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ORIGINAL RESEARCH **CORONA EXPERIENCE**

Individual components of metabolic syndrome as a prognostic factor for morbidity and mortality in COVID-19

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ABSTRACT

Background: COVID-19 has emerged as a rapidly spreading pandemic with millions of deaths. We aimed to investigate whether metabolic syndrome can be used as a prognostic factor for the outcome of patients infected with this viral disease, regarding the ICU stay, the requirement of mechanical ventilation (MV) and mortality.

Methodology: This retrospective study included 90 patients admitted to intensive care unit (ICU) of Ain Shams University for pneumonic COVID-19 with a confirmed positive RT-PCR for COVID-19 and positive changes on chest computed tomography, over a period of 10 months from July 2021 to April 2022. They were divided into two groups according to the presence or absence of metabolic syndrome. The primary outcome measured was the length of ICU stay. Secondary outcome was the percentage of patients requiring mechanical ventilation (MV) and the mortality rate in the two groups.

Results: Patients with metabolic syndrome had higher liver transaminases, random blood glucose, triglycerides, ferritin, and P/F ratio compared to those without metabolic syndrome ($P < 0.05$). Components of metabolic syndrome such as hypertension, type 2 diabetes mellitus, and obesity significantly increased the risk of hospitalization and mortality in COVID-19 patients ($P < 0.05$).

Conclusion: Metabolic syndrome is a better prognostic indicator for severe disease outcomes in patients with COVID-19 than its individual components. Although patients with metabolic syndrome didn't have a higher need for mechanical ventilation, they had longer duration of ICU stay and a higher mortality rate.

Abbreviations: ACE-2: angiotensin-converting enzyme-2, hs-CRP: High sensitivity C-reactive protein,ICU: Intensive care unit, MV: Mechanical ventilation, MS: Metabolic syndrome, ROC: Receiver operating characteristic

Key words: Metabolic Syndrome; COVID-19; ICU; Mechanical ventilation; Mortality

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1. INTRODUCTION

The primary route of transmission of SARS-CoV-2 is droplet infection, though other routes remain a topic for investigation, as the virus has also been found in the stool and urine of the affected individuals.[1]

The disease severity varies from mild upper respiratory tract infection to severe pneumonia, respiratory failure and death. Risk groups identified for higher rates of morbidities, and mortalities included, patients with cardiovascular diseases, hypertension, chronic respiratory diseases, metabolic syndrome (MS), and diabetes mellitus (DM).[2,3] MS consists of a group of risk factors including central obesity, hypertension, dysglycemia, atherogenic dyslipidemia, and pro-inflammatory state.[4]

Clinically, MS is defined according to the ATP-III guidelines as the presence of 3 or more of the following factors: increased waist circumference, hypertriglyceridemia (>150 mg/dL or on treatment for hypertriglyceridemia), elevated blood pressure (systolic > 130 mmHg and/or diastolic > 85 mmHg) reduced high-density lipoproteins (< 40 mg/dL in males; < 50 mg/dL in females), and dysglycemia (blood sugar levels that go too low or too high or on treatment for hyperglycemia).[5] Components of MS are among the risk factors for morbidity and mortality in patients with COVID-19.[6]

The pathophysiologic mechanisms for these observations remain obscure. An interaction between SARS-CoV-2 and the angiotensin-converting enzyme-2 (ACE2) facilitating viral entry into the host cells has been suggested. ACE2 is present in many tissues especially pancreatic islets, vascular endothelium, and adipose tissue. The SARS-CoV-2 -ACE2 interaction in these tissues, maybe responsible for the severity of clinical manifestations among COVID-19 patients with MS.[4, 7]

The pro-inflammatory sequalae observed in individuals with MS has been suggested to contribute in the COVID-19-mediated immune dysregulation, including abnormal immune reactions, hyper inflammatory sequalae, and thrombotic vulnerability.[8]

We aimed to investigate to what extent various components of MS can be used as a prognostic factor for outcomes of patients suffering from COVID-19.

