High Atherogenic Index of Plasma at-admission of COVID-19 patients can predict Upcoming Cardiac Morbidity and Mortality in Non-Cardiac patients

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Abstract

Background: The coronavirus disease 2019 showed multiple modifications since the start of the pandemic not only in the viral structure but also in its clinical presentation. Cardiac presentation and infection of cardiac patients is serious and necessitates early prediction

Objectives: Evaluation of the relation between incidentally detected dyslipidemia at-admission of COVID-19 non-cardiac patients and their outcome.

Patients and methods: Plasma lipid profile and the Atherogenic Index of Plasma [AIP] were determined in 302 COVID confirmed patients. Patients were evaluated using the COVID-GRAM [CG] critical illness score and during hospital stay the rates of admission to intensive care unit [ICU], development of cardiac insults and need for admission to cardiac ICU [CCU] and its outcome were determined.

Results: 114 patients were dyslipidemic with increasing incidence with increased disease severity. The AIP cardiac risk was high in 92 and the CG critical illness risk was medium in 231 patients. Forty-seven and 63 patients were admitted to the CCU and ICU, respectively, and unfortunately; 21 and 22 patients died at CCU and ICU, respectively. High at-admission CG-risk percentage was defined as predictor for progress to critical grade by 63% and total mortality by 37%, while high at-admission AIP score was the only important predictor for mortality secondary to cardiac insult.

Conclusion: Dyslipidemia was detected in about 40% of low cardiac risk COVID patients and about 15.6% developed cardiac insult and 7% had died. Combined estimation of AIP and CG scores might accurately differentiate patients liable to develop cardiac complications and predict both mortalities.

Keywords: Dyslipidemia, Non-cardiac patients, COVID-19 disease, Atherogenic Index of Plasma, Cardiac insults.

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Introduction

The coronavirus disease 2019 pandemic presents itself by different and modifying symptoms that made it difficult to approach the diagnosis, or predict the course and mortality of the disease **(Huyut, 2022)**. During the first wave of the pandemic, COVID-related mortality rate [MR] was more than 20% of all-cause mortality and occurred among middle-aged and older adults **(Vila-Corcoles et al, 2021)**. This could be attributed to COVID-induced cytokine storm which is responsible for development of acute lung injury, acute respiratory distress syndrome, multiorgan dysfunction, shock, and thrombosis **(Nair, 2022)**.

The COVID-GRAM [CG] score provides an estimate of the risk of development of critical illness among patients with COVID-19 admitted to the hospital **(Liang et al., 2020)**. However, the predictability of scoring systems for the prognosis of COVID patients is still controversial because these systems depend on multiple clinical, laboratory and radiological findings and this provided contradiction of the results of multiple comparative studies **(Gidari et al., 2020; Armiñanzas et al., 2021; De Socio et al., 2021)** and indicated the need for refining these scoring systems to be easily applicable and provide highly accurate prediction for patients' outcome **(Ngiam et al., 2021; Gu & Wang, 2021)**.

Early identification and treatment of cardiovascular disease risk factors through screening of apparently healthy individuals is crucial for the primary prevention of cardiac insults **(Amadi et al., 2020)**. During COVID era, the cardiac risk of COVID patients was extensively investigated; speckle tracking echocardiography detected subclinical left ventricular systolic dysfunction in mildly symptomatic COVID-19 patients **(Gul et al., 2021)**. The three-dimensional echocardiography to measure the right ventricular ejection fraction provided a higher predictive value for mortality in COVID-19 patients over conventional parameters **(Zhang et al., 2021)**. Moreover, cardiovascular magnetic resonance of recently recovered COVID-19 patients, revealed cardiac involvement in 78% and ongoing myocardial inflammation in 60% of patients, thus indicates the need for early prediction and evaluation of the long-term cardiovascular consequences of COVID-19 **(Puntmann et al., 2020)**.

