Original Article

Unmasking the Role of Obesity in COVID-19: Effects on Laboratory parameters, inflammatory Markers and Clinical outcome

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Objectives: To compare the outcome in obese and non-obese covid positive patients.

Methodology: In this retrospective study, data were obtained from the records of 150 COVID-positive patients, aged 18-80 years, admitted to Railway Hospital Rawalpindi and Riphah International Hospital Sihala from July 2021 to November 2022. Patients were divided into two groups on the basis of BMI. They were categorised into two groups: obese and non-obese. Laboratory parameters, inflammatory markers and outcomes were compared in two groups.

Results: Blood gas analysis revealed significantly higher pCO_2 levels (62.01±21.98 vs 54.35±12.43 mmHg, p=0.011) and lower PO2 in obese as compared to non-obese (62.96±12.07 vs 65.85±11.09 mmHg, p=0.038). No significant differences were observed between the two groups for ferritin, d-dimers, lactate dehydrogenase (LDH) and C-reactive protein (CRP). Obese patients had significantly higher glycosylated hemoglobin (Hb-A1c) levels (6.98±1.85% vs 6.17±1.64%, p=0.005). Oxygen requirements at discharge and mortality rate were significantly higher in obese as compared to non-obese (1.48±1.3 vs 0.70±1.05 L/min, p<0.001, and 33 (40.2%) deaths compared to 10 (14.7%), p=0.001).

Conclusion: Obese covid positive patients were more likely to have poor outcome in terms of increase mortality.

Keywords: C-reactive protein, D-Dimers, ferritin, inflammatory markers, obesity, outcome.

INTRODUCTION

COVID-19 was first reported in China in 2019-2020.[1] Numerous factors associated with an increased death rate among COVID positive patients include old age, presence of comorbidities and length of hospital stay.[2] Recent data suggest that obesity is a risk factor for assisted mechanical ventilation, ICU admissions, progression to ARDS and disease severity,[3] and so is high BMI.[4,5]

Severe COVID-19 is believed to cause cytokine release syndrome (CRS), which is a heightened inflammatory response that can cause organ failure and death.[6] Inflammatory response is characterized by an increased production of CRP, d-dimers and ferritin.[7,8] Direct tissue damage by the toxins and cytokine can lead to increased production of LDH.[9] The Lungs are the commonest site of injury by cytokine storm and patients can progress to acute respiratory distress syndrome.[10]

Obese patients have other comorbidities like diabetes, HTN, that make them more vulnerable to poor outcomes.[11] Obese patients have decreased vital capacity and functional residual lung capacity that make them more prone to hypoxemia. Obesity creates a condition of inflammation in the body and puts a stress by increasing cytokine releases in the body.[12] This study was carried out to compare Lab parameters and inflammatory markers between obese and non-obese Covid-19 patients and to compare their clinical outcomes and comorbidities.

METHODOLOGY

This retrospective cohort study obtained data from the records of 150 COVID-19 positive patients, aged 18-80 years admitted in the wards of Railway Hospital Rawalpindi and Riphah International Hospital, Sihala from July 2021 to November 2022. It gained approval from Islamic International Dental Hospital (Ref No: IIDC/IRC/2022/012/006).

By using Rao soft sample size calculator, sample size came out to be 252 with Confidence interval of 95%. However, patients with missing BMI and lab values, smokers, pregnant females, patients with incomplete records, patients with a history of COPD, tuberculosis, any autoimmune disease and cancer were excluded from the study. Finally, 150 patients were included in the analysis. Patients were grouped on the basis of their BMI: Group I included non obese (n=68) BMI (18-29.9kg/m^2) and Group II included obese patients (n= 82) (BMI >30kg/m^2).

We retrieved the baseline data, symptoms including fever, malaise loss of taste and smell, cough, shortness of breath, and laboratory parameters such as lymphocytic count, LDH, serum ferritin and blood gases, from patients

record.

Statistical Analysis: We used SPSS version 25. Independent sample t-test and Man Whitney U test were employed for comparison of the variables between the groups. Chi-square test was applied for comparison bet-ween categorical variables. Correlation of BMI with lab parameters and outcomes in COVID-19 positive patients was done using Pearsons's correlation. And noticing a significant correlation of BMI with HbA1c, the role of HbA1c in predicting outcome was estimated by ROC analysis. $p<0.05$ was considered significant.

