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Association between Elevated Liver Enzymes and Acute Myocardial Infarction: A Comprehensive Literature Review

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Abstract

Elevated liver enzymes, particularly alanine aminotransferase (ALT) and aspartate aminotransferase (AST), are increasingly recognized as potential markers in patients with acute myocardial infarction (AMI). This review explores the association between liver enzyme elevation and AMI, focusing on the underlying mechanisms, including ischemic liver injury, systemic inflammation, and metabolic comorbidities. Studies suggest that elevated liver enzymes may not only reflect the extent of myocardial injury but also have prognostic significance in predicting worse outcomes. However, their nonspecific nature necessitates cautious interpretation in clinical practice. Further research is required to clarify their role and potential use as biomarkers in AMI.

Keywords: Acute Myocardial infarction, Liver enzymes, De Ritis ratio, Association.

Introduction

The Coronary Vasculature – Anatomical Considerations

The human heart has a weight of approximately 250-300 g and a size similar to a closed fist. The four-chambered heart is positioned in the thorax with the fibrous sac, the pericardium (fibrous and serous). The external layer of the heart tissue is called the epicardium and the innermost layer in association to the ventricles is the endocardium. The tissue between the two layers is called as the myocardium. It is responsible for ventricular contraction and consists of muscular tissue. The heart is divided into left and right side by the septal wall.[1,2]

Blood Supply of the Heart

The myocardium is supplied with oxygen-rich blood through the coronary arteries, the left anterior descending coronary artery (LAD), the left circumflex coronary artery (LCX), and the right coronary artery (RCA). The la-corona or the royal crown is the term used for coronary arteries.[1,2]

The right and left coronary arteries together form an oblique inverted vascular crown. The LCA supplies a larger volume of the myocardium as compared to the right coronary artery. The LCA is also more variable than its right counterpart in origin, distribution, branching pattern and luminal size.

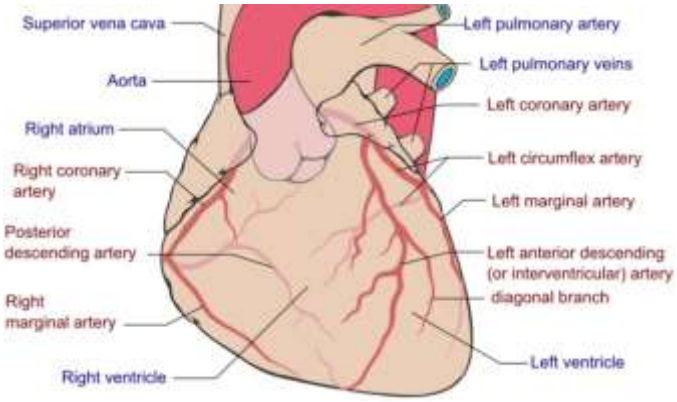

Figure 1: Showing Coronary Artery

The structures that are routinely observed are referred to as "n coronary anatomy." Variations that affect fewer than 1% of the general population are referred to as "anomalies".[3,4]

The first blood vessels to emerge from the aorta are the coronary arteries, which typically begin at the sinotubular junction, which is located below the point where the ascending aorta and bulbus meet. The coronary orifices are situated just above the cusp's free margin and in the centre of the corresponding aortic sinuses. The right coronary artery typically branches off from the aorta wall at an angle of 95 degrees, whereas the left coronary artery branches off at a somewhat lower angle.[3,4]

The coronary arteries are vessels located in the epicardium, although they may penetrate into the myocardium for part of their route. Here, they form a dense network known as the arterio-cameral connections, which are sporadic links between the ventricular chambers and the venous circulation made possible by the cardiac capillaries.[1,3].

Acute myocardial infarction (AMI)

Acute myocardial infarction (AMI), also known as a MI, is primarily caused by a reduction or cessation of blood flow to a specific area of the heart, resulting in the death of cardiac myocyte tissue.

Typically, this occurs due to an occlusion of the vessel by a blood clot or thrombus formed in the epicardial artery that provides blood to that specific area of the cardiac muscle. It is currently recognized that not all cases of AMI require a thrombus as the reason for ischemia.

