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Serum Uric Acid Levels in Patients with Acute Myocardial Infraction and its Correlation with the Severity of myocardial infarction

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Abstract

Background: Acute myocardial infarction is life threatening condition. Prompt action is essential as it has very high mortality in hospital and long-term mortality and morbidity. Recent studies which states the association between killip class and uric acid level. So our goal is to find out the any quantal relationship between killip class and serum uric acid in acute myocardial infarction in our population. This study aims to determine the serum uric acid levels in patients with acute myocardial infraction and to corelate the levels of uric acid with the severity of myocardial infraction. **Material and Methods:** 100 Patients more than 18 years of age who were diagnosed as a case of ST elevation myocardial infarction were included. The subjects were diagnosed with history, physical examination, electrocardiographic changes and biochemical markers. **Results:** The results in our study shows that Serum Uric acid levels are significantly higher in Killip Class 3 & 4 that is correlated similarly to ECHO cardiographic findings (moderate and severe LV dysfunction). **Conclusion:** The study results show that elevated Uric acid level had an objective correlation with ECHO cardio graphic evaluation of LV dysfunction. Combination of Serum Uric acid and Killip's class after STEMI is a good predictor of mortality and severity of heart failure.

Keywords: uric acid, myocardial infarction,

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Introduction

Ischemic heart disease is the leading cause of death worldwide for both men and women1. In more than 90% of cases, the cause of myocardial ischemia is reduced blood flow due to obstructive atherosclerotic lesions in the coronary arteries. IHD is often termed coronary artery disease (CAD). It is the generic designation for a group of pathophysiologically related syndromes resulting from myocardial ischemia - an imbalance between the supply (perfusion) and demand of the heart for oxygenated blood.[1] Acute coronary syndrome (ACS) refers to a spectrum of clinical presentations ranging from unstable angina to Myocardial Infarction (MI). MI includes both ST - segment Elevation Myocardial Infarction (STEMI) and Non-ST - segment Eleavtion Myocardial Infarction (NSTEMI) pathophysiology of myocardial infarction:

STEMI usually occurs when coronary blood flow decreases abruptly after a thrombotic occlusion of a coronary artery previously affected by atherosclerosis.[2] Slowly developing, high-grade coronary artery stenosis do not typically precipitate STEMI because of the development of a rich collateral network over time. Instead, STEMI occurs when a coronary artery thrombus develops rapidly at a site of vascular injury. MI affects predominantly the left ventricle (LV), but damage may extend into the right ventricle (RV) or the atria.

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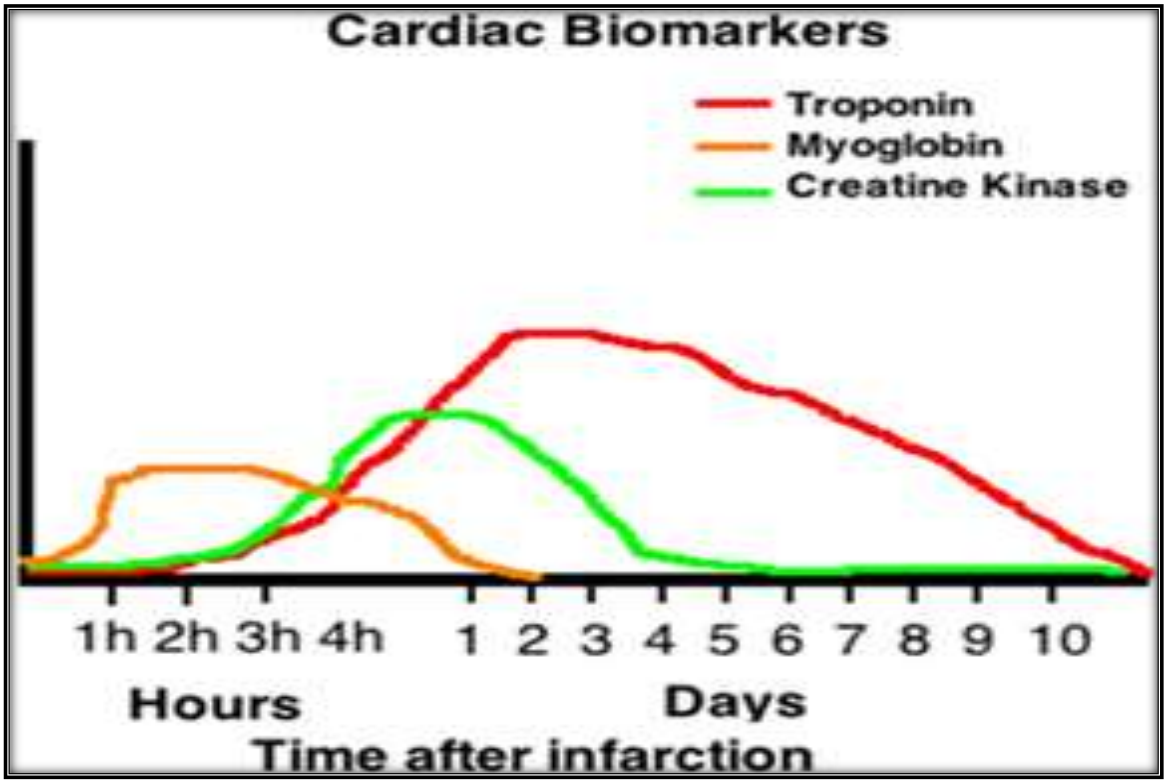
Symptoms: pain, which is usually described as pressure, squeezing, or a burning sensation across the precordium and may radiate to the neck, shoulder, jaw, back, upper abdomen, or either arm.[2]
Palpitations
Exertional dyspnea that resolves with pain or rest.
Diaphoresis from sympathetic discharge.
Nausea from vagal stimulation.
Decreased exercise tolerance.