RESULTS

Out of 150 patients, 82 (54.7%) were obese and 68 (45.3%) were non-obese. Mean age was 61.1 years (range 18-80) and 84(56%) were males and 66(44%) females. Co-morbidities showed that 79(52.7%) were hypertensive, 43(28.7%) were diabetic, 32(21.34%) had ischemic heart disease, 11(7.3%) had obstructive sleep apnea and 6(4%) had acute on chronic kidney disease.

Blood gas and biomarkers: Statistical analysis of blood gases revealed significant differences between obese and non-obese patients. In terms of inflammatory biomarkers, no significant differences were observed between the two groups (Table 1).

Glycemic control and oxygen requirements: Obese patients had higher HbA1c levels (6.98±1.85%) vs. the non-obese patients (6.17±1.64%), (p=0.005). Baseline blood sugar levels (BSF) were also elevated in obese patients ((Table 1).

Clinical outcomes and mortality: The mortality rate was significantly higher in obese patients, with 33(40.2%) deaths compared to 10(14.7%) in the non-obese group (p=0.001). No difference was found regarding disease severity, mechanical ventilation and presence of radiological findings in two groups (Table 2).

Correlation of laboratory parameters and outcomes with BMI: Significant positive correlation of BMI was observed with PCO_2 (r =.274, p=0.001), LDH (r =.228, p=0.005), HbA1c (r =.223, p=0.006), outcome (r =.263, p=0.001) and comorbidity (r =.262, p=0.001) reinforcing the notion that higher BMI is linked with respiratory compromise, tissue damage, and worsened glycemic control (Table 3).

ROC curve analysis of HbA1c for predicting clinical outcomes: At a cutoff value of 5.1%, HbA1c has sensi-

Table 1: Comparison of blood gas analysis and inflammatory biomarkers.

Laboratory Parameters	Non-obese (n= 68)	Obese (n= 82)	p-value
BMI (kg/m^2)	23.37±3.53	35.75±4.1	.000
SpO_2 (%)	80.17±8.97	80.69 ± 10.3	.713
pH	7.26±.14	7.24±.15	.478
pCO^2 (mmHg)$^{\$}$	54.35±12.43	62.01±21.98	.011
pO^2 (mmHg) $^{\$}$	65.85±11.09	62.9613±12.07	.038
HCO_3(mmHg)	20.9509±4.06	22.6524±6.77	.071
Total Leucocyte count × 10^9 per L	14.5132±5.74	14.6146±5.66	.914
Lymphocytes × 10^9 per L	2.9191±1.46	3.3528±1.53	0.080
Ferritin (ng/mL)	900.45±390.04	936.72±416.35	0.586
LDH (IU/L)	457.79±334.03	549.80±293.98	0.07
D-Dimers (ng/mL)	6.2472±5.08	22.2261±121.70	0.281
CRP (mg/mL)	137.13±74.00	125.86±72.40	0.349
O2 Requirement at Baseline (%)	4.1471±1.10	5.02±6,27	0.257
O_2 Requirement at Discharge (%)	0.70±1.05	1.48±1.3	0.000
HbA1c (%)	6.1696±1.64	6.98±1.85	0.005
Baseline BSF (mg/dL)	113.41±33.89	142.7683±54.04	0.000
Baseline BSR (mg/dL)	161.37±69.32	229.33±220.44	0.016

$^{\$}$Denotes that comparison was done via Man-Whittney U test

Table 2: Comparison of clinical outcomes and comorbidities.

Parameters		Non-Obese n= 68	Obese n= 82	p-value
Comorbidity	Present	19(23.2%)	31(45.6%)	0.004*
	Absent	37(54.4%)	63(76.8%)	
Severity	Mild	9(13.2%)	17(20.7%)	0.227
	Severe	59(86.8%)	65(79.3%)	
Radiological Findings	ARDS	6(8.8%)	15(18.3%)	0.312
	>50% on X ray	49(72.05%)	50(60.75%)	
	< 50 % on X ray	8(11.76%)	14(17.07%)	
	Nonspecific on X ray without typical HRCT	3(4.41%)	2(2.44%)	
	Typical X ray and HRCT	2(2.94%)	1(1.21%)	
Outcome	Cured	58(85.3%)	49(59.8%)	0.001*
	Died	10(14.7%)	33(40.2%)	
Mechanical ventilation	Yes	45(66.2%)	47(57.3%)	0.267
	No	23(33.8%)	35(42.7%)	

Chi square used for comparison

Table 3: Correlation of laboratory parameters and outcomes with BMI.

