ORIGINAL ARTICLE

Prognostic Significance of ALT/AST in diabetic patients having Myocarditis secondary to COVID Pneumonia

MUHAMMAD RASHID ALI[1], MARYAM HAROON[2], RUMLA SAMAYYAH[3], FAREEHA SALMAN[4], AMBREEN BUTT[5]
[1]Senior Registrar of Medicine, Department & Hospital: Medical Unit-IV, Services Hospital Lahore.
[2]Postgraduate Resident of Internal Medicine, Department & Hospital: Medical Unit-IV, Services Hospital Lahore
[3]WMO
[4]PGR Medicine, Services Hospital Lahore.
[5]Professor of Medicine Services Hospital Lahore.
Correspondence to Dr Maryam Haroon, Contact number: 03245764244

ABSTRACT

Aim: To compare the predictive accuracy of raised ALT/AST ratio in diabetic patients for survival and myocarditis due to COVID-19 pneumonia.

Study design: It was a cross-sectional study, conducted at Department of Medicine, Services Hospital, Lahore for about 6 months (March 2020 to September 2020)

Methods: A cross-sectional study was conducted for six months at Services Hospital in Lahore (March 2020 to September 2020). A total of 350 patients' ALT and AST levels will be tested in blood. Patients' survival rates will be tracked. Patients with myocarditis and ALT/AST ratios below 0.90 had a dismal prognosis.

Results: The average female age was 47.87.15.82. There were 142 men (40%) and 208 women (59.4%). There were 131 light (36.4%), 77 moderate (22%), 83 severe (23.7%), and 59 serious cases (16.9%). Mean ALT/AST was 0.89 0.33. 58 patients (16.6%) had myocarditis, and 66 (18.9%) died in the hospital. Sensitivity, specificity, PPV, NPV, and diagnostic accuracy of the ALT/AST ratio for predicting diabetic patient survival were 56.1%, 39.1%, 17.6%, 79.3%, and 42.3%. The ALT/AST ratio's sensitivity, specificity, PPV, NPV, and diagnostic accuracy were 78%, 42.9%, 20%, 91.3%, and 48.3% for predicting the survival of diabetic patients with COVID-19 pneumonia-related myocarditis.

Conclusion: This study found that ALT/AST ratio is not a strong predictor of mortality in diabetic patients with COVID-19-related myocarditis.

Keywords: ALT, AST, diabetes mellitus, myocarditis, COVID-19 pneumonia

INTRODUCTION

The global pandemic of Coronavirus disease 2019 (COVID-19) has spread to over 185 nations and affected over 3 million individuals as of April 28, 2020. Coronavirus 2 employs[1] Angiotensin-converting enzyme[2] receptors for entry into cells and induction of COVID-19. This virus causes severe symptoms of acute respiratory syndrome. Myocardial damage occurs in over 7% of persons infected with the COVID-19 virus (22% of critically ill patients). If you have prior cardiovascular conditions or have an acute heart injury as a result of COVID-19, you are more likely to get this sickness. Clinicians must have a full awareness of the relationship between COVID-19 and cardiovascular disease in order to provide appropriate care for these patients[4,5].

The incidence of hepatic involvement in adults with acute enteroviral peri-myocarditis may be substantially higher than previously recognised. Recognizing liver involvement alongside enteroviral peri-myocarditis has the potential to improve diagnostic sensitivity and modify treatment methods for acute viral myocarditis[6]. As a reserve of blood volume, the liver is an essential organ[7]. As it gets over a quarter of the entire cardiac output, it is very sensitive to hemodynamic changes. The liver, heart muscle, and other tissues contain the highest concentrations of AST and ALT. In instances of liver cell damage, the AST/ALT ratio is commonly employed[8]. The ratio of AST to ALT is often used to diagnose liver disease. In 1957, Fernando De Ritis described for the first time how the AST/ALT ratio may be used to determine the likelihood of disease[9]. Even though hepatic transaminases have historically been associated with an increased risk of cardiovascular illness, few studies have explored the AST/ALT ratio in individuals with heart failure.

In order to determine the predictive significance of the ALT/AST ratio for survival in diabetic patients with myocarditis, we conducted a study. ALT/AST is an important signal. Myocarditis prognosis can be predicted, despite the absence of supporting evidence. Therefore, this study would contribute to the corpus of knowledge.

METHODOLOGY

In the study, 350 diabetes patients with a COVID-19 diagnosis were included. The participant's demographic information was also recorded following their explicit agreement after ethical permission. Observations revealed the presence of clinical indications and symptoms. A clinical history and list of co-morbidities were also gathered. After obtaining a blood sample and submitting it to the hospital laboratory for analysis, additional tests were performed, including an electrocardiogram, polymerase chain reaction, x-ray, and computed tomography scan, and the results were recorded. Myocarditis was also investigated to establish whether or not patients have it. ECG (evidence of arrhythmias), LV and RV systolic and diastolic dysfunction, regional wall motion abnormalities, change in LV dimensions and thickening of myocardial wall secondary to oedema on echocardiography, and cardiac enzymes including elevated troponins, CK-MB, CK, AST, LDH, and others of non-cardiac origin, especially ALT, were utilised to diagnose myocarditis in Myo. The patients were subsequently observed in the COVID-19 wards until they were released, at which time their status (alive or deceased) was recorded. Permission from Ethical Committee was granted.