Investigations
Electrocardiography
The initial ECG may be normal or nondiagnostic in one-third of cases. Repeated ECGs are important, especially where the diagnosis is uncertain or the patient has recurrent or persistent symptoms. The earliest ECG change is usually ST-segment deviation. In non-ST segment elevation acute coronary syndrome, there is partial occlusion of a major vessel or complete occlusion of a minor vessel, causing unstable angina or partial thickness (subendocardial) MI. In the emergency setting, ECG is the most important diagnostic test for angina. A normal ECG or one that remains unchanged from the baseline does not exclude the possibility that chest pain is ischemic in origin.

Two-dimensional echocardiography
Complete 2-D echocardiographic examination typically includes color-coded assessment of blood movement (red indicates movement toward the transducer; blue, away), which reveals valvular leaks and septal defects. Transoesophageal echocardiography is the most preferred one.



Cardiac Markers:
Cardiac markers (serum markers of myocardial cell injury) are Cardiac enzymes (eg, CK-MB)

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Cell contents (eg, troponin I, troponin T, myoglobin CK-MB, the isoenzyme specific to the heart muscle, was the principal biomarker of cardiac injury until troponin supplemented it. In the setting of myocardial infarction, plasma CK-MB concentrations typically rise about 4-6 hours after the onset of chest pain. They peak within 12-24 hours and return to baseline levels within 24-48 hours.[3]

The troponins are regulatory proteins found in skeletal and cardiac muscle. The 3 subunits that have been identified include troponin I (TnI), troponin T (TnT), and troponin C (TnC).

The cardiac troponins are sensitive, cardiospecific, and provide prognostic information for patients with ACS. They have become the cardiac markers of choice for patients with ACS.

Measurement of Myoglobin Levels

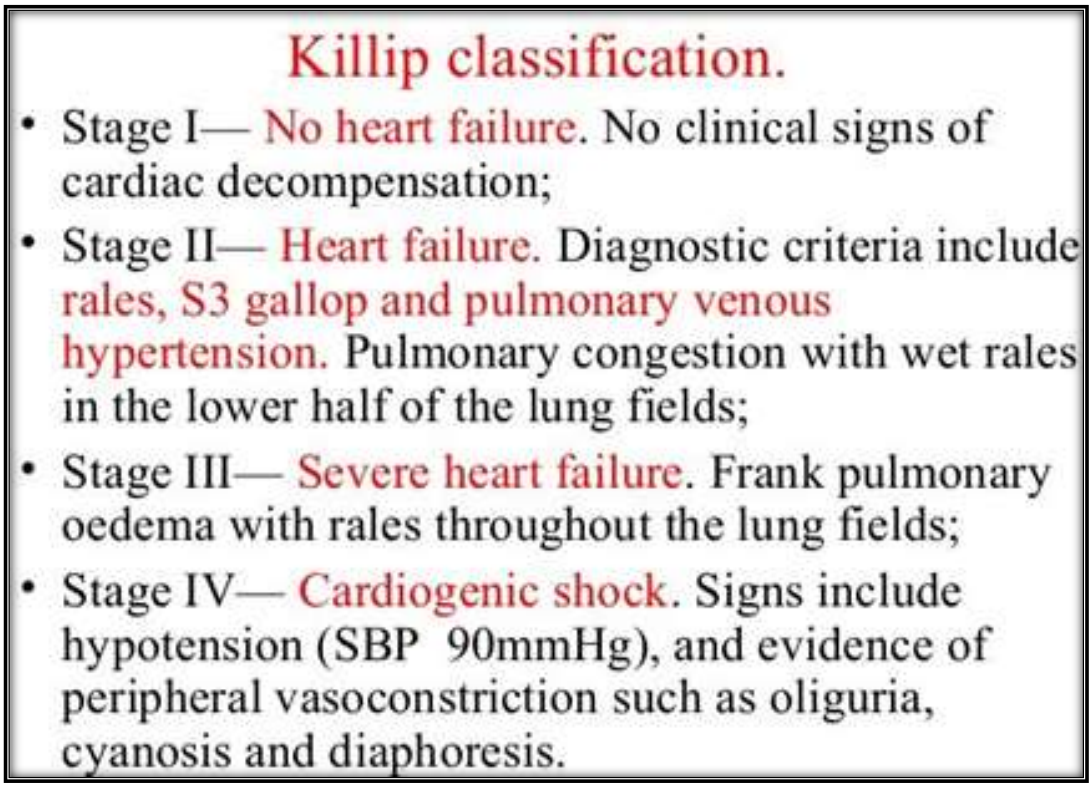
Myoglobin is not cardiac specific, but it may be detected as early as 2 hours after myocardial necrosis starts. Myoglobin values have a high negative predictive value when blood is sampled in the first 4-8 hours after onset.

