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ORIGINAL ARTICLE

Outcomes of Nonalcoholic Fatty Liver Disease in Covid Positive Diabetic Patients: Cross Sectional Study

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ABSTRACT

Background: SARS-CoV-2 principally invades the respiratory system. ACE receptor are also abundant throughout the hepatobiliary system and their increased expression on hepatocyte make patients with NAFLD more vulnerable.
Aim: To see outcomes of COVID positive diabetic patients suffering from Nonalcoholic fatty liver disease (NAFLD).
Study design: Cross Sectional Study.
Methodology: 150 diabetic and COVID PCR positive were recruited from COVID ward of Services Hospital in Lahore. Clinical parameters like BMI, SpO2, Hepatomegaly and lab parameters like HbA1C, AST ALT were noted in spreadsheet. Statistical analysis was done using SPSS v.25. Statistical significance for difference in proportions is calculated using Pearson's Chi-Squared test. P less than 0.05 was considered statistically significant.
Results: Around 84(56%) were males and 66(44%) females, smoked were 27(18%), mean age (years) was 59.7333 ±11.35023, mean BMI (kg/m²) was 30.1425±7.30673, 87(58%) patients had NAFLD, who experienced sever disease (53.2%; $x^2 = 0.010$) and more mortalities (60.2%;$x^2 = 0.453$) as compared to those who do not had condition.
Conclusion: We concluded that NAFLD makes COVID-19 infected patients more fragile. Such patients experienced sever disease and more mortalities however need of mechanical ventilation remains almost equal between those who has NAFLD and those who didn't had.
Keywords: Nonalcoholic fatty liver disease, COVID-19, Diabetes, Mortality and Severity.

INTRODUCTION

December 2019 was time of an outbreak of a novel coronavirus, the severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) was first reported in the Wuhan City, China[1], Since then, this infection has precipitously spread like a storm globally. According to few estimates, most of its infected cases were in Europe followed by the US and South America[2,3].

There are many risk factors causing its diverse and severe infectious trend. Obesity is one of them thus leading to its severe course of infection[4-6]. There are many illnesses like DM, HTN, CVD, and COPD that coexist with COVID-19 as reported by various epidemiological studies[6,7]**.** It has been shown by pathological studies that metabolic conditions like obesity and NAFLD are linked with elevated pro-inflammatory cytokines such as TNF-a. It has been documented that this pathogen uses angiotensin-converting enzyme-2 (ACE2) receptor for cellular entry. Increased expression of ACE2 receptors on hepatocytes of patients with NAFLD may defiantly pose an increased risk in NAFLD patients[8,9]. Different mechanisms have been proposed for liver injury.

Direct cytotoxicity because of active viral replication in hepatic cells and cholangiocytes with normal ALP in majority of patients is against this proposed mechanism[10,11]. Another idea named cytokine storm proposed that damage caused by immune mediated markers due to the severe inflammatory response following COVID-19 infection include C reactive protein (CRP), serum ferritin, LDH, IL-6, IL-2, were significant raised[12,13].

Patients with chronic liver diseases make up less than 1% of reported cases[14], So it can be inferred that patients with chronic liver disease are not at increased risk of contracting acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[15]**.** Present study can defiantly help us not only clear direction of management but also guide allocating precious health resources.

The objective of the study was to see outcomes of COVID positive diabetic patients suffering from Nonalcoholic fatty liver disease (NAFLD).

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METHODOLOGY

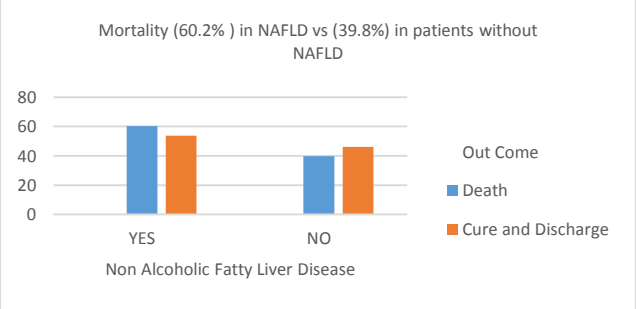
Informed written consent was taken. 150 diabetic and COVID PCR positive were recruited from COVID ward of Services Hospital in Lahore. Clinical parameters like BMI, SpO2, Hepatomegaly and lab parameters like HbA1C, AST ALT were noted in spreadsheet.
Statistical Analysis: Statistical analysis was done using SPSS v.25. Stratification of NAFLD was done with age, gender, BMI, diabetes control, smoking and outcome measures like mortality, severity of disease and need of mechanical ventilation. Statistical significance for difference in proportions are calculated using Pearson's Chi-Squared test. P less than 0.05 was considered statistically significant.

