrane especially cholesterol-enriched lipid rafts [5]. Mass Spectrometry (MS)-based proteomics analysis suggested that the derangements in lipid metabolism may favour the progression of COVID-19 [6]. After replication inside the cytoplasm, virus is released from cell membrane. A cell culture based study has shown that cellular SARS-CoV-2 infectivity is increased by cholesterol present inside the cell [7]. Virus modifies the lipid and carbohydrate metabolic pathways of host cell. A specific lipidomic fingerprint has been observed in COVID-19 patients by a metabolomics study [8]. Apart from forming bio membranes and providing energy, lipids are important cell signaling molecules. The metabolic derivatives of cholesterol may have immunomodulatory properties like affecting the regulatory T-cell proliferation [9] [Table/Fig-1].

Viral infections hamper these biological functions of lipids and promote cell apoptosis and death [4]. Inflammatory mediators synthesised during the infection derange lipid metabolism by lowering cholesterol synthesis and absorption, reducing clearance of triglyceride-rich lipoprotein and decreasing production of Apolipoprotein A1. Earlier a study noticed a fall in HDL-C and Low Density Lipoprotein (LDL)-Cholesterol (sometimes) levels along with maintained or raised Triglyceride levels during infections [10]. In COVID-19, low LDL-C, HDL-C and Triglyceride (TG) levels have strong correlations with disease severity. Another factor linked with severity is Sterol Regulatory Element-Binding Protein 2 (SREBP-2) C-terminal fragment activated by COVID-19 in patient's blood which may become a therapeutic target for preventing cytokine storm [11].



[Table/Fig-1]: Mechanisms underlying the effects of COVID-19 on lipid profile. Effect of sex hormones and more visceral fat makes men more prone to atherogenic dyslipidaemia.
ACE2: Angiotensin converting enzyme 2; TMPRSS2: Transmembrane protease, serine 2

Lipid profile of populations of various countries showed considerable ethnic differences in a study. Asian Indians were reported to have higher adverse lipid pattern due to low HDL-C and high TG as compared to other countries, making them more prone to high prevalence of Cardiovascular Disease (CVD) and diabetes mellitus. Decreased HDL-C was more common in Asian Indians even with desirable LDL-C levels, irrespective of their diabetic status. Factors responsible for this included genetic, environmental, psychosocial, cultural and unexplained causes [12].

Taking into account the high prevalence of lipid disorders and their cardinal role in COVID-19, differences of lipid profile in Indian population from other countries, this study was planned to evaluate the levels of total cholesterol, triglyceride and HDL-C along with C-Reactive Protein (CRP) and ferritin in COVID-19 patients in rural district of Haryana, India where no such study has been conducted so far.

Hence, the present study was performed to assess the relationship between serum total cholesterol, triglyceride and HDL-C with serum CRP and serum ferritin which are markers of inflammation in COVID-19 patients. Also to evaluate any differences in male and female patients in lipid parameters and their correlation with inflammatory markers i.e, serum CRP and ferritin.

MATERIALS AND METHODS

This retrospective study was conducted in Department of Biochemistry at SHKM, GMC, Mewat, Haryana, India (tertiary care health centre) on COVID-19 positive patients attending Outpatient Department (OPD) and Inpatient Department (IPD), from October 2020 to December 2020. Data were analysed in February 2021. The study was approved by the Ethics Committee of the Institution (EC/OA-26/2020).

Inclusion criteria: All COVID-19 positive patients, confirmed by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and who were prescribed for lipid profile laboratory examination along with C-Reactive Protein (CRP) and serum ferritin were included in the study.

Exclusion criteria: Children younger than five years were excluded from the study.

Sample size calculation: The sample size was calculated using confidence interval 95%, margin of error 5% and population proportion 5%, i.e, N=73. But for final sample size, the retrospective data of 85 COVID-19 positive patients including 46 males and 39 females were collected in the study.

Data Collection

Values of all the parameters were recorded from patient files along with other demographic details (age and gender) available in Medical Record Department (MRD). The values of serum Triglycerides (TG), total cholesterol, High Density Lipoprotein (HDL), serum CRP and serum ferritin values were entered in patient performa and a masterchart for statistical analysis was made in Apple MacBook Air Numbers App. Very Low Density Lipoprotein (VLDL) is a calculated parameter from TG in the machine and no separate kit is used. So, the results of VLDL are actually same as TG. Tests were performed on Roche auto analyser C501 using methods and reference intervals as mentioned in [Table/Fig-2] [13-15].