2. METHODOLOGY

The ethical approval from the institutional Research Ethics Committee (No. MS 640/2021) was obtained. Patients or their caregivers were informed about the purpose and the anticipated benefits of the research and confidentiality of data was ensured. This study is compliant with the ethical principles of declaration of Helsinki for medical research involving human subjects.

Ninety patients admitted to ICU for pneumonia associated with COVID-19 infection, diagnosed using positive RT-PCR and confirmed by chest computed tomography findings. Patients were divided into two groups depending on the association of MS. This study was conducted over a period of 10 months from July 2021 to April 2022 on patients admitted to ICU of Ain Shams University. Patients were divided into equally into two groups; Group MS included COVID-19 patients with MS, and Group NMS included COVID-19 without MS. Patients who received any COVID vaccine were excluded. Egyptian people began receiving the vaccine regularly only several months after the study.

A sample size was determined using Power and Sample Size (PASS) software, setting alpha error at 5% and power at 80%; the minimum needed sample was 35 patients for each group.

2.1. Study Procedure

All patients were subjected to complete history taking including personal history, history of the current illness, past medical history of chronic illness (diabetes mellitus and hypertension). General physical examination included body built, BMI calculation and SpO_2 using pulse oximeter.

Review of patients' laboratory investigations during admission included; complete blood count (CBC), random blood sugar, routine liver and kidney function tests, fasting lipid profile; serum total and high-density lipoprotein (HDL), cholesterol and triglycerides. Inflammatory markers including measurement of high sensitivity C-reactive protein (hs-CRP), serum ferritin, lactate dehydrogenase (LDH) and D-dimer were also analyzed. Arterial blood gases (ABG's) and PaO_2 / FiO_2 (P/F) ratio were measured. CT chest was used for evaluation of severity of lung disease and detection of extra-pulmonary complications. Any need for invasive mechanical ventilation and total duration of hospital and ICU stay were recorded.

All patients received the treatment which included inj. dexamethasone 6 mg OD, prophylactic anticoagulation, and remdesivir 200 mg on the first day, and then 100 mg/day for 7 days in severe cases. While critically ill patients received the same dose of remdesivir, therapeutic anti coagulation, and methyl prednisolone 2 mg/kg. Patients who didn't improve on steroids within 24 h received tocilizumab 4–8 mg/kg/day for 2 doses.

2.2. Statistical Analysis

The Statistical Package for Social Science (IBM SPSS) version 23 was used for data analysis. The qualitative data were analyzed in terms of number and percentages

Table 1: Comparison between two groups regarding the presence of co-morbidities

Co-morbidities	Group MS N = 45	Group NMS N = 45	Test value*	P-value
Co-morbidities	28 (62.2)	45 (100.0)	20.959	**0.000**
Rt breast cancer	0 (0.0)	2 (4.4)	1.279	0.258
HCC	1 (3.6)	0 (0.0)	1.629	0.202
CKD	1 (3.6)	0 (0.0)	1.629	0.202
IHD	4 (14.3)	8 (17.8)	0.153	0.695
Obesity	0 (0.0)	45 (100.0)	73.000	**0.000**
DM	10 (35.7)	45 (100.0)	38.396	**0.000**
HTN	14 (50.0)	45 (100.0)	27.839	**0.000**
Bronchial asthma	1 (3.6)	0 (0.0)	1.629	0.202

*Data presented as n (%); P < 0.05 considered as significant; * Chi-square test, ** Independent t-test*

while quantitative data are presented as mean, standard deviations and ranges.

Chi-square test was used to compare two groups with qualitative data and Fisher exact test was used when the expected count in any cell was found less than 5. Independent t-test and Mann-Whitney test were used to compare quantitative data between two independent groups using parametric and non-parametric distribution respectively. Pearson's correlation coefficient was used to detect correlation studies. Logistic regression analysis was used to determine the relation between hospital stay and other variables. Receiver operating characteristic (ROC) curve was employed to determine the best cut-off value of serum ferritin and absolute lymphopenia as risk factors for the need of mechanical ventilation.

The confidence interval was adjusted to 95%. $P < 0.05$ was considered significant.