However, these diagnostic modalities could not be applied as screening methods and this necessitated evaluation of more simple, inexpensive and accurate methods. Thus the current study targets to evaluate the relation between incidentally detected dyslipidemia during routine investigations at time of admission of COVID-19 patients and the progress and outcome of the disease with special regard to cardiac insults and mortalities **(Bray, 1992).**

Patients and methods

Study design and participants

A prospective comparative multicenter study was performed at Cardiology Department, Faculty of Medicine, Tanta University and Quarantine hospitals, Ministry of Health, Al-Gharbia Governorate.

Patients diagnosed to have COVID-19 disease according to the diagnostic protocol settled by the WHO and approved by the Egyptian Ministry of Health either admitted to ICU, CCU, quarantine hospitals or general wards.

Exclusion criteria: The presence of morbid obesity, immunosuppressive disorders, indications for ICU or CCU admission

other than complicated Covid-19 disease, or malignancy anywhere in the body are the exclusion criteria.

Ethical consideration

The study protocol was approved by the Ethical Committee of Tanta Faculty of Medicine [35069/11/21] in 22/11/2021, and a written informed patient's consent was obtained from patient or the nearest relative according to the conditions of the Local Ethical Committee. The study protocol was registered at ClinicalTrials.gov; the Identifier number is NCT05226377 and the first posted date is (07/02/2022).

Clinical evaluation

All patients were evaluated with application of strict personal protection for history taking, determination of demographic data including age, sex, weight and height for calculation of body mass index (BMI) as weight in kg divided by height in square meter and was graded according to guidelines of **WHO, 1995**. Diagnostic laboratory and radiologic workup was applied assess the disease severity.

Evaluation tools

1. **COVID-19 disease severity** was graded as mild Illness was defined as the presence of any manifestations of COVID-19 without abnormal chest imaging. The presence of evidence of lower respiratory disease during clinical assessment or imaging with oxygen saturation of oxygen [SpO2] of ≥94% indicated moderate and if SpO2 was <94% indicated severe grade. Critical Illness was defined by the presence of organ failure **(Yang et al., 2023)**.
2. **COVID-GRAM Critical Illness Risk Score** for assessment of the risk of progression to critical illness according to the protocol proposed by **Liang et al. 2020** as numerical risk score and percentage of probability for progress to critical illness depending on age, number of comorbidities, neutrophil/lymphocyte ratio (N/L), lactate dehydrogenase (LDH) and direct bilirubin levels are continuous variables, and X-ray abnormality, hemoptysis, dyspnea and unconsciousness were scored by 1 if positive and 0 if negative. .
3. **Atherogenic index of plasma [AIP]** which is defined as the base 10 logarithms of the ratio of plasma triglyceride [TG] to high-density lipoprotein cholesterol [HDL-c] **(Holmes et al., 2008)** and an index of ≥0.1 is the optimum for prediction of CR **(Dobiásová et al., 2006)**.

Laboratory investigations

A- Routine and infection severity parameters including serum urea, creatinine, direct bilirubin, LDH were estimated.

B- Estimation of plasma lipids after 12-hr fasting for determination of plasma levels of TG **(Mcgowan, 1983)** and HDL-c **(Friedwald et al., 1972)**.

Study outcomes

1. Primary outcome is the incidence of at admission dyslipidemia that was defined as elevated levels of TC >200 mg/dl or LDLc >130 mg/dl or low levels of HDLc <60 mg/dl **(Rifai & Warnick, 2006; Fodor, 2011)**.
2. Secondary outcomes included
   - The incidence of development of critical illness or cardiac insult that necessitated ICU or CCU admission, invasive ventilation or resulted in death among the enrolled non-cardiac patients
   - The predictive value of at admission determination of AIP

and/or COVID-GRAM score for the incidence of progress to critical disease grade, development of cardiac or no-cardiac complications and mortality rates [MR] secondary to these events.

