ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

Original Research

Study of Prognostic impact of hyponatremia occurring at various time points during hospitalization in patients with acute myocardial infarction.

Dheeraj Garg[1], Pankaj Singh Jadon[2], Ishwer Tayal[3], Parul Garg[4]

1.Junior resident, 2-Associate Professor;- Department of General Medicine, Jaipur National University Institute for Medical Science and Research Centre, Jagatpura, Jaipur, Rajasthan. 3.Associate Professor (Forensic Medicine) 4.Associate Professor (Immuno-hematology and Blood Transfusion)- GGS Medical College and Hospital, Faridkot, Punjab

Corresponding author -Dr Parul Garg, Associate Professor (Immuno-hematology and Blood Transfusion)- GGS Medical College and Hospital, Faridkot, Punjab. Email id:

ABSTRACT

Introduction- Hyponatremia is an important predictor of mortality in AMI , it is important to assess the influence of hyponatremia at various time points during hospitalization. However there is dearth of literature on the prognostic consequences of the changes in serum sodium levels in patients with AMI.

Aim - To assess the prognostic importance of hyponatremia in patients of acute myocardial infarction.

Material and Methods- Hospital based observational study conducted in In Department of General Medicine at Jaipur National University Institute for Medical Sciences and Research Centre, Jaipur from June 2022 to April 2024.

Results- In the present study, the mean levels of Trop-T, CPK-MB, and Pro-BNP were significantly higher in the hyponatremia group compared to the normonatremia group. LVEF, SBP, and DBP were significantly lower in the hyponatremia group compared to the normonatremia group. Additionally, the mean hospital stay duration for ACS patients was significantly longer in the hyponatremia group compared to the normonatremia group.

Conclusion- Patients with acute coronary syndrome (ACS) who have hyponatremia experience significantly higher morbidity and mortality rates, as well as longer hospital stays, compared to those with normal sodium levels. The development of hyponatremia at admission and within the first 48 hours in acute myocardial infarction (MI) patients is an effective determinant of short-term outcomes. Therefore, serum sodium levels can serve as a simple and affordable marker to assess the risk status of patients with myocardial infarction. However, further studies are needed to investigate the effects of hyponatremia as a prognostic marker in patients with acute coronary syndrome (ACS).

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

Introduction

The incidence of acute myocardial infarction (AMI) from 2025 to 2050, is projected to increase by 194.4%, rising from 482 to 1,418 cases per 100,000 population. Among individuals with AMI, the largest percentage increase in metabolic risk factors is expected to be overweight/obesity, with an 880.0% increase. This is followed by hypertension (248.7% increase), type 2 diabetes mellitus (T2DM) (215.7% increase), hyperlipidemia (205.0% increase), and active/ previous smoking (164.8% increase). The number of AMI-related deaths is predicted to rise by 294.7% in individuals with overweight/obesity. However, mortality is expected to decrease by 11.7% in individuals with hyperlipidemia, 29.9% in those with hypertension, 32.7% in those with T2DM, and 49.6% in active/previous smokers from 2025 to 2050. Compared to Chinese individuals, Indian and Malay individuals are expected to experience a disproportionate burden of overweight/obesity incidence and AMI-related mortality.1

Clinically, MI is a syndrome that can be recognized by a set of symptoms, chest pain being the hallmark of these symptoms in most cases, supported by biochemical laboratory changes, electrocardiographic(ECG) changes, or findings on imaging modalities able to detect myocardial injury and necrosis.[2]

Hyponatremia, defined as serum sodium levels <135 mEq/L, is the most commonly encountered electrolyte abnormality in hospitalized patients. and has been considered a marker of underlying disease severity and prognosis in various clinical settings.[3-5]

Hyponatremia is an important predictor of mortality and morbidity in patients with acute myocardial infarction (AMI).[6-10] The prevalence of hyponatremia in patients with myocardial infarction ranges from 12.5%–23.2%.[11-12] In AMI the underlying mechanism of hyponatremia is complex and it involves neurohormonal activation, involving nonosmotic release of vasopressin and activation of the sympathetic nervous system and renin–angiotensin–aldosterone system.[13-14]

Hyponatraemia has been identified as a predictor of short-term mortality in ST-segment elevation myocardial infarction (STEMI) patients as well as of long-term mortality, and rehospitalisation due to heart failure .[15]

Heart failure (HF) is associated with various electrolyte abnormalities, including hyponatraemia, hypokalaemia, and hypochloraemia besides acid–base disturbances, the causes of which are multifactorial. Maladaptive activation of neurohormonal mechanisms, such as an increase in arginine vasopressin, results in free water absorption and thirst activation, causing dilutional hyponatraemia and hypochloraemia.[16-18] The use of drugs such as loop and thiazide diuretics also results in disproportionately higher solute loss than free water loss.[19]

During periods of hospitalization, the neurohormonal activation can be mediated by factors such as the restoration of flow in the stenosed artery, and this is especially important

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

in the era where primary angioplasty is a preferred method of primary management of AMI.[20] In addition, pharmacologic interventions such as β-blocker, angiotensin converting enzyme (ACE) inhibitor, and angiotensin receptor blocker (ARB) also attenuate neurohormonal activation.[21]Therefore, many patients who survive the acute event may show altered serum sodium levels during the hospitalization period.