One of the prerequisites for survival is oxygen. The coronary arteries are responsible for providing the necessary blood supply that is required for the cardiac

muscle to survive. There is a supply-demand ratio. It is now recognized that an imbalance in this ratio, such as an excessive heart rate or a decrease in blood pressure, can result in myocardial injury even without the presence of a thrombus.[5,6,7]

In the past decade, a universally accepted definition of AMI has been established to assist clinicians in diagnosing the condition. This criteria specifies that in order to diagnose Acute Myocardial Infarction (AMI), there is an increase in a blood test that detects cardiac myocyte damage (troponin I). Additionally, at least one of these values must be higher than the upper reference limit's 99th percentile. Furthermore, there should be clinical evidence supporting the diagnosis of AMI. This clinical evidence encompasses symptoms of ischemia, such as electrocardiographic signs indicating ischemia like ST segment changes or new left bundle branch occlusion , the appearance of pathological Q waves on electrocardiogram (ECG), or the emergence of new wall motion abnormalities during cardiac testing, or a combination of these indicators.[7,8]

It was Reimer et al in the year 1977 , who showed that myocardial infarction has the ability to gradually progress over time.(9) It begins as a waveform from the level of the level of the endocardium to the level of the myocardium to the level of the epicardium . They stated that a myocardial infarct has a gradual progression with time, and it progresses in a waveform from the endocardium but the entire myocardial is at risk and the time of onset of occlusion to restoration to perfusion of the ischemic myocardium.[9,10]

Because of this concept, the expression time is muscle, and the Golden hour came into existence referring to the time during which a large proportion of myocardium at risk can be salvaged. Various studies have shown that within one hour of onset of symptoms if the medications are given, it results in a 50% reduction in the mortality and morbidity; and treatment within the first six hours of onset of symptoms will result in a decrease in mortality approximately twice that, compared to if treatment was given between 6th and 12 hours of time of onset.

Acute coronary infection is also referred to as AMI or MI refers to the necrosis of the tissue of the myocardial as a result of prolonged ischemia, because of the occlusion of the coronary artery. As a result of the ischemic insult, there will be reversible damage to the myocardium that is affected, which will impair its function leading to arrhythmias, and cardiac arrest.

Classification

The History

Since the 1970s, there have been multiple revisions to the terminology used to describe myocardial infarction (MI). In the 1960s and 1970s, MI was classified as either transmural MI or non-transmural MI. Transmural myocardial infarction (MI) refers to a condition where the lack of blood flow and subsequent damage occurs throughout the full thickness of the heart muscle, affecting the endocardium, myocardium, and epicardium.[2,4]

This commonly occurs due to a total occlusion of a major coronary artery by a blood clot, leading to reduced blood flow to all three layers of the heart muscle. Non-transmural myocardial infarction (MI) refers to ischemia and injury that does not include all three layers of the heart muscle, usually sparing the outer layer known as the epicardium. This was believed to be caused by a substantial reduction in blood flow to the area, either with or without full occlusion of a coronary artery or its branch. In the 1980s, the terminology was modified to incorporate electrocardiogram (ECG) findings indicating

myocardial infarction (MI). The term "Q wave MI" has replaced the previous definition of "transmural MI". It refers to a myocardial infarction that affects all three layers of the heart muscle, resulting in the presence of a pathological Q wave on an electrocardiogram (ECG) in two adjacent leads. Non-transmural myocardial infarction (MI) was later referred to as non-Q wave MI, based on the hypothesis that Q waves would not be present on an electrocardiogram (ECG) unless the full thickness of the cardiac myocyte was affected. Nevertheless, in the following ten years, autopsies were unable to verify that Q-wave MI was equivalent to a transmural MI. Consequently, during the 1990s, the medical fraternity embraced the terms ST segment elevation MI (STEMI) and non-STEMI (NSTEMI) as the preferred terminology. This revised terminology would categorize myocardial infarction based on the electrocardiogram (ECG) alterations observed. STEMI is characterized as a myocardial infarction (MI) with ST segment elevations in two adjacent leads on an electrocardiogram (ECG). The specific criteria for ST segment elevations may vary depending on the leads involved. Typically, STEMI is associated with full occlusion of a major coronary artery on the outer surface of the heart. On the other hand, an NSTEMI was characterized as ST depressions or other ECG ischemia alterations that did not fulfil the criteria for STEMI. Angiographic studies have shown that non-Q wave myocardial infarction (similar to non-ST elevation myocardial infarction or NSTEMI) can occur due to three main factors: complete occlusion of a small branch, complete occlusion followed by spontaneous reopening (reperfusion) of a major artery, or collateral blood flow from another area that mitigates the impact of complete occlusion. In the last two cases, the extent of necrosis was significant enough to prevent or just briefly manifest ST elevation.

A consensus statement was issued in 2007 by the leading American and European cardiac associations, establishing a universal definition of myocardial infarction (MI). This definition broadened the prior terminology by incorporating laboratory tests and clinical history. Myocardial infarction (MI) is now defined as an occurrence where there is an increase or decrease (or both) in a blood test that detects cardiac myocyte injury (troponin I or T), together with clinical evidence that confirms a diagnosis of acute myocardial infarction (AMI) as described above. Under this comprehensive definition, numerous factors leading to NSTEMI did not necessarily involve the presence of a blood clot in a coronary artery located on the outer surface of the heart.