Parameter	Name of the test	Normal range
Serum total cholesterol [13]	Cholesterol Oxidase Phenol 4-aminoantipyrine Peroxidase (COP-PAP) method	140-200 mg/dL
Serum triglyceride [13]	Glycerol Phosphate Oxidase (GPO) Trinder method	Male: 50-150 mg/dL Female: 40-150 mg/dL
Serum HDL-C [13]	Direct estimation	Male 30-60 mg/dL Female 35-75 mg/dL
Seum C-reactive protein [14]	Particle enhanced immunoturbidimetric assay	<0.5 mg/dL
Serum ferritin [15]	Particle enhanced immunoturbidimetric assay	Male: 30-400 ng/dL, Female: 15-150 ng /dL

[Table/Fig-2]: Methods and reference intervals of the parameters [13-15].

Definitions were taken from National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) guidelines [Table/Fig-3] [16]. Atherogenic dyslipidaemia: Elevated levels of TG and small-dense low-density lipoprotein and low levels of HDL-C [16].

Analyte	Units
Hypercholesterolemia: Serum cholesterol	≥200 mg/dL
Hypertriglyceridemia: Serum triglyceride levels	≥150 mg/dL
Low HDL-C levels	Men <40 mg/dL Women <50 mg/dL

[Table/Fig-3]: National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) guidelines [16].

STATISTICAL ANALYSIS

Data was collected in numbers application and statistically analysed using Pyscripter software. Mean and Standard deviation (SD) were calculated for continuous variables with normal distribution. Differences between groups were tested using Student's parametric t-test for continuous variables. A p-value <0.05 was taken as significant. Pearson's correlation coefficient was used to estimate the strength of correlation between parameters.

RESULTS

Total 85 (46 males and 39 females) COVID-19 patients were included in the study with age of 42.56±15.31 years. Mean age in male and female patients were 43.02±15.52 and 42.02±15.25 years, respectively. Serum triglyceride levels were significantly higher in males (233.63±146.92 mg/dL) than females (171.10±127.99 mg/dL), (p-value=0.0413). The HDL-C however was significantly higher in females (48.23±12.92 mg/dL) than males (38.52±12.20 mg/dL) (p-value=0.0006). All values of lipid profile parameters and inflammatory markers between male and female are presented in [Table/Fig-4].

Nine (19.57%) male patients and 4 (10.26%) females had CRP levels >5 mg/dL. Inflammatory marker, serum ferritin in 18 (39.13%) male patients was above 400 ng/dL and 5 (10.86%) male patient had <30 ng/dL. Ferritin <15 ng/dL (lower limit) was noticed in

Parameter	Total (Mean±SD)	Male (Mean±SD)	Female (Mean±SD)	p-value (Student's t-test)
Age (years)	42.56±15.31	43.02±15.52	42.02±15.25	0.7662
Total cholesterol (mg/dL)	187.058±45.75	182.04±45.84	192.97±45.52	0.2750
Triglyceride (mg/dL)	204.94±141.27	233.63±146.92	171.10±127.99	0.0413
HDL (mg/dL)	42.97±13.38	38.52±12.20	48.23±12.92	0.0006
CRP (mg/dL)	2.325±4.90	2.96±5.76	1.56±3.59	0.1918
Ferritin (ng/dL)	360.52±535.81	550.76±626.88	136.12±271.58	0.0002

[Table/Fig-4]: Comparison of lipid profile and inflammatory markers between males and females.
p-value <0.05 was considered as statistically significant, HDL: High density lipoprotein cholesterol; CRP: C-reactive protein

4 (10.26%) females while 8 (20.51%) females had ferritin >150 ng/dL (higher limit). Out of total, 3 (7.7%) females patients had serum ferritin >400 ng/dL. These results indicate more inflammation in male subjects as compared to females in COVID-19.

A statistically significant negative correlation between cholesterol and CRP was found in male patients (r-value=-0.3538, p-value=0.016). The correlation between cholesterol and ferritin was a very weak negative correlation (r-value=-0.1717) in total cases [Table/Fig-5].

