INDUS JOURNAL OF SCIENCE
https://induspublishers.com/IJS
Volume 1, Issue 1 (2023)

Original Article

EVALUATION OF HYPERLIPIDEMIA AND ELEVATED ISCHEMIA MODIFIED ALBUMIN (IMA) AS KEY RISK FACTORS FOR ACUTE CORONARY SYNDROME IN TUBERCULOSIS PATIENTS: A CROSS-SECTIONAL STUDY AT LUMHS

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ARTICLE INFO

Received: 01 April 2023
Revised: 30 April 2023
Accepted: 12 June 2023
Published: 30 June 2023

Key Words:
*Tuberculosis
*Hyperlipidemia
*Ischemia Modified Albumin
*Acute Coronary Syndrome
*Cross-Sectional Study
*Risk Factors

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ABSTRACT

Background: Tuberculosis (TB) patients may have an increased risk of Acute Coronary Syndrome (ACS) due to associated hyperlipidemia and elevated Ischemia Modified Albumin (IMA) levels. However, the extent of this association has not been thoroughly evaluated.

Objective: To assess the significance of hyperlipidemia and elevated IMA levels as risk factors for ACS among TB patients.

Methods: A cross-sectional study was conducted at Liaquat University of Medical & Health Sciences (LUMHS), involving 200 participants diagnosed with TB. Non-convenience sampling was used to ensure a representative sample. Participants underwent a comprehensive physical exam and blood sampling for lipid profile and IMA concentration analysis.

Results: The study found a wide range of BMI, blood pressure, and cholesterol levels among participants. IMA levels were relatively stable across the cohort. A significant positive correlation between IMA levels and BMI ($p<0.05$) was identified, suggesting that higher BMI is associated with increased IMA levels. Participants were categorized into three groups based on IMA levels, revealing that higher IMA levels correlate with poorer lipid profiles and more severe TB status.

Conclusion: Elevated IMA levels and hyperlipidemia are associated with an increased risk of ACS in TB patients. This association underscores the need for careful cardiovascular risk assessment and management in this population.

INTRODUCTION

IMA (ischemia-modified albumin) is a new tissue ischemia marker. IMA is now well recognized as an indicator of oxidative stress. IMA, a novel biochemical marker for detecting myocardial damage, has sparked a lot of attention in recent literature publications. The assessment of the IMA test for the identification and evaluation of ischemic insult to the myocardium and other acute coronary syndromes in emergency patients receives special emphasis. The IMA specificity for myocardial ischemia is unknown since ischemia and the accompanying biochemical alterations can occur in any artery [1.]

Ischemia-modified albumin (IMA) is albumin that has been "N-terminally modified" as a result of myocardial ischemia. Reduced cobalt binding affinity, due to a modified N-terminus on the albumin, is used to diagnose IMA. Although the albumin cobalt binding test was considered a potentially powerful diagnostic for distinguishing acute coronary syndrome from non-ischemic chest pain, it was shown to be ineffective. Patients with acute myocardial ischemia have a fast rise in fatty acid levels in their blood. Almost all released FAs (fatty acids) bind tightly to albumin, causing structural changes in the protein and a reduction in cobalt binding affinity. The blood levels of fatty acid and ischemia-modified albumin, as assessed by albumin cobalt binding tests, have a strong metabolic and temporal connection. We conclude that "FA-occupied albumin" is a better representative of IMA in ACS [2-3.]

Transition metal ions, like nickel, copper, and cobalt are known to bind to the N-terminal residues of human serum albumin. In the presence of ischemia, the N-terminal residues experience a loss in binding ability, most likely because of hypoxia, acidosis, damages due to free radicals, and membrane disruption (energy- dependent). IMA estimate is so easy that it may be done in a laboratory with very modest equipment, or even at the bedside. By adding a known quantity of cobalt to the patient's serum, the changes may be assessed. The quantity of free cobalt remaining in the combination, which is unable to attach to albumin owing to a change in the N-terminal binding residue, is used to bind to Dithiothreitol (DTT), and the color formed as a result of DTT binding with cobalt is detected using a 470 nm colorimeter. As a result, the binding of albumin to cobalt varies depending on the level of damage in the N-terminal residue, and it is known that human albumin is less stable than that of other species. As a result, using albumin from different species to simulate the same circumstances as in the Ischemia process will not operate in the same way [4-5.] In the initial phase of vascular injury Ischemia modified albumin rises stays increased for several hours allowing detection before necrosis in the myocardium develops, .this necrosis is also shown by isoenzyme creatine kinase (CK- MB), troponin, and myoglobin. IMA rises from a normal circulating value of 2% to a higher value of 8% in ischemic patients [6-7.]