Laboratory Parameter	Correlation with BMI	
	Correlation Coefficient (r)	p-value
PCO_2	.274	0.001*
HCO_3	.107	0.194
Ferritin	.086	0.293
LDH	.228	0.005*
HbA1c	.223	0.006*
Outcome	.263	0.001*
Comorbidity	.262	0.001*

tivity of 80% and specificity of 80%. The area under the curve (AUC) for HbA1c in predicting adverse outcomes was 0.796, (p<0.001), indicating that HbA1c is a strong predictor of mortality and poor outcome in COVID-19 patients (Fig. 1).

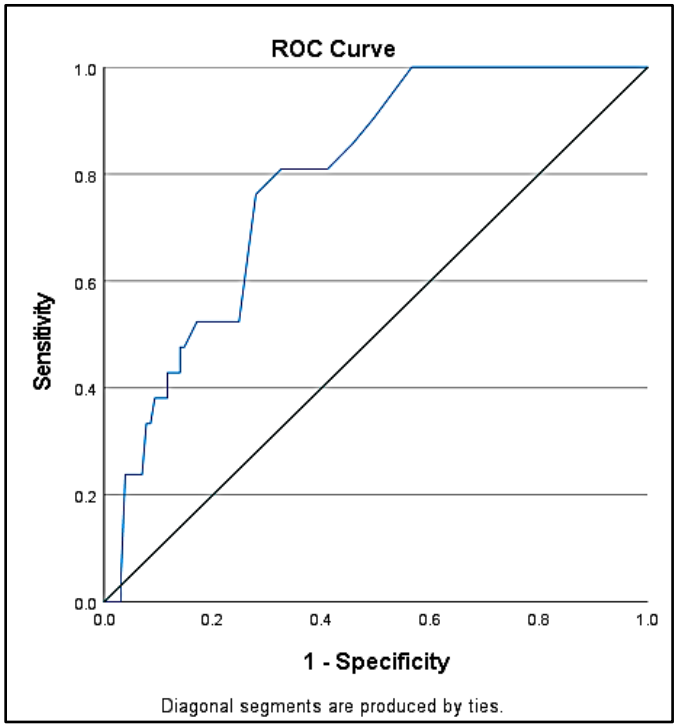

Fig. 1: ROC curve analysis for HbA1c in predicting outcomes in Covid-19 positive patients.

DISCUSSION

In this retrospective cohort study, we found a significant association between obesity and adverse outcomes, including increased mortality. Adipose tissue serves as a seed of subclinical inflammation causing infiltration of macrophages by triggering release of proinflammatory cytokines. SARS-CoV-2 enters the fat cells after binding with

ACE-2 receptors present on fat cells, favouring its rapid multiplication.[13] However, in our study, there was no difference in total leucocyte count, lymphocytic count, LDH, D-Dimers, serum ferritin and CRP between the obese and non-obese patients, as was reported by Friedman et al.[14] Another study suggested decreased ferritin and d-dimers in obese patients, however no significant differences were reported in CRP and LDH on first day of admission.[15]

Baseline BSF, HbA1c and BSR were significantly higher in obese patients as compared to those who did not suffer from obesity, showing strong association of impaired glycemic control and diabetes with obesity, reported by previous studies.[16,17] Regarding clinical outcomes, Smati et al, reported that BMI was associated with early severity of disease but not with mortality, a finding contrary to our results.[18] This difference could be due to various disease patterns in different regional locations that have also contributed to diverse findings regarding the clinical outcomes.

In another study, Al-Sabah et al, reported that severe obesity and diabetes mellitus were significantly associated with increasing mortality and ICU admission.[19] Conversely, in our study, due to small sample size and the limited number of patients with only one comorbid condition, we analysed only the association between clinical outcomes and the presence or absence of comorbid diseases, that yielded significant results.

We found positive correlation of BMI with mortality, as reported by previous studies.[20-22] However, Friedman et al, found no independent relationship between obesity and an increasing risk of mortality.[14] The disparity may be due to our smaller sample size, the presence of comorbid conditions, and a larger proportion of patients with severe disease, which could have acted as confounding factors.

While the risk of acute respiratory distress syndrome (ARDS) increases with increasing BMI, the current study found no significant difference between the obese and non-obese groups in terms of ARDS prevalence. These results contrast with those of Cai et al.[23]

CONCLUSION

Our study shows that obesity can significantly worsen the clinical outcomes for COVID-19 patients. We did not find major differences in inflammatory markers of the two groups, obese patients had higher HbA1c levels and worse blood gas results. These findings highlight the importance of keen monitoring and the need for provision of targeted care for obese patients with COVID-19, as they are more vulnerable to worse outcomes.

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