Statistical analysis

Statistical analyses were conveyed using IBM® SPSS® Statistics [Version 22, 2015; Armonk, USA]. Results were analyzed using ANOVA test, Mann-Witney test and Chi-square test [X2 test]. Correlation analysis was performed by Spearman's correlation analysis and predictability of at-admission variate for outcome was estimated using the Receiver characteristic curve (ROC) analysis. Significance was defined at cutoff point of P=0.05.

Results

The enrolment data of the included 302 patients as shown in table 1; majority of patients were males with mean age of about 53 years and BMI of 30.3 kg/m^2. Patients were mostly of mild severity, but all lab findings were out of normal range (**Table.1**).

Table 1. Patients' at admission data

Variables		Findings
Age [years]	**30-39**	16 [5.3%]
	40-49	76 [25.2%]
	50-59	154 [51%]
	60-69	50 [16.5%]
	≥70	6 [2%]
	Mean ±SD [range]	53.2±7.8 [33-74]
Sex	**Males**	211 [69.9%]
	Females	91 [30.1%]
BMI [kg/m^2]	**<25**	11 [3.6%]
	25-30	108 [35.8%]
	>30-35	183 [60.6%]
	Mean ±SD [range]	30.3±2.6 [22.7-34.9]
Clinical disease severity	**Mild**	195 [64.6%]
	Moderate	76 [23.2%]
	Severe	37 [12.2%]
Laboratory variables*	**TLC [10^3 cells/cc]**	12.3 [10.4-13.2]
	N/L ratio	3.81 [3.38-4.19]
	Serum CRP [mg/dl]	79 [54-96]
	Serum IL-6 [ng/ml]	43 [31-58]
	Serum D-dimer [µg/ml]	581 [436-702]
	Serum ferritin [ng/ml]	482 [349-684]
	Serum LDH [U/L]	285 [243-309]
	Serum direct bilirubin [mg/dl]	0.31 [0.25-0.38]

Data are presented as numbers and percentages; mean and standard deviation [SD]; *median and interquartile range [IQR]; BMI: Body mass index; TLC: Total leucocytic count; N/L ratio: Neutrophil/Lymphocyte counts; CRP: C-reactive protein; IL-6: Interleukin-6; LDH: Lactate dehydrogenase

According to estimated levels of plasma lipids, 114 patients [37.7%] were dyslipidemic; 59 of patients had mild COVID [30.3%], 31 of patients

had moderate disease [44.3%] and 24 of patients had severe COVID disease [64.9%] with significantly lower incidence of dyslipidemia among patients had mild COVID disease in comparison to those had moderate [p=0.0335] and severe [p=0.0006] and a significantly higher incidence of dyslipidemia among patients had severe [p=0.043] than those had moderate COVID disease. Moreover, according to computed AIP score, 92 patients had high, 133 patients had medium and 77 patients had low CR with significantly higher incidence of patients had high CR among patients with severe COVID than patients had mild [p=0.00002] and moderate [p=0.0018] COVID disease, but non-significantly [p=0.645] higher incidence of patients had high CR among patients had moderate than patients had mild COVID. Moreover, the computed AIP score of patients with high CR was significantly [p<0.0001] higher in patients had severe COVID disease than score of patients had either mild or moderate COVID disease with non-significantly [p=0.645] higher score among patients had moderate than those had mild COVID disease (**Table.2**).