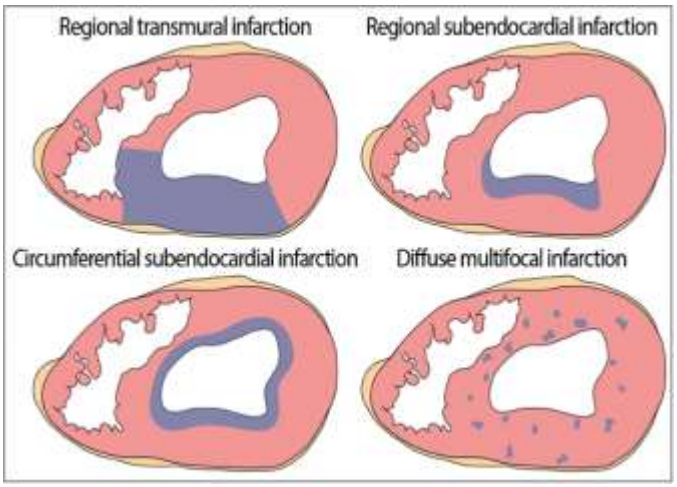

Figure 2: Types of Infarction

Etiology of MI

The most common cause of acute myocardial infarction is atherosclerosis. But there are a number of non atherosclerosis causes that are of known to cause myocardial infarction that have been listed below in the figure.

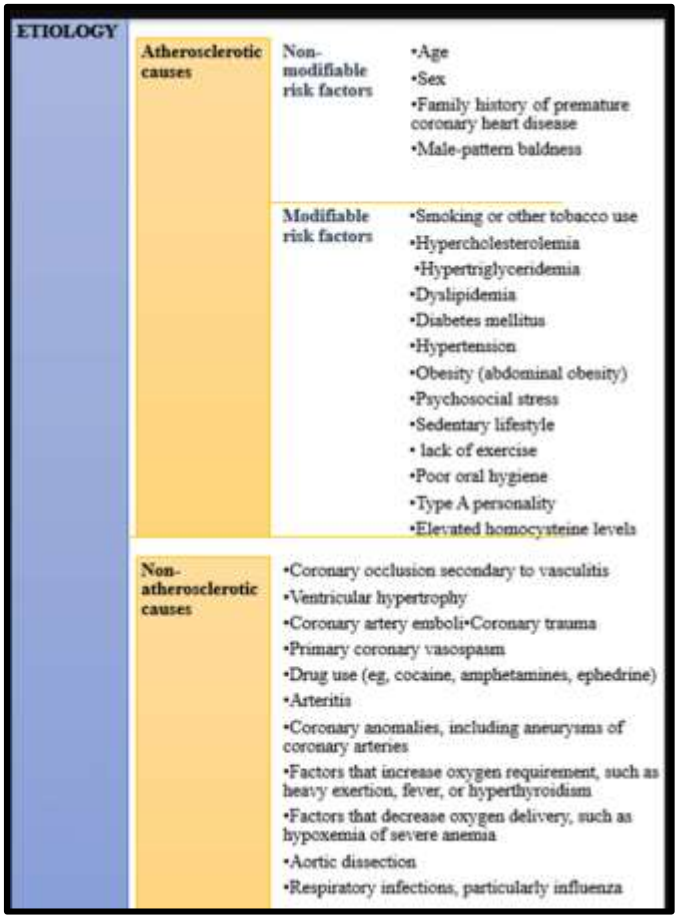

Figure 3: Causes of Mi.

Risk Factors for Acute Myocardial Infarction (AMI)

Acute myocardial infarction (AMI) is a multifactorial disease influenced by a combination of genetic, environmental, and lifestyle factors. Understanding the various risk factors associated with AMI is crucial for risk stratification, preventive interventions, and optimizing patient outcomes.

Hypertension

Hypertension, defined as persistently Elevated blood pressure, is a well-established risk factor for AMI. Elevated blood pressure increases cardiac workload, leading to left ventricular hypertrophy, endothelial dysfunction, and arterial stiffness, predisposing individuals to atherosclerosis and AMI.

Diabetes Mellitus

Diabetes mellitus, especially type 2 diabetes, is strongly associated with an increased risk of AMI. Chronic hyperglycemia promotes endothelial dysfunction, oxidative stress, inflammation, and dyslipidemia, contributing to accelerated atherosclerosis and plaque instability.

Dyslipidemia

Dyslipidemia, characterized by elevated levels of low-density lipoprotein cholesterol (LDL-C) and/or reduced levels of high-density lipoprotein cholesterol (HDL-C), plays a pivotal role in the pathogenesis of AMI. LDL-C contributes to atherosclerotic plaque formation, whereas HDL-C exerts antiatherogenic effects by promoting reverse cholesterol transport.

Smoking

Cigarette smoking is a major modifiable risk factor for AMI, exerting detrimental effects on the cardiovascular system through various mechanisms, including endothelial dysfunction, oxidative stress, inflammation, thrombosis, and accelerated atherosclerosis.

