Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Medicine

Pattern of Liver Enzymes Change in Patients with STEMI Admitted in Comilla Medical College & Hospital, Bangladesh

Dr. Mohammad Mohibul Alam[1*], Dr. Jabed Ahmed[2], Dr. Nazmoul Hassan[3], Dr. SM Ali Hassan[4], Dr. Isha Abdullah Ali[5]

[1]Junior Consultant, Department of Medicine, Upazila Health Complex, Haziganj, Chandpur, Bangladesh.
[2]Medical Officer, Department of Cardiology, Cumilla Medical College Hospital, Bangladesh.
[3]Medical Officer, Department of Medicine, Cumilla Medical College Hospital, Bangladesh.
[4]Medical Officer, Department of Gastroenterology, Cumilla Medical College Hospital, Bangladesh.
[5]Assistant Professor and Associate Consultant, Department of Cardiology, Ibrahim Cardiac Hospital and Research Institute, Dhaka, Bangladesh.

DOI: https://doi.org/10.36347/sjams.2024.v12i08.016 | **Received:** 02.07.2024 | **Accepted:** 11.08.2024 | **Published:** 21.08.2024

***Corresponding author:** Dr. Mohammad Mohibul Alam
Junior Consultant, Department of Medicine, Upazila Health Complex, Haziganj, Chandpur, Bangladesh

Abstract **Original Research Article**

Background: Serum glutamic pyruvic transaminase (SGPT) and Serum glutamic oxaloacetic transaminase (SGOT) are the liver transaminases. Nowadays, there is intensified interest in studying the role of liver transaminases in independently predicting cardiac-related morbidity and mortality. In recent years, coronary heart disease has increased to an alarming rate throughout the world including Bangladesh. There are several mechanisms by which liver enzymes including SGPT, SGOT, and ALP are raised following ST-segment elevation myocardial infarction (STEMI). Few studies have demonstrated that gamma-glutamyltransferase (GGT), lactate dehydrogenase (LDH) and alkaline phosphate (ALP) are also increased in patients with acute myocardial infarction. We have studied the associations of liver enzymes change due to ST-segment elevation myocardial infarction (STEMI). ***Aims and Objectives:*** To observe the pattern of liver enzymes change among the ST elevation MI (STEMI) patients in the hospitalized patients and to associate the changes to outcomes of the patients. ***Study design and study setting:*** This was a hospital based prospective observational study conducted in the Department of Cardiology, Comilla Medical College & Hospital, Cumilla, during the period from January 2021 to June 2021. ***Methods:*** 100 randomly selected patients hospitalized in the Cardiology Department of the Comilla Medical College & Hospital from January 2021 to June 2021 with Acute ST elevation MI (STEMI) was enrolled in the study. All patient's history and clinical examination was done and demographic variables was noted in the "Data collection sheet". We had study the liver enzymes change at the baseline day 1 and at 6th day and note all the clinical and laboratory parameters. Data was analyzed using SPSS 24 version. Values of $p<0.05$ was considered statistically significant. ***Results:*** The mean ($\pm$SD) age of the patients was 56.06±12.016. The peak age incidence of STEMI was found in 55 to 64 years' age group (37%). The male: female ratio was 74:26. We had 57% participants from rural background and 51 percent were illiterate. In sixty percent of the cases the inferior surface of heart was involved. The most common type of complication was heart failure (30%), followed by pericarditis (19%), arrhythmia (16%), and cardiogenic shock (12%). At baseline (day 1), SGPT, SGOT, and ALP are raised by 54%, 47% and 29% respectively. But at 6th day it further increased to 75%, 77% and 54%. SGPT (p=0.000) and SGOT (p=0.03) increased significantly in the heart-failure than the non-heart failure patient, ALP (p=0.69) was not significantly increased. Five percent (5%) patients died and rest 95% are improved clinically. The most common mode of death was heart failure (60%). SGPT and SGOT trend line were significantly inclined from day 1 to day 6, but ALP was not inclined in the dead patients. Adjusted odd ratio of SGPT, SGOT and ALP are 4.56(4.11-5.10), 4.236(3.901-4.696), and 1.421 (1.401-1.442) respectively for dead patients, but for improved patients these are not significant. ***Conclusion:*** Our findings are clear about the association of the liver enzymes change with ST segment elevation myocardial infarction (STEMI). Liver enzyme elevation is more prominent in the heart failure patients. Mortality and morbidity were more significantly associated with the liver transaminases (SGPT and SGOT) but very less significantly with ALP.

Keywords: Liver transaminases, morbidity and mortality, heart disease, Cardiology, SGPT and SGOT.

INTRODUCTION

Alanine transaminase (ALT) or Serum glutamic pyruvic transaminase (SGPT) and aspartate aminotransferase (AST) or serum glutamic-oxaloacetic transaminase (SGOT) are referred to as liver transaminases. ALT is found predominantly in hepatocytes and is a widely used specific serum marker of liver disease. AST is mainly derived from the liver; although, a significant portion is derived from other

tissues, such as heart, red blood cells, and muscle, which makes it an imperfect marker of liver function. Recent studies have demonstrated an increasing interest in investigating the role of liver transaminases in independently predicting cardiac-related morbidity and mortality [1-3]. Several prospective epidemiological studies have suggested that hepatic dysfunction is common in cardiac disease [4, 5]. If no other causes of liver injury are identified, the elevations of liver aminotransferases are associated with a higher incidence of cardiac-related mortality [6]. However, the results from these studies have been inconsistent and have revealed geographical variations in the association between ALT and all-cause mortality [7-11].

In several studies, acute heart failure and congestive heart failure were identified as the causative culprits for hypoxic hepatitis that is the core mechanism of elevated liver enzymes [12,13]. In recent years, coronary heart disease has increased to an alarming rate throughout the world including Bangladesh. Few studies have demonstrated that gamma-glutamyltransferase (GGT), lactate dehydrogenase (LDH)and alkaline phosphate (ALP) are also increased in patients with acute myocardial infarction [12,14].