Data Analysis: SPSS version 20.0 was used to analyse the data. To determine the sensitivity, specificity, positive and negative predictive value (PPV) as well as the non-prognostic value (NPV), 2x2 tables were produced for each patient and for those with a positive myocarditis test result.

RESULTS

The average age of female participants was 47.8715.82 years old. There were 142 men (40.6% of the total) and 208 women (59.4% of the total). 40 instances (11.4%), 69 (19.7%), and 241 (68.9%) were from rural areas, while 69 (19.7%) came from suburban areas. Symptoms began to appear on average after 4.38 days, with a standard deviation of 1.81 days. A meeting with a positive family member accounted for 669% of all infections, while social gatherings accounted for 28% of all infections and international travel accounted for 8.6% of all infection cases. Fever (74.6%), cough (73.7%), shortness of breath (70.9%), and

anorexia (697.7%) were the most prevalent symptoms, and the mean ALT/AST ratio was 0.890.33. There were 131(37.4%) light cases, 77(22%) moderate cases, 83 (23.7%) severe cases, and 59(16.9%) critical cases in the study. More than one-fifth of patients had myocarditis (58/16.6%) (Table 1).

Table 1: Demographics of patients included in the study

N	350
Age (year)	47.87±15.82
Gender	
Male	25 (43.1%)
Female	33 (56.9%)
Residence	
Rural	40 (11.4%)
Sub-urban	69 (19.7%)
Urban	241 (68.9%)
Onset (days)	4.38±1.81
Source of infection	
Positive family member	234 (66.9%)
Social gathering	28 (8.0%)
Travel abroad	30 (8.6%)
Unknown	58 (16.6%)
Sign & Symptoms	
Fever	261 (74.6%)
Cough	258 (73.7%)
SOB	248 (70.9%)
Anorexia	244 (69.7%)
Sore throat	194 (55.4%)
Sputum production	185 (52.9%)
Haemoptysis	181 (51.7%)
Palpitation	177 (50.6%)
Chest pain	171 (48.9%)
Fatigue	168 (48.0%)
Muscle pain	160 (45.7%)
Lower limb weakness	59 (16.9%)
Quadriplegia	16 (4.6%)
Medical history	
Pulmonary disease	13 (3.7%)
Hypertension	126 (36.0%)
Epilepsy	31 (8.9%)
Rheumatic arthritis	6 (1.7%)
Laboratory findings	
Lymphomas	19.52±17.23
Neutrophils	75.75±18.10
Platelet count	262.27±90.84
CK	212.67±244.71
CK-MB	35.23±36.98
LDH	468.76±346.03
Urea	44.85±39.78
Creatinine	1.44±1.99
Bilirubin	0.75±0.31
Alkaline phosphatase	227.04±78.23
ALT	49.01±55.90
AST	65.76±70.59
ALT/AST	0.89±0.33
O2	0.96±0.98
Cell score	
<6	195 (55.7%)
>6	155 (44.3%)
Lung involvement on Chest X-ray	
<25%	67 (19.1%)
>25%	14 (4.0%)
<50%	8 (2.3%)
>50%	152 (43.4%)
>80%	6 (1.7%)
Normal	103 (29.4%)
ECG findings	
Atrial fibrillation	6 (1.7%)
Ischemia	66 (18.9%)
Normal	228 (65.1%)
ST-changes	33 (9.4%)
Tachycardia	17 (4.9%)
Echocardiography findings	
LV and RV systolic & diastolic dysfunction	210 (60%)
Regional wall motion abnormalities	52 (14.8%)
Change in LV dimensions	18 (5.1%)
Thickening of myocardial wall secondary to wall oedema	105 (30%)
Condition of patient	
Mild	131 (37.4%)
Moderate	77 (22.0%)
Severe	83 (23.7%)
Critical	59 (16.9%)
Myocarditis	58 (16.6%)

Myocarditis was found in 58 of the patients, and 66 of the patients died during their stay in the hospital (Figure 1). 56.1%, 39.1%, 17%, 79.3% and 42.3% of diabetic patients' survival was predicted by the ALT/AST ratio's specificity, PPV and NPV. The diagnostic accuracy of the ALT/AST ratio was 42.3% (Table 2). It was found that ALT/AST ratio had a sensitivity of 78%, specificity of 42.9%, NPV of 91.3%, and diagnostic accuracy of 48.3% for predicting the survival of diabetic patients with myocarditis caused to COVID-19 pneumonia (Table 3). The ROC and the area under the curve are shown in Figure 2. When looking at diabetic patients with myocarditis caused by COVID-19, the area under the curve was found to be just 0.530, indicating that ALT/AST ratio is not a reliable predictor of outcome.
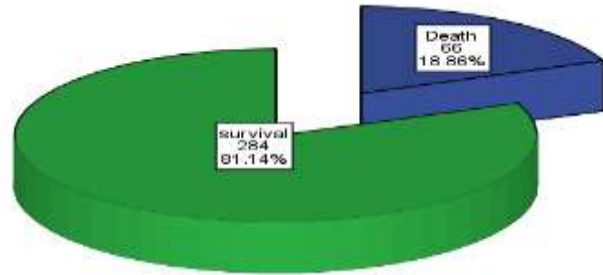
Fig 1: Distribution of outcome of patients