3. RESULTS

Patients in both groups were comparable regarding age; 47.47 ± 2.35 y vs 47.42 ± 2.51 y (P = 0.931), and gender distribution; M:F ratio 26:19 vs 34:21 (P = 0.671) in Group MS vs. Group NMS; while, there was a significant difference between both groups regarding BMI; 32.69 ± 1.16 in Group MS vs 27.36 ± 1.21 in Group NMS (P < 0.001).

Additionally, patients with MS showed significantly higher comorbidities particularly obesity, diabetes and hypertension (Table 1).

There were no significant differences between both groups regarding the onset of symptoms (days) and CT-chest findings (P > 0.05) (Table 2).

Regarding the laboratory findings of the studied groups, we found a significant difference between the two groups regarding the presence of absolute lymphopenia, elevated liver transaminases, kidney functions, random blood glucose, lipid profile, and markers of acute phase reaction (ferritin and LDH) and P/F ratio (P < 0.05) (Table 3).

Although the number of patients requiring mechanical ventilation in the MS group was more than those requiring mechanical ventilation in the Group NMS, statistical analysis showed no significant difference, [11 (26.7%) vs. 5 (11.1%), P = 0.099], but further analysis of the individual components of MS showed that patients

Table 2: Comparative onset of symptoms (days) and CT-chest findings in two groups

Variable		Group MS N = 45	Group NMS N = 45	Test value	P-value
Onset of symptoms (days)		6.00 ± 0.48	6.02 ± 0.62	-0.190**	0.849
CT-Chest	Bilateral mild GGO	40 (88.9)	45 (100.0)	5.294*	0.151
	Bilateral mild to moderate GGO	1 (2.2)	0 (0.0)		
	Bilateral moderate GGO	3 (6.7)	0 (0.0)		
	bilateral sever GGO	1 (2.2)	0 (0.0)		

Data presented as mean ± SD or n (%); P < 0.05 considered as significant;
** Chi-square test, ** Independent t-test; GGO = Ground-glass opacities*

Table 3: Comparison between the groups regarding laboratory findings

Laboratory findings		Group MS N = 45	Group NMS N = 45	Test value	P-value
Hemoglobin (mg/dl)	Mean ± SD	13.34 ± 1.62	13.21 ± 1.46	0.396**	0.693
	Range	9.2–17	10.6–16.8		
Total leucocytic count (/mm^3)	Mean ± SD	8.68 ± 4.68	7.24 ± 2.80	1.771**	0.080
	Range	3.3–24	3.2–13.8		
Absolute lymphopenia	Mean ± SD	1.38 ± 1.69	0.72 ± 0.31	2.578**	0.012
	Range	0.2–11.7	0.3–1.3		
Platelet (/mm^3)	Mean ± SD	264.04 ± 90.81	260.00 ± 169.18	0.141**	0.888
	Range	63–587	119–841		
Ferritin (micro/Ll)	Median (IQR)	436 (356–634)	946 (752–1498)	-6.191 ß	0.000
	Range	47–974	328–2979		
D-Dimer (mg/L)	Median (IQR)	0.7 (0.4–0.9)	0.5 (0.4–2.4)	-0.466 ß	0.641
	Range	0.2–5.7	0.2–4		
C reactive protein (mg/L)	Median (IQR)	44 (22–87)	40 (28–158)	-1.054 ß	0.292
	Range	3.7–311	2–375		
Lactate dehydrogenase (LDH)(u/L)	Median (IQR)	215 (153–314)	369 (294–486)	-3.854 ß	0.000
	Range	20–642	120–877		
Aspartate transaminase (AST)(IU/L)	Mean ± SD	36.76 ± 14.75	46.89 ± 21.18	-2.633**	0.010
	Range	11–112	17–85		
Alanine transaminase (ALT)(IU/L)	Mean ± SD	27.53 ± 12.01	56.40 ± 50.93	-3.701**	0.000
	Range	6–67	16–231		
Urea (mg/dl)	Mean ± SD	23.91 ± 8.98	27.78 ± 11.68	-1.760**	0.082
	Range	10–52	10–55		
Creatinine (mg/dl)	Median (IQR)	1 (0.8–1.1)	1.1 (1–1.2)	-2.624 ß	0.009
	Range	0.4–3.2	0.7–1.7		
Random blood sugar (mg/dl)	Mean ± SD	124.84 ± 43.01	231.18 ± 56.32	-10.065**	0.000
	Range	79–240	158–375		
P/F ratio	Mean ± SD	272.62 ± 66.72	212.18 ± 94.49	3.505**	0.001
	Range	110–400	70–450		
Triglycerides (mg/dl)	Mean ± SD	162.89 ± 41.31	289.16 ± 43.03	-14.199**	0.000
	Range	110–265	216–374		
High density lipoprotein (mg/dl)	Mean ± SD	47.89 ± 7.47	37.67 ± 3.98	8.101**	0.000
	Range	30–58	31–45		