New Biomarkers

Levels of brain natriuretic peptide (BNP) and N-terminal pro-BNP (NT-pro-BNP) are elevated in acute MI and provide predictive information for risk stratification across the spectrum of ACS.[4]

Killip classification

The Killip classification is widely used in patients presenting with acute MI for the purpose of risk stratification, as follows:[5]



Day MORTALITY RATE

Killip class I -	6 %
Killip class II -	17 %
Killip class III -	38 %
Killip class IV -	81 %

TIMI (Thrombolysis In Myocardial Infarction)

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TIMI Indices	Point Score
Age≥ 75 years	3
74 y. ≥ Age ≥ 65 years	2
History Of DM or HTN or Angina	1
Systolic blood pressure <100 mm Hg	3
Heart rate >100 beat/min.	2
Killip class ≥II	2
Body weight >67 Kg	1
Anterior STEMI	1
Time of beginning of pain to treatment >4 hours	1
Total score	0 to 14

URIC ACID

The final breakdown product of purine catabolism in humans is uric acid. The liver and intestinal mucosa produce most of the uric acid. Uric has a pKa of 5.75 and 10.3 and thus is a weak acid. Plasma is saturated with monosodium urate at a concentration of 405 µmol/L (6.8 mg/dL) at 37°C.

The reference ranges for uric acid are as follows:

Men: 2.5-8 mg/dL

Women: 1.9–7.5 mg/dL

Serum urate concentrations in most children range from 3-4 mg/dL. Ionized forms of uric acid in urine include monosodium, disodium, potassium, ammonium, and calcium urates. Normally, two-thirds to three- fourths of urate is excreted by the kidneys, and most of the remainder is eliminated through the intestines.

Serum Uric Acid and CAD

There are many studies that have proven the relationship between hyperuricemia and some cardiovascular diseases.

One of the explanations about the pathogenic role of uric acid in cardiovascular morbidity is from the formation of free radicals, platelet adhesiveness and aggregation, which are responsible for the formation of thrombi.[6] In addition, high levels of uric acid are also related to endothelial dysfunction, antiproliferative effects, alteration in the production of nitric oxide, lipid peroxidation and smooth muscle proliferation.[7]

There are some evidences that oxidative stress may have a role in atherosclerosis and pathogenesis of coronary artery disease (CAD). Uric acid is the main quantitative determinant of total antioxidant capacity of plasma (TAOC), and hence expected to protect against progression of atherosclerosis.[8] In other hand, it is a component of the metabolic syndrome and associates to CAD positively.

TAOC and UA also showed significant correlation not only with the occurrence but also with the severity of CAD.

However, recently a study by Patetsios et al.[9] found the existence of a significant linear correlation between serum uric acid levels and endothelial dysfunction, even after having adjusted the analysis for confounding variables. Additionally, the study conducted by

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Alderman et al,[10] took 2142 healthy individuals older than 65 years and determined that high levels of UA are able to predict, independently, the risk of CAD.
It is possible to explain the results obtained by knowing the role played by uric acid as an oxidizing molecule: forming free radicals; stimulating platelet aggregation and thrombus formation, endothelial dysfunction, smooth muscle proliferation and alteration in the production of nitric oxide.[11] All these are pathophysiological events that alter coronary arteries, thus aggravating the coronary artery disease.[12]
Overall, serum uric acid may be a powerful tool to help stratify risk for cardiovascular disease.
Killip class is a bed side assessment test which is useful in predicting mortality in acute myocardial infarction. Hyperuricemia is associated in increased cardiovascular mortality in high risk patients.[13]
So our goal is to find out the any quantal relationship between killip class and serum uric acid in acute myocardial infarction in our population.