Table 2. Incidence of dyslipidemia among enrolled patients and their distribution according to the AIP score

Group / Variable		Mild [n=195]	Moderate [n=70]	Severe [n=37]	Significance of difference		
					Mild vs. moderate	Mild vs. severe	Moderate vs. severe
Dyslipidemia		59 [30.3%]	31 [44.3%]	24 [64.9%]	0.0335	0.0006	0.043
Eulipidemia		136 [69.7%]	39 [55.7%]	13 [35.1%]			
AIP score	**Low**	58 [29.7%]	18 [25.7%]	1 [2.7%]	0.683	0.00002	0.0018
	Medium	88 [45.1%]	31 [44.3%]	14 [37.8%]			
	High	49 [25.1%]	21 [30%]	22[59.5%]			
	Median [IQR]	0.156 [0.11-0.266]	0.1945 [0.102-0.25]	0.347 [0.215-0.397]	0.645	<0.0001	<0.0001

Data are presented as numbers and percentages; median and interquartile range [IQR]; P<0.05 indicates significant difference; AIP: Atherogenic index of plasma

According to the COVID-GRAM critical illness score, only 71 of patients had mild disease severity had low critical illness risk, while the remaining 231 patients had medium risk of critical illness. Patients had at-admission mild disease severity had a median COVID-GRAM score of 61 [53-68] points, while those had moderate disease severity had a median score of 97 [92.75-108.25] and patients had severe disease had a median score of 119 [113-123] points with significantly [p<0.0001] higher median score than patients had mild or moderate disease severity and significantly [p<0.0001] higher score for patients had moderate than those had mild disease severity. There were 204 patients [67.5%] had COVID-GRAM risk of critical disease of <5%, 43 patients [14.2%] had risk of critical disease ranging between >5-10%, 27 patients [8.9%] had risk range of >10-

20%, 25 patients [8.4%] had risk of >20-30 %, while 3 patients [1%] had risk >30% to progress to critical disease (**Table. 3**).

Table 3. Patients' evaluation for liability for progress to critical disease according to the COVID-Gram Risk score for evaluation of the risk of critical illness

COVID-Gram score		Mild [n=195]	Moderate [n=70]	Severe [n=37]
Risk of critical illness	Low	71 [36.4%]	0	0
	Medium	124 [63.6%]	70 [100%]	37 [100%]
Score points; median {IQR]		61 [53-68]	97 [92.75-108.25]*	119 [113-123]*†
Risk percentage; median [IQR]	<5	185 [94.9%]	18 [25.7%]	1 [2.7%]
	>5-10	10 [5.1%]	33 [47.1%]	0
	>10-20	0	16 [22.9%]	11 [27%]
	>20-30	0	3 [4.3%]	22 [62.2%]
	>30	0	0	3 [8.1%]

* indicates the significance of difference versus patients had mild moderate; † indicates the significance of difference versus patients had severe COVID disease at P<0.05 for significance

During the duration of the study, 192 patients [63.6%] passed uneventful hospital stay and were discharged without developing complications secondary to the disease or the hospital stay. Unfortunately, 110 patients [36.4%] progressed to the critical disease severity and required intensive care. The incidence of progress to critical grade was significantly lower [p<0.0001] among patients had at-admission mild disease in comparison to those had at-admission moderate or severe disease with significantly [p=0.0013] higher incidence among patients had at-admission severe disease than patients had at-admission moderate disease. Among the 110 patients who progressed to critical disease grade; 47 patients [42.7%] developed cardiac insults and were admitted to the CCU, while 63 patients [57.3%] developed non-cardiac complications and were admitted to ICU. There were non-significant differences between patients developed cardiac or non-cardiac complications among studied patients categorized according to at-admission disease severity grade (**Table. 4**).

Unfortunately, 43 patients [39.1%] died during their ICU stay with significantly higher mortality rate among patients had at-admission severe disease than those had at-admission mild [p=0.0004] or moderate [p=0.026] disease severity with non-significantly [p=0.095] higher MR among those had moderate than those had mild at-admission disease severity. MR at CCU showed non-significant difference between patients who developed cardiac insults and categorized according to their at-admission disease severity grade. On contrary, MR secondary to non-cardiac complications was significantly lower among patients had at-admission mild disease in comparison to those had at-admission moderate [p=0.036] or severe [p=0.0015] disease severity with non-significantly higher among patients had at-admission severe disease (**Table. 4**).

