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## INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/17709

DOI URL: <http://dx.doi.org/10.21474/IJAR01/17709>



### RESEARCH ARTICLE

#### PROGNOSTIC IMPORTANCE OF HYPONATREMIA OCCURRING AT VARIOUS TIME POINTS DURING HOSPITALISATION IN PATIENTS WITH ST ELEVATION MYOCARDIAL INFARCTION - AN OBSERVATIONAL STUDY AT A TERTIARY CARE HOSPITAL

Prof. Dr. V.V Agrawal<sup>1</sup>, Dr. Narendra Sharma<sup>2</sup>, Dr. Prashank Ajmera<sup>2</sup> and Dr. Rajat Pachori<sup>2</sup>

1. Professor and Head, Department of Cardiology, SMS Medical College and Attached Group of Hospitals.
2. Senior Resident, Department of Cardiology, SMS Medical College and Attached Group of Hospitals.

#### Manuscript Info

##### Manuscript History

Received: 15 August 2023

Final Accepted: 18 September 2023

Published: October 2023

##### Key words:-

Stemi, Hyponatremia, Heart Failure

#### Abstract

ST-elevation myocardial infarction (STEMI) and heart failure (HF) are common, big-budget, debilitating and expanding diseases. Cardiovascular diseases, especially STEMI and heart failure have been known to cause 17.3 million deaths worldwide annually. Hyponatremia, delineated as a serum sodium (sNa) concentration  $<135$  mmol/l, is a frequently seen electrolyte disturbance in practice and the prevalence, clinical impact; the prognostic factor of low sNa in STEMI/heart failure patients vary widely. The aim of this review is to assess its existence and comparing survival difference between hypo and normonatremic patients. Hyponatremia is the most frequently encountered electrolyte abnormality in clinical practice and has a poor prognosis in both STEMI and heart failure patients. It exacerbates both short and long term mortality, rehospitalization rates, as well as the average length of stay in the hospital. Although it is still a mystery whether hyponatremia is just a marker of iller patients or the core of poor prognosis in patients with STEMI and HF, one thing is certain: timely recognition of patients at risk for developing hyponatremia could help to commence early treatment.

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#### Introduction:-

Hyponatremia has been identified as an independent predictor of short- term mortality, long- term mortality, and re-hospitalization because of heart failure.<sup>(1-3)</sup>

In acute STEMI, baroreceptor activation leads to activation of sympathetic nervous system releasing hormones like vasopressin and also activation of renin angiotensin system. Magnitude of these neuro-hormonal changes is related to the severity of the myocardial damage.

Hyponatraemia (serum sodium  $<135$  meq/ l) as a marker of these hormonal changes may serve as a simple, easily available and cost effective marker to identify patients at high risk . Hyponatremia is common after MI, and clinical improvement is accompanied by rise in plasma sodium concentration.<sup>(4)</sup> Hyponatremia develops in early phases of acute myocardial infarction.

**Corresponding Author:-Dr. Narendra Sharma**

Address:-Senior Resident, Department of Cardiology, SMS Medical College and Attached Group of Hospitals.

Recently, several studies shows the importance of hyponatremia as important early prognostic tool. Many studies shown that significant increase in plasma AVP level was in patients who had associated with complication as heart failure and fatal outcome after acute MI, and clinical improvement was noted following the rise in serum plasma level of sodium. [4,5] The neurohormonal activation that accompanies acute myocardial infarction is similar to that which accompanies heart failure. While the prognostic value of hyponatremia in chronic heart failure is well established, data in the setting of acute STEMI are lacking.

Whether hyponatremia (sodium <135mEq/L) in the acute phase of ST segment elevation myocardial infarction is just a marker of “more ill” patients or decreased sodium concentration is able to exert a direct adverse effect on the cardiovascular system is still unknown.

Thus, the aim of this study was to evaluate the importance of hyponatremia as a predictor of prognosis in patients with acute STEMI. My concept of this dissertation was to study the prognostic importance of hyponatremia in acute ST elevation myocardial infarction and also to determine its usefulness in finding its short term survival.

### **Aims And Objectives:-**

To determine the prognostic importance of hyponatremia in acute ST segment elevation myocardial infarction and to find out its usefulness in predicting short time mortality.

### **Materials And Methods:-**

The Prospective observational study was carried out in the Department of Cardiology, SMS Medical College & Hospital, Jaipur for the period of 1 year from 1 April 2022 to 31 march 2023.

Sample size was calculated at alpha error 5% and study power 80 % assuming mortality 4.6 % and 26.9 % in STEMI patient with normal Na and hyponatremia respectively. It came out to be 220 after adding 10% non-response rate and finally a total 220 patients were taken.

### **Inclusion Criteria:**

All patients with myocardial infarction having following criteria will be selected -

1. More than 20 minutes of chest pain
2. ECG alteration consisting of new pathological Q waves or ST Segment and T wave changes which are diagnostic of STEMI in ECG.
3. Elevation of cardiac enzymes such as creatinine kinase (CKMB) or cardiac troponin T and I levels.

### **Exclusion Criteria**

1. Patients with prior h/o CAD or structural heart disease
2. Acute coronary syndrome without ST elevation in ECG was excluded.
3. Patient with known renal disorder/ liver disease
4. Patient already on medication which may cause hyponatremia like carbamazepine, antidepressants specially SSRI, thiazide diuretics.

Hyponatremia: It was considered when serum sodium level <135meq/ L.

Dyslipidaemia: It was considered if any of the lipid profile parameter found to be abnormal.

### **Statistical Analysis:**

The collected data was entered in Microsoft excel spread sheet and analysed using Statistical Package for Social Sciences software (SPSS version 24.0). Categorical data are to be presented as absolute values and percentages, whereas continuous data was summarized as mean value  $\pm$  standard deviation. Independent sample ‘t’ test was used for continuous data and for categorical data, Chi - square tests was used. A p-value <0.05 was considered to be statistically significant.