Correlation	Total cases (r-value)	p-value	Male (r-value)	p-value	Female (r-value)	p-value
Cholesterol and CRP	-0.2874	0.0077	-0.3538	0.016	-0.1442	0.381
Triglyceride and CRP	-0.0297	0.0077	0.0122	0.936	-0.0332	0.842
HDL and CRP	-0.0488	0.662	0.0034	0.982	0.0035	0.983
Ferritin and CRP	0.4064	0.000114	0.4243	0.0032	0.2327	0.153
Cholesterol and ferritin	-0.1717	0.117	-0.19	0.205	-0.0259	0.297
Triglyceride and ferritin	0.2285	0.035	0.1568	0.2980	0.193	0.163
HDL and ferritin	-0.3578	0.00079	-0.3917	0.0070	0.0035	0.025

[Table/Fig-5]: Gender-wise correlation of serum ferritin and CRP with lipid profile.
Pearson's correlation test

Another significant inverse correlation was discovered between serum ferritin and HDL in male patients (r-value=-0.3917, p-value=0.0070). Females patients had no correlation between HDL and ferritin (r-value=0.0035). Weak positive correlation was noted between TG and ferritin (r-value=0.2285, p-value=0.035).

In COVID-19 positive females, triglycerides increases with age (r-value= 0.3047; p-value=0.0045). Similarly ferritin concentrations also rises with progressing age in female (r-value=0.3013) and male (r-value=0.284) subjects [Table/Fig-6].

Correlation coefficient	Total cases (r-value)	p-value	Male (r-value)	p-value	Female (r-value)	p-value
Age and cholesterol	0.0218	0.843	-0.0447	0.689	0.1116	0.309
Age and triglyceride	0.1415	0.196	0.0175	0.873	0.3047	0.0045
Age and HDL	-0.0658	0.554	0.0119	0.913	-0.137	0.2111
Age and CRP	0.108	0.325	0.2507	0.020	-0.171	0.1176
Age and ferritin	1.0	<0.0001	0.284	0.0084	0.3013	0.005

[Table/Fig-6]: Correlation of age with lipid profile and inflammatory markers.
Pearson's correlation test

DISCUSSION

The present study is the first study on lipid profile in COVID-19 patients in north India. Number of cases included in the study was 85 as lipid profile was a less requested investigation in COVID-19 patients as compared to blood glucose and inflammatory markers. Masana L et al., also highlighted the low prescription of lipid profile in COVID-19 patient care [17].

The results of present study demonstrated hypolipoproteinemia and hypertriglyceridemia in COVID-19 patients. Decrease in HDL-C concentration and elevation of triglyceride level was positively correlated with ferritin levels. CRP and ferritin levels were negatively correlated with total cholesterol level.

A meta-analysis performed on 19 studies supported the role of lipid profile in both severity and prognosis of COVID-19 [18]. Significantly decreased levels of total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol were found in the severe group when compared with the non severe group in a random effect model. However, no significant difference was observed in the level of TG between severe and non severe groups or survivor and non survivor groups [18].

These derangements in lipid metabolism were more pronounced in male patients as compared to females. Triglycerides levels and ferritin levels were associated with progressing age in females. This gender bias has been less studied in previous studies [19-21]. Lipid profile derangements with growing inflammation may be used to assess severity and prognosis of COVID-19 and help in better patient care. Being one of the major metabolic pathway of body, the effect of alterations in lipid chemistry is going to be paramount.

The severity of COVID-19 is reflected by rise in inflammatory markers like CRP and ferritin. In COVID-19 pandemic, it was noticed that patients who were overweight and obese required more IMV and had higher peaks of CRP and ferritin than patients with normal weight [22]. Few studies on effects of COVID-19 on lipid profile have been conducted [19,20].

It was shown that the increased concentration of total cholesterol, low density lipoprotein, high density lipoprotein and triglycerides in the serum was inversely correlated with the severity of COVID-19 [4]. Another study concluded, that low HDL-C levels and high triglyceride levels are important high risk markers for COVID-19 hospital admitted cases [17].

Most of the studies analysed lipid results of patients after becoming COVID-19 positive, but Barman HA et al., reported that the temporal changes in lipid parameters before and after COVID-19 may be associated with mortality and in-hospital adverse outcomes [19,20,23].