Table 4. Patients' distribution according to progress to critical severity grade and survival outcome

Disease severity grade / Outcome		Mild [n=195]	Moderate [n=70]	Severe [n=37]	Total [n=302]
Progressed to critical severity grade	**Yes**	32 [16.4%]	44 [62.9%]	34 [91.9%]	110 [36.4%]
	No	163 [83.6]	26 [37.1%]	3 [8.1%]	192 [63.6%]
	P1		<0.0001	<0.0001	
	P2			0.0013	
Type of complications	**Cardiac**	12 [37.5%]	20 [45.5%]	15 [44.1%]	47 [42.7%]
	Non-cardiac	20 [62.5%]	24 [54.5%]	19 [55.9%]	63 [57.3%]
	P1		0.488	0.585	
	P2			0.906	
Total MR of patients progressed to critical grade	**Died**	6 [18.8%]	16 [36.4%]	21 [61.8%]	43 [39.1%]
	Survived	26 [81.2%]	28 [63.6%]	13 [38.2%]	67 [60.9%]
	P1		0.095	0.0004	
	P2			0.026	
MR of patients developed cardiac complications	**Survived**	8 [66.7%]	13 [85%]	5 [33.3%]	26 [55.3%]
	Died	4 [33.3%]	7 [15%]	10 [66.7%]	21 [44.7%]
	P1		0.923	0.085	
	P2			0.064	
MR of patients developed non-cardiac complications	**Survived**	18 [90%]	15 [62.5%]	8 [42.1%]	41 [65.1%]
	Died	2 [10%]	9 [37.5%]	11 [57.9%]	22 [34.9%]
	P1		0.036	0.0015	
	P2			0.183	

P1 indicates the significance of difference versus mild; P2 indicates the significance of difference versus moderate severity at P<0.05; MR: Mortality rate

Spearman's correlation analysis indicated a positive significant correlation between the computed AIP score, COVID-Gram score points and percentage of risk for progressing to critical illness and the reported outcome rates (**Table. 5**).

Table 5. Spearman's correlation analysis of AIP and COVID-Gram scores and patients' outcome regarding progress to critical severity grade and survival outcome

Evaluated scores / Studied variables	AIP score		COVID-Gram score points		COVID-Gram risk percentage	
	Rho.	p	Rho.	P	Rho.	P
Progress to critical severity grade	0.597	<0.001	0.427	<0.001	0.473	<0.001
Development of cardiac insult	0.477	<0.001	0.369	<0.001	0.381	<0.001
Total MR	0.407	<0.001	0.411	<0.001	0.427	<0.001
Cardiac MR	0.331	<0.001	0.315	<0.001	0.328	<0.001
Non-cardiac MR	0.223	<0.001	0.244	<0.001	0.254	<0.001

AIP score: Atherogenic index of plasma; Rho: Spearman's coefficient; MR: Mortality rate; P<0.05 indicates significant difference; P>0.05 indicates non- significant difference

ROC curve analysis could not differentiate between high at-admission AIP score and COVID-Gram score or critical risk percentage as predictors for progress of non-cardiac patients who were admitted with mild-to-severe COVID to critical grade or development of cardiac insult or subsequent total or cardiac mortality (**Table. 6**).

Table 6. ROC curve analysis of AIP and COVID-Gram scores and patients' outcome regarding progress to critical severity grade and survival outcome