Aims and Objectives

- To estimate the serum uric acid levels in patients with acute myocardial infraction
- To corelate the levels of uric acid with the severity of myocardial infraction

Methodology

Study Design: Observational Cross-sectional study
Study Period: Data collection done for a period of 1 year between January 2021 to January 2022
Place of Study: KRIMS, Karwar
Study population: Patients more than 18 years of age who were diagnosed as a case of ST elevation myocardial infarction (diagnosed with history, physical examination, electrocardiographic changes and biochemical markers)
Sample Size: 100

Inclusion Criteria

Patients more than 18 years of age who were diagnosed as a case of ST elevation myocardial infarction (diagnosed with history, physical examination, electrocardiographic changes and biochemical markers)

Exclusion Criteria

Patients with:

- Chronic Kidney Disease
- Gout
- Hematological malignancies
- Hypothyroidism
- Chronic alcoholism
- Patients with H/O drug intake like Aspirin, Diuretics, Ethambutol, Pyrazinamide (that increases serum uric acid level)
- VSA/SA Malingency

After Ethical Committee approval and obtaining written informed consent from nearest relative of the patient, this cross sectional observational study on patients who are diagnosed as ST ELEVATION Myocardial Infarction with the protocol based inclusion and exclusion criteria, the samples for biochemical analysis of:

- Random Blood Sugar

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- Renal Function Test
- Serum Uric Acid
- Fasting Lipid Profile
- ECG
- ECHO

Statistical Analysis

The data were coded and entered in MS-excel office 2010. The data were analyzed using Graph Pad Prism version 5. The categorical data were represented as n(%) and numerical data in mean with SD. Fisher's exact test was used to compare the proportions between the groups for sample less than 30. Unpaired 't' test was used to compare the means between groups. $P<0.05$ was considered statistically significant.

RESULTS

Table 1: Occurrence of hyperuricemia and gender ratio in the study.

S.No	Parameter		n	%
1	Hyperuricemia status	Present	29	29
		Absent	71	71
2	Gender	Male	76	76
		Female	24	24

Data are expressed as n with %. The total N=100

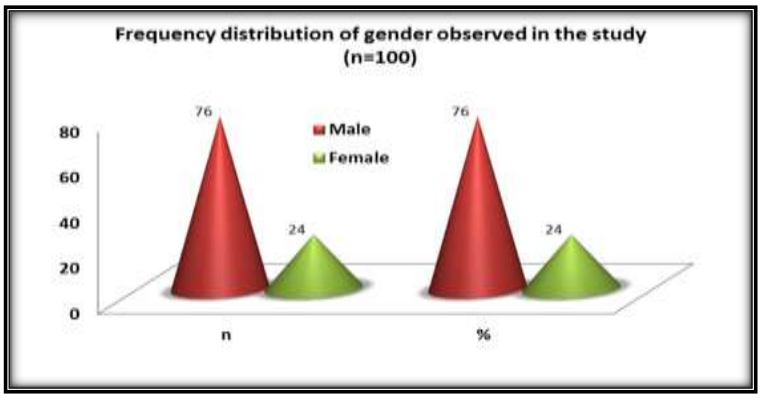

Figure 1: Vertical cone diagram depicting the frequency distribution of gender observed in the study

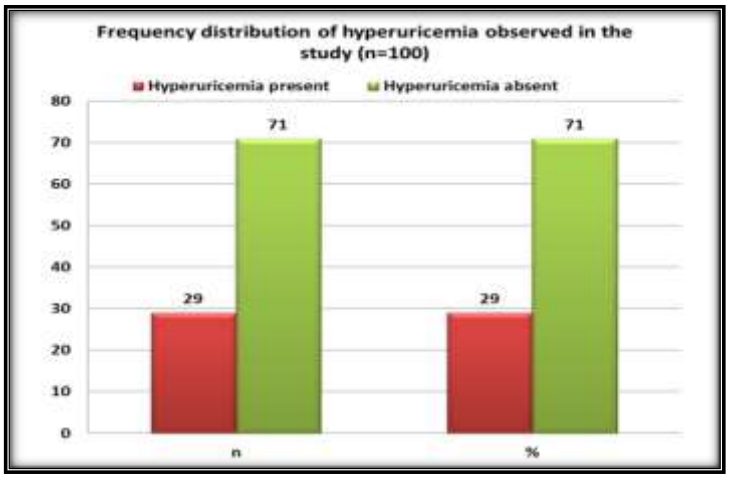

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Figure 2: Vertical bar diagram depicting the frequency distribution of hyperuricemia observed in the study.

Table 2: Frequency distribution of age category in years observed in the study.

S.No	Age category	n	%
1	≤40 years	10	10
2	41 – 50 years	23	23
3	51 – 60 years	42	42
4	61 – 70 years	15	15
5	>70 years	10	10

Data are expressed as n with %. The total N=100

Table 3: Comparison of age category with respect to gender in the study.

S.No	Age category	Male (n=76)		Female (n=24)		Chi square value	df	p value
		n	%	N	%			
1	≤40 years	10	13.2	0	0	10.62	4	0.031*
2	41 – 50 years	17	22.4	6	25			
3	51 – 60 years	33	43.4	9	37.5			
4	61 – 70 years	12	15.8	3	12.5			
5	>70 years	4	5.3	6	25*			

Data are expressed as n(%). Fisher's exact test was used to compare the frequencies between the genders. *indicates p<0.05 and considered statistically significant.