Little is known about the association between hepatic dysfunction and mortality in patients with ST-segment elevation myocardial infarction (STEMI) treated with thrombolysis or percutaneous coronary intervention for acute coronary artery disease. Our study may unveil this association of STEMI and the elevated liver enzymes in causation of mortality and morbidity. This study evaluated the outcomes of the patients who were treated with thrombolysis or LMWH.

OBJECTIVES

General Objective

- To observe the pattern of liver enzymes change among the ST elevation MI (STEMI) patients.

Specific Objective

- To observe the demographics characteristic of the patients having liver enzymes changes presented with STEMI.
- To observe the trends of liver enzymes in STEMI.
- To see the liver enzymes change in heart failure with STEMI.

MATERIALS AND METHODS

This was a Hospital based Prospective observational Study. The patients were selected purposively. A total of 100 patients were included in this study. The study was conducted in the Department of Cardiology, Comilla Medical College Hospital (COMCH), Cumilla, Bangladesh. At January' 2021 to June' 2021

Inclusion criteria:

- Patient with 1st attack of STEMI

Exclusion criteria:

- Patients having documented viral hepatitis, cirrhosis of liver, alcholic liver disease, non alcholic fatty liver disease,

Procedure of preparing and organizing materials

All patients who admitted in Cardiology department were thoroughly informed about the aims, objectives and detail procedure of the study. He /She were encouraged for voluntary participation and allowed freedom to withdraw from the study whenever he/she liked even after participation. From all eligible subjects after getting consent clinical history were taken and clinical examination were done to elicit findings related to disease (STEMI patients admitted in cardiology department with non-liver cause and its complication). 5 ml of venous blood were collected and sent for analysis of liver enzymes like SGPT, SGOT and ALP. All investigation was done in the laboratory of Comilla medical college @hospital. All relevant were be noted in the pre-tested data sheet. All data were checked and rechecked to avoid error. Data were collected by the researcher himself.

Procedure of data collection data analysis and interpretation

Findings of observation was recorded on prescribed data collection form (attached here with). Categorical data (types of disease, modalities of treatment, anemia, jaundice etc) expressed as either percentage or proportion and presented by bar diagram and pie chart. Numerical data (age, BP, Temperature, level of different liver enzymes) were expressed as (means ± SD). Probability (p) was fixed at 0.05. Data were processed and analyzed by using computer based software SPSS- 24 (Chicago, Illinois, USA).

Ethical implications

Written consent from the patients or legal guardian was taken and ethical clearance was taken from the institutional Ethical Review committee.

RESULTS

This prospective observational study was carried out in Cardiology department of Comilla Medical College Hospital, a tertiary care hospital in Bangladesh during the period from January 2021 to June 2021. We studied the data of the 100 participants those were enrolled according to specific criteria. The results of the study are detailed here:

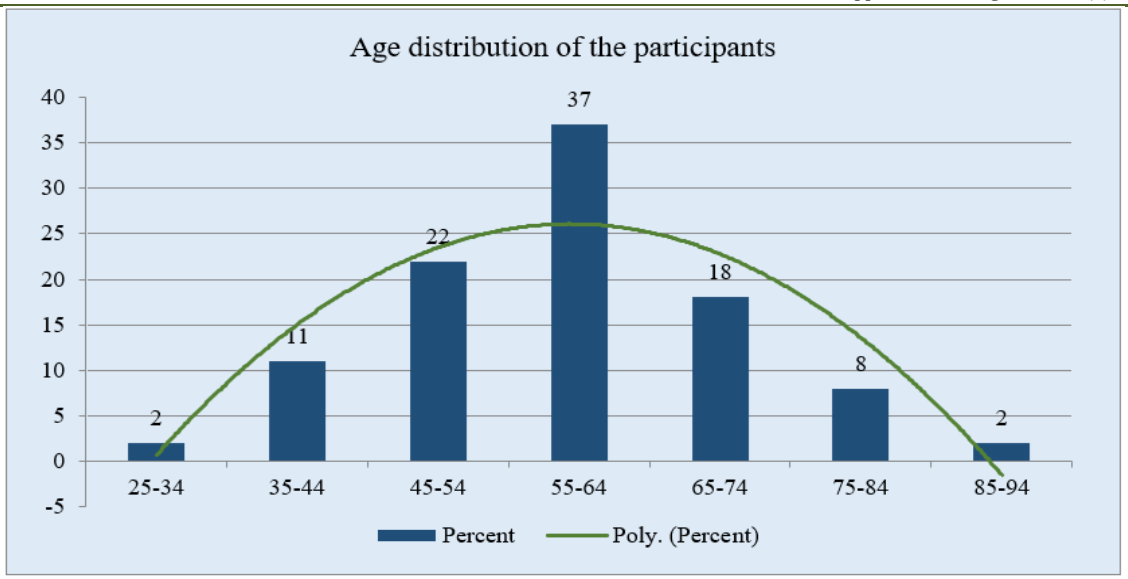

Figure 1: Column chart showed frequency distribution of age group of participants and polygonal trend line (N=100)

Figure 1 showed the range of age in the STEMI participants was 30 to 90 years of age and the mean age of the participants was (56.06±12.016). Highest numbers of STEMI patients were belong to 55-64 years of age group (37%). After that, 45-54 years group (22%), 65-74 years group (18%), 35-44 years group (11%), 75-84 years group (8%), 25-34 years group (2%), and 85-94 years group (2%).