Review article by Surma S et al., found a similar potential link between the incidence of lipid disorders and the prognosis of COVID-19 patients along with a role of statins in the treatment [24]. Lowering of serum lipid concentrations probably leads to worsening of inflammation, hypercoagulation and impairment of oxygen which results in multiorgan failure [6].

Multiple hypotheses have emerged by accruing research on mechanisms underlying the link between lipids and COVID-19. Earlier, it was thought that a hypercatabolic state and poor nutritional status of patient during infection is the reason for lower lipids values [25]. Patients infected with a virus strain which is more evolved presents with significantly raised triglyceride and decreased HDL-C levels [26]. Robust scientific proofs are available to support the changes in lipid pathways, in presence of inflammation or infections [27].

It is well known that numerous cytokines and inflammatory markers are released during infections. These molecules interacts with Lipoprotein lipase (LPL) and its regulatory proteins. The LPL is also inhibited by bacterial products and modified lipoproteins [28]. The LPL is a chief enzyme involved in lipid abnormalities during infections. When LPL activity is hampered, triglyceride rich lipoproteins are less converted into LDL, resulting in hypertriglyceridemia and low HDL levels. Other causes of low HDL levels are decreased Cholesteryl

Ester Transfer Protein (CETP) activity, poor app A1 synthesis and faster HDL clearance [28].

Lipoproteins enriched with triglycerides can bind toxins, thus play a role in innate immune response. HDL is also a key molecule in inflammation that binds toxins and help in its clearance from liver. So another player of innate immunity, the HDL when lowered may affect the course of disease. Drug-induced effects of statins and corticosteroids could not explain the atherogenic dyslipidaemia seen in COVID-19 [29].

A substantial difference in severity of COVID-19 has been suggested between men and women, with women having better prognosis and outcome than men. Prevalence of COVID-19 infection in male and female was 53.3% and 46.7%, respectively in a study done in 2020 and the death rate was also higher in males (58.3%) than females (41.7%) [30]. Sex hormone testosterone in male was hypothesised to be a risk factor and oestrogen in female subjects was assumed to be protective in COVID-19 [31]. Bhatia V et al., noted that inflammatory mediators continue to remain elevated in men having lower levels of testosterone [31].

Klein SL and Flanagan KL, studied the sex differences in immune responses and found that in men, severity of COVID-19 is more due to enhanced Angiotensin-Converting Enzyme 2 (ACE2) expression in lungs and stimulation of Transmembrane Protease, Serine 2 (TMPRSS2) expression. TMPRSS2 is a protein present on endothelial cell surface protein that participates in viral entry and spread of SARS-CoV-2. In females, on the other hand less severity of COVID-19 was probably due to two reasons, one is decreased ACE2 expression in lung and second is inhibition of TMPRSS2 expression by oestrogen [32].

As per scientific data, females have less risk factors for cardiovascular diseases than males. Factors like protein, lipidome, insulin resistance and messenger Ribonucleic Acid (mRNA) expression are comparatively favourable in females than males [33]. Accumulation of more visceral fat in males as compared to females is an important hypothesis to explain more severe COVID-19 in males [34]. Adipose tissue in men have greater number of macrophages and immune cells which can secrete more cytokines for longer duration than female adipose tissue. So, visceral fat can function as a source for flaring up cytokine levels in men [35].

Limitation(s)

Due to retrospective design of study, it was difficult to derive causal relationships. It was not ascertained that the lipid profile was always fasting. Another limitation was that the severity of COVID-19 disease was not taken into account. The kit for LDL was not available in the department.

CONCLUSION(S)

Lipid profile is a basic investigations available in even small laboratory setups where inflammatory markers like ferritin and CRP may not be available. Lipids are important biomarkers of inflammation and infection and will be helpful in COVID-19 patient care. Lipids participate in immune response and also modulate course of disease. Triglyceride, cholesterol and HDL-C are associated with inflammatory markers and hence, may be used for assessing severity and prognosis of COVID-19. Studies with large sample size needs to be explored in India.

REFERENCES

[1] Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. JAMA. 2020;323(16):1574-81. Doi: 10.1001/jama.2020.5394.

[2] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet. 2020;395(10223):507-13.

[3] Potere N, Valeriani E, Candeloro M, Tana M, Porreca E, Abbate A, et al. Acute complications and mortality in hospitalized patients with coronavirus disease 2019: A systematic review and meta-analysis. Crit Care. 2020;24(1):389. Doi: 10.1186/s13054-020-03022-1. PMID: 32616077.