RESULTS

Table-1: Demographic Characteristics of population studied (n=150)

Variables	n	Mean	SD
Age (in completed years)	150	59.7333	±11.35023
BMI (kg/m²)	150	30.1425	±7.30673
Lab Parameters			
SpO2	150	80.6673	±9.15820
ALT (IU/l)	150	72.0667	±39.11464
AST (IU/l)	150	61.5067	±33.92407
HbA1C (%)	150	8.7189	±1.92502

Figure-1: Depicting Outcome in COVID +ve pts with and without NAFLD



Total of 150 patients who were COVID PCR positive diabetics were recruited, Table-1 showed various demographic characteristics of the sample under study. Table-1 demonstrated mean age (years) of patients was 59.7333±11.35023, mean BMI (kg/m²) was 30.1425±7.30673, mean SpO2 80.6673±9.15820, mean ALT(IU/l) was 72.0667±39.11464, mean AST (IU/l) was 61.5067 ±33.92407 mean HbA1C (%) 8.7189±1.92502.

Table 2 showed bivariate analysis of NAFLD with different confounding variables of studied. Among Non-Obese (BMI:18-29.9) 14(20.6%) out of 68(100%) and among Obese (BMI ≥30), 73(89%) people out of 82 (100%) were having NAFLD. And these results are significant as shown by ($x^2 = 0.000$). Area of special interest was to see relationship with control of diabetes, it was observed that prevalence of NAFLD remains almost same between both groups (56.5% patients within HbA1C (5.7-6.4%) and 58.3% were observed in HbA1C (>6.5%) group, however results were statistically not significant($x^2 = 0.876$). Among those people who smoked 21(77.8%) out of 27(100%) had NAFLD these results were significant ($x^2 = 0.021$) . As regards Outcome, NAFLD shows significant result in bivariate analysis with severity of disease ($x^2 = 0.010$) , 21 (80.8%) out of 26 (100%) patient who had mild (SpO2 ≥94%) disease and 66 (53.2%) out of 124 (100%) who had moderate to severe (SpO2 <94%) COVID-19 infection.

Table 2: Stratification of Non-Alcoholic Fatty Liver Disease with different confounding variables

Variables	**Sub Groups**	**Non-Alcoholic Fatty Liver Disease**		**Total**	(p_value)
		Yes (n=87)	**No (n=63)**		
Age (in completed years)	18-40 years	03(27.3%)	08(72.7 %)	11(100%)	0.097
	41-60 Years	40(61.5%)	25(38.5%)	65(100%)	
	61-80 Years	44 (59.5%)	30 (40.5 %)	74 100%)	
	Total	87 (58%)	63 (42%)	150(100%)	
Obesity(kg/m²)	Non-Obese (BMI:18-29.9)	14 (20.6%)	54 (79.4%)	68 (100%)	**0.000***
	Obese (BMI ≥30)	73 (89%)	9 (11%)	82 (100%)	
	Total	87 (58%)	63(42%)	150 (100%)	
Gender	Male	46 (54.8%)	38 (45.2%)	84 (100%)	0.365
	Female	41 (62.1%)	25 (37.9%)	66 (100%)	
	Total	87(58%)	63(42%)	150(100%)	
Smoking status	Smokers	21(77.8%)	6(22.2%)	27(100%)	**0.021***
	Non-Smokers	66(53.7%)	57(46.3%)	123(100%)	
	Total	87(58%)	63(42.0%)	150(100%)	
Diabetes Control	HbA1C 5.7-6.4%	13(56.5%)	10(43.5%)	23(100%)	0.876
	HbA1C >6.5%	74(58.3%)	53(41.7%)	127(100%)	
	Total	87(58.0%)	63(42%)	150(100%)	
Out Come					
Severity of Disease	Mild (SpO2 ≥94%)	21 (80.8%)	5 (19.2%)	26 (100%)	**0.010***
	Moderate to Sever (SpO2 <94%)	66 (53.2%)	58 (46.8%)	124 (100%)	
	Total	87 (58%)	63 (42%)	150 (100%)	
Mode of Ventilation	NRBM	26 (68.4%)	12 (31.6%)	38 (100%)	0.143
	Nasal Canula	11 (73.3%)	4 (26.7%)	15 (100%)	
	Face Mask Ventilation	22 (56.4%)	17 (43.6%)	39 (100%)	
	IPVV	28 (48.3%)	30 (51.7%)	58 (100%)	
	Total	87 (58%)	63 (42%)	150 (100%)	
Mortality Out Come	Mortality	59 (60.2%)	39 (39.8%)	98 (100%)	0.453
	Cure & and Discharge	28 (53.8%)	24(46.2%)	52 (100%)	
	Total	87(58%)	63 (42%)	150 (100%)	