Table I: Demographic characteristics of the participants (N=100)

Demographic parameters	Group	Percent (%)
Gender	Male	74.0
	Female	26.0
Marital status	Married	93.0
	Widow	07.0
	Non-married	0.0
Religion	Muslim	94.0
	Hindu	06.0
Education	Illiterate	51.0
	Primary	33.0
	SSC	8.0
	HSC	5.0
	Degree/Honours	3.0
Inhabitant	Urban	43.0
	Rural	57.0
Occupation	House wife	27.0
	Day laborer	42.0
	Office worker/Service	07.0
	Professional	14.0
	Business	10.0

The demographic characteristics shows that 74.0% of the participants were male and rest 26.0% were female. Here, 93.0% of the STEMI patients were in current marital relationship and the rest 07.0% were widow. Maximum (94%) were Muslim background and rest 6% were Hindu. Interestingly, 51.0% of the participants were illiterate, 33% were primary passed, 8% were SSC passed, 5% were HSC passed and only 3% were Degree/Honours passed. Most (57%) of the participants came from rural area and the rest (43%) were from urban area. A good number (42%) of the participants were day laborer and 27.0% were house wives, professional (14%), business (10%) and office worker (7.0%).

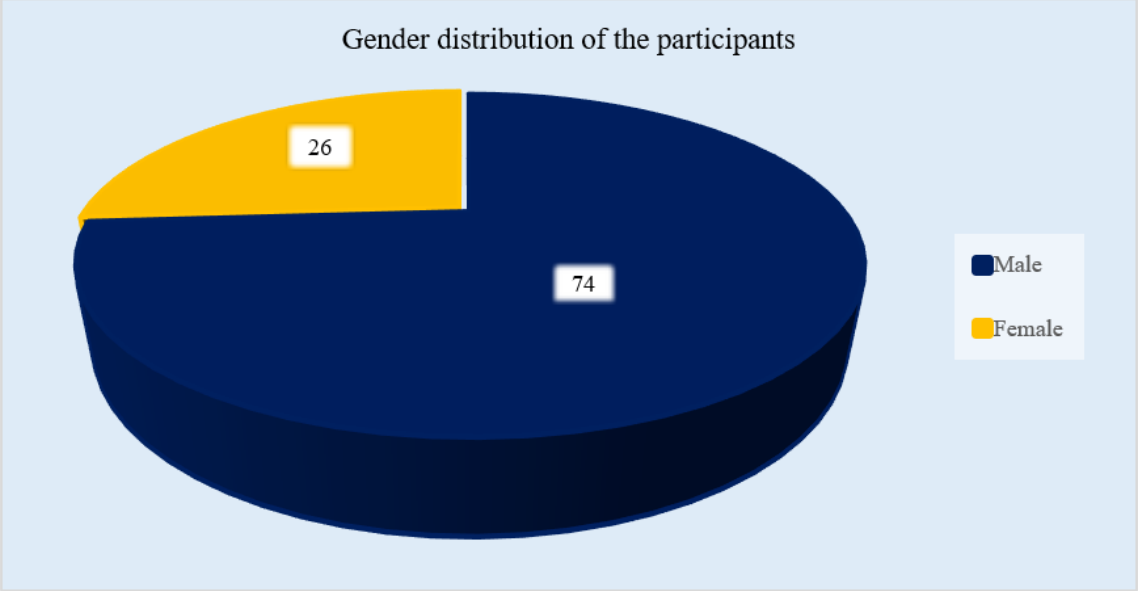

Figure 2: Pie chart showed gender wise participants distribution (N=100)

Table II: Clinical and laboratory (qualitative) parameters (N=100)

Clinical and Lab parameter	Group	Percent (%)
Chest pain	Present	97
	Absent	03
Sweating	Present	90
	Absent	10
Anemia	Present	11
	Absent	89
Jaundice	Present	5
	Absent	95
Vomiting	Present	44
	Absent	56
HBsAg	Positive	6
	Negative	94
Anti HCV	Positive	4
	Negative	96

Table II showed 97.0% of the STEMI patients had chest pain, 90.0% complaints for sweating and 44.0% complaint for vomiting. Out of them, 11.0% were anemic, 5.0% were icteric.

Table III: Distribution of clinical parameters (quantitative) (N=100)

Parameter	mean	SD
Age (yrs)	56.06	12.016
Monthly income (taka)	13550.00	7510.51
Pulse (bpm)	77.31	10.87
SBP (mm Hg)	115.0	22.35
DBP (mm Hg)	74.54	13.99
Weight (kg)	57.74	6.51
Resp. Rate (br/min)	23.00	3.54

Table III showed quantitative clinical parameters, showing age (mean±SD) 56.06±12.016, monthly income (mean±SD) 13550.00±7510.51, pulse (bpm) (mean±SD) 77.31±10.87, systolic blood pressure (mean±SD) 115.0±22.35 mm Hg, diastolic BP (mean±SD) 74.54±13.99 mm Hg, weight (kg) (mean±SD) 57.74±6.51 and respiratory rate (breath/min) (mean±SD) 23.0±3.54.

Table IV: Distribution of various laboratory parameters (Quantitative) (N=100)

Parameter	Mean	SD
Hb%	12.37	1.72
TC WBC (cells/mm³)	5274.59	6496.09
Neutrophil (%)	71.16	8.59
Lymphocyte (%)	19.35	8.13
Eosinophil (%)	3.39	0.84
Monocyte (%)	6.02	1.55
Blood urea (mg/dl)	31.41	6.26
S. Creatinine (mg/dl)	1.10	0.32
S. Bilirubin (mg/dl)	0.79	0.31
RBS (mmol/L)	8.55	4.52
SGPT (U/L) day 1	61.27	47.12
SGPT (U/L) day 6	82.45	85.07
SGOT (U/L) day 1	52.82	42.35
SGOT (U/L) day 6	70.11	73.73
ALP (U/L) day 1	209.73	68.59
ALP (U/L) day 6	266.67	433.82

Table IV showed quantitative laboratory parameters. Hemoglobin (mg/dl) (mean±SD) 12.37±1.72, serum creatinine (mg/dl) (mean±SD) 1.10±0.32, serum bilirubin (mg/dl) (mean±SD) 0.79±0.31, RBS (mmol/l) (mean±SD) 8.55±4.55, SGPT (U/L) on day1(mean±SD) 61.27±47.12, on day 6 (mean±SD) 82.45±87.07, SGOT (U/L) on day1(mean±SD) 52.82±42.35, on day 6 (mean±SD) 70.11±73.73, and ALP (U/L) on day1(mean±SD) 209.73±68.59, on day 6 (mean±SD) 266.67±433.82.