[4] Gordon DE, Jang GM, Bouhaddou M, Xu J, Obernier K, White KM, et al. A SARS-CoV-2 protein interaction map reveals targets for drug repurposing. Nature. 2020;583:459-68. Doi: 10.1038/s41586-020-2286-89.

[5] Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): A review. JAMA. 2020;324:782-93.

[6] Shen B, Yi X, Sun Y, Bi X, Du J, Zhang C. Proteomic and metabolomic characterization of COVID-19 patient sera. Cell. 2020;182(1):59-72. Doi: 10.1016/j.cell.2020.05.032.e15.

[7] Wang H, Yuan Z, Pavel MA, Jablonski SM, Jablonski J, Hobson R, et al. The role of high cholesterol in age-related COVID19 lethality. Preprint. bioRxiv. 2021;2020.05.09.086249.

[8] Song JW, Lam SM, Fan X, Cao JW, Wang SY, Tian H, et al. Omics-driven systems interrogation of metabolic dysregulation in COVID-19 pathogenesis. Cell Metab. 2020;32:188-02.

[9] Zeng H, Yang K, Cloer C, Neale G, Vogel P, Chi H. mTORC1 couples immune signals and metabolic programming to establish T(reg)-cell function. Nature. 2013;499:485-90. Doi: 10.1038/nature12297.

[10] Trinder M, Boyd JH, Brunham. Molecular regulation of plasma lipid levels during systemic inflammation and sepsis. Curr Opin Lipidol. 2019;30:108-16.

[11] Lee W, Ahn JH, Park HH, Kim HN, Kim H, Yoo Y. COVID-19-activated SREBP2 disturbs cholesterol biosynthesis and leads to cytokine storm. Signal Transduct Target Ther. 2020;5(1):186.

[12] Zhang L, Qiao Q, Tuomilehto J, Janus ED, Lam TH, Ramachandran A, et al. Distinct ethnic differences in lipid profiles across glucose categories. J Clin Endocrinol Metab. 2010;95(4):1793-01.

[13] Vasudevan DM and Sreekumari S. Textbook of Biochemistry (For Medical students) 6th ed. New Delhi, India: Jaypee Brothers Medical Publishers (P) Ltd. 2011; pp.149.

[14] Dati F, Schumann G, Thomas L. Consensus of a group of professional societies and diagnostic companies on guidelines for interim reference ranges for 14 proteins in serum based on the standardisation against the IFCC/BCR/CAP reference material (CRM 470). Eur J Clin Chem Clin Biochem 1996;34:517-20.

[15] Lotz J, Hafner G, Prellwitz W. Reference study for Ferritin assays. Kurzmitteilung Clin Lab. 1997;43:993-94.

[16] National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report Circulation. 2002;106:3143-21.

[17] Masana L, Correig E, Ibarretxe D, Anoro E, Arroyo JA, Jericó C, et al. Low HDL and high triglycerides predict COVID-19 severity. Sci Rep. 2021;11:7217. https://Doi.org/10.1038/s41598-021-86747-5.

[18] Mahat RK, Rathore V, Singh N. Lipid profile as an indicator of COVID-19 severity: A systematic review and meta-analysis. Clin Nutr ESPEN. 2021;45:91-101.

[19] Chen Q, Huang M, Luo Y. Alteration of lipid profile and prognostic value of lipids on the length of hospital stay in COVID-19 pneumonia patients. Circulation. 2020;142:A14904.

[20] Ding X, Zhang J, Liu L, Yuan X, Zang X, Lu F, et al. High-density lipoprotein cholesterol as a factor affecting virus clearance in covid-19 patients. Respir Med. 2020;175:106218.

[21] Siordia JA. Epidemiology and clinical features of COVID-19: A review of current literature. J Clin Virol. 2020;127:104357. Available from: https://dx. Doi.org/10.1016/j.jcv.2020.104357.

[22] Bettini S, Bucca G, Sensi C, Dal Prà C, Fabris R, Vettor R. Higher levels of c-reactive protein and ferritin in patients with overweight and obesity and SARS-CoV-2-related pneumonia. Obes Facts. 2021;14:543-549. Doi: 10.1159/000517851).