*P < 0.05 considered as significant; * Chi-square test, ** Independent t-test, ß Mann-Whitney test*

requiring mechanical ventilation had higher incidence of DM, higher BMI, and higher triglycerides levels (P < 0.05). And there was a significant difference between both groups regarding ICU stay; (P = 0.034). The mean duration of mechanical ventilation amongst the MS group was 8 ± 7.1 vs. 6.6 ± 5.9 days, with P = 0.7 and a non-significant difference between hospital stay (P < 0.001). Meanwhile, no significant difference was detected between both groups regarding time from onset of symptoms till mechanical ventilation (P = 0.063).

A negative correlation was found between the duration of *ICU stay* and HDL (-0.222, P = 0.035), while no significant correlation was found with BMI, triglycerides and cholesterol (P > 0.05).

Table 4: Univariate and multivariate logistic regression analysis for factors associated with presence of MS and Hospital Stay

Factor	Univariate				Multivariate			
	P-value	B	95% CI for OR		P-value	B	95% CI for OR	
			Lower	Upper			Lower	Upper
BMI	0.007	-9.133	-15.674	-2.593	0.000	30.667	30.066	31.269
TG	0.391	-3.333	-11.064	4.397	0.000	240.283	224.625	255.941
HDL	0.099	5.500	-1.064	12.064	0.000	41.662	40.090	43.233
Serum cholesterol	0.109	-10.33	-23.329	2.662	0.000	260.866	245.826	275.905

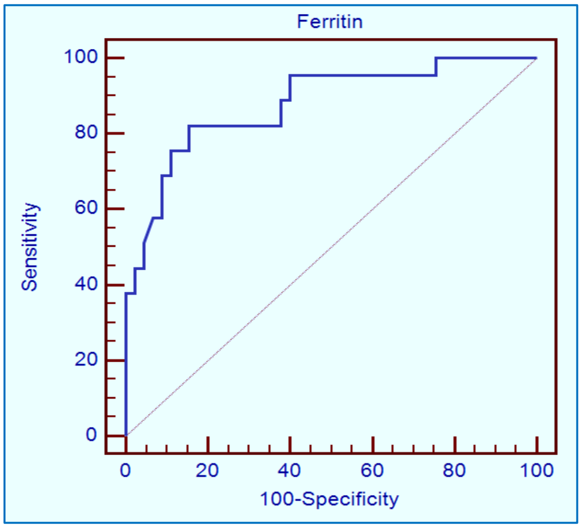

Figure 1: ROC curve for detection of serum Ferritin as risk factor for mortality and need of mechanical ventilation

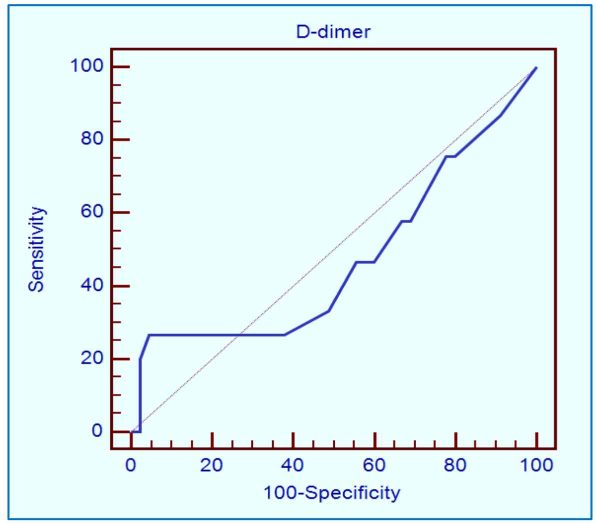

Figure 3: ROC curve for detection of D-dimer as risk factor for mortality and need of mechanical ventilation