### **Results:-**

In the present study, mean age of study participants was  $55.85 \pm 12.67$  years with maximum 110 (50%) in age of 41-60 years. Maximum participants were male i.e. 167/220 (75.9%), had hypertension history i.e. 61/220

(27.7%) and Killip class I i.e. 176/220 (80%). Most of the patients were diagnosed as anterior wall MI i.e. 122(55.5%) (Table 1).

In this study, mean value of Trop-T was  $1.33 \pm 0.88$ , LVEF was  $38.8 \pm 4.12$ , baseline sodium level was  $138.7 \pm 4.5$  and  $137.7 \pm 4.5$  meq/L. (Table 2)

In our study, 30 days mortality was found to be 10.9% and hyponatremia at admission and after 72 hours was found to be 14.5% and 20.0% respectively. (Table 3, figure 1)

Current study revealed that, older age > 60 years, diabetes, hypertension, smoking, increasing Killip class, 30 days mortality, Trop-T were found to statistically significant high while LVEF was found to be statistically significant low among the patients had hyponatremia at admission. (Table 4)

Current study also revealed that, older age > 60 years, dyslipidaemia, Killip class I, 30 days mortality were found to statistically significant high while LVEF was found to be statistically significant low among the patients had hyponatremia at 72 hours. (Table 5)

In our study, mortality was increased as Killip class increases and Trop-T was found to be statistically significant high among the patients who were died. (Table 6)

**Table 1:-** Sociodemographic and clinical profile of study participants (N=220):

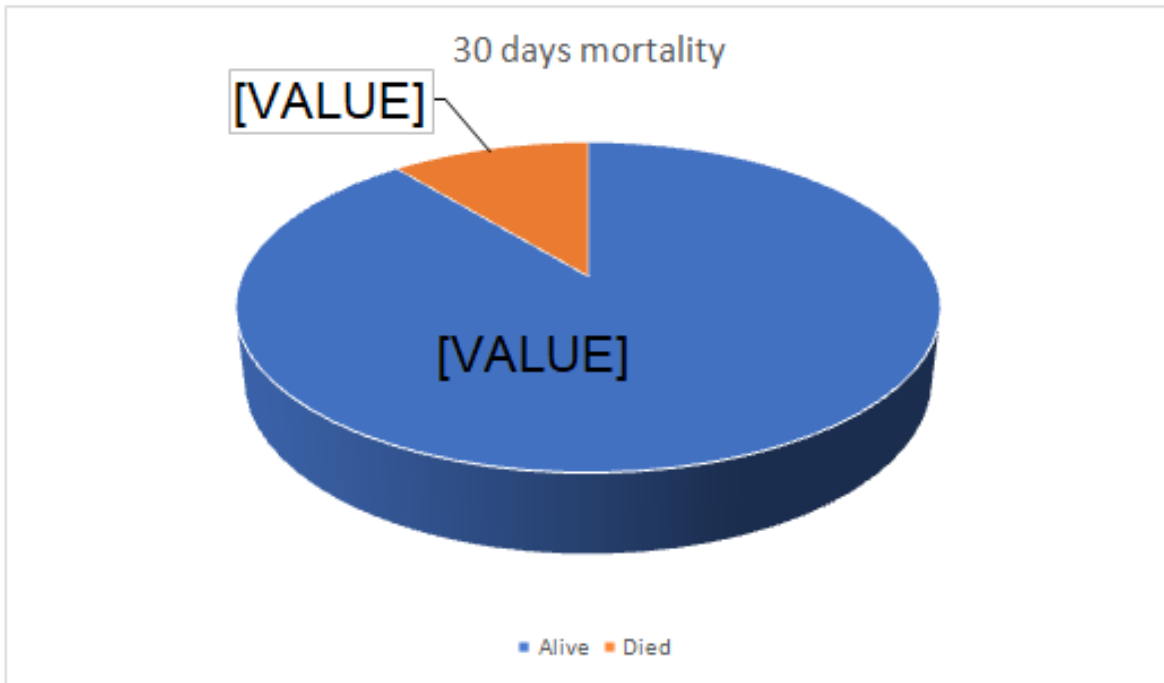
Variables	Frequency	Percent
Age (Mean±SD)	55.85±12.67	
Age:		
≤40 years	22	10.0
41-60 years	110	50.0
>60 years	88	40.0
Gender:		
Female	53	24.1
Male	167	75.9
Risk Factors:		
Hypertension	61	27.7
Diabetes	33	15.0
Dyslipidemia	7	3.2
Smoking	11	5.0
STEMI:		
ALWMI	15	6.8
AWMI	122	55.5
Iw+PwMI	15	6.8
Iw+RvMI	6	2.7
IWMI	60	27.3
LWMI	2	.9
Killip Grade		
I	176	80.0
II	41	18.6
III	2	.9
IV	1	.5

**Table 2:-** Distribution of investigation among the study participants:

	Trop-T	LVEF	Baseline Na	Na at 72hr
Mean	1.335011	38.800	138.723	137.882
Median	.875000	38.000	139.000	139.000
SD	1.1096396	4.1243	4.5138	4.5254
Minimum	.5550	30.0	125.0	127.0