[23] Barman HA, Pala AS, Dogan O, Atıcı A, Yumuk MT, Alici G, et al. Prognostic significance of temporal changes of lipid profile in COVID-19 patients, Obesity Medicine. 2021;28:100373. ISSN 2451-8476. Available from: https://Doi.org/10.1016/j.obmed.2021.100373.

[24] Surma S, Banach M, Lewek J. COVID-19 and lipids. The role of lipid disorders and statin use in the prognosis of patients with SARS-CoV-2 infection. Lipids Health Dis. 2021;20(1)141. Doi: 10.1186/s12944-021-01563-0. PMID: 34689776; PMCID: PMC8542506.

[25] Sittiwet C, Simonen P, Gylling H, Strandberg TE. Mortality and cholesterol metabolism in subjects aged 75 years and older: The Helsinki businessmen study. J Am Geriatr Soc. 2020;68(2)281-87.

[26] Orkaby AR. The highs and lows of cholesterol: A paradox of healthy aging? J Am Geriatr Soc. 2020;68:236-37.

[27] Filippas-Ntekouan S, Liberopoulos E, Elisaf M. Lipid testing in infectious diseases: Possible role in diagnosis and prognosis. Infection. 2017;45(5):575-88.

[28] Trinder M. Cholesteryl ester transfer protein influences high-density lipoprotein levels and survival in sepsis. Am J Respir Crit Care Med. 2019;199:854-62.

[29] Wu Q, Zhou L, Sun X, Yan Z, Hu C, Wu J, et al. Altered lipid metabolism in recovered SARS patients twelve years after infection. Sci Rep. 2017;7:01-12.

[30] Yu C, Lei Q, Li W, Wang X, Liu W, Fan X, et al. Clinical characteristics, associated factors, and predicting COVID-19. Mortal Science. 2020;368(6495):1038-39.

[31] Bhatia V, Chaudhuri A, Tomar R, Dhindsa S, Ghanim H, Dandona P. Low testosterone and high C-reactive protein concentrations predict low hematocrit in type 2 diabetes. Diabetes Care. 2006;29(10):2289-94.

[32] Klein SL, Flanagan KL. Sex differences in immune responses. Nat Rev Immunol. 2016;16(10):626-38.

[33] Elzinga SE, Savelieff MG, O'Brien PD, Mendelson FE, Hayes JM, Feldman EL. Sex differences in insulin resistance, but not peripheral neuropathy, in a diet-induced prediabetes mouse model. Dis Model Mech. 2021;14dmm048909.
[34] Földi M, Farkas N, Kiss S, Dembrovszky F, Szakács Z, Balaskó M, et al. Visceral adiposity elevates the risk of critical condition in COVID-19: A systematic review and meta-analysis. Obesity (Silver Spring). 2021;29(3):521-28.
[35] Camporez JP, Lyu K, Goldberg EL, Zhang D, Cline GW, Jurczak MJ, et al. Anti-inflammatory effects of oestrogen mediate the sexual dimorphic response to lipid-induced insulin resistance. J Physiol. 2019;597(15):3885-3903. J Physiol. 2019;597:3885-03.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Biochemistry, Shaheed Hasan Khan Mewati Government Medical College, Nalhar, Nuh, Mewat, Haryana, India.
2. Assistant Professor, Department of Biochemistry, Shaheed Hasan Khan Mewati Government Medical College, Nalhar, Nuh, Mewat, Haryana, India.
3. Professor and Head, Department of Biochemistry, Shaheed Hasan Khan Mewati Government Medical College, Nalhar, Nuh, Mewat, Haryana, India.
4. Associate Professor, Department of Biochemistry, Shaheed Hasan Khan Mewati Government Medical College, Nalhar, Nuh, Mewat, Haryana, India.
5. Demonstrator, Department of Biochemistry, Shaheed Hasan Khan Mewati Government Medical College, Nalhar, Nuh, Mewat, Haryana, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Asha Kumari,
House No. 504, C-2 Block, Shaheed Hasan Khan Mewati Government Medical College, Nalhar, Nuh, Mewat-122107, Haryana, India.
E-mail: drashatigraniya@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Feb 22, 2022
- Manual Googling: May 17, 2022
- iThenticate Software: Jul 19, 2022 (14%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Feb 05, 2022**
Date of Peer Review: **Mar 01, 2022**
Date of Acceptance: **May 27, 2022**
Date of Publishing: **Aug 01, 2022**