ORIGINAL ARTICLE

CORRELATION BETWEEN TRIGLYCERIDE LEVEL AND SEVERITY OF COVID-19 PATIENTS.

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Abstract:

Objective: To determine the correlation of serum triglyceride levels with severity of admitted Covid-19 in patients.

Methodology: An observational and analytical study was conduct in which All patients between 20 years to 70 years of age, either sex, who had presented with a confirmed diagnosis of Covid-19 to Amina Hospital, Sialkot, from May 15th 2020 till April 15th 2021 were included in this study.

Results: There were a total of 81 Covid-19 confirmed cases in our study. Out of 81 Covid-19 patients, there were (26.4%) mild, (46%) moderate, (19.6%) severe and (8%) critical patients. Sixty-five patients (39.9%) were between 20 to 45 years of age, and (60.1%) were between 46 to 70 years of age. There were (54%) male patients and (46%) female patients. The spearmen rank's correlation between triglyceride levels and Covid-19 severity was p (rho) 0.174 (p value 0.02). There was a positive and statistical significant correlation present.

Conclusion: Hypertriglyceridemia was a common feature in patients presenting with Covid-19 and its frequency kept on increasing with the severity of Covid-19. Positive and statistical correlation was noted between triglyceride levels and severity of Covid-19.

Keywords: Adults, triglyceride, COVID-2019, COVID-19-developing country, SARS-CoV-2, severity of illness.

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Introduction

The COVID-19 disease has quickly spread globally, so researchers tried to determine which primary pathophysiological processes were involved in its progression to severity. However, merely few aspects have been recognized. Some patients have an asymptomatic course while others succumb to mortality. Since there are restricted treatments available for Covid-19 infection, hence the documentation of risk factors associated with severe COVID-19 is of extreme significance in order to improve the prognosis of patients affected by Corona virus infection. [1, 2]

Impaired glucose levels, raised blood pressure, and deranged lipid levels have been documented to be linked with a poor prognosis of disease. [2, 3] A few studies have provided some evidence of altered triglyceride levels among Covid-19 patients.[4] Covid-19 virus is enclosed by a lipid bilayer. Process of infection requires lipids, as they are essential components of membranes,

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and they participate in the regulation, such as movement of infectious materials. [6]

Corona virus multiplies by using the metabolic mechanism of the host cell, which it has invaded and entered.[7]

In addition to this, Covid-19 virus, once when inside the host cell, amends cellular metabolism activity by changing the pathways for energy production.[8]

Lipid metabolism process is thus affected by these means, simultaneously, altering the intracellular lipids, which also act as transcription factors, Viral particles alter host cell's physiology and result in apoptosis and cell death.[10]

The routine clinical method used in evaluating modifications in the metabolism of lipid involves measuring the serum triglyceride levels. [4, 5, 7]

Studies are being conducted to develop a better understanding of how these factors will play a role in improving our comprehension of cellular lipids in Covid-19 infection. Giving consideration to these mechanisms and triglyceride being a potential marker for the disease progression, we consider that it would be beneficial to study the correlation between deranged serum triglyceride levels and severity of Covid-19 infection.

Methodology

A total of 81 patients were included in this observational descriptive study from May 15th 2020 till April 15th 2021. All patients between 20-70 years of age, either sex, who had presented with the confirmed diagnosis of Covid-19 at Amina Hospital, Sialkot, were included in this research. Permission from the ethics committee was taken prior to conduct the study. Informed consent was obtained from all patients, after full disclosure of risk and benefits of the study. Patients who were unable to give consent it was taken from their attendants. Data were collected, a unique identifier was assigned to each patient in the data sheet, and confidentiality was maintained throughout study period. Pharyngeal swab samples of all the patients in this research were collected, and Covid-19 RNA was identified by a reverse transcription polymerase chain reaction (RT-PCR).

Adults with asthma, pulmonary tuberculosis, acute coronary syndrome, chronic renal failure, chronic liver disease, stroke, chronic obstructive pulmonary disease (COPD), sarcoidosis, and immunosuppression were excluded from this study.