Obesity

Obesity, characterized by excess adiposity, is associated with an increased risk of AMI due to its adverse effects on metabolism, inflammation, insulin resistance, dyslipidemia, and endothelial function. The studies have demonstrated a positive association between obesity and the risk of coronary heart disease, including AMI. Furthermore, weight loss interventions, through lifestyle modifications or bariatric surgery, have been shown to improve cardiovascular risk factors and reduce the incidence of AMI in obese individuals.

Physical Inactivity

Physical inactivity is an independent risk factor for AMI, contributing to the development of obesity,

hypertension, dyslipidemia, insulin resistance, and endothelial dysfunction. the protective effects of regular physical activity, with individuals engaging in moderate physical activity experiencing a significantly reduced risk of AMI compared to sedentary individuals.

Atherosclerosis initiates when low-density lipoprotein (LDL) is absorbed into the intima and undergoes oxidation, leading to a series of events that trigger the creation of inflammatory cytokines, enzymes, and cell adhesion molecules. This mechanism leads to the recruitment of T cells and monocytes into the subintimal region. The build-up of oxidised LDL exacerbates the damage to endothelial cells, leading to increased generation of free radicals originating from cytokines and oxygen in the subintimal region. Monocyte-derived macrophages consume oxidised LDL and convert it into foam cells. Over a period of time, smooth muscle cells move from the middle layer of the blood vessel wall to the inner layer, and fat builds up beneath a protective layer made up of smooth muscle cells, elastin, and collagen. In addition, chronic inflammation characterised by an increased level of C-reactive protein, regardless of LDL levels, has been demonstrated to play a role in cardiac events and is therefore believed to contribute to the development and advancement of atherosclerotic disease. As stated before, inflammatory cells, specifically macrophages and T lymphocytes, have a direct impact on the development and destabilisation of atherosclerotic plaques. Inflammation also indirectly triggers the intrinsic and extrinsic clotting pathways, hence exacerbating the development and destabilisation of atherosclerotic plaques.

The thin-cap fibroatheroma is a type of plaque that is considered fragile due to its lipid-rich, necrotic core. It might burst unexpectedly as a result of macrophage infiltration and breakdown of the fibrous cap. This leads to a series of events where platelets clump together and form blood clots, which can cause reduced blood flow to the cardiac myocyte leading to myocardial ischemia or a future heart attack (infarction), or both.

Plaque erosion, which is less common than plaque rupture, can cause coronary thrombosis. It can happen in a lesion that has a lot of proteoglycans and smooth muscle cells, but not necessarily in one that is rich in lipids. The thrombus in this case arises from a malfunction in the endothelium layer that lines the inside surface of all blood arteries. Plaque erosions often have a lower presence of inflammatory cells in comparison to plaque ruptures.

The third mechanism of thrombus formation, which is rare and observed in less than 10% of cases, happens when a calcified nodule extends through the thin fibrous cap, leading to platelet aggregation and the formation of a thrombus. The accuracy of these post-mortem observations was initially validated in vivo through coronary angiography conducted during an acute transmural infarction. This procedure confirmed that thrombosis played a crucial role in causing AMI. Subsequently, intravascular devices like optical coherence tomography were used just before coronary stent implantation during the acute event to further confirm these findings. These intravascular devices can accurately identify the specific forms of plaque that are linked to acute myocardial infarction (AMI).

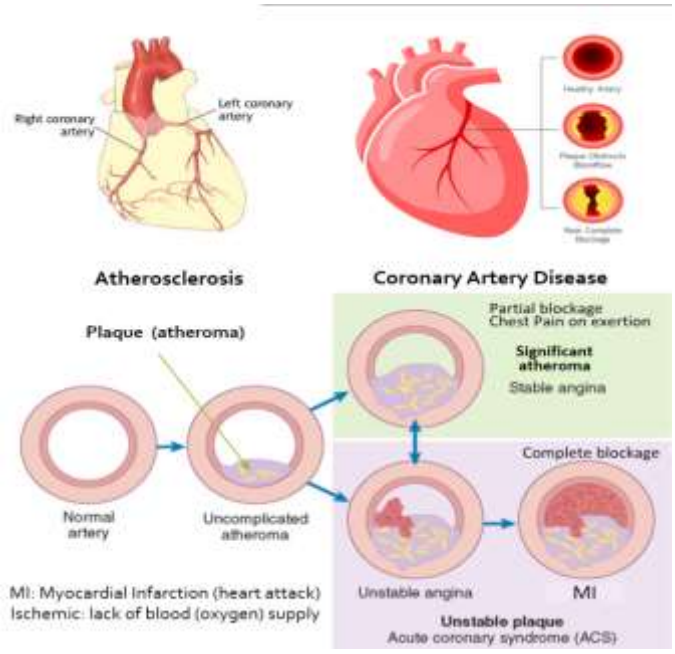

Figure 4: Atherosclerosis and Mi

Classification of MI

Acute myocardial infection can be classified into various subgroups based on the degree of alterations of the biochemical markers of myocardial injury, based on the echocardiographic alterations that are seen following the onset of the disease and the clinical presentation of the disease.