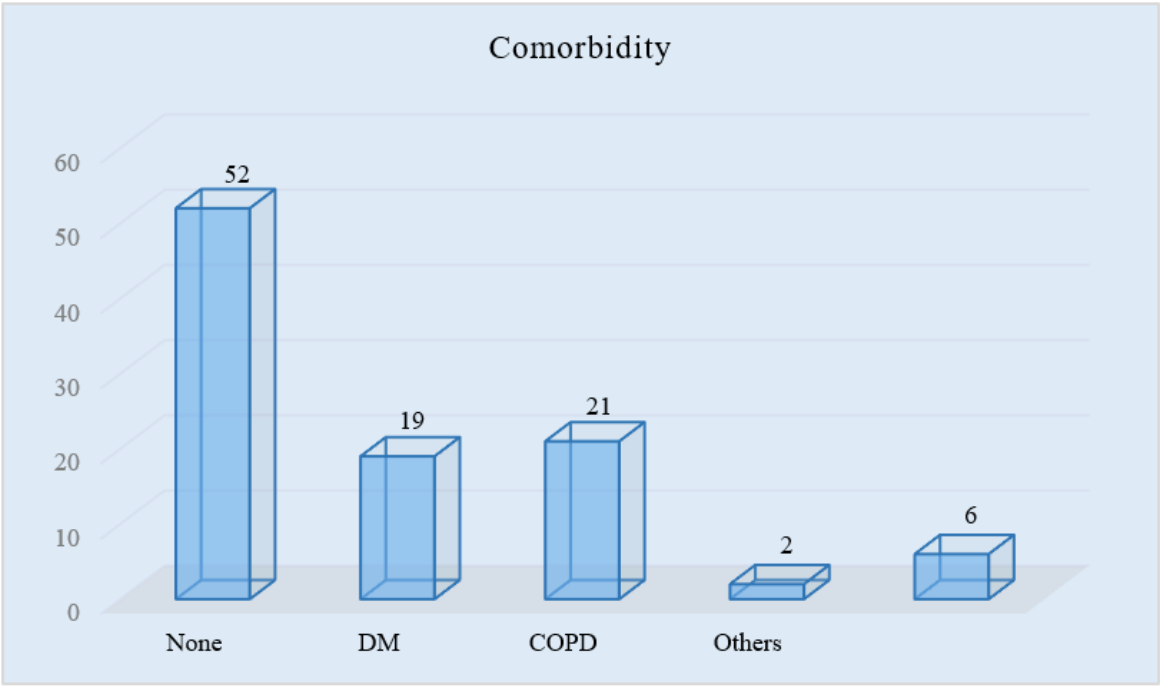

Figure 3: Column chart showed distribution of comorbidity in the STEMI Patients (N=100)

Figure 3 showed about half of the patients (48%) had various comorbidities including Hypertension (21%), Diabetes mellitus (19%), COPD (2%), and rest 6% had other (i.e.- RA, Thyrotoxicosis, stroke, CKD etc) comorbidities.

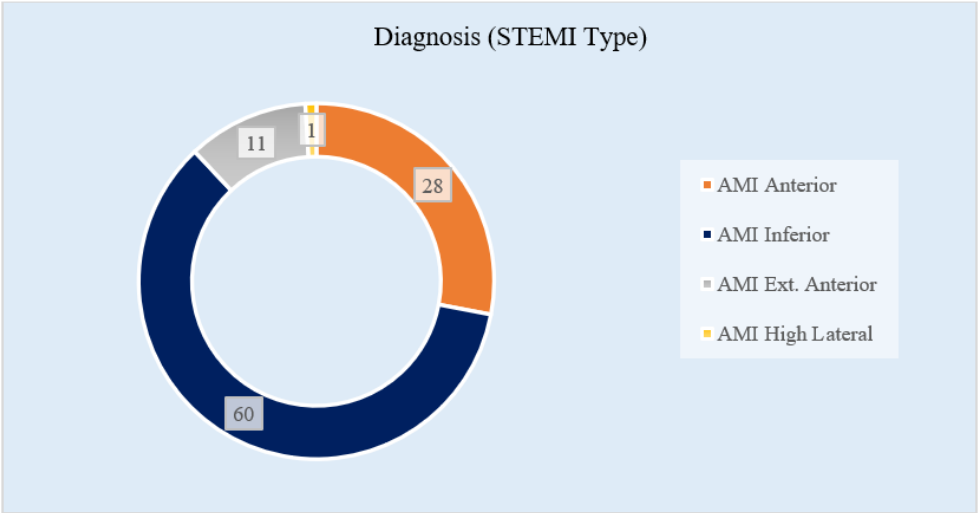

Figure 4: Ring chart showed distribution of STEMI types in the participants (N=100)

Figure 4 showed the most common variety of STEMI in our participants was AMI inferior (60%). Other surface areas including Anterior (28%), extensive anterior (11%) and high lateral (1%) were involved relatively less frequently.