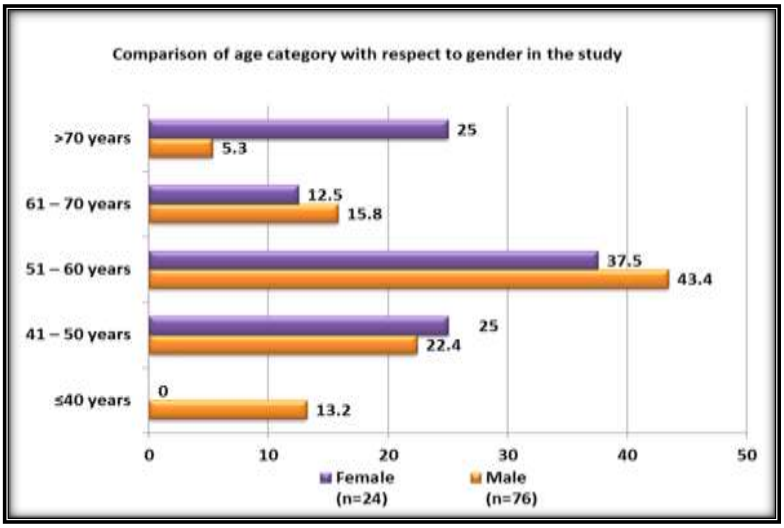

Figure 3: Horizontal bar diagram depicting the comparison of frequency distribution of age category with respect to gender in the study. Data are expressed as %.

Table 4: Description of prevalence of various risk factors observed in the study.

S.No	Risk factors	Present in (n)	Present in (%)
1	Age >50 years	67	67
2	Male sex	76	76
3	Smoking	43	43
4	Hypertension	51	51
5	Diabetes	41	41
6	Dyslipidemia	10	10

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7	Hyperuricemia	29	29

Data are expressed as n with %. The total N=100.

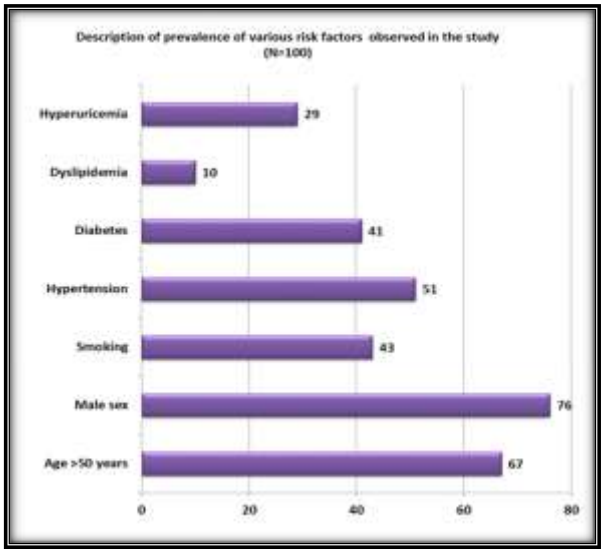

Figure 4: Horizontal bar diagram depicting the description of prevalence of various risk factor observed in the study (n=100).

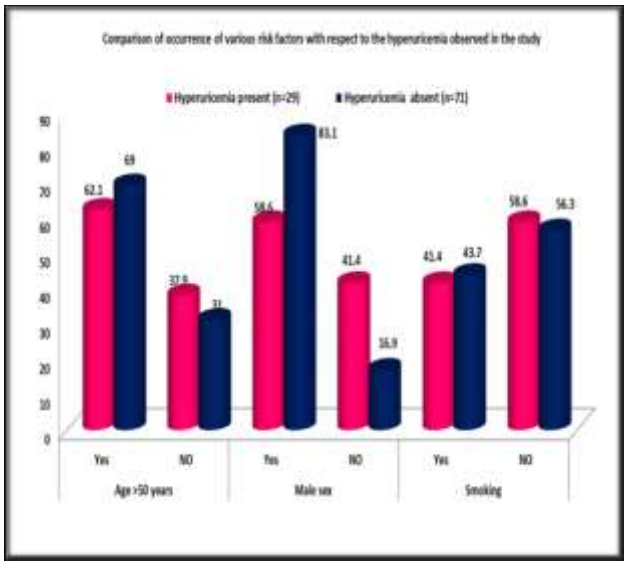

Figure 5: Vertical cylindrical diagram depicting the comparison of occurrence of various risk factors with respect to the hyperuricemia observed in the study. Data are expressed as %.

Table 5: Comparison of occurrence of various risk factors with respect to the hyperuricemia observed in the study.

S. No	Risk factor		Hyperuricemia				Chi square value	df	p value
			Present (n=29)		Absent (n=71)				
			n	%	n	%			
1	Age >50 years	Yes	18	62.1	49	69	0.449	1	0.639 (NS)
		No	11	37.9	22	31			
2	Male sex	Yes	17	58.6	59	83.1	6.746	1	0.018*
		No	12	41.4	12	16.9			
3	Smoking	Yes	12	41.4	31	43.7	0.044	1	>0.999

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		No	17	58.6	40	56.3			(NS)
4	Diabetes	Yes	11	37.9	30	42.3	0.159	1	0.823
		No	18	62.1	41	57.7			(NS)
5	Hypertension	Yes	14	48.3	37	52.1	0.121	1	0.827
		No	15	51.7	34	47.9			(NS)
6	Dyslipidemia	Yes	5	17.2	5	7	2.381	1	0.144
		No	24	82.8	66	93			(NS)

Data are expressed as n(%). Fisher's exact test was used to compare the frequencies between the groups. *indicates $p<0.05$ and considered statistically significant. NS = not significant.