Evaluated scores / Studied variables	AIP score			COVID-Gram score points			COVID-Gram risk percentage		
	AUC [SE]	p	95%CI	AUC [SE]	p	95%CI	AUC [SE]	p	95%CI
Progress to critical disease	0.858 [0.022]	<0.001	0.815-0.901	0.758 [0.031]	<0.001	0.697-0.819	0.784 [0.030]	<0.001	0.725-0.843
Development of cardiac insult	0.855 [0.026]	<0.001	0.805-0.906	0.795 [0.036]	<0.001	0.723-0.866	0.803 [0.034]	<0.001	0.736-0.870
Total MR	0.836 [0.029]	<0.001	0.779-0.892	0.839 [0.034]	<0.001	0.772-0.907	0.853 [0.032]	<0.001	0.790-0.916
Cardiac MR	0.875 [0.030]	<0.001	0.815-0.935	0.858 [0.038]	<0.001	0.784-0.932	0.872 [0.026]	<0.001	0.820-0.924
Non-cardiac MR	0.747 [0.043]	<0.001	0.662-0.832	0.771 [0.054]	<0.001	0.665-0.876	0.782 [0.055]	<0.001	0.675-0.889

AIP score: Atherogenic index of plasma; AUC: Area under curve; SE: Standard error; CI: Confidence interval; MR: Mortality rate; P<0.05 indicates significant difference; P>0.05 indicates non- significant difference

However, the automatic linear modeling regression analysis for the importance of high at-admission COVID-Gram score or critical risk percentage and AIP score for outcome prediction showed high at-admission CG-score could predict progress to critical grade by 39%, total mortality by 47% and mortality secondary to cardiac insult by 14% (**Fig.1**), while high at-admission CG-risk percentage could predict progress to critical grade

by 63% and total mortality by 37%, but could not predict the oncoming development of cardiac insult or its related mortality (**Fig.2).** On contrary, high AIP score at time of admission was found to be the only important predictor mortality secondary to oncoming cardiac insult, but could not predict development of other morbidities or total mortality.

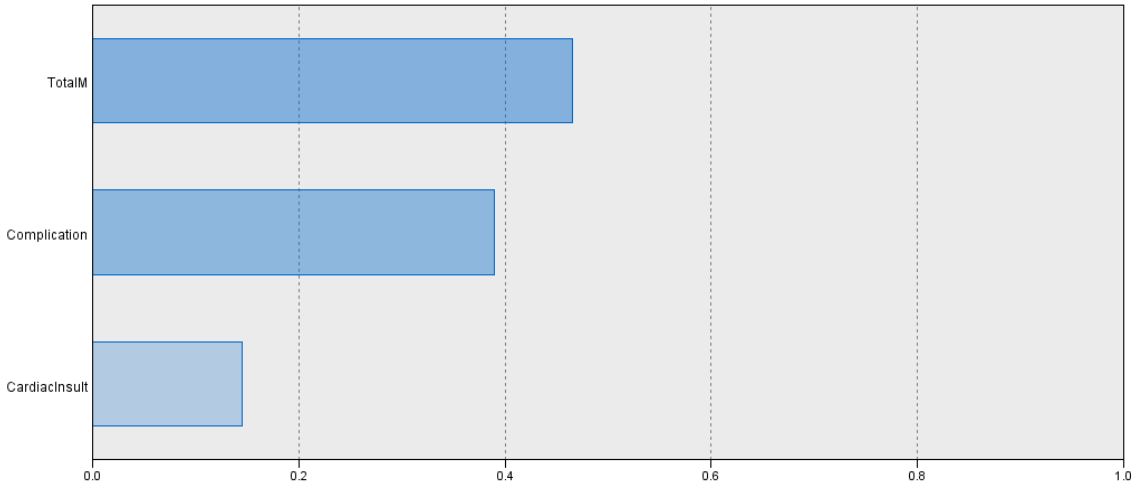

Fig. 1. The Automatic Linear Modeling regression analysis for the predictability of high CG score for outcomes of non-cardiac patients with COVID-19 of mild-severe disease severity