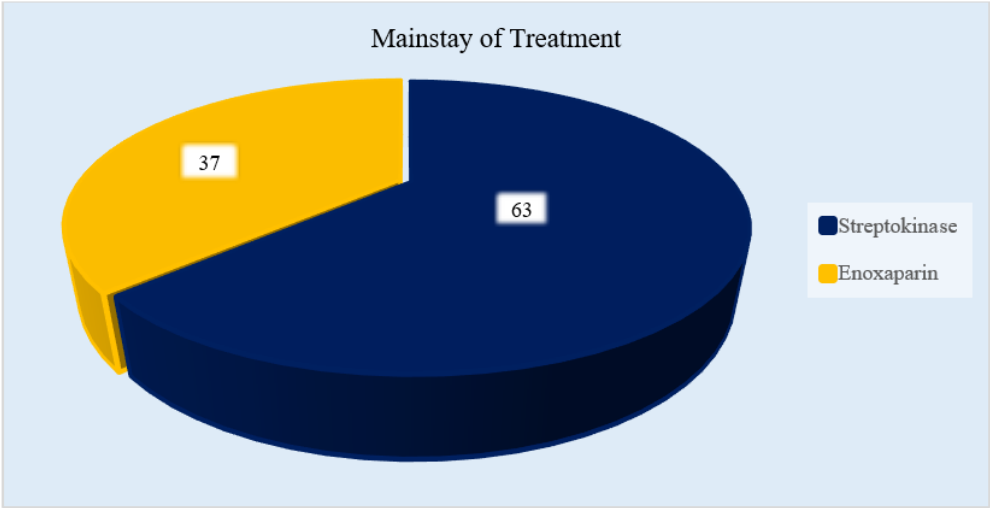

Figure 5: Pie chart showed distribution of the mainstay of treatment (N=100)

Figure 5 showed all the patients were treated according to standard protocol for the locally available medicines. We did not include the patients who were referred for Angioplasty or CABG as these are available in CoMCH. The maximum patients were treated with injectable streptokinase (63%) and they were not eligible for thrombolysis that's why they were treated with LMWH (Enoxaparin- 37%).

Table V: Distribution of in-hospital complications of the STEMI patients (N=100)

Complications	Number (n)	Percent (%)
None	23	23
Heart failure	30	30
Arrhythmia	16	16
Pericarditis	19	19
Shock	12	12
Total=	100	100

Table V showed 23 percent of the patients had no in-hospital complications. The most common type of complication was heart failure (30%), followed by pericarditis (19%), arrhythmia (16%), and cardiogenic shock (12%).

Table VI: Distribution of the outcome (N=100)

Outcome	Percent (%)	P value
Improved	95	0.000
Death	05	

Table VI showed in-hospital outcome (who stayed ≥ 6days) was favorable in our study. Death was noted in 5% of the patients and rest 95% were discharged with improvement. This difference was statistically significant (p value= 0.000).

Table VII: Distribution of modes of death in the STEMI patients (N=100)

Modes of death	Number (n)	Percent (%)
Arrhythmia	1	20
Heart failure	3	60
Cardiogenic shock	1	20
Total	5	100

Table VII showed the most common type of mode of death was heart failure (60%). Arrhythmia and cardiogenic shock were noted in 20% each.

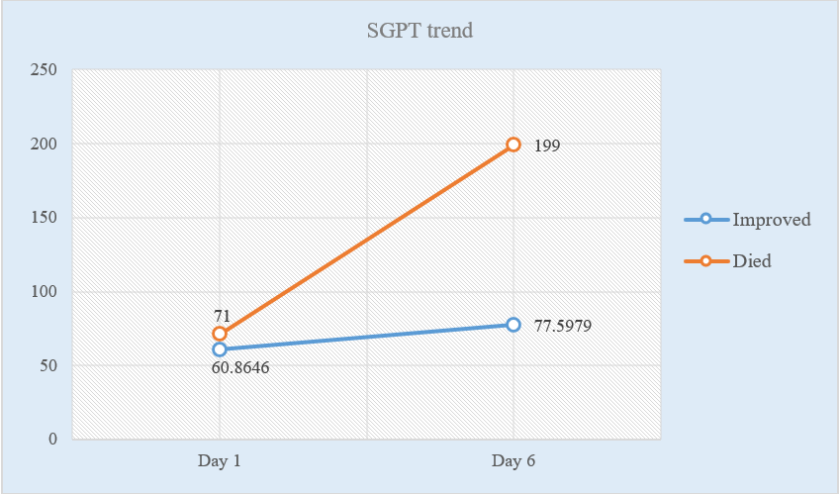

Figure 6: Line chart showed trend of SGPT according to outcome of patients (N=100)

Figure 6 showed SGPT trend line clearly shows that SGPT was rising from day 1 to day 6 in the patients who died in the hospital 6 days onwards. But the level of SGPT in the improved patients was not that much inclined.

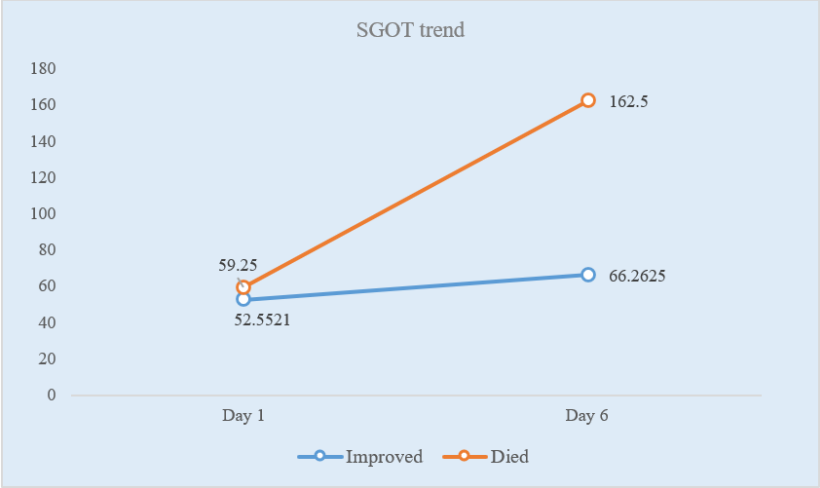

Figure 7: Line chart showed trend of SGOT according to outcome of patients (N=100)

Figure 7 showed the trend line of SGOT is very similar to that of SGPT; much inclined in death patients and minor change in the improved patients.