Hyponatremia is an important predictor of mortality in AMI , it is important to assess the influence of hyponatremia at various time points during hospitalization. However there is dearth of literature on the prognostic consequences of the changes in serum sodium levels in patients with AMI . We therefore undertook this study to assess the prognostic impact of hyponatremia occurring at various time points during hospitalization on short term and long-term mortality in survivors of AMI.

Aim and Objectives- To assess the prognostic importance of hyponatremia in patients of acute myocardial infarction.

Material and Methods-

Hospital based observational study conducted in In Department of General Medicine at Jaipur National University Institute for Medical Sciences And Research Centre, Jaipur from June 2022 to April 2024 on 50 patients of ACS.

Inclusion Criteria

All patients diagnosed to have Acute Myocardial Infarction using the case definition were included in the study.

Exclusion Criteria

1. Patients with previous MI.
2. Patients with congestive cardiac failure.
3. Patients with Cirrhosis of liver, nephrotic syndrome , renal failure.
4. Patients on diuretics.
5. All those who do not give consent.

Results-

Table 1: Demographic Profile of study subjects

Parameter		**N**	**%**
Age group (years)	**<50 Years**	9	18
	50-69 Years	33	66
	>=70 Years	8	16
	Total	50	100

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

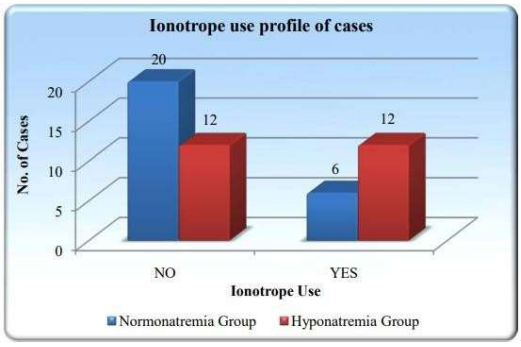
Sex	**Male**	30	60
	Female	20	40
	Total	50	100

Out of 50 patients the number of patients in age category of <50 Years, 50-69 Years, and >=70 Years were 9, 33, and 8 respectively.Out of 50 patients 30 were male and 20 were females.

Table-2 Ionotrope use profile of cases as per Hyponatremia at admission

Parameter		**Normonatremia Group**		**Hyponatremia Group**		**Total**		**P Value**
		No.	**%**	**No.**	**%**	**No.**	**%**	
IONOTROPE Use	**NO**	20	62.5%	12	37.5%	32	64.0%	.048
	YES	6	33.3%	12	66.7%	18	36.0%	
	Total	26	52.0%	24	48.0%	50	100.0%	

Out of 50 patients 32 patients have no requirement of Ionotrope (20 in Normonatremia Group and 12 in Hyponatremia Group) and 18 patients have no requirement of Ionotrope (6 in Normonatremia Group and 12 in Hyponatremia Group).



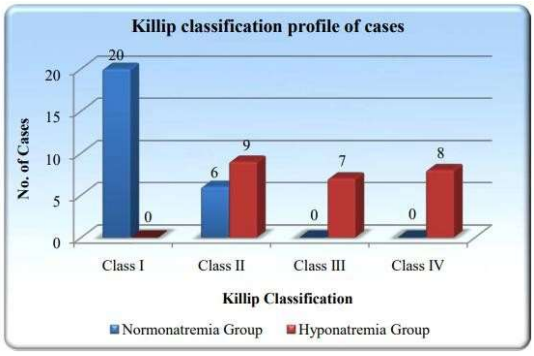


Table- 3 Killip classification of cases as per Hyponatremia at admission

Parameter		**Normonatremia Group**		**Hyponatremia Group**		**Total**		**P Value**
		No.	**%**	**No.**	**%**	**No.**	**%**	
Killip Classification	**Class I**	20	100.0%	0	0.0%	20	40.0%	<.001
	Class II	6	40.0%	9	60.0%	15	30.0%	
	Class III	0	0.0%	7	100.0%	7	14.0%	
	Class IV	0	0.0%	8	100.0%	8	16.0%	
	Total	26	52.0%	24	48.0%	50	100.0%	

According to Killip Classification out of 50 patients 20 patients were in Class I (all 20 in Normonatremia Group) 15 patients were in Class II (6 in Normonatremia Group and 9 in

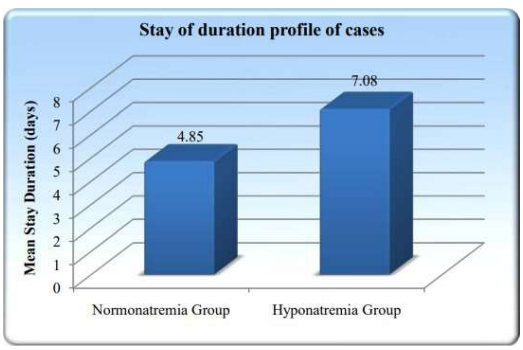
ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

Hyponatremia Group), 7 patients were in Class III (0 in Normonatremia Group and 7 in Hyponatremia Group), 8 patients were in Class IV (0 in Normonatremia Group and 8 in Hyponatremia Group).