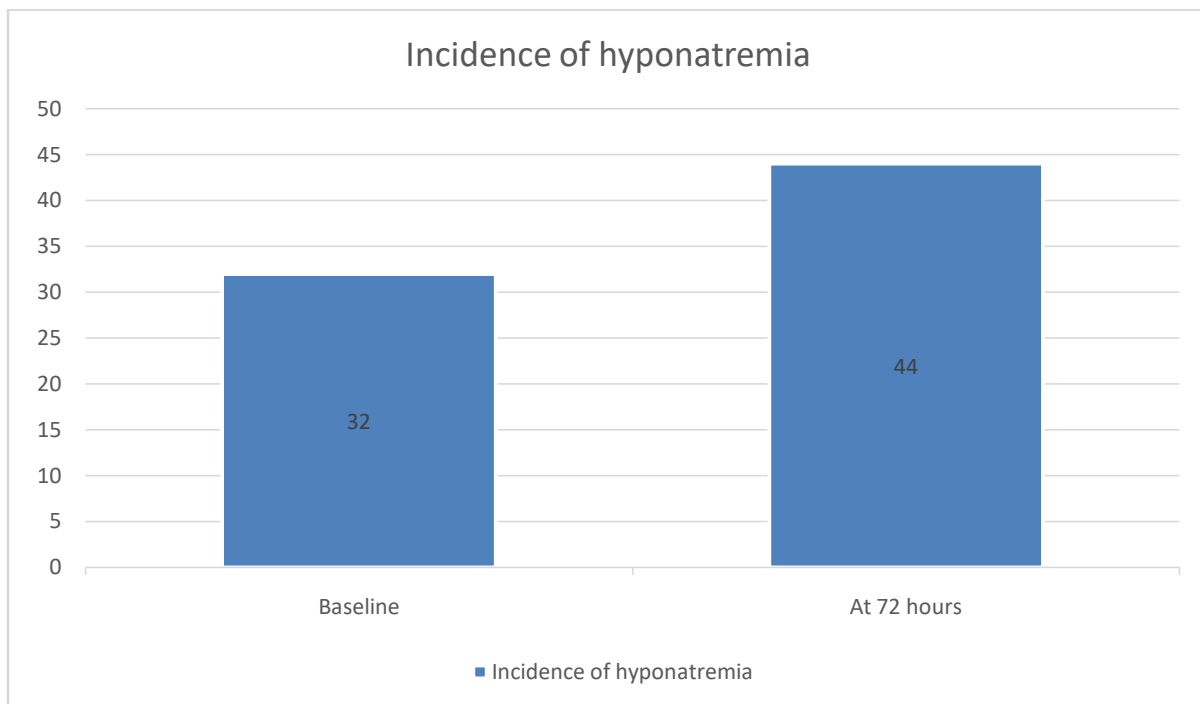
Maximum	6.0050	48.0	145.0	145.0
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**Figure 1:-** Distribution of participants according to 30 days mortality.



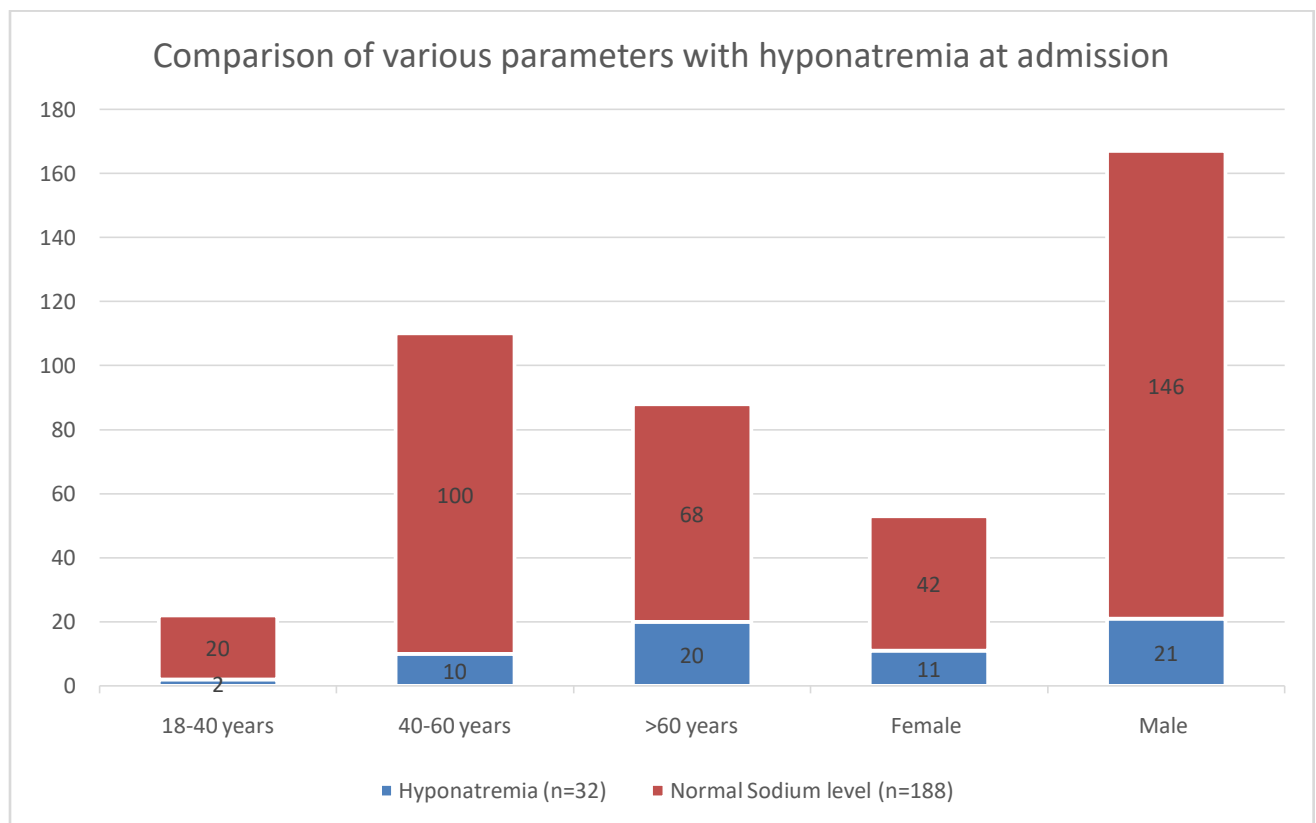
**Table 3:-** Incidence of hyponatremia:

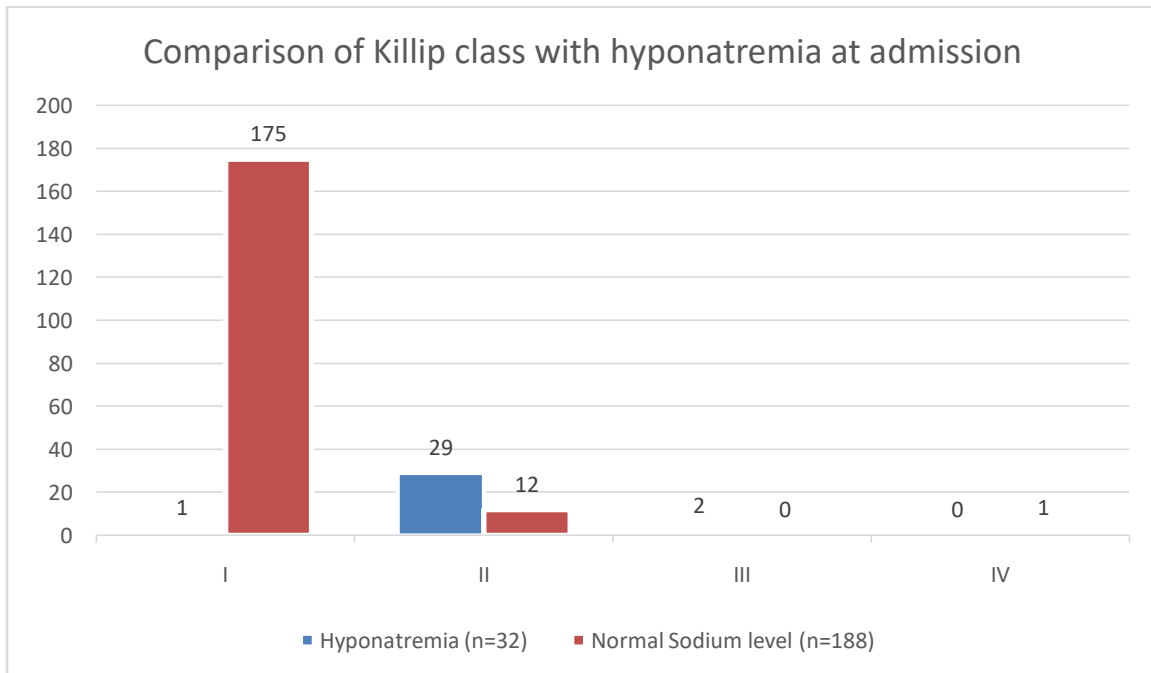
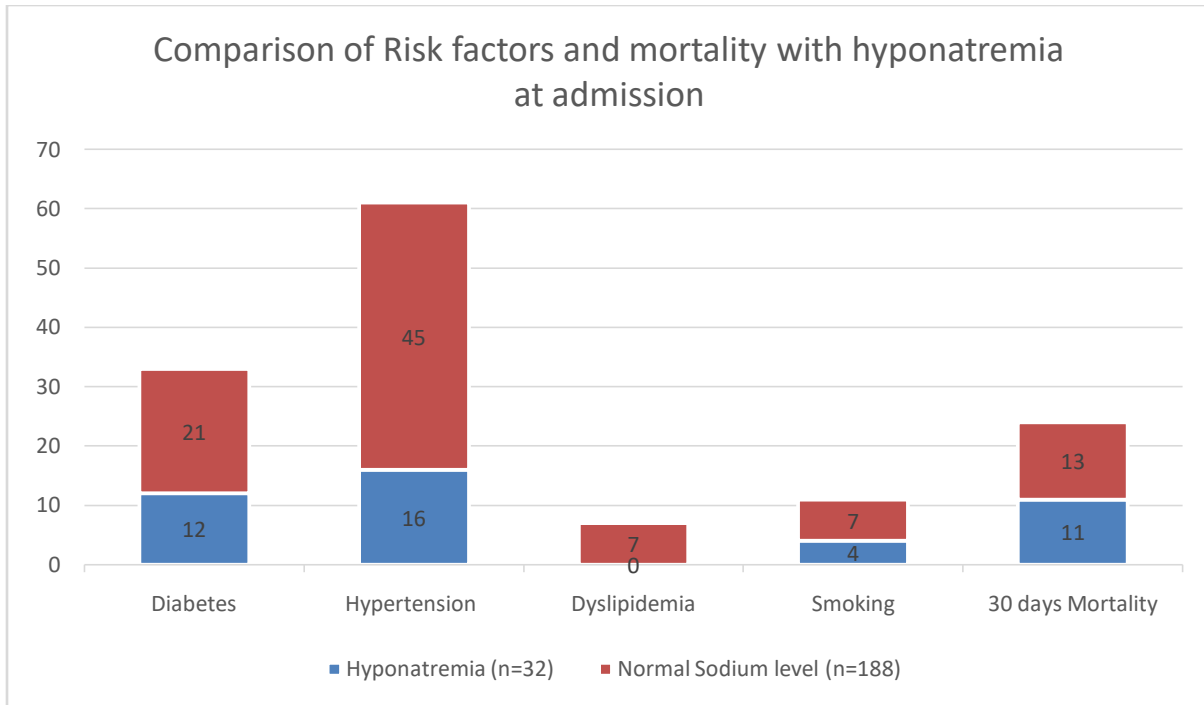
	Frequency	Percent
Baseline	32	14.5
At 72 hours	44	20.0