The N-terminal part of albumin was sequenced in several individuals with elevated IMA, and no indication of degradation of the N-terminal was detected. Other causes for the dramatic increase in IMA have been suggested. They observed fatty acids as they are produced in ischemic coronary conditions, they interact with albumin at its binding sites, blocking albumin from binding to cobalt, resulting in the appearance of IMA despite the absence of IMA. Although it was assumed to be an obvious biomarker for the process of ischemia in AMI and ACS, there is no question that the increases are also present in a variety of other conditions where ischemia is present. IMA is associated with systemic diseases like diabetes and hypertension. Smokers, and other individuals having peripheral vascular disease, ischemia of skeletal muscles, end-stage renal illness, cirrhosis of the

liver, and systemic sclerosis, to mention a few, have all been linked to an increase in IMA [8-9] IMA, which was recently shown to be a marker for acute myocardial ischemia, aids in the early detection of cardiogenic ischemic disorders. The FDA (Food and Drug Administration) approved IMA as a diagnostic indicator of early coronary ischemia in patients with the acute coronary syndrome (ACS), and it can help to lower the rate of missed diagnoses in patients with cardiovascular disease. Many new investigations have discovered that the blood level of IMA can also be dramatically elevated in non-cardiogenic ischemic disorders in recent years. Furthermore, IMA is a reliable indicator of the severity and prognosis of illnesses such as acute ischemic chest pain, continuous ambulatory peritoneal dialysis, and patients with profound sepsis [10].

The primary aim of this cross-sectional study was to evaluate the significance of hyperlipidemia and elevated IMA levels as risk factors for ACS among the tuberculosis patients.

METHODOLOGY

Study Setting: This cross-sectional investigation was carried out at the Department of Physiology, Liaquat University of Medical & Health Sciences (LUMHS), in collaboration with the Diagnostic and Research (DR) lab, the Medicine Ward, and several clinical wards. To guarantee statistical robustness, particular emphasis was placed on the recruitment of tuberculosis patients for the 200-participant sample, which was computed using the Epi Info software. To assemble a cohort that accurately reflects the population, a non-convenience sampling technique was employed, ensuring stringent adherence to the inclusion criteria and a specific emphasis on patients who had received a tuberculosis diagnosis.

Data Collection: All participants, including individuals who had received a tuberculosis diagnosis, were provided with a thorough explanation of the study's aims, methodologies, potential hazards, and advantages, thereby guaranteeing their informed consent. Participants were subjected to a comprehensive physical examination (blood pressure, pulse rate, height, and weight) after providing informed consent. A sterile sample of 5cc of blood was obtained from each participant. The blood samples were processed without delay for laboratory analysis, where the primary objectives were to assess Ischemia Modified Albumin (IMA) concentrations and perform a comprehensive Lipid Profile. The participation of tuberculosis patients was essential for determining the precise objectives of the study. A statistical analysis was conducted on the data, including a subset consisting of tuberculosis patients, utilizing SPSS software version 25.0. For quantitative data, analysis techniques included ANOVA and the Student's T-test; for qualitativedata, the Chi-Square Test or Fischer's Exact Test was utilized. To ascertain statistical significance, a p-value threshold of 0.05 was applied in conjunction with a 95% confidence interval.

Ethical Considerations: In regard to tuberculosis patient data, which is particularly sensitive, ethical authorization was obtained from the ERC at LUMHS. A commitment to maintaining confidentiality and integrity was also upheld. Ensuring that all participants, including those with tuberculosis, provided informed consent, the ethical underpinnings of the research were further strengthened.

RESULTS

The data provided encompasses a variety of health indicators for the participants of the study, with a moderate variation in age between 35 and 50 years and a BMI ranging from 16.5 to 36 kg/m², which suggests a heterogeneous body weight profile. Systolic blood pressure readings exhibit substantial variability, spanning from 110 to 180 mmHg, while diastolic blood pressure values range from 70 to 110 mmHg. Cholesterol levels exhibit significant variation as well, ranging from 150 to 240 mg/dL for total