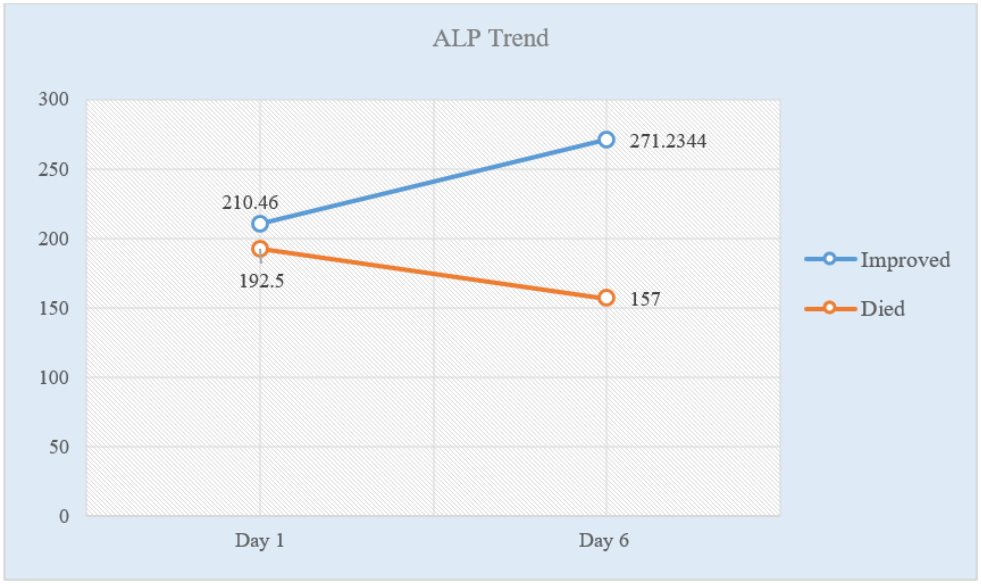

Figure 8: Line chart showed trend of ALP according to outcome of patients (N=100)

Figure 8 showed the ALP trend line does the follow the previous two. Here, the improved patients had some inclination of the level from day 1 to day 6 and the reverse in noted in the dead patients.

Table VIII: Comparison of mean SGPT (U/L) level in heart failure and non-heart failure STEMI patients (N=100)

Parameter	Day 1	Day 6	p value
Heart failure	46.4	104.7	0.001
Non heart failure	36.5	45.5	

Table VIII showed the SGPT level was significantly increased from day 1 to day 6 in heart failure patients than the non-heart failure patients (p value 0.000)

Table IX: Comparison of mean SGOT (U/L) level in heart failure and non-heart failure STEMI patients (N=100)

Parameter	Day 1	Day6	p value
Heart failure	38.8	112.8	0.03
Non heart failure	32.9	51.5	

Table IX showed the SGOT level was significantly increased from day 1 to day 6 in heart failure patients than the non-heart failure patients (p value 0.03).

Table X: Comparison of mean ALP (U/L) level in heart failure and non-heart failure STEMI patients (N=100)

Parameter	Day 1	Day6	p value
Heart failure	230.8	222.7	0.69
Non heart failure	223.95	261.8	

Table X showed alkaline phosphatase (ALP) was not significantly changed in the patients with heart failure. Non-heart failure patients show few increase in the level of ALP (U/L), but it wasn't significantly associated (p value 0.69).

Table XI: Percentage of Participants with raised liver enzymes (N=100)

Liver enzymes	Day 1 (%)	Day 6 (%)
SGPT	54	75
SGOT	47	77
ALP	29	54

Table XI showed all the liver enzymes (SGPT, SGOT, and ALP) are raised in STEMI. At baseline, these are 54%, 47% and 29% respectively. But at the 6th day, they increased to 75%, 77% and 54%.

Table XII: Crude odds ratio and Adjusted odds ratios of Liver enzyme elevation in STEMI population stratified by clinical outcome (N =100)

Liver enzyme		Improved (n=95)		Death (n=5)	
		Odds Ratio (OR)	p-value	Odds Ratio (OR)	p-value
SGPT	Crude	0.464(0.264-0.664)	0.602	3.10(2.85-3.35)	0.000
	Adjusted	0.667(0.567-0.767)	0.660	4.56(4.11-5.10)	0.000
SGOT	Crude	0.486(0.286-0.686)	0.205	2.559(2.157-3.100)	0.004
	Adjusted	0.870(0.670-0.970)	0.348	4.236(3.901-4.696)	0.000
ALP	Crude	0.447 (0.047-0.847)	0.170	1.911 (1.892-1.931)	0.007
	Adjusted	0.956 (0.948-0.963)	0.080	1.421 (1.401-1.442)	0.060

Table XI showed crude odds ratio and adjusted odds ratios of Liver enzyme elevation in STEMI population stratified by clinical outcome (death and improved). In case of SGPT and SGOT all the odds are higher in dead patients and all the odds are lower in case improved patients. Here the relations are statistically significant in death patients. But for ALP, all the odds are slightly higher in death patients and the relation significant in case of crude value only.