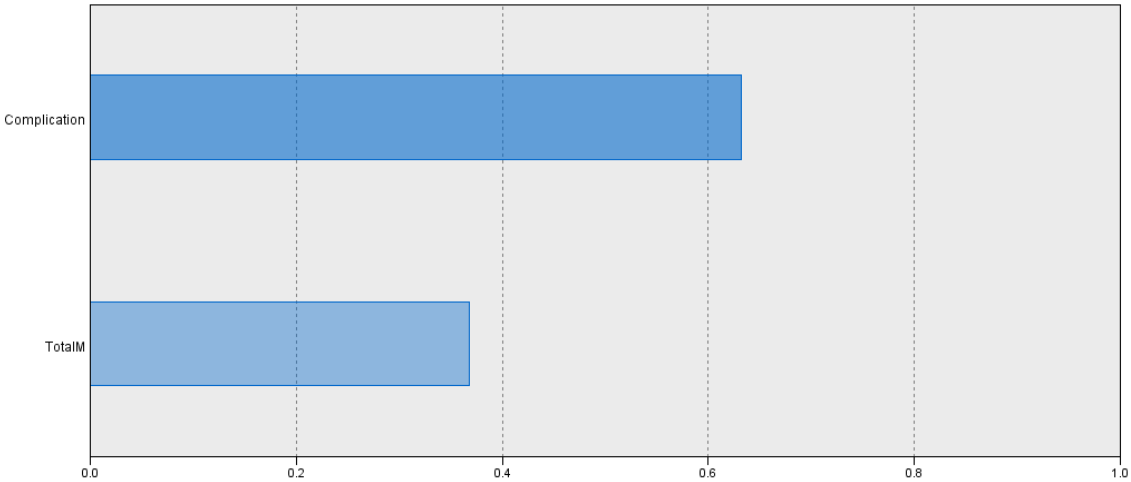

Fig. 2. The Automatic Linear Modeling regression analysis for the predictability of high CG-percentage for outcomes of non-cardiac patients with COVID-19 of mild-severe disease severity

Discussion

Estimation of plasma lipid levels at time of admission was not included in the routine laboratory evaluation of COVID-19 patients; however, the current study detected an incidence of dyslipidemia of 37.7% among the studied non-cardiac COVID patients and the incidence increases with the increased disease severity. Similarly, **Urbistondo et al. 2021** detected an incidence of dyslipidemia during evaluation of newly admitted COVID patients of 32.2%, and **Galyfos et al. 2021** detected dyslipidemia in 20.5% of patients who

had COVID-associated acute limb ischemia.

The current study detected high plasma TG and low plasma HDL-c levels in all dyslipidemic patients, but with more extensive changes with increasing COVID disease severity. These results coincided with **Masana et al. 2021** who detected high TG and low HDL-c levels in blood samples obtained on hospitalization of COVID patients with severe or critical disease and with **Zhong et al. 2021** who found plasma TG levels positively correlate with COVID disease severity markers. Also, **Bellia et al. 2021** detected low HDL levels and high TG in COVID patients and found TG levels were significantly associated with inflammatory biomarkers' levels and poorer in-hospital outcome of COVID-19 patients, irrespective of being dyslipidemic or not. Moreover, these results go in hand with studies that detected low HDL-c levels in COVID patients (**Mahat et al., 2021; Zhu et al., 2021; Yue et al., 2021**).

The AIP score, which entails a relation between TG and HDL-c levels, was high in the studied COVID patients and showed a positive significant correlation with both at-admission disease severity and development of COVID-induced morbidities and mortalities. Also, **Salari et al. 2021** identified high plasma TG among the independent risk factors of COVID-19 mortality and **Sampedro-Nuñez et al. 2021** detected a decrease in HDL-c in 42.9% and increased TG levels in 76.8% of COVID patients and found an inverse relation between plasma HDL levels and ICU admission and mortality. Also, using NMR spectroscopy, **Ballout et al. 2021** detected markedly reduced HDL particle numbers, especially the small HDL-P with high counts of TG-rich lipoprotein particle particularly the very small and small subfractions at presentation of patients of patients with severe COVID-19.