The basic classification system that is outlined in the 4th universal definition of acute myocardial infection, the 2018 update gives a clear differentiation between five different types of myocardial infarction.

The five varieties are:

- The type 1 or the spontaneous acute myocardial infection.
- The type 2 or the secondary acute myocardial infarction.
- The type 3 or the acute myocardial infarction associated with death.
- The type 4 or the procedure related acute myocardial infection.
- The type 5 or the myocardial infarction associated with cabg or coronary artery bypass graft.

1. **Type 1 (Spontaneous AMI):** This type of AMI occurs due to atherosclerotic plaque rupture, fissuring, erosion, or dissection, leading to coronary artery thrombosis and subsequent myocardial ischemia. It is further subclassified based on the presence or absence of ST-segment elevation on electrocardiography (ECG) as STEMI (ST-segment elevation myocardial infarction) or NSTEMI (non-ST-segment elevation myocardial infarction).
2. **Type 2 (Secondary AMI):** Secondary AMI is attributed to an imbalance between myocardial oxygen supply and demand, without direct coronary artery involvement. This imbalance may result from conditions such as severe hypotension, severe hypertension, severe anemia, or coronary artery spasm.
3. **Type 3 (Cardiac Death Due to AMI):** This type refers to cases where death occurs before reaching the hospital due to an AMI event. The diagnosis is typically based on postmortem examination findings or clinical history suggestive of AMI.
4. **Type 4 (Periprocedural AMI):** Periprocedural AMI occurs within 48 hours following coronary revascularization procedures, such as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), due to procedure-related complications or thrombotic events.
5. **Type 5 (Myocardial Infarction Associated with Coronary Artery Bypass Grafting):** This type of AMI is characterized by myocardial infarction occurring in the setting of CABG, typically manifested by new Q waves or imaging evidence of new loss of viable myocardium.

Epidemiology of Acute Myocardial Infarction (AMI)

Global Epidemiology*:* Acute myocardial infarction (AMI) remains a leading cause of morbidity and mortality globally, with significant variations in incidence and prevalence across different regions and populations. According to the World Health Organization (WHO), cardiovascular diseases, including AMI, accounted for approximately 17.9 million deaths worldwide in 2019, representing nearly a third of all global deaths. The burden of AMI is expected to rise further due to aging populations, urbanization, and changes in lifestyle factors such as smoking, unhealthy diet, and physical inactivity.[54] [m]A meta analysis, twenty-two qualifying studies including 2,982,6717 people (under 60) were included in the sample size. The global incidence of MI in people under 60 years of age was 38%. Additionally, this value was found at 9.5% when 20 qualifying investigations were evaluated, resulting in a sample size of 5,071,185 people (> 60 years old).

Epidemiology in Asia: In Asia, AMI poses a substantial health challenge, with diverse epidemiological patterns observed across countries and regions. Rapid economic development, urbanization, and transitions in lifestyle and dietary habits have contributed to an increasing burden of cardiovascular diseases, including AMI, in many Asian countries. Additionally, disparities in healthcare infrastructure, access to medical services, and preventive measures influence the prevalence and outcomes of AMI in different Asian populations.

Nicholas W.S. Chew et al noted that the incidence of AMI is expected to increase by 194.4% between 2025 and 2050, from 482 to 1418 cases per 100,000 people. Overweight/obesity (880.0% increase) is predicted to have the biggest percentage rise in metabolic risk factors within the AMI population. This is followed by increases in hypertension (248.7%), T2DM (215.7%), hyperlipidemia (205.0%), and active/previous smoking (164.8%). Between 2025 and 2050, it is anticipated that the number of AMI-related deaths will rise by 294.7% among overweight/obesity adults, while mortality will drop by 11.7% in those with hyperlipidemia, 29.9% in those with hypertension, 32.7% in those with type 2 diabetes, and 49.6% in those who smoke actively or formerly. Indians and Malay people are disproportionately affected by the incidence of overweight/obesity and AMI-related mortality as compared to Chinese people.