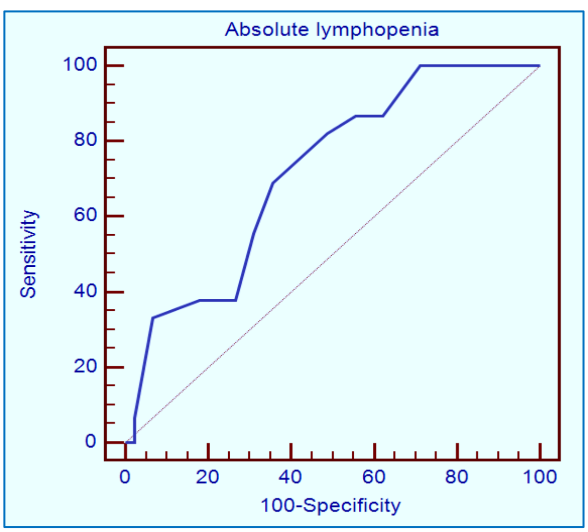

Figure 2: ROC curve for detection of absolute lymphopenia as risk factor for mortality and need of mechanical ventilation

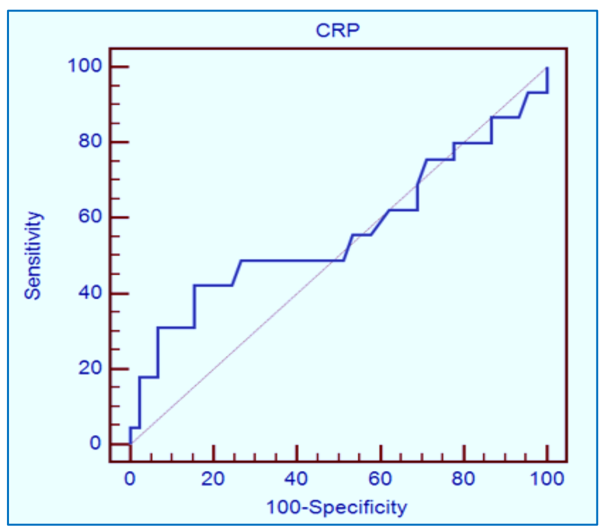

Figure 4: ROC curve for detection of CRP as risk factor for mortality and need of mechanical ventilation

Table 5: Univariate and multivariate logistic regression analysis for factors associated with presence of MS and need of mechanical ventilation

Factor	Univariate				Multivariate			
	P-value	B	95% C.I. for OR		P-value	B	95% C.I. for OR	
			Lower	Upper			Lower	Upper
BMI	0.754	0.067	-0.356	0.505	0.000	31.529	29.823	33.236
TG	0.000	-0.625	-0.952	-0.298	0.000	263.294	221.222	305.367
HDL	0.147	0.300	-0.108	-0.708	0.000	41.588	38.492	44.684
Serum cholesterol	0.147	-0.667	-1.604	0.271	0.000	269.471	229.565	309.376

positive correlation was found between the duration of *hospital stay* and BMI (r = 0.557, P < 0.001), triglycerides (r = 0.432, P < 0.001), cholesterol (r = 0.511, P < 0.001); meanwhile, there was negative correlation with HDL (r = -0.327, P = 0.002). Also, a significant relation was found between hospital stay and the presence of hypertension (P = 0.026) and diabetes (P < 0.001).

Logistic regression analysis revealed that BMI is the most significant factor for hospital stay (Table 4), while levels of triglycerides represent the significant factor for the need of mechanical ventilation (Table 5).

ROC curve analysis detected serum ferritin > 700 µg/l and absolute lymphopenia < 0.9 as risk factors for the need of mechanical ventilation and high mortality rate with high sensitivity and specificity (Figure 1 and 2).