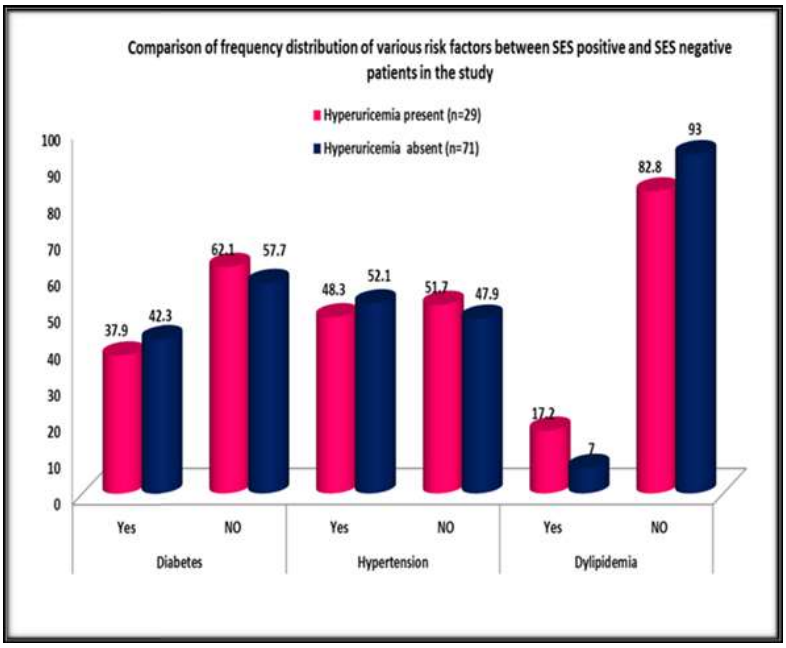

Figure 6: Vertical cylindrical diagram depicting the comparison of occurrence of various risk factors with respect to the hyperuricemia observed in the study. Data are expressed as %.

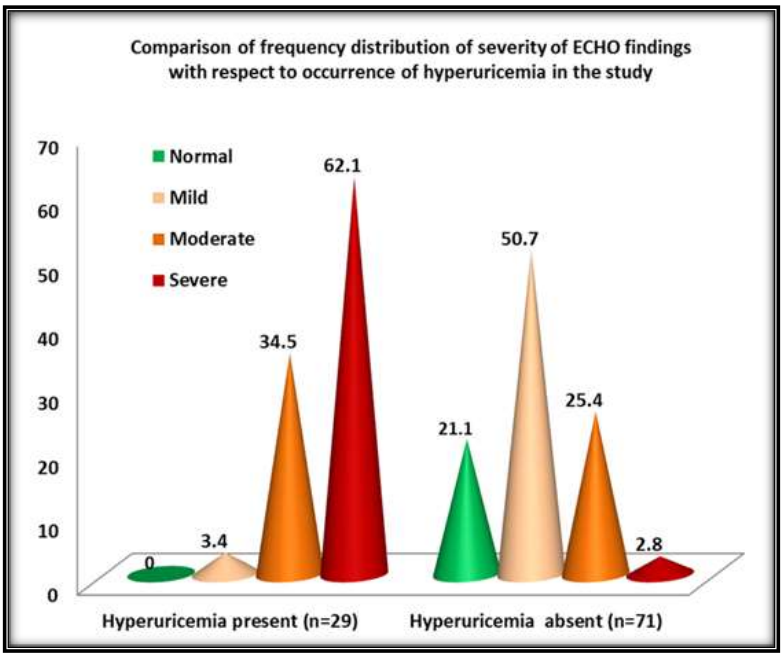

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Figure 7: Vertical cone diagram depicting the frequency distribution of severity of ECHO findings with respect to occurrence of hyperuricemia in the study. Data are expressed as %.

Table 6: Comparison of frequency distribution of severity of ECHO findings with respect to occurrence of hyperuricemia in the study.

S.No	ECHO findings	Hyperuricemia				Chi square value	Df	p value
		Present (n=29)		Absent (n=71)				
		n	%	n	%			
1	Normal	0	0	15	21.1*	55.3	3	<0.0001 *
2	Mild	1	3.4	36	50.7*			
3	Moderate	10	34.5*	18	25.4			
5	Severe	18	62.1*	2	2.8			

Data are expressed as n(%). Fisher's exact test was used to compare the frequencies between the genders. *indicates p<0.05 and considered statistically significant.