Cholesterol and from 40 to 60 mg/dL for HDL cholesterol. It is noteworthy that the Ischemia Modified Albumin (IMA) concentrations remain comparatively stable throughout the cohort, fluctuating between 0.55 and 0.95 absorbance units. The presented tableau of measurements is essential for analyzing health risks and outcomes, as it reflects the diverse health landscape of the study population (Table 1). The distribution within a population of three distinct classes of BMI. Class I comprises the plurality of the population, comprising 59% of the total. Class II comprises 21% of the total, whereas Class III comprises 20%. The data indicates that Class I BMI comprises the largest proportion of the population, while Classes II and III are comparatively infrequent but nearly equivalent in distribution (Figure 1). The data presented indicates a statistically significant positive correlation (r-value) of 0.718 and p-value of 0.0193 between IMA levels and BMI. This Suggests that an increase in BMI is associated with a corresponding increase in IMA levels (Table 2). Three distinct groups according to IMA levels: Control group (IMA <80 u/ml), which has normal lipid values and no evidence of tuberculosis; Borderline group (IMA = 81- 100 u/ml), which has slightly elevated lipid values and was recently diagnosed with tuberculosis; and Raised group (IMA >101 u/ml), which has the highest lipid values and active TB ($p<0.05$). The disparities in lipid profiles and tuberculosis status between each group were statistically significant; higher IMA levels are associated with worse lipid profiles and more severe TB status (Table 3). The deviation of 9.7903 units from the mean IMA concentration of 11.946 pg/mL indicated that there was considerable variation among the measurements ($p<0.05$). The BMI has a mean value of 9.126 and a significantly high t-value of 14.808 ($p<0.05$) (Table 4).

Table 1: Demographic features of participants

Variables	Minimum	Maximum	Mean	Std Deviation
Age(in years)	35	50	42.5	6.296
BMI(kg/m2)	16.5	36	21.5	3.951
Systolic BP (mmHg)	110	180	140	15.2
Diastolic BP (mmHg)	70	110	85	10.1
Total Cholesterol (mg/dL)	150	240	195	23.5
HDL Cholesterol (mg/dL)	40	60	50	5.2
IMA (Absorbance Units)	0.55	0.95	0.75	0.1

Graph: 1 shows Range of BMI in sample was calculated from as low as 30 to as high as 45, as shown in

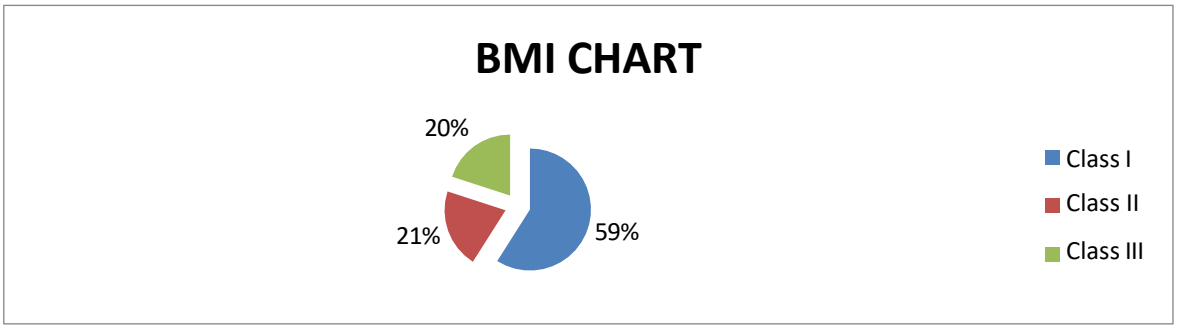

Table: 2 shows relation of IMA in different classes of obesity in population of our sample size

ISI SCORE		BMI (kg/m2)
IMA LEVELS (pg/mL)	r -value	.718**
	p value	.0193

Table: 3 Comparison of IMA levels with Lipid Profile markers using ANOVA

Classification	IMA levels (u/ml) Mean	HDL Mean	LDL Mean l	Cholestero Mean	Tag's Mean	TB status	P-value
CONTROL IMA <80	78	49	109	264	189	No TB	0.0001
BORDER LINE IMA= 81-100	84	31	169	311	201	Recently diagnosed	0.0001
RAISED IMA> 101	117	28	187	348	239	Active TB	0.0001

Table: 4 showing One-Sample Statistics between IMA levels and diastolic BP

	Mean	Std. Deviation	Std. Error Mean	T	P
IMA LEVELS (pg/mL)	11.946	9.7903	.9992	12.956	0.0193
BMI	9.126	6.789	.693	14.808	

DISCUSSION

This study conducted on 200 sample population of hypertensive patients in the setting of Liaquat University of medical and health sciences Jamshoro have shown that there is strong positive correlation of serum IMA (Ischemia Modified Albumin) with hypertension (diastolic blood pressure) (as shown in table: 2-4).