DISCUSSION

In our study, the average age of STEMI patients was 56.06 (± 12.016) and the peak age group of incidence was 55 to 64 years age. This was slightly lower than *DK Djakpo et al.*, 61.43(±13.702), but very close to *Ming Gao et al.*, 59.5 (± 11.1). Sex distribution (male: female) in our study (74:26) was nearly to *DK Djakpo et al.*, (76.7:23.3) and *Ming Gao et al* (72:28) [14, 33]. Liver function tests usually comprise SGPT, SGOT, ALP, GGT, other nonenzymatic proteins (e.g., albumin), and heme metabolites, such as bilirubin. Among these markers, SGPT and SGOT are often elevated in patients with STEMI [31] In this study, SGPT, SGOT and ALP are increased from day 1 to day 6. The baseline (day1) SGPT 61.27(±47.12) is similar to *Gao et al.*, 55.5(± 108.3), But SGOT 52.82(± 42.35) and ALP 209.73(±62.59) were not same; 165.3(± 283.1) and 72.4 (± 24.4) respectively. Random blood sugar in this current study was 8.55(±4.52) was slightly higher than *Gao et al.*, which was 7.1 ± 3.1. This may be due to having more diabetic patients in this study. Serum bilirubin level was similar to Teodor Baars *et al.*, 0.79±0.32 and 0.63 ± 0.03 respectively [12,16]. *Lofthus et al.*, have shown that Aspartate transaminase (AST) was elevated above the upper limit of normal in 85.6% and alanine transaminase (ALT or SGPT) was elevated in 48.2% of patients at baseline or day 1. Those who have any degree of elevation of liver enzymes in first 24 hours, AST levels had returned to baseline in 57% (740/1307) by day 6 or discharge. Similarly, 43% (323/749) of patients with any degree of ALT elevation during the first 24 h had normal levels by day 6 or discharge. Some patients live enzyme cannot reach to normal, but there is decrement from the initial elevated level in 91% and 57% of the participants in case of SGOT and SGPT respectively. In this study, at baseline (day 1), SGPT, SGOT, and ALP are 54%, 47% and 29% respectively. But at the 6th day, they increased to 75%, 77% and 54%. This difference may be due to the unawareness of the level of the enzymes and the fact that the enzymes were elevated, but not reaching the 3 times upper limit of normal value, which is the indication of stopping the statins. The Lofthus *et al.*, [14] had introduced the statins during the discharge when the enzymes had reached to a tolerable limit. In this study, the inferior surface of heart was involved maximally (60%) and anterior surface was involved in 29% of cases. But *Gao et al.*, [12] showed both are nearly equal (anterior 48%, inferior 49%). Current study shows, the maximum number patients died (mode of death) from heart failure (60%). There was difference in the liver enzyme elevation according to present and absent of heart failure. SGPT and SGOT elevation are significantly associated with heart failure. The p values are 0.001 and 0.003 respectively. In case of ALP, the p value was 0.69.

Crude odds ratio and adjusted odds ratios of Liver enzyme elevation in STEMI population stratified by clinical outcome (died and improved) showed that in case of SGPT and SGOT all the odds are higher in dead patients and all the odds are lower in case improved patients. Here the relations are statistically significant in death patients.

LIMITATION OF THE STUDY

The limitation of the study was that we had follow up the patient for 6 days only, didn't wait to see the return of the liver enzymes to normal level. So, we could not evaluate the actual duration required to return of liver enzymes to normal. We had only taken the patients who are treated with LMWH and streptokinase. As our facility lacks angioplasty, we could not assess if there is any differences among them. Another limitation is that we had measured liver enzymes only two times. If we could measure these more frequently i.e.- 12 hourly or 24 hourly, we could find the actual time when it comes to peak. Another important thing is that we found only 100 cases to study this complicated relationship, though we had shown the association correctly.

RECOMMENDATION

From our study, we would recommend to follow up vigorously regarding the changes of liver enzymes in STEMI patients. It will help us to lower the morbidity and mortality related to acute hepatic failure. To get more precise and accurate association between liver enzymes changes and STEMI, we should undertake larger and well-designed prospective study. We also recommend including patients from all modalities of treatment and conducting the study in multiple centers to ensure better coverage and avoid confounding.

CONCLUSIONS

In conclusion, the association of STEMI with liver enzymes elevation are clear. SGPT and SGOT elevations are common in STEMI. Both markers are correlated and are independently associated with worse clinical outcomes. ALP also increases in STEMI, but the association is not clinically significant. This study shows, there is persistence rise of liver enzymes till 6th day following ST-segment elevation myocardial infarction. This points out that we are not aware about the rise of these enzymes or using statins vigorously. So, we should pay attention to liver enzyme rise to reduce the death due to acute liver failure.

REFERENCES

1. Poelzl, G., Ess, M., Mussner-Seeber, C., Pachinger, O., Frick, M., & Ulmer, H. (2012). Liver dysfunction in chronic heart failure: prevalence, characteristics and prognostic significance. *European journal of clinical investigation*, *42*(2), 153-163.
2. Batin, P., Wickens, M., McEntegart, D., Fullwood, L., & Cowley, A. J. (1995). The importance of abnormalities of liver function tests in predicting mortality in chronic heart failure. *European heart journal*, *16*(11), 1613-1618.
3. Allen, L. A., Felker, G. M., Pocock, S., McMurray, J. J., Pfeffer, M. A., Swedberg, K., ... & CHARM Investigators. (2009). Liver function abnormalities and outcome in patients with chronic heart failure: data from the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program. *European journal of heart failure*, *11*(2), 170-177.
4. Alvarez, A. M., & Mukherjee, D. (2011). Liver abnormalities in cardiac diseases and heart failure. *International Journal of Angiology*, *20*(03), 135-142.
5. Fouad, Y. M., & Yehia, R. (2014). Hepato-cardiac disorders. *World journal of hepatology*, *6*(1), 41.
6. Yun, K. E., Shin, C. Y., Yoon, Y. S., & Park, H. S. (2009). Elevated alanine aminotransferase levels predict mortality from cardiovascular disease and diabetes in Koreans. *Atherosclerosis*, *205*(2), 533-537.
7. Kunutsor, S. K., Apekey, T. A., Seddoh, D., & Walley, J. (2014). Liver enzymes and risk of all-cause mortality in general populations: a systematic review and meta-analysis. *International journal of epidemiology*, *43*(1), 187-201.
8. Lee, T. H., Kim, W. R., Benson, J. T., Therneau, T. M., & Melton III, L. J. (2008). Serum aminotransferase activity and mortality risk in a United States community. *Hepatology*, *47*(3), 880-887.
9. Prati, D., Taioli, E., Zanella, A., Torre, E. D., Butelli, S., Del Vecchio, E., ... & Sirchia, G. (2002). Updated definitions of healthy ranges for serum alanine aminotransferase levels. *Annals of internal medicine*, *137*(1), 1-10.
10. Lee, J. K., Shim, J. H., Lee, H. C., Lee, S. H., Kim, K. M., Lim, Y. S., ... & Suh, D. J. (2010). Estimation of the healthy upper limits for serum alanine aminotransferase in Asian populations with normal liver histology. *Hepatology*, *51*(5), 1577-1583.
11. Al-Hamoudi, W., Ali, S., Hegab, B., Elsiesy, H., Hashim, A., Al-Sofayan, M., ... & Abaalkhail, F. (2013). Revising the upper limit of normal for levels of serum alanine aminotransferase in a Middle Eastern population with normal liver histology. *Digestive diseases and sciences*, *58*, 2369-2375.
12. Lofthus, D. M., Stevens, S. R., Armstrong, P. W., Granger, C. B., & Mahaffey, K. W. (2012). Pattern of liver enzyme elevations in acute ST-elevation myocardial infarction. *Coronary artery disease*, *23*(1), 22-30.
13. Henrion, J., Schapira, M., Luwaert, R., Colin, L., Delannoy, A., & Heller, F. R. (2003). Hypoxic hepatitis: clinical and hemodynamic study in 142 consecutive cases. *Medicine*, *82*(6), 392-406.
14. Gao, M., Cheng, Y., Zheng, Y., Zhang, W., Wang, L., & Qin, L. (2017). Association of serum transaminases with short-and long-term outcomes in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. *BMC cardiovascular disorders*, *17*, 1-8.
15. Thygesen, K., Alpert, J. S., Jaffe, A. S., Chaitman, B. R., Bax, J. J., Morrow, D. A., ... & Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. (2018). Fourth universal definition of myocardial infarction (2018). *Circulation*, *138*(20), e618-e651.
16. Baars, T., Neumann, U., Jinawy, M., Hendricks, S., Sowa, J. P., Kälsch, J., ... & Canbay, A. (2016). In acute myocardial infarction liver parameters are associated with stenosis diameter. *Medicine*, *95*(6), e2807.
17. Liu, Y., Cheng, Z., Ding, L., Fang, F., Cheng, K. A., Fang, Q., & Shi, G. P. (2010). Atorvastatin-induced acute elevation of hepatic enzymes and the absence of cross-toxicity of pravastatin. *International*