Patient history and demographic information was noted. The patients were examined and clinical features were observed. Severity of Covid-19 was recorded using the National Institutes of Health's (NIH) guidelines.[11]

Blood sample were drawn by using 5 cc disposable syringes from peripheral vein under aseptic measures and sent to the hospital's laboratory for the measurement of serum triglyceride. After obtaining laboratory results. serum triglyceride was categorized into (a) normal (<150 mg/dL), (b) borderline high (150-199 mg/dL), (c) high (200-499 mg/dL) and (d) very high levels ($\geq$ 500 mg/dL), based on NCEP ATP III criterion.[12]

Covariates, from the patient's history and laboratory, were noted to calculate the severity of Covid-19 category, based on the severity criterion like mild, moderate, severe and critical. (Table-1)

Continuous variables were shown as mean (standard deviation). Categorical variables were presented as frequency (%).

Categorical data is presented as number of subjects (%), Spearman rank's correlation test was used to calculate the relationship between serum triglyceride and severity of Covid-19. Post stratification, chi-square was used to compare categorical data. The P-value of <0.05 was considered statistically significant. Student T-test was used to find the mean difference in triglyceride levels.

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Data was analysed using the Statistical Package for the Social Sciences (SPSS) version 20.

Results

There were a total of 81 Covid-19 confirmed cases in our study. Out of 81 Covid-19 patients, there were (26.4%) mild, (46%) moderate, (19.6%) severe and (8%) critical patients. The 39.9% patients were between 20 to 45 years of age, and (60.1%) were between 46 to 70 years of age. There were 44 (54%) male patients and 37 (46%) female patients. Among the patients in our research, however, 15 patients (18.4%) had diabetes mellitus, 18 patients (22.1%) had hypertension, and 24 (29.4%) had reported being smokers. (Table 2) The spearmen rank's correlation between triglyceride levels and Covid-19 severity grades was p (rho) = 0.174 (P-value 0.02). There was a positive and statistically significant correlation was present.

The mean ± SD triglyceride level among the males was ± 472.73 whereas among the females patients it was ± 429.33 (p value = 0.085). Even though the mean triglyceride level was lower among females, yet the difference was not statistically significant as p value cut off was <0.05. Both groups were statistically comparable. The distribution of males and females was similar across all categories of triglyceride levels (p value = 0.37). More females had severe Covid-19 (n=10) as compared to the males (n=6) However, there were more males in mild (n=14), and moderate (n=20) categories, as compared to females, who were n=7 and n=17 respectively. (Table 3) Among both moderate and severe Covid-19 patients who were hypertensive and diabetic, the frequency of raised triglyceride levels was subsequently higher.

		n	%
	Total	81	100
Age in years	20 to 45	33	39.9
	46 to 70	49	60.1
Diabetes Mellitus	Yes	15	18.4
Hypertension	Yes	63	77.9
Smoking Status	Yes	24	29.4
Triglyceride Levels	Borderline high	1	0.6
	High	4	4.9
	Very High	75	93.3
	Normal	1	1.2
Severity of Covid-19	Mild	23	26.4
	Moderate	36	46
	Severe	16	19.6
	Critical	6	8

Table-2: Overall Distribution of Patient Characteristics

'Severity of Covid-19 criterion	**"Mild Illness:** Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging. **Moderate Illness:** Individuals who show evidence of the lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO2) ≥90% on room air at sea level. **Severe Illness:** The individuals who have SpO2 < 90% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300 mm Hg. The respiratory frequency 30 breaths/min, or lung infiltrates >50%. **Critical Illness:** Individuals who have the respiratory failure, septic shock, and/or multiple organ dysfunctions."
	*https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/

Table-1: Criterion used for severity of Covid-19 patients.