*Statistically Significant

Mortality is clearly high (60.2%) in patients with NAFLD as compared to those patients (39.8%) who did not have it as shown in fig-1.

DISCUSSION

Although the main target of SARS-CoV-2 infection is considered to be respiratory tract as this can lead to potentially fatal outcomes[16-19]. Now there is sufficient evidence that COVID-19 is not only of respiratory concern it may be considered as a systemic infectious and inflammatory disease as it involves organs like liver and gastrointestinal tract that are receiving increasing attention[20].

We studied cohort of 150 patients that had mean age of (59.7±11.35023) years, mean BMI was (30.14±7.30), NAFLD was present in (58.3%) subjects. 65 out of 150 patients were in (41-60 years) age group and 74 were in (61-80 years) group however prevalence of NAFLD was found more in middle age group (40-60 years) that was (61.5%), higher BMI (>30 kg/m²) and poor glycemic control defined by HbA1C >6.5% with 74(58.3%) patients having NAFLD, more females (62.1%) as compared to males (54.8%) had condition. People with NAFLD experienced sever disease (53.2%; $x^2 = 0.010$) and more mortalities (60.2%; $x^2 = 0.453$) as compared to those who do not had condition however need of mechanical ventilation remains almost equal between those who has NAFLD (48.3%) and those who didn't had NAFLD (51.7%), while Dong ji et al studied 202 consecutive patients with confirmed COVID-19 and NAFLD there were (55.9%) male patients, mean age was 44.5 (years), mean BMI (24.0 ± 2.8), (37.6%) patients had NAFLD out of which (87.2%) had progressive illness, overall (13.9%) patient had sever disease[20].

In another study conducted by Mahamid et al, showed that NAFLD was present in (31%) of the study group. Out of 71, 13(18.3%) suffered from severe COVID-19. NAFLD patients had more severe COVID-19 compared with non-NAFLD subjects, 8/22 (36.3%) vs. 5/49(10.2%), (P<0.005), respectively[21]. Kenneth I. Zheng et al reported obesity as a possible risk factor for severe COVID-19 illness in patients with MAFLD they had mean age of 47 years and 74.2% were female, mean BMI (26.5 ± 3.9) and sever COVID-19 was present in 19 (28.8%)[21].

Limitations: This study was limited because some hospitals do not allow research work and data collection in their respective department so we were supposed to gather data from single hospital. Our sample size was limited.

CONCLUSION

We concluded that metabolic disorders like NAFLD and diabetes makes COVID-19 infected patients more fragile. People with NAFLD experienced sever disease (53.2%; $x^2 = 0.010$) and more mortalities (60.2%; $x^2 = 0.453$) as compared to those who do not had condition however need of mechanical ventilation remains almost equal between those who has NAFLD and those who didn't had. The deleterious interplay of inflammatory pathways which are

chronically active in NAFLD and acutely in COVID-19-infected patients, may explain worse outcome in metabolically compromised NAFLD patients.

Authors Contribution: AH&MI: Conception & design of study, **AR&ML:** Data collection & Analysis, **MJA, SZ:** Drafting of manuscript, **TL:** Final approval and revisions,
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Financial Disclosure: None

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