journal of clinical pharmacology and therapeutics, *48*(12), 798.

18. Writing Committee Members, Hunt, S. A., Abraham, W. T., Chin, M. H., Feldman, A. M., Francis, G. S., ... & Riegel, B. (2005). ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart Rhythm Society. *circulation*, *112*(12), e154-e235.
19. 2009 Writing Group to Review New Evidence and Update the 2005 Guideline for the Management of Patients with Chronic Heart Failure Writing on Behalf of the 2005 Heart Failure Writing Committee, Jessup, M., Abraham, W. T., Casey, D. E., Feldman, A. M., Francis, G. S., ... & Yancy, C. W. (2009). 2009 focused update: ACCF/AHA guidelines for the diagnosis and management of heart failure in adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the International Society for Heart and Lung Transplantation. *Circulation*, *119*(14), 1977-2016.
20. Sherlock, S. (1951). The liver in heart failure relation of anatomical, functional, and circulatory changes. *British heart journal*, *13*(3), 273.
21. Safran, A. P., & Schaffner, F. (1967). Chronic passive congestion of the liver in man. Electron microscopic study of cell atrophy and intralobular fibrosis. *The American journal of pathology*, *50*(3), 447.
22. Dunn, G. D., Hayes, P., Breen, K. J., & Schenker, S. (1973). The liver in congestive heart failure: a review. *The American journal of the medical sciences*, *265*(3), 174-189.
23. Safran, A. P., & Schaffner, F. (1967). Chronic passive congestion of the liver in man. Electron microscopic study of cell atrophy and intralobular fibrosis. *The American journal of pathology*, *50*(3), 447.
24. Lefkowitch, J. H., & Mendez, L. (1986). Morphologic features of hepatic injury in cardiac disease and shock. *Journal of hepatology*, *2*(3), 313-327.
25. Weisberg, I. S., & Jacobson, I. M. (2011). Cardiovascular diseases and the liver. *Clinics in liver disease*, *15*(1), 1-20.
26. Henrion, J., Minette, P., Colin, L., Schapira, M., Delannoy, A., & Heller, F. R. (1999). Hypoxic hepatitis caused by acute exacerbation of chronic respiratory failure: a case-controlled, hemodynamic study of 17 consecutive cases. *Hepatology*, *29*(2), 427-433.
27. Mathurin, P., Durand, F., Ganne, N., Mollo, J. L., Lebrec, D., Degott, C., ... & Bernuau, J. (1995). Ischemic hepatitis due to obstructive sleep apnea. *Gastroenterology*, *109*(5), 1682-1684.
28. Ellenberg, M., & Osserman, K. E. (1951). The role of shock in the production of central liver cell necrosis. *The American journal of medicine*, *11*(2), 170-178.
29. KILLIP III, T. H. O. M. A. S., & Payne, M. A. (1960). High serum transaminase activity in heart disease: circulatory failure and hepatic necrosis. *Circulation*, *21*(5), 646-660.
30. Clarke, W. T. W. (1950). Centrilobular Hepatic Necorsis Following Cardiac Infarction. *The American Journal of Pathology*, *26*(2), 249.
31. Giallourakis, C. C., Rosenberg, P. M., & Friedman, L. S. (2002). The liver in heart failure. *Clinics in liver disease*, *6*(4), 947-967.
32. Vyskočilová, K. & Špinarová, L. &Špinar, J. &Vítovec, Jiří&Littnerova, Simona & Mikušová, T. &Pařenica, J. &Jarkovsky, Jiri. (2014). Prognostic significance of liver enzyme elevations in acute coronary syndromes. Kardiologicka Revue. 16. 25-30
33. Djakpo, D. K., Wang, Z. Q., & Shrestha, M. (2020). The significance of transaminase ratio (AST/ALT) in acute myocardial infarction. *Archives of Medical Science-Atherosclerotic Diseases*, *5*(1), 279-283.