Table 2: Accuracy of ALT/AST ratio taking outcome as gold Standard in whole cohort

| ALT/AST ratio	Survival		Total
	Dead	Alive	
Positive	37	173	210
Negative	29	111	140
Total	66	284	350

Sensitivity=56.1%, Specificity=39.1%, PPV=17.6%, NPV=79.3% and Diagnostic Accuracy=42.3%

Table 3: Accuracy of ALT/AST ratio taking outcome as gold Standard in myocarditis patients

ALT/AST ratio	Survival		Total
	Dead	Alive	
Positive	7	28	35
Negative	2	21	23
Total	9	49	58

Sensitivity=77.8%, Specificity=42.9%, PPV=20.0%, NPV=91.3% and Diagnostic Accuracy=48.39%

Fig 2: ROC curve showing Area under the curve (AUC: 0.530)

Diagonal segments are produced by ties.
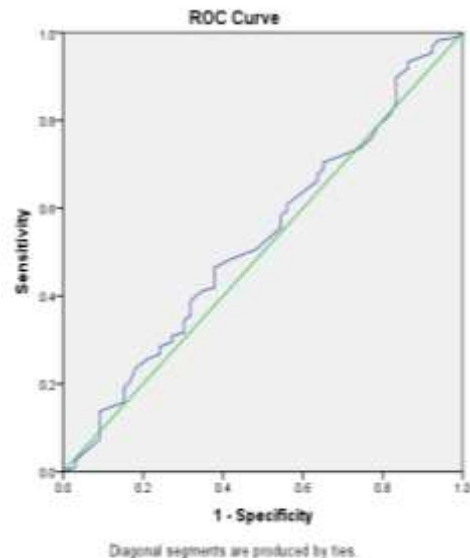
DISCUSSION

Coronavirus illness significantly compromises the cardiovascular system, microvascular injury, thrombosis, and endothelial dysfunction are characteristics of severe COVID-19, which is distinguished by substantial systemic inflammation and an immune response. Heart disease and viral load are associated with myocardial damage and poorer patient outcomes[12]. Due to its association with other organ failure, particularly cardiovascular disease, hepatic fibrosis is no longer considered an exclusively hepatic disorder. Now, hepatic fibrosis can be recognised and monitored without invasive procedures[14]. Among the scientifically validated indices are the AST/ALT ratio, the AST to platelet ratio indicator, the Fibrosis-4 score, and the non-alcoholic fatty liver disease fibrosis score[15-17].

The research we conducted revealed that 58 patients (16.6%) had myocarditis. Sixty-eight patients (16.6%) were diagnosed with myocarditis, resulting in the deaths of sixty-six patients (18.9%). 56.1%, 39.1%, 17.5%, 77.3%, and 42.3 were the respective sensitivities for predicting survival in diabetes patients using the ALT/AST ratio. There was a sensitivity of 78%, specificity of 42.9%, negative predictive value (NPV) of 91.3%, and diagnostic accuracy of 48.3% for predicting diabetic patients with myocarditis attributable to COVID-19 pneumonia. The ROC curve revealed that ALT/AST has an AUC of only 0.530, indicating that it is ineffectual. Numerous tissues, including the heart and liver, emit AST, but only the liver emits ALT. Therefore, an increase in the AST/ALT ratio is anticipated if myocardial injury is significant[18]. People with a greater AST/ALT ratio are more prone to develop hepatic fibrosis, which is associated to cardiovascular disease aetiology via multiple routes, including increased plasma inflammatory mediators, insulin resistance, oxidative stress, and metabolic syndrome.

Several studies, like those by Ruhl et al and Fraser et al[20, 21], did not, however, detect a significant correlation between ALT and cardiovascular disease. Possible explanation for their findings could be that they did not include AST or AST/ALT ratio in their analysis of cardiovascular disease. The ratio of AST/ALT was found to be an independent predictor of the functional condition of the left ventricle in patients with heart failure and a low ejection fraction. AUC was also reported to be 0.643%[10]. In this regard, additional study is required to corroborate the results and provide fresh information about liver enzymes' significance.

CONCLUSION

According to the findings of this research, the ratio of ALT to AST cannot be relied upon as an accurate predictor of survival in diabetic individuals who developed myocarditis as a result of COVID-19 pneumonia. These findings need to be verified by conducting more examinations.

Conflict of interest: Nil

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