Patients with D-dimer > 1.4 were at increased risk of mechanical ventilation and mortality. Figure 4 shows ROC analysis for detection of the value of CRP above which the patient is at risk for mechanical ventilation and mortality and was found to be >120 mg/dL (normal value is < 1.0 mg/dL).

4. DISCUSSION

The coronavirus disease 2019 (COVID-19) which has rapidly spread, was considered as a global pandemic with high mortality worldwide. Acute respiratory distress syndrome (ARDS), septic shock, and multiorgan failure were considered the leading causes of several deaths following severe infections with COVID-19.[9]

We wanted to find to what extent MS can be used as a prognostic factor for the outcomes of patients infected with COVID-19. We found significant relationship between the presence of hypertension, DM, and obesity and hospital stay and mortality. Although the number of patients requiring mechanical ventilation in the MS group was more than those requiring mechanical ventilation in the other group, statistical analysis showed no significant difference, which could be attributed to the relatively small sample size of our study, but further analysis of the individual components of MS showed that patients with DM, a higher BMI, and higher triglyceride levels required mechanical ventilation more than those who had normal values of these parameters.

There was no significant difference between both groups regarding their age and sex, but there was a highly significant difference found between two groups regarding BMI.

In contrast to our results, some recent studies stated that the mortality rate was increased in females with MS compared to male gender with COVID-19 infection. Additionally, patients younger than 65 years of age suffered from a higher mortality rate when compared to those with older age group. In the same context, several previous studies have reported that although MS is more prevalent in elderly patients, the mortality decreased with age. This was similar to what was seen in our studied individuals with COVID-19.[10]

Anderson and his colleagues declined the association between obesity and mortality among their studied patients with COVID-19 who were older than 65 years.[11] This was explained by the possibility of better management of the individual components of MS in the elderly.[12] According to the National Health and Nutrition Examination Surveys (NHANES), data collected from 2011 to 2016 revealed that the prevalence of MS among females has increased significantly. Also, several studies suggested increased susceptibility to cardiovascular diseases in females with MS in comparison to male gender.[13]

Hypertension and diabetes were frequently reported among hospitalized patients with COVID-19 which affect the clinical outcomes among those patients.[14] Our study reports a significant association between hypertension and mortality, and this is consistent with a recent study which reported similar results.[15]

In our study, although obesity was associated with increased need for mechanical ventilation, no association was observed with increased mortality in those individuals. Nevertheless, a positive correlation was found between the duration of hospital stay and BMI. An earlier study reported similar findings among their studied population.[16] On the other hand, Ni and colleagues reported decreased mortality among their studied critically ill patients with pneumonia who were obese.[17]

We found that hyperlipidemia was one of the associated risk factors of critical outcomes including the length of stay at ICU and the total hospital stay. A possible explanation can be related to the immune-modulating properties of statin and decreased cytokine production.[18] This was in disagreement with a recent study that stated that among individual with MS, only DM was the main factor associated with significant critical outcomes.[19]

Our study also reports that patients with MS had a significantly increased need for mechanical ventilation and a longer ICU admission. The study highlights that the presence of MS is a good predictor of clinical outcomes in COVID-19 compared with other comorbidities.

Regarding the laboratory findings of the studied patients, we found that there was no difference between both groups regarding their Hb, TLC, platelet counts, D-dimer, CRP, and urea levels. Meanwhile, there was a significant difference found between them regarding absolute lymphopenia and AST, and there was highly significant difference between two groups regarding ferritin, LDH, ALT, creatinine, random blood sugar, P/F ratio, triglycerides and HDL. In accordance with our study, Zhang et al. reported association between MS and abnormal liver transaminases especially in those with severe COVID-19 infection.[20]

In our study, patients with MS had significantly higher liver enzymes within 24 h of admission compared to those without, which can be associated with mortality and other clinical outcomes. In contrast to our study, another study noted no association between these inflammatory markers and morbidity among patients with COVID-19, irrespective of its association with MS.[21]

As regards the need of MV, ICU stay and hospital stay, we found that there was no significant difference found between both groups regarding the need for MV. Meanwhile, the duration of ICU stay was significantly higher in those with MS. A negative correlation was found between the duration of ICU and hospital stay and HDL and a positive correlation was found between the duration of hospital stay and BMI ($r = 0.557$, $P < 0.001$), triglycerides ($r = 0.432$, $P < 0.001$), and cholesterol. On the other hand, a previous study observed higher frequency of dyslipidemia in hospitalized patients.[22]

In our study, when DM was evaluated as part of MS, the syndrome was significantly associated with morbidities, especially when combined with other underlying conditions, suggesting that DM might be a risk factor for severe clinical outcomes.