Variables	Males (n)	Females (n)	P value
Triglyceride mg/dL			0.085

Variables	Categories	n	%
Sex	Males	44	54
	Females	37	46

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Mean Standard Deviation	472.73 242.43	429.33 211.058	
Triglyceride Level			0.37
Borderline high	0	1	
High	2	2	
Very High	40	34	
Normal	1	0	
Covid-19 Severity			0.12
Mild	14	7	
Moderate	20	17	
Severe	6	10	
Critical	3	1	

TABLE 3: Distribution of Triglycerides And Severity Between Male And Female Patients

Discussion

The primary finding of our research is that Corona virus infection has an impact on triglyceride level. Literature supports this that infectious diseases are correlated with altered lipid metabolism.[4, 5,7-9,13-16]

The research has shown that the Covid-19 infection results in the altered levels of triglycerides among patients.[5,13,15,16]

These results corroborate with the outcome of our study, as we found raised triglyceride levels. Among our patients, triglycerides above 150 mg/dL were correlated with an increased severity of Covid-19 disease with p (rho) 0.174 (p value=0.02). The numerous causes could explain this positive and statistically significant correlation. For instance, among patients with impaired triglyceride levels, the accumulation triglycerides will result in endothelial dysfunction.[17,18]

This endothelial dysfunction could be more aggravated among those who suffer from Covid-19 infection since the receptor for Corona virus is ACE2 receptor, and this is correspondingly expressed in endothelial cells as well. This would eventually result in the development of cardiac problems that can result in a severe outcome of the Covid-19 patients.[19] This notion is comparable to the results obtained from our data, which showed that there were 15 (18.4%) diabetics in our data set, and 18 (22.1%) hypertensive patients. Similar to other infectious diseases, a few studies have provided some evidence of observed modifications in triglycerides in among Covid-19 patients.[4-8] Covid-19 virus multiplies by using the metabolic mechanism of the host cell, which it has invaded and entered.[16, 20, 21, 22]

These processes thus affect the lipid metabolism[14], which in turn affects the lipids within the cells, thus impacting the transcription factors. Masana et al, in 2021 reported that patients with severe Covid-19 have altered triglyceride levels.[15] However, the literature is still evolving on this subject. As in another study the triglyceride levels were variable.[22] Researchers had used the UK Biobank data and it was noted that raised HDL-C levels were correlated with the decreased risk of testing positive Covid-19. Whereas, the researchers did not find triglyceride levels to be significantly correlated with an increased risk of Covid-19. This disparity in evidence further highlights the need for more studies in this area.

This provides researchers an opportunity to open up a clinical narrative about triglycerides being a biomarker. They could thus be prognostic for patients hospitalized with severe Covid-19. In our analysis of triglyceride levels and severity of Covid-19, we found increased correlation, when maximum triglyceride level was greater than 150 mg/dL. Studies are being conducted to develop a better understanding of how these factors will play a significant role in improving our comprehension of cellular lipids in Covid-19 infection. Few Covid-19 studies have demonstrated that deranged trigly-ceride levels have been observed to be correlated with the severity of Covid-19 infection.[14,15]

Consequently, more such studies are to be needed. This suggests that inflammatory

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mediators, cytokine, and the modified lipids produced during Covid-19 infection delay the process of metabolism of lipids, by reducing the rate of clearance triglyceride-rich lipoprotein.[23] This leads us to hypothesize that the increase in triglycerides may be associated with Corona virus infection, though how exactly this happens within the human body is still unclear. We also consider, based on our results, that altered triglyceride levels which were observed in this study, could be utilized for assessing Covid-19 patient response to treatment. This could be proxy measure and not a direct measure. However, to establish levels of triglyceride as a proxy measure of the severity of Covid-19, more evidence-based studies with bigger sample size are needed. If possible, then longitudinal studies should be conducted to illustrate the correlation between deranged triglyceride levels and severity of Covid-19.

Conclusion

Our study supports that deranged triglyceride levels are correlated with severity of Covid-19.

Limitations

This is a single center study, and not a multi centre study. Due to this the research does not provide information about causes or effects relationship. Thus, we do not know how many patients had dyslipidemia prior to having Covid-19 infection. We did not have their baseline lipid profile. The patients we had included in this study were those who were diagnosed with having Covid-19, and in this way we did not have a comparison group. Although we found a significant correlation, but further studies are needed to investigate the clinical significance of the role of triglyceride as a bio-marker for severity of Covid-19.

Recommendation

We would suggest that more studies are to be conducted to compare the triglyceride biomarker on the longitudinal timeline, in the Covid-19 infection. There is initial evidence present to suggest that there is value in checking for triglyceride levels.

Conflict of Interest:

Author declared that he had no conflict of interest and he got no funding.

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