Table 7: Comparison of frequency distribution of type so Killip class with respect to occurrence of hyperuricemia in the study.

S.No	Killip class	Hyperuricemia				Chi square value	df	p value
		Present (n=29)		Absent (n=71)				
		n	%	n	%			
1	Class I	2	6.9	50	70.4*	67.7	3	<0.0001*
2	Class II	2	6.9	17	23.9*			
3	Class III	11	37.9*	4	5.6			
5	Class IV	14	48.3*	0	0			

Data are expressed as n(%). Fisher's exact test was used to compare the frequencies between the genders. *indicates p<0.05 and considered statistically significant.

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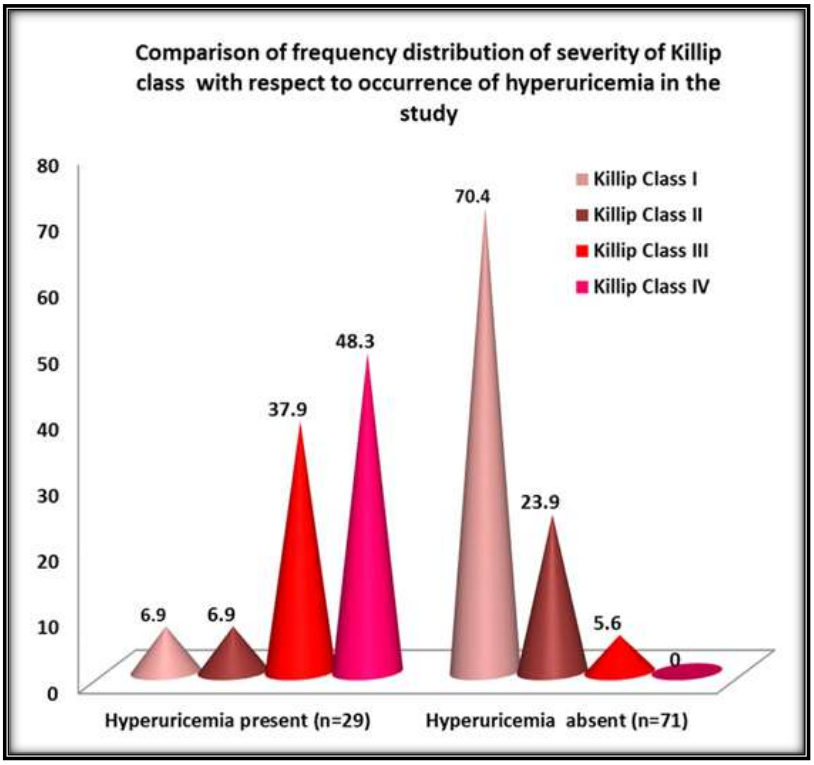

Figure 8: Vertical cone diagram depicting the frequency distribution of Killip class with respect to occurrence of hyperuricemia in the study. Data are expressed as %.

Table 8: Comparison of frequency distribution of type of MI with respect to occurrence of hyperuricemia in the study.

S.No	MI type	Hyperuricemia				Chi square value	Df	p value
		Present (n=29)		Absent (n=71)				
		n	%	n	%			
1	AWMI	21	72.4	38	53.5			
2	IWMI	7	24.2	24	33.8	3.619	2	0.163 (NS)
5	LWMI	1	3.4	9	12.7			

Data are expressed as n(%). Fisher's exact test was used to compare the frequencies between the genders. NS = not significant.

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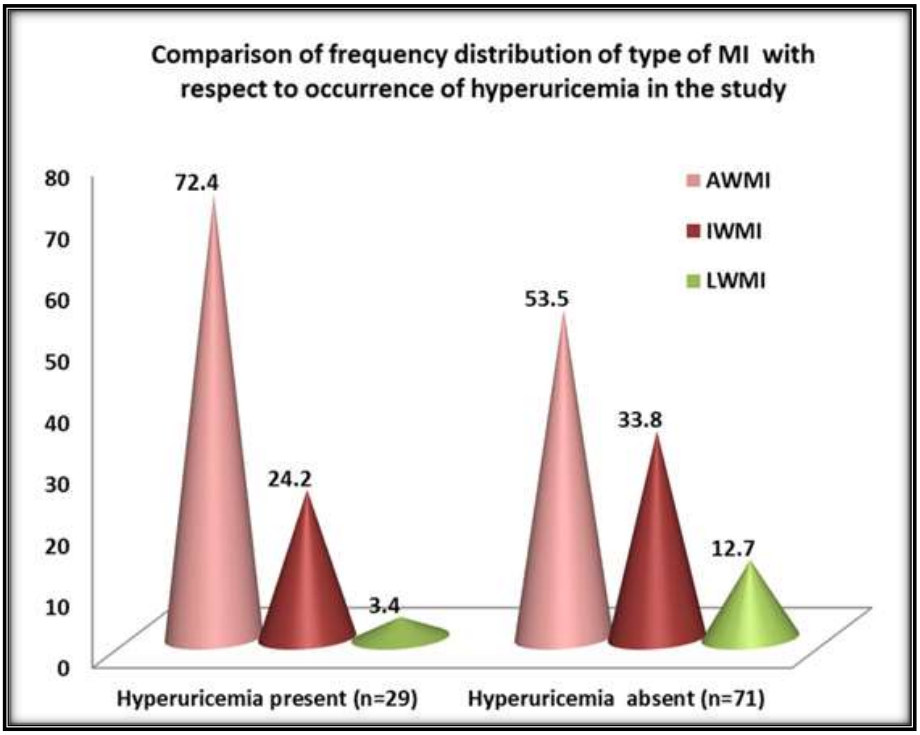