MS has been found to be associated with multiple negative outcomes among hospitalized COVID-19 patients. This was in agreement with the study by Xie et al.[6] done on type 1 and type 2 DM and they reported the same findings. Another earlier study by Sisó-Almirall et al., which evaluated patients with diabetes during COVID pandemic reported its risk association with prolonged hospitalization and morbidities.[23]

5. CONCLUSION

Metabolic syndrome is a prognostic indicator for severe disease outcomes in patients with COVID-19 more than its individual components. Patients with metabolic syndrome have a significantly higher need for ICU and hospital admission. The need for mechanical ventilation is also higher across all patients with metabolic syndrome.

Future studies and the development of a clinical risk score for mortality/severe outcomes in COVID-19 should consider incorporating metabolic syndrome. Longitudinal studies with larger representative sample are required for providing evidence on nature of association between metabolic syndrome and COVID-19 morbidity and mortality.

6. Availability of data

All data generated or analyzed during this study are included in this published article. All data are available for sharing.

7. Conflict of interest

Authors declare no conflict of interests.

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This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

9. Authors contributions

All authors contributed to the conception, design of the work and interpretation of data, drafted the work and revised it, approved the submitted version.

10. REFERENCES

1. Del Rio C, Malani PN. COVID-19 - New Insights on a Rapidly Changing Epidemic. JAMA. 2020;323(14):1339–1340. [PubMed] DOI:10.1001/jama.2020.3072
2. Gupta R, Ghosh A, Singh AK, Misra A. Clinical considerations for patients with diabetes in times of COVID-19 epidemic. Diabetes and Metabolic Syndrome: Clinical Research and Reviews, 2020;14(3):211–212. [PubMed] DOI: 10.1016/j.dsx.2020.03.002

3. Marhl M, Grubelnik V, Magdič M, Markovič R. Diabetes and Metabolic Syndrome as risk factors for COVID-19. Diabetes Metab Syndr. 2020;14(4):671–677. [PubMed] DOI: 10.1016/j.dsx.2020.05.013

4. Bansal R, Gubbi S, Muniyappa R. Metabolic syndrome and COVID 19: Endocrine-immune-vascular interactions shapes clinical course. Endocrinology. 2020;161(10):1-15. [PubMed] DOI: 10.1210/endocr/bqaa112

5. Ranjan P, Kumar A, Chowdhury S, Pandey S, Choudhary A, Bhattacharya A, et al. Is excess weight a risk factor for the development of COVID 19 infection? A preliminary report from India. Diabetes Metab Syndr. 2020;14(6):1805–1807. [PubMed] DOI: 10.1016/j.dsx.2020.09.012

6. Xie J, Zu Y, Alkhatib A, Pham TT, Gill F, Jang A, et al. Metabolic syndrome and COVID-19 mortality among adult black patients in new orleans. Diabetes Care. 2021;44(1):188-193. [PubMed] DOI: 10.2337/dc20-1714

7. Cure E, Cumhur Cure M. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may be harmful in patients with diabetes during COVID-19 pandemic. Diabetes Metab Syndr. 2020;14(4):349–350. [PubMed] DOI: 10.1016/j.dsx.2020.04.019

8. Pal R, Bhadada SK. COVID-19 and diabetes mellitus: An unholy interaction of two pandemics. Diabetes Metab Syndr. 2020;14(4):513–517. [PubMed] DOI: 10.1016/j.dsx.2020.04.049

9. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708- 1720. [PubMed] DOI: 10.1056/NEJMoa2002032