Rajesh Kumar et al noted that the 466 (9.9%) of the 4,686 patients overall were young (≤40 years old). Young patients had a higher frequency of smoking (33% vs 24.7%, p <0.001), positive family history (8.2% vs 3.2%, p <0.001), single-vessel involvement (60.1% vs 33.2%, p <0.001), and lower prevalence of hypertension (40.8% vs 54.5%, p <0.001), diabetes (26.6% vs 36.4%, p <0.001), metabolic syndrome (14.8% vs 24%, p <0.001), and history of IHD (5.8% vs 9.3%, p = 0.013). In younger patients, the composite unfavourable clinical outcome occurrence was significantly lower (p = 0.006), at 14.2% vs 19.5%. Multivariable analysis revealed that pre-procedure left ventricular end-diastolic pressure, ejection fraction <40%, age, Killip class III/IV, intubation, arrhythmias at arrival, diabetes, and history of IHD were associated with lower risk of heart attack and stroke were discovered to be the independent predictors of a poor clinical result in elderly individuals.

Epidemiology in India: India, with its large and diverse population, is experiencing a significant rise in the incidence and prevalence of AMI. According to studies conducted in India, the burden of cardiovascular

diseases, including AMI, has been steadily increasing over the past few decades. Factors such as urbanization, sedentary lifestyles, high prevalence of risk factors like hypertension, diabetes, dyslipidemia, and tobacco use contribute to the rising epidemic of AMI in India. Moreover, disparities in healthcare access and quality exacerbate the challenges in managing AMI effectively in India.

Epidemiology in Karnataka and Mangalore: Specific data on the epidemiology of AMI in Karnataka and Mangalore may be limited; however, studies conducted in India provide insights into the regional trends. Karnataka, a southern state in India, including Mangalore as one of its major cities, is likely to reflect the broader epidemiological patterns observed in the country. Factors such as urbanization, lifestyle changes, genetic predispositions, and environmental factors influence the incidence and outcomes of AMI in these regions. Local studies examining the burden of cardiovascular diseases and risk factors in Karnataka and Mangalore would provide more specific insights into the epidemiology of AMI in these areas.

Clinical Presentation of Acute Myocardial Infarction (AMI)

The occlusion of a coronary artery deprives the downstream myocardium of oxygen and nutrients, leading to ischemia. Inadequate oxygen supply compromises cellular metabolism, resulting in the accumulation of metabolic by-products, including lactate. Prolonged ischemia leads to irreversible cellular damage, primarily through the disruption of cellular membranes and the induction of apoptosis and necrosis. This myocardial injury manifests clinically as AMI, characterized by electrocardiographic changes, elevation of cardiac biomarkers, and clinical symptoms such as chest pain and dyspnea.[7]

Acute myocardial infarction (AMI) presents with a spectrum of clinical manifestations, ranging from asymptomatic cases to life-threatening complications such as cardiogenic shock and cardiac arrest. Timely recognition and diagnosis of AMI are crucial for initiating appropriate management strategies and improving patient outcomes.

Typical Symptoms: The hallmark symptom of AMI is chest pain or discomfort, often described as crushing, pressure-like, or squeezing in nature. The pain may radiate to the neck, jaw, shoulders, arms (usually the left arm), back, or epigastrium. Patients may also experience associated symptoms such as dyspnea, diaphoresis, nausea, vomiting, and light-headedness. However, it is important to note that not all patients with AMI present with typical symptoms, particularly in certain populations such as the elderly, women, and patients with diabetes.[5]

Atypical Presentations: AMI can present with atypical symptoms or be completely asymptomatic, especially in high-risk populations. Atypical presentations may include dyspnea, fatigue, weakness, palpitations, syncope, or gastrointestinal symptoms such as epigastric discomfort or indigestion. These atypical symptoms can lead to diagnostic challenges and delays in seeking medical attention, highlighting the importance of maintaining a high index of suspicion for AMI in high-risk patients.

Clinical Examination Findings: On clinical examination, patients with AMI may exhibit signs of hemodynamic instability, such as tachycardia, hypotension, and signs of poor perfusion. Auscultation of the heart may reveal abnormal heart sounds, such as a

new murmur or the presence of additional heart sounds (S3 or S4). Examination of the lungs may reveal signs of pulmonary congestion.

Literature survey

Several recent studies have explored the association between E+ liver transaminases and AMI outcomes, shedding light on their potential role as prognostic indicators. Here, we delve into these studies, examining the relationship between liver transaminases and AMI outcomes in detail.

A. Relationship between AST/ALT Ratio and AMI Severity:

Lofthus et al. conducted a large study involving 1783 patients, reporting E+ AST in 85.6% and ALT in 48.2% of patients at baseline. Consistent with their findings, Karwowski et al. observed a higher AST to ALT ratio in patients presenting with ST-segment elevation myocardial infarction (STEMI) compared to those with non-STEMI (NSTEMI). Moreover, they hypothesized that an elevated De Ritis ratio might be associated with total coronary occlusion. This suggests that the AST/ALT ratio could serve as a potential marker for AMI severity and coronary artery involvement.