**Table 4:-** Comparison of various parameters with hyponatremia at admission.

	Hyponatremia (n=32)		Normal Sodium level (n=188)		p-value
	n	%	n	%	
<b>Age</b>					
18-40years	2	6.3%	20	10.6%	0.019
40-60years	10	31.3%	100	53.2%	
>60years	20	62.5%	68	36.2%	
<b>Gender</b>					
Female	11	34.4%	42	22.3%	0.141
Male	21	65.6%	146	77.7%	
<b>Risk factors</b>					
Diabetes	12	37.5%	21	11.2%	0.001
Hypertension	16	50.0%	45	23.9%	0.002
Dyslipidemia	0	0.0%	7	3.7%	0.267
Smoking	4	12.5%	7	3.7%	0.035
<b>Killip class</b>					
I	1	3.1%	175	93.1%	0.0001
II	29	90.6%	12	6.4%	
III	2	6.3%	0	0.0%	
IV	0	0.0%	1	0.5%	
<b>30 days Mortality</b>					
Survived	21	65.6%	175	93.1%	0.001
Died	11	34.4%	13	6.9%	
<b>Investigations:</b>					
Trop-T(Mean±SD)	2.99±1.74		1.05±0.62		0.001
LVEF(Mean±SD)	36.78±4.73		39.14±3.92		0.003