10. Wang J, Ruotsalainen S, Moilanen L, Lepistö P, Laakso M, Kuusisto J. The metabolic syndrome predicts cardiovascular mortality: a 13-year follow-up study in elderly non-diabetic Finns. Eur Heart J. 2007 Apr;28(7):857-64. [PubMed] DOI: 10.1093/eurheartj/ehl524

11. Anderson MR, Geleris J, Anderson DR, Zucker J, Nobel YR, Freedberg D, et al. Body Mass Index and Risk for Intubation or Death in SARS-CoV-2 Infection: A Retrospective Cohort Study. Ann Intern Med. 2020 Nov 17;173(10):782-790. [PubMed] DOI: 10.7326/M20-3214

12. Hildrum B, Mykletun A, Dahl AA, Midthjell K. Metabolic syndrome and risk of mortality in middle-aged versus elderly individuals: the Nord-Trøndelag Health Study (HUNT). Diabetologia. 2009 Apr;52(4):583-90. [PubMed] DOI: 10.1007/s00125-009-1271-5

13. Hirode G, Wong RJ. Trends in the Prevalence of Metabolic Syndrome in the United States, 2011-2016. JAMA. 2020;323(24):2526–2528. [PubMed] DOI:10.1001/jama.2020.4501

14. Chen Y, Yang D, Cheng B, Chen J, Peng A, Yang C, et al. Clinical Characteristics and Outcomes of Patients With Diabetes and COVID-19 in Association With Glucose-Lowering Medication. Diabetes Care. 2020 Jul;43(7):1399-1407. [PubMed] DOI: 10.2337/dc20-0660

15. Kim L, Garg S, O'Halloran A, Whitaker M, Pham H, Anderson EJ, et al. Risk Factors for Intensive Care Unit Admission and In-hospital Mortality Among Hospitalized Adults Identified through the US Coronavirus Disease 2019 (COVID-19)-Associated Hospitalization Surveillance Network (COVID-NET). Clin Infect Dis. 2021 May 4;72(9):e206-e214. [PubMed] DOI: 10.1093/cid/ciaa1012

16. Goyal P, Ringel JB, Rajan M, Choi JJ, Pinheiro LC, Li HA, et al. Obesity and COVID-19 in New York City: A Retrospective Cohort Study. Ann Intern Med. 2020 Nov 17;173(10):855-858. [PubMed] DOI: 10.7326/M20-2730

17. Ni YN, Luo J, Yu H, Wang YW, Hu YH, Liu D, et al. Can body mass index predict clinical outcomes for patients with acute lung injury/acute respiratory distress syndrome? A meta-analysis. Crit Care. 2017;21(1):36. [PubMed] DOI:10.1186/s13054-017-1615-3

18. Geovanini GR, Libby P. Atherosclerosis and inflammation: overview and updates. Clin Sci (Lond). 2018 Jun 21;132(12):1243-1252. [PubMed] DOI: 10.1042/CS20180306

19. Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. BMJ. 2020 May 22;369:m1966. [PubMed] DOI: 10.1136/bmj.m1966

20. Zhang C, Wu Z, Li JW, Zhao H, Wang GQ. Cytokine release syndrome in severe COVID-19: interleukin-6 receptor antagonist tocilizumab may be the key to reduce mortality. Int J Antimicrob Agents. 2020 May;55(5):105954. [PubMed] DOI: 10.1016/j.ijantimicag.2020.105954

21. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, et al. Hematological findings and complications of COVID-19. Am J Hematol. 2020 Jul;95(7):834-847. [PubMed] DOI: 10.1002/ajh.25829

22. Alali AS, Alshehri AO, Assiri A, Khan S, Alkathiri MA, Almohammed OA, et al. Demographics, comorbidities, and outcomes among young and middle-aged COVID-19 patients in Saudi Arabia. Saudi Pharm J. 2021 Aug;29(8):833-842. [PubMed] DOI: 10.1016/j.jsps.2021.06.005

23. Sisó-Almirall A, Kostov B, Mas-Heredia M, Rotllan SV, Sequeira-Aymar E, Sans-Corrales M, et al. Prognostic factors in Spanish COVID-19 patients: A case series from Barcelona. PLoS One. 2020;15(8):e0237960. [PubMed] DOI: 10.1371/journal.pone.0237960