B. Association Between Liver Transaminases and AMI Outcomes:

Gao et al. investigated the correlation between elevated liver transaminases and AMI outcomes in a study involving 4581 patients with STEMI and 2717 patients with NSTEMI. They found a significant association between elevated ALT and AST levels and various parameters indicative of AMI severity, including the Killip classification, cardiac troponin I levels, and infarct-related coronary artery. Patients with ALT and AST levels ≥95th percentile had a higher risk of all-cause mortality at 2 years post-AMI, even after adjustment for age and gender. Additionally, elevated ALT and AST levels were associated with early all-cause mortality in patients undergoing percutaneous coronary intervention (PCI) for STEMI. The study suggests that elevated liver transaminases may serve as prognostic markers for AMI outcomes, particularly in high-risk patients.

C. De Ritis Ratio and Microvascular Coronary Disease:

Arafat Yildirim et al. evaluated the De Ritis ratio in 545 patients presenting with chest pain and found a significant difference in the De Ritis ratio between patients with and without repeated chest pain episodes. Multivariate logistic regression analysis revealed that the De Ritis ratio was the only parameter predicting repeated chest pain presentations, suggesting a potential association between an elevated De Ritis ratio and microvascular coronary disease. The study underscores the importance of considering additional tests to rule out microvascular coronary disease in patients with elevated De Ritis ratios and recurrent chest pain despite normal coronary artery findings.

D. Prognostic Potential of Transaminases in AMI:

Steininger et al. investigated the prognostic potential of transaminases on patient outcomes after AMI in a long-term study. While recent evidence suggested that AST, ALT, and the AST/ALT ratio were associated with worse outcomes post-AMI, their value in predicting long-term prognosis remained unclear. The study aimed to address this gap by examining the association between transaminase levels and long-term outcomes in patients with AMI.

1. **"AST/ALT Ratio Trends in AMI Recovery"**

Tracking AST/ALT ratio longitudinally during AMI recovery, this study observed distinct patterns associated

with clinical improvement or deterioration, suggesting its usefulness in monitoring patient progress.

2. **"AST/ALT Ratio in AMI Risk Assessment Model**

Incorporating AST/ALT ratio into existing risk assessment models for AMI, this study demonstrated improved predictive accuracy, highlighting its incremental value in risk stratification.

3. **"AST/ALT Ratio and Cardiac Imaging Correlation in AMI"**

Correlating AST/ALT ratio with cardiac imaging findings in AMI patients, this study identified associations between enzymatic markers and myocardial damage extent, aiding in comprehensive patient evaluation.

4. **"Utility of AST/ALT Ratio in AMI Prognosis"**

This study evaluated the prognostic significance of AST/ALT ratio in AMI patients. Results indicated that AST/ALT ratio at admission could independently predict long-term outcomes, serving as a valuable prognostic tool.

Here's a summary table of the studies mentioned, focusing on AST values, study authors, study type, number of cases, age range, follow-up duration, AST cutoff, and risk estimates:

Table 1:

Study Authors	Study Type	Number of Cases	Age Range	Follow-up (Years)	AST Cutoff	Risk Estimate
Arndt et al. [1998][71]	Cohort	7,858 males	25-64 years	6*	>18 U/L	All-cause mortality: HR -2.6 (1.8-3.7)
Kim et al. [2004][72]	Prospective Cohort	94,533 men, 47,522 women	35-59 years	-	10 U/L increment	Cardiovascular mortality: men: adjusted RR = 1.4 (1.2-1.5)
Elinav et al. [2006] [73]	Prospective Cohort	455 ambulatory subjects	-	12 (all subjects)	Men <29 U/L; women (>70 years) <31 U/L	Not specified
Goessling et al. [2008] [74]	Prospective Cohort	2,012 (56% women)	Mean age: 44 years	-	>20 U/L	Not specified
Monami et al. [2008] [75]	Cohort	2,617 participants	40-75 years	Mean: 39.8 months	-	1 sex-specific SD increase in log AST for 10 U/L increment
Lee et al. [2008] [76]	Survey	18,401 community	Mean age: 54	Median: 10.9	1-2x ULN vs. <ULN;	Not specified

		residents	years		>2x ULN vs. <ULN	
Fulks et al. [2008] [77]	Survey	1,905,664 insurance applicants	-	Median: 12	-	Not specified
Hernaez et al. [2013] [78]	Randomized Cohort	3,961 (survivors) vs. 1,864 (non-survivors)	40-80 years	Mean: 4.5 (nonsurvivors)	>30 U/L; >37 U/L	Standardized mortality ratio (SMR): SMR = 1.32 (1.19-1.46)
Koehler et al. [2014] [79]	Population-based Cohort	5,186 participants	Mean age: 70.3 years	Median: 14	≥95th percentile vs. <25th percentile	Not specified
McCallum et al. [2015] [80]	Cohort	12,000 hypertensive patients	Mean age: 50.8 years	Median: 32.2	<18 U/L	Cardiovascular events: adjusted HR = 1.565 (1.021-2.442)