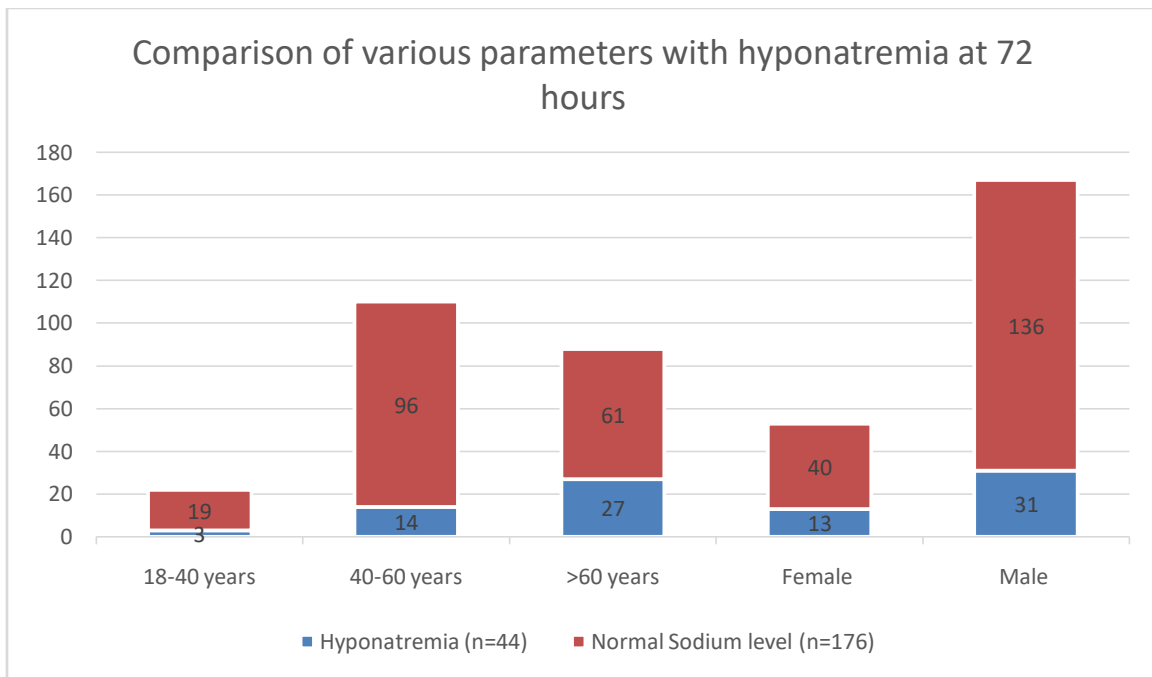


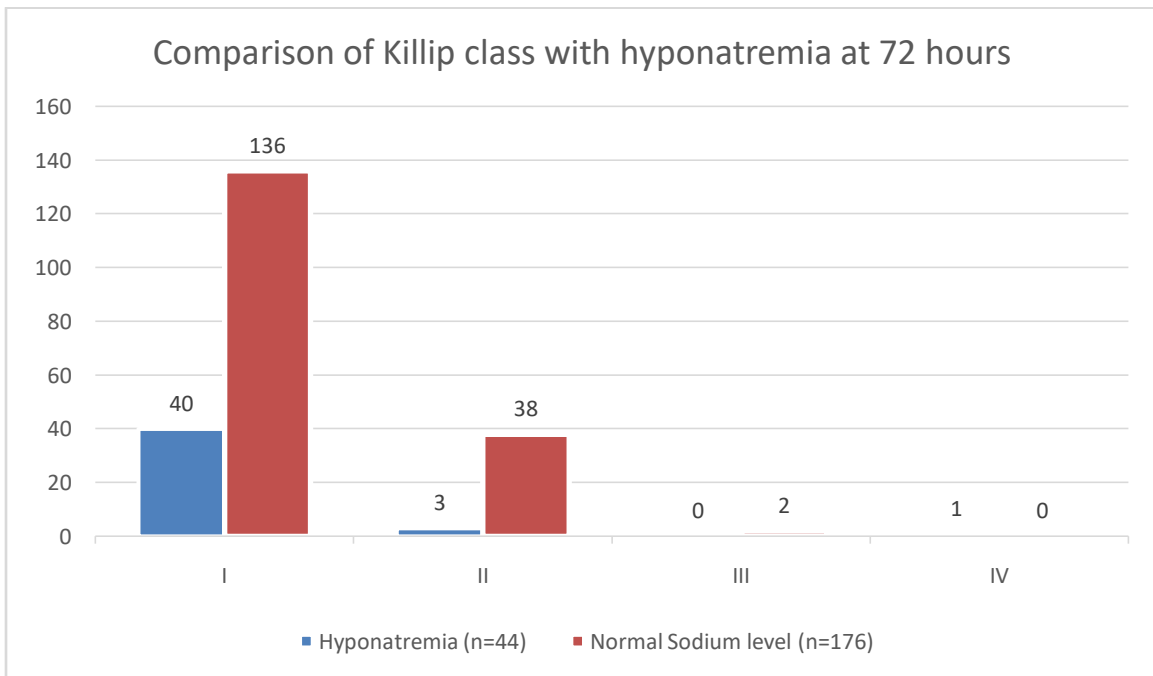
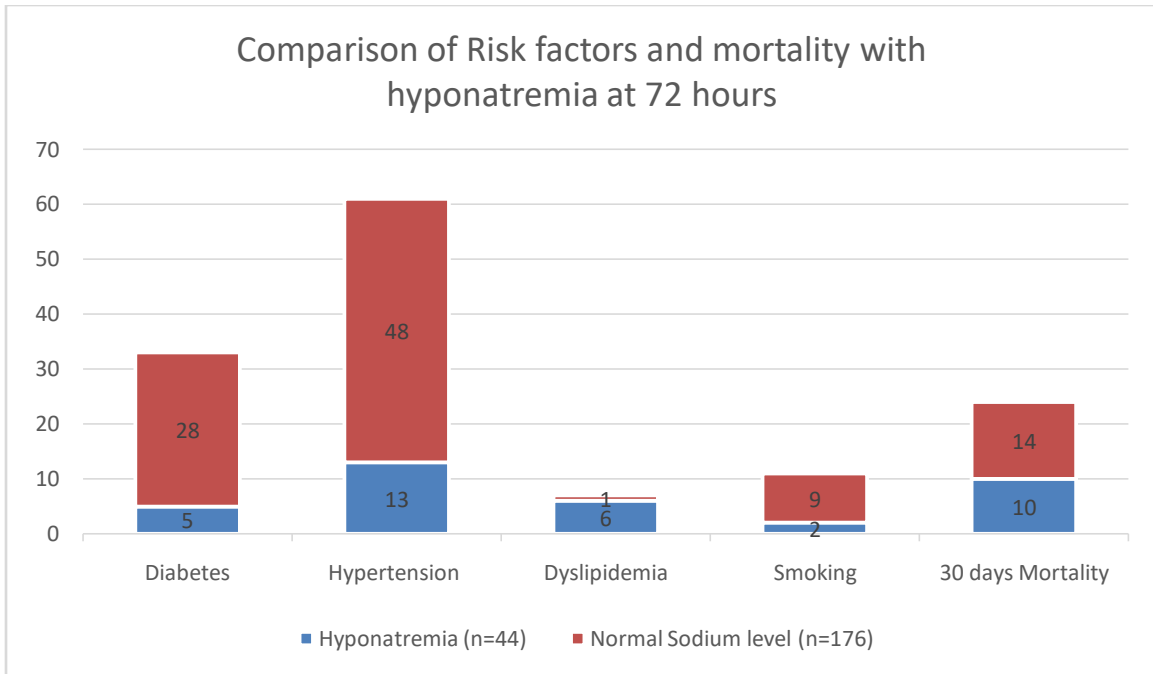


**Table 5:-** Comparison of various parameters with hyponatremia at 72 hours.

	Hyponatremia (n=44)		Normal Sodium level (n=176)		p-value
	n	%	n	%	
<b>Age</b>					
18-40years	3	6.8%	19	10.8%	0.005
40-60years	14	31.8%	96	54.5%	
>60years	27	61.4%	61	34.7%	
<b>Gender</b>					
Female	13	29.5%	40	22.7%	0.344

Male	31	70.5%	136	77.3%	
Risk factors					
Diabetes	5	11.4%	28	15.9%	0.450
Hypertension	13	29.5%	48	27.3%	0.763
Dyslipidemia	6	13.6%	1	0.6%	0.001
Smoking	2	4.5%	9	5.1%	0.877
Killip class					
I	40	90.9%	136	77.3%	0.024
II	3	6.8%	38	21.6%	
III	0	0.0%	2	1.1%	
IV	1	2.3%	0	0.0%	
30 days Mortality					
Survived	34	77.3%	162	92.0%	0.005
Died	10	22.7%	14	8.0%	
Investigations:					
Trop-T(Mean±SD)	1.23±0.84		1.36±1.16		0.496
LVEF(Mean±SD)	37.3±4.7		39.17±3.9		0.007