One study conducted by Sinha [10] showed that "In the context of PCI, IMA serves as an early warning sign of myocardial ischemia. In individuals who had chest discomfort and ischemia ECG abnormalities after PCI, IMA levels were found elevated., Furthermore Sinha confirms and expands previous suggestions given by Bar- Or D [11] that "For PCI patients, IMA is an excellent measure of ischemia. The function of IMA in individuals with hypertension and dyslipidemia has to be studied in a larger therapeutic context".

Marx G [12] have shown that "When IMA levels rise, it's an indication that myocardial ischemia and the generation of oxygen free radical species are causing albumin's metal binding ability to be lowered. Furthermore according to one research "Reperfusion damage may be reduced by the "sacrificial" antioxidant effect of albumin [13].

It was shown that HTN is also accompanied with rise in IMA levels Kumar A. Prognostic implications of ischemia modified albumin in known cases of 86 elderly hypertensive patients [14]. Our findings are very much in line with those of the authors. We believe this is the first time we've seen a rise in serum IMA levels in HR and Obesity. A rise in serum IMA levels in hypertensive individuals has been linked to an increased risk of cardiovascular diseases.

One study conducted by Menon B [15] have estimated the "Serum IMA levels in 50 stroke patients were found to be considerably higher than in controls, when compared to 50 age- and sex-matched controls. This only applied to individuals who had a stroke during the first eight hours, therefore the study had a small sample size. The IMA levels of the control participants did not vary from those of the experimental subjects." IMA levels in ischemic lesions of all sizes and areas were shown to rise, demonstrating that "IMA levels increase in stroke regardless of size and area." Both the IMA levels and stroke severity did not change". This finding is consistent with our own research, which found that IMA is a predictive and determining factor in hypertension patients.

Gunduz suggest that "IMA level increases in stroke patients, particularly in ischemic stroke patients [16]. According to National Institute of Neurological Disorders and Stroke [17] "Toxicology of the N-terminus of albumin, which is ordinarily able to bind transition metals, is responsible for the patient's decline in clinical status after a stroke. Localized acidity and the production of free radicals are the results of a decreased oxygen supply to the brain. Protein-binding sites in the plasma release copper and zinc ions, which typically circulate as free ions [18].

Studies have shown that IMA is a biomarker of ischemia and that tissue hypoxia is the cause of oxidative stress [19-20]. As a result of the OS' participation in the development of various disorders, the IMA value in the serum was dramatically elevated.

There is increasing evidence that IMA is linked to ischemic stroke, intracranial hemorrhage, skeletal and mesenteric muscle ischemia, peripheral atherosclerosis and hyperlipidemia, obesity, and metabolic syndrome. IMA has also been linked to hepatosteatosis, preeclampsia, ovarian torsion, fetal distress, thalassemia and diabetes, as well as advanced renal disease and liver cirrhosis. [21-25]. Serum IMA value was significantly increased in almost all the above-named cases, due to the role of the OS in the development of these diseases.

Many studies have shown that obesity is the primary factor in the development of hypertension, and many studies have shown that hypertension leads to various inflammatory disorders such as stroke, aneurysm, heart failure, and various metabolic syndromes, so obesity is the leading cause of developing hypertension. Because stroke is still the biggest cause of death worldwide, symptoms must be identified and treated as quickly as feasible. As

a consequence, the degree of oxidative stress decreases, resulting in a decrease in IMA levels, as proven by our study. As a result, having a biomarker at the primary care level is critical so that we can make some type of diagnostic conclusion and bring the patient to the hospital inside the window time. Incorporating biomarkers into the diagnosis process will undoubtedly result in the inclusion of new data, assisting in the prompt referral of the patient to a specialist for treatment. In conclusion, our data showed that the IMA might be a reliable, quick, and cost- effective biomarker for early hypertension screening, particularly in rural locations. More well organized validation studies are required in order to develop blood biomarkers that will improve the treatment of people with hypertension.

CONCLUSION

The findings of this research indicated that there is a noteworthy correlation between heightened levels of Ischemia Modified Albumin (IMA), hyperlipidemia and an elevated susceptibility to Acute Coronary Syndrome (ACS) among individuals diagnosed with tuberculosis. IMA levels increase in tandem with BMI; these levels are associated with more severe lipid profile abnormalities and active tuberculosis. In order to reduce the risk of ACS, tuberculosis patients must be closely monitored and managed cardiovascularly, according to these findings, which emphasizes the need for integrated care approaches in this vulnerable population.

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