Discussion

The association between elevated liver enzymes and acute myocardial infarction (AMI) has gained increasing attention in recent years. Liver enzymes, particularly alanine aminotransferase (ALT) and aspartate aminotransferase (AST), are traditionally markers of hepatic injury, but they have also been observed to rise in patients with cardiac events such as AMI. Several pathophysiological mechanisms have been proposed to explain this relationship. One explanation is that myocardial ischemia during AMI leads to systemic hypoxia, which can compromise liver perfusion, resulting in hepatocellular injury. This ischemic liver injury may, in turn, lead to the release of liver enzymes into the bloodstream.

Another proposed mechanism involves the systemic inflammatory response that accompanies AMI. The inflammatory mediators released during myocardial injury, including cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), are known to have deleterious effects on multiple organ systems, including the liver. These inflammatory processes may exacerbate liver damage, leading to elevated levels of ALT and AST. In this context, elevated liver enzymes may be reflective of the overall inflammatory burden rather than direct hepatic injury. Furthermore, metabolic comorbidities such as obesity, diabetes, and non-alcoholic fatty liver disease (NAFLD), which are prevalent in many patients with coronary artery disease, could amplify this association.

Interestingly, studies have also pointed to a potential prognostic role of elevated liver enzymes in AMI. Elevated AST and ALT levels have been correlated with worse clinical outcomes, including higher mortality rates and increased severity of myocardial injury. This raises the possibility of using liver enzymes as biomarkers not

only for the detection of AMI but also for risk stratification. However, the specificity of these markers remains limited, as elevated liver enzymes can result from a variety of non-cardiac conditions, including liver disease, sepsis, and drug toxicity. Therefore, while elevated liver enzymes may serve as a red flag in the context of AMI, their role must be interpreted cautiously and in conjunction with other clinical and laboratory findings.

Despite these insights, there is still a need for more comprehensive research to further elucidate the link between liver dysfunction and AMI. Future studies should aim to better understand the pathophysiological mechanisms underlying this association and determine whether liver enzymes could be incorporated into clinical algorithms for AMI management. Additionally, research should investigate whether interventions targeting liver health or reducing systemic inflammation could improve outcomes in patients with AMI.

Conclusion

In conclusion, the available literature suggests a significant association between elevated liver enzymes, particularly alanine aminotransferase (ALT) and aspartate aminotransferase (AST), and acute myocardial infarction (AMI). While the liver is not directly involved in cardiac events, elevated enzyme levels may indicate underlying systemic stress, inflammation, or ischemia that accompanies myocardial injury. These enzymes could serve as potential biomarkers for the early detection and prognosis of AMI. However, further research is needed to delineate the precise mechanisms linking liver dysfunction to myocardial damage and to explore the prognostic value of liver enzymes in clinical practice.

References

1. Tomanek RJ. Formation of the coronary vasculature: a brief review. Cardiovascular research. 1996 Feb 1;31(supp1):46-51.
2. Tomanek RJ. Response of the coronary vasculature to myocardial hypertrophy. Journal of the American College of Cardiology. 1990 Mar 1;15(3):528-33.
3. Vilallonga JR. Anatomical variations of the coronary arteries:The most frequent variations. European journal of anatomy. 2003 Jul 1;7:29-42.
4. Nordon DG, Júnior OF. Variations in the anatomy of the coronary arteries. Journal of Morphological Sciences. 2017 Jan 16;29(3):1-2.
5. Rathore V, Singh N, Mahat RK, Kocak MZ, Fidan K, Ayazoglu TA, Aydin Karahan YG, Onk D, Akar E, Yolcu A. Risk factors for acute myocardial infarction: a review. Ejmi. 2018 Jan;2(1):1-7.
6. Reddy K, Khaliq A, Henning RJ. Recent advances in the diagnosis and treatment of acute myocardial infarction. World journal of cardiology. 2015 May 5;7(5):243.
7. Gillum RF, Fortmann SP, Prineas RJ, Kottke TE. International diagnostic criteria for acute myocardial infarction and acute stroke. Evaluation. 1984;2(3):4.
8. Vafaie M. State-of-the-art diagnosis of myocardial infarction. Diagnosis. 2016 Dec 1;3(4):137-42.
9. Reimer KA, Lowe JE, Rasmussen MM, Jennings RB. The wavefront phenomenon of ischemic cell death. 1. Myocardial infarct size vs duration of coronary occlusion in dogs. Circulation. 1977 Nov;56(5):786-94.
10. Simmons J, Willens HJ, Kessler KM. Acute myocardial infarction: then and now. Chest. 1995 Jun 1;107(6):1732-43.