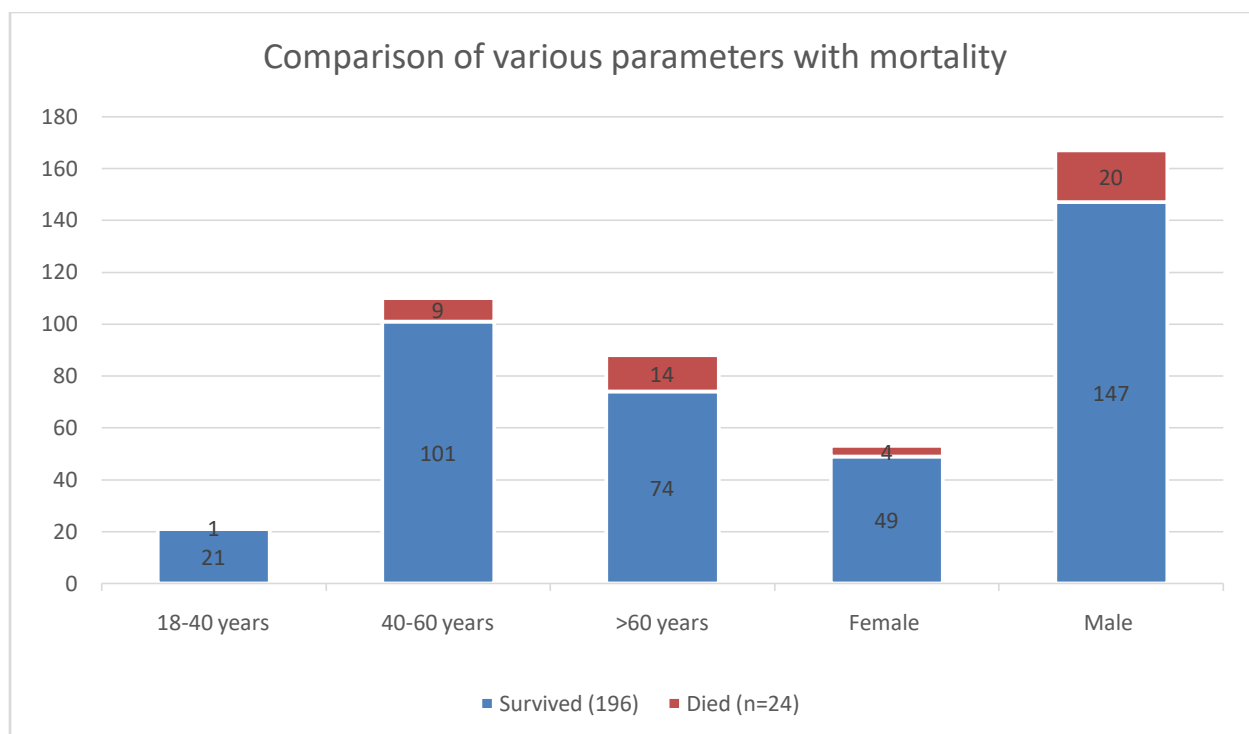


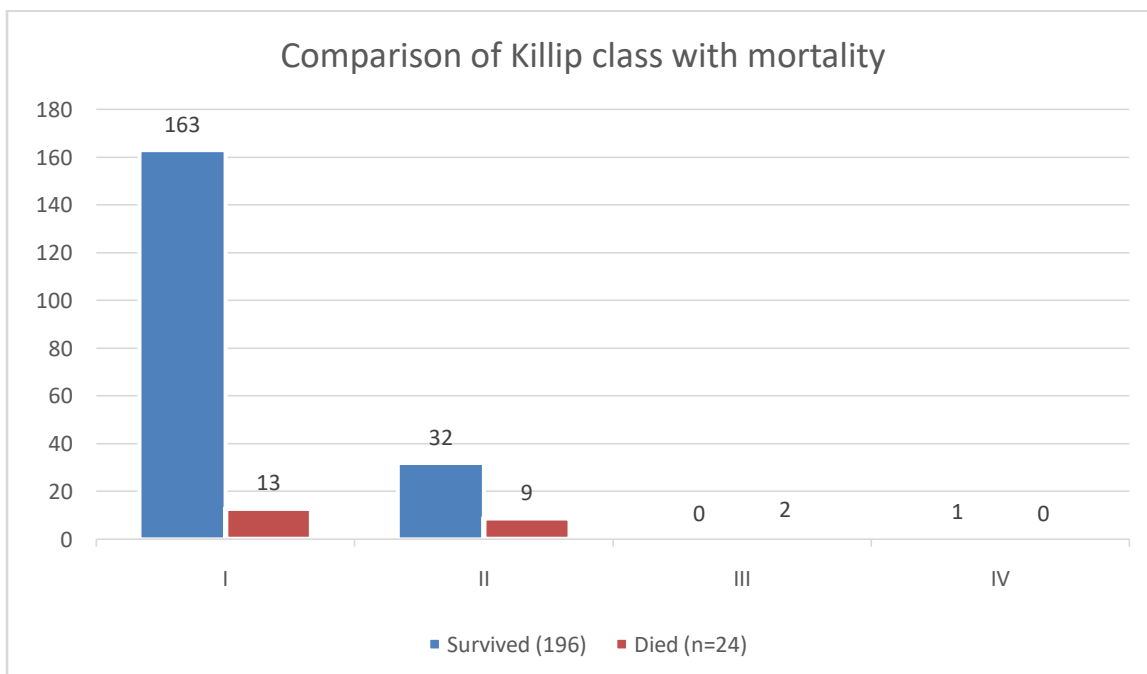
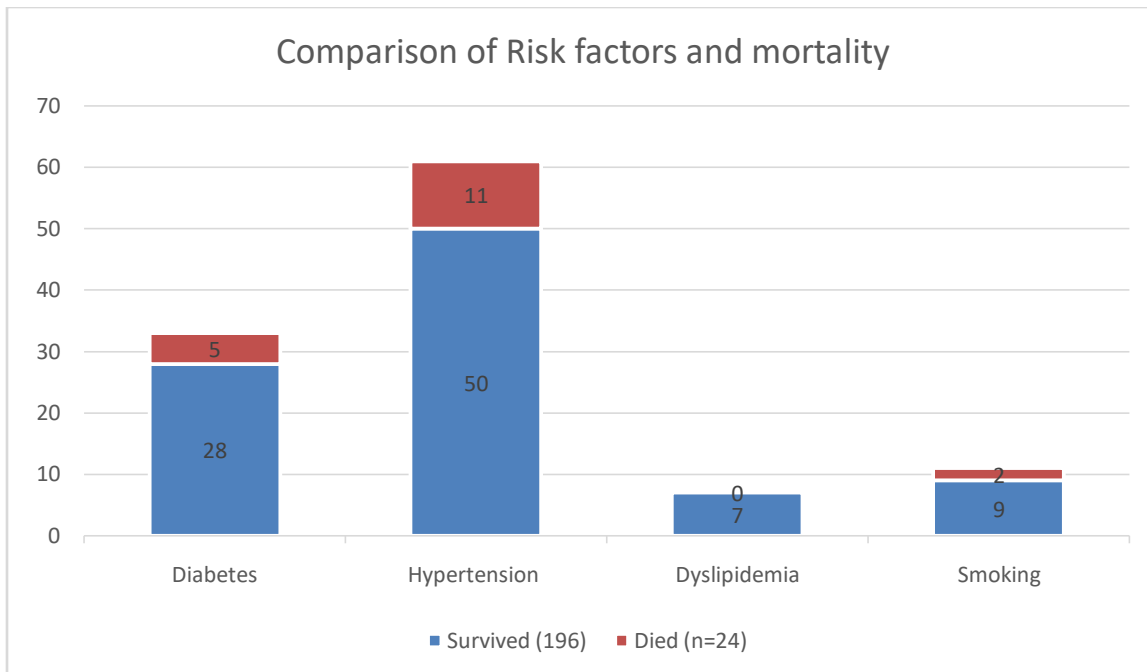
**Table 6:-** Comparison of various parameters with 30 days mortality.