Figure 9: Vertical cone diagram depicting the frequency distribution of type of MI with respect to the occurrence of hyperuricemia in the study

Table 9: Comparison of uric acid levels between the various risk factors observed in the study.

S. No	Risk factor	Uric acid level (mg/dl)			t value	Df	p value
		N	Mean	SD			
1	Age>50 present	67	5.44	1.38	1.54	98	0.127 (NS)
	Age >50 absent	33	5.89	1.43			
2	Male sex present	76	5.49	1.44	1.18	98	0.239 (NS)
	Male sex absent	24	5.88	1.26			
3	Smoking present	43	5.66	1.34	0.47	98	0.643 (NS)
	Smoking absent	57	5.53	1.46			
4	Hypertension present	51	5.49	1.36	0.67	98	0.504 (NS)
	Hypertension absent	49	5.68	1.46			
5	Diabetes present	41	5.45	1.33	0.82	98	0.416 (NS)
	Diabetes absent	59	5.68	1.46			
6	Dyslipidemia present	10	6.12	1.31	1.26	98	0.209 (NS)
	Dyslipidemia absent	90	5.52	1.41			

Data are expressed as mean with SD. Unpaired 't' test was used to compare the means between the group. NS = not significant.

DISCUSSION

Myocardial Infarction is a spectrum of cardiac disorder comprising of STEMI, Non-STEMI and Unstable angina. These are differentiated with clinical features, specific ECG changes and Cardiac enzymes like Troponin I & T and CK-MB Blood pressure, Killip Class, localization of infarct and TIMI score are some methods useful in risk stratification and estimation of mortality in intensive coronary unit. Killip classification is a bedside evaluation test to predict mortality in STEMI. It has four classes of which Class 3 & 4 has higher mortality than 1&2. Class 4 has mortaliy rate of 81% while Class 3 is 37%. A recent study conducted by Kojimo et al,[14] on 90 patients revealed Hyperuricemia in Killip class 3&4

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compared to 1&2 and it's elevation is proportional to mortality rate in Class 3&4. Our study was conducted to assess the prognostic significance of Serum Uric acid in STEMI related to Sex, Age, Diabetes, Hypertension, Smoking, Hyperlipidemia, Killip class and ECHO finding. In our study total of 100 patients were included who were admitted in ICCU. All patients are included in the study after getting written consent. Detailed history and clinical examination were made after ruling out exclusion criteria. Out of 100 patients, 76 were male and 24 were female. This distribution shows the predominance of male sex affected STEMI which was similar to other studies with regard to male predominance in STEMI. There was significant rise of Uric acid in female patients particularly more than 70 years of age($p=0.031$) in contrast to other age groups. Risk factors like Diabetes, Hypertension, Hyperlipidemia and Smoking were taken into consideration in our study. Of total patients taken into study, 43 patients had smoking habit predominantly in males. This shows smoking is much prevalent in male population in our study. Among total study population, 51 patients were hypertensive; 41 patients were diabetics and 10 patients were dyslipidemia. Out of 100 patients 59 had Anterior wall MI(AWMI), 31 had Inferior wall MI(IWMI) and 10 had Lateral wall MI(LWMI). Of total study patients, 52 patients were Killip class 1 and 19 patients were Killip class 2 while 15 patients belonged to Class 3 and 14 patients were Class 4. Among 4 Killip classes, Class 3 and 4 patients had significant hyperuricemia($p<0.0001$). Out of 100 patients, 28 had Moderate LV systolic dysfunction while 20 patients had severe LV dysfunction. These two group of patients i.e., 10 out of 28 in Moderate LV dysfunction and 18 out of 20 Severe LV dysfunction had significant elevation of Uric acid ($p<0.0001$). The results in our study shows that Serum Uric acid levels are significantly higher in Killip Class 3 & 4 that is correlated similarly to ECHO cardiographic findings(moderate and severe LV dysfunction).

CONCLUSION

Measuring serum Uric acid level is one of the predictable prognostic indicator in STEMI and one of the early and short term predictor. Significant elevation of Uric acid is commonly seen in patients with Killip class 3 & 4. Elevated Uric acid level had an objective correlation with ECHO cardiographic evaluation of LV dysfunction. Combination of Serum Uric acid and Killip's class after STEMI is a good predictor of mortality and severity of heart failure.

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