Statistical analyses showed high ability of estimated AIP score to predict the probability of getting cardiac insult during course of COVID disease in these non-cardiac patients. This finding goes in hand with recent studies documented that AIP might be a strong biomarker that could be used to predict the risk of cardiovascular events in diabetic patients (**Fu et al., 2021**) and functional outcome of patients with acute ischemic stroke (**Liu & Li, 2021**). Regarding COVID patients, the obtained results coincided with **Yıldırım & Kaya, 2021** who detected significantly lower HDL-c and higher TG levels in deceased patients in comparison to survivors and found the area under ROC curve for the AIP to predict mortality is 0.850.

In support of the application of AIP for prediction of cardiac insults in non-cardiac patients, **Kim et al. 2021** documented that higher AIP levels in non-cardiac non-diabetics may precede and predict the development of ischemic heart disease.

Concerning the relation between plasma TC and LDL-c levels and COVID disease severity, multiple studies detected low plasma TC and LDL-c levels in COVID patients (**Bellia et al., 2021; Mahat et al., 2021; Zhu et al., 2021; Yue et al., 2021**), while the current study detected high at-admission plasma TC and LDL-c in all dyslipidemic patients; this contradiction could be attributed to the design of these studies that were either retrospective study (**Bellia et al., 2021**) or meta-analysis of published works (**Mahat et al., 2021**) and all did not document timing of estimation of lipid profile, while **Yue et al. 2021** in their retrospective study documented that lipid profile was

estimated on 2-3 days after admission. Thus, the hallmark of the current study is the early estimation of plasma lipid levels that detected high levels of TC, LDL-c and TG, but its pitfall is absence of re-estimation during course of disease but this is because the study hypothesis was to detect incidental dyslipidemia in non-cardiac COVID patients and not to follow-up the level changes during the course of the disease.

COVID-GRAM critical illness score showed positive significant correlation with COVID disease severity and its related morbidities and could predict total and non-cardiac mortality, but its predictive value for cardiac mortality is minimal. In line with the reliability of COVID-Gram score for prediction of in-hospital mortality of COVID patients, **Al-Hassan et al. 2020** found AUC for the COVID-GRAM score, the CALL score and the nomogram was 0.636, 0.500 and 0.628, respectively. Also, **Shi et al. 2021** documented that the COVID-GRAM score demonstrated acceptable predictive performance for in-hospital death and **Covino et al. 2021** found COVID-GRAM calculated at ED admission, had the best performance for prediction of in-hospital death of elderly COVID patients.

The ability of AIP score to predict cardiac mortality and COVID-GRAM score to predict non-cardiac mortality points to its complementary function to achieve high prediction rates of outcome of COVID patients especially patients with unpredicted mortality as the studied population in the current study who were non-cardiac, non-morbidly obese, not elderly and mostly free of special pre-COVID morbidities. In line with the use of complementary scores, **Boero et al. 2021** found Lung Ultrasound Score of >15 points was associated with a high risk ratio of critical illness and COVID-19 Worsening Score accurately identify patients who are unlikely to need ICU admission, thus combined estimation could accurately differentiate COVID patients into high and low risk groups.

Conclusion

Dyslipidemia affects all subjects with an incidence of about 40% despite being non-cardiac, non-diabetic, not elderly nor morbidly obese. Dyslipidemia in COVID disease patients may deleteriously affect their outcome. Cardiac insult in non-cardiac COVID patients is an actual event with an incidence of 15.6% and was the cause of death of 7% of studied patients. Combined estimation of AIP score and COVID-GRAM critical illness score might accurately differentiate patients liable to develop complications especially cardiac insults and predict both cardiac and non-cardiac mortalities.

Limitations

Follow-up estimation of plasma lipid levels during hospital stay is a limitation of the study.

Recommendations

Estimation of plasma lipid levels is cheap investigation that could predict cardiac insults and mortality in COVID patients and thus needs to be included in the diagnostic protocol of COVID disease.

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