	Survived (196)		Died (n=24)		p-value
	n	%	n	%	
<b>Age</b>					
18-40years	21	10.7%	1	4.2%	0.134
40-60years	101	51.5%	9	37.5%	
>60years	74	37.8%	14	58.3%	
<b>Gender</b>					
Female	49	25.0%	4	16.7%	0.368
Male	147	75.0%	20	83.3%	



Risk factors					
Diabetes	28	14.3%	5	20.8%	0.396
Hypertension	50	25.5%	11	45.8%	0.036
Dyslipidemia	7	3.6%	0	0.0%	0.347
Smoking	9	4.6%	2	8.3%	0.427
Killip class					
I	163	83.2%	13	54.2%	0.0001
II	32	16.3%	9	37.5%	
III	0	0.0%	2	8.3%	
IV	1	0.5%	0	0.0%	
Investigations:					
Trop-T(Mean±SD)	1.26±0.95		1.96±1.88		0.003
LVEF(Mean±SD)	38.9±3.8		37.9±6.2		0.291





**Discussion:-**

The most common electrolyte imbalance in hospitalized patients is hyponatremia, which is defined as serum sodium levels below 135 mEq/L. It has been used in a variety of clinical contexts as a sign of the severity and prognosis of underlying diseases.[1-4] In people who have recently had an acute myocardial infarction (AMI), hyponatremia is a significant predictor of mortality. In the current study, the prevalence of hyponatremia in STEMI patients was reported to be 14.5% at admission and 20.0% after 72 hours. From the time of admission to 72 hours afterward, hyponatremia increased. Similar types of findings were made in the Vikash et al study, where hyponatremia upon admission and after 72 hours was discovered to be 14% and 20%, respectively. Hyponatremia upon admission and after 72 hours was 11% and 15%, according to Sharma HK et al. The results of our investigation agreed with those of the study by Madhaw G et al, which revealed that hyponatremia was 11% and 18%, respectively, at admission and after 72 hours.

In individuals with AMI, hyponatremia is caused by a complex set of processes. The onset of AMI, as well as reactions to pain, nausea, and stress, may cause the nonosmotic release of vasopressin, which may contribute to the emergence of hyponatremia.[17,24,25] Through the insertion of aquaporin-2 channels into the collecting duct cell membrane, elevated vasopressin enhances water permeability in the renal collecting duct. In AMI, hyponatremia also develops as a result of neurohormonal activation. Vasoconstriction occurs in AMI patients due to significant activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system.[11,26] Free water retention is also aided by the glomerular filtration rate's subsequent decline and the transfer of tubular fluid to the dilution section of nephrons.[27,28] Hyponatremia in AMI may therefore be a reflection of the disease's severity, including the degree of neurohormonal activation, hemodynamic change, and left ventricular failure. These characteristics of hyponatremia help to explain, in part, the relationship between hyponatremia and higher fatality rates among AMI patients. It's important to note that changes to these risk variables can alter serum sodium levels while a patient is in the hospital. This hypothesis is supported by our data, which demonstrates that the incidence of hyponatremia varied by time point over the hospitalization stay.

In our study, the 30-day death rate for STEMI patients was 10.9%. According to the current study, there was a 34.4% and a 22.7% death rate for hyponatremic patients at admission and after 72 hours. Similar to this, Goldberg et al. [5,6] proposed that hyponatremia at the time of admission or soon after is an independent predictor of short-term and long-term mortality in STEMI. In 1858 STEMI patients who underwent primary angioplasty, Klopotoski et al[8] examined the impact of hyponatremia on in-hospital mortality. Only in patients with an eGFR of less than 60 mL/min/1.73 m<sup>2</sup> or an LVEF of less than 40% did they find that hyponatremia upon admission was an independent predictor of in-hospital death. Hyponatremia was recently demonstrated to be unrelated to short- and long-term mortality in STEMI patients getting primary angioplasty by Lazzeri et al[29] after adjusting for baseline variables. These researchers proposed that hyponatremia in STEMI patients should be seen as a measure of disease severity rather than a standalone predictor of both short- and long-term mortality. The inconsistent outcomes mentioned above are mostly related to variations in how AMI was managed across studies, notably in terms of primary intervention and evidence-based medical care.

According to a recent case-control research, hyponatremia is an independent predictor of in-hospital mortality, and hyponatremia alone is probably responsible for the excess mortality between cases and persistently normonatremic controls (serum sodium level 135–145 mEq/L).[30] Furthermore, Qureshi et al. [31] shown that, in contrast to persistent hyponatremia, a corrected serum sodium level >134 mEq/L at discharge had no effect on the short-term mortality of patients with AMI but had a positive effect on long-term mortality.

### **Conclusion:-**

According to the results of our study, the serum sodium concentration may be a predictor of STEMI in patients. After a STEMI, hyponatremia has a substantial predictive value for death in patients. Therefore, identifying high risk patients and risk stratifying for best management may be aided by the dynamic monitoring of serum sodium levels.

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