Table 4- Duration of stay profile of cases as per Sodium Status at admission

Parameter	Hyponatremia at admission			P Value
	Normonatremia Group	Hyponatremia Group	Total	
	Mean (SD)	Mean (SD)	Mean (SD)	
Stay Duration (days)	4.85±1.91	7.08±1.98	5.92±2.23	.001

The mean Stay Duration ± SD of ACS patients was 5.92±2.23 days. The mean Stay Duration of ACS patients in hyponatremia group was 7.08±1.98 days and the mean Stay Duration of ACS patients in normonatremia group was 4.85±1.91 days.



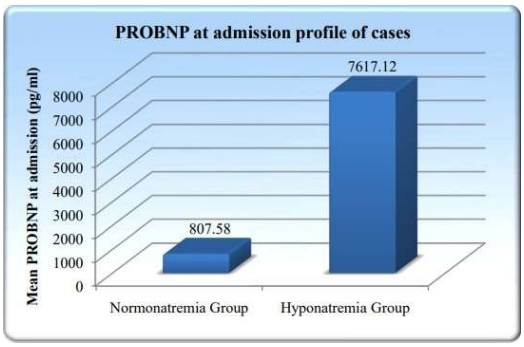
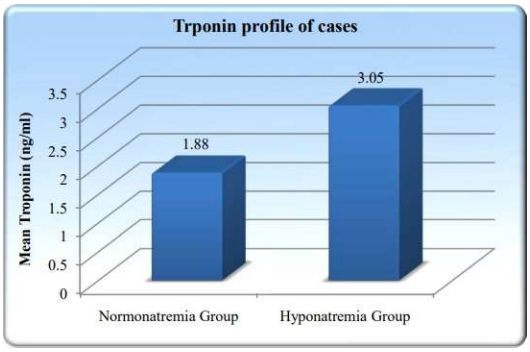


Table- 5 Cardiac Enzymes profile of cases as per Hyponatremia at admission

Parameter	Normonatremia Group	Hyponatremia Group	Total	P Value
	Mean (SD)	Mean (SD)	Mean (SD)	
Troponin T (ng/ml)	1.88±.73	3.05±.88	2.44±.99	<.001
CPK-MB (IU/L.)	57.08±19.51	70.58±21.67	63.56±21.47	.014
PROBNP at admission(pg/ml)	807.58±1466.68	7617.12±7906.10	4076.16±6499.80	<.001

The mean Troponin T of ACS patients in hyponatremia group was 3.05±.88 ng/ml and the mean Troponin T of ACS patients in normonatremia group was 1.88±.73 ng/ml and
The mean CPK-MB of ACS patients 63.56±21.47 IU/L . The mean CPK-MB of ACS patients in hyponatremia group was 70.58±21.67 IU/L . The mean PROBNP at admission of ACS patients in hyponatremia group was 7617.12±7906.10 pg/ml and the mean PRO-BNP at admission of ACS patients in normonatremia group was 807.58±1466.68 pg/ml

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024



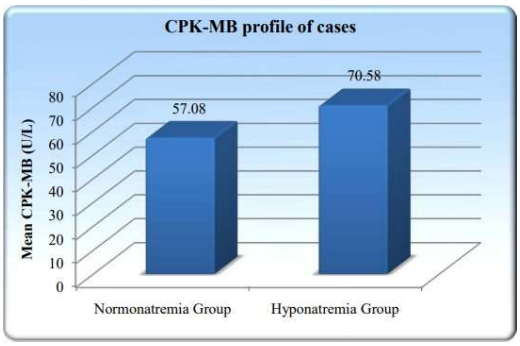
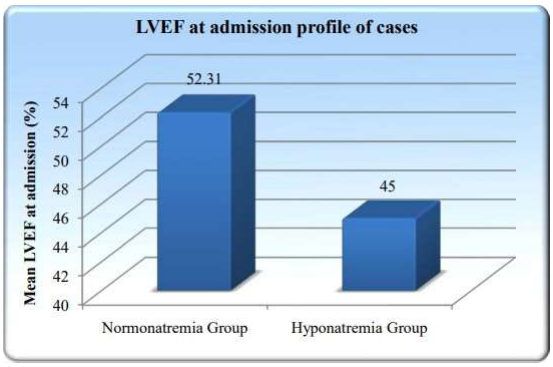


Table-6 LVEF (at admission) and at 1 month profile of cases as per Hyponatremia

Parameter	Hyponatremia at admission			P Value
	Normonatremia Group	Hyponatremia Group	Total	
	Mean (SD)	Mean (SD)	Mean (SD)	
LVEF at admission (%)	52.31±4.74	45.00±8.85	48.80±7.86	.001
LVEF at 1 month (%)	51.92±5.33	48.00±7.15	51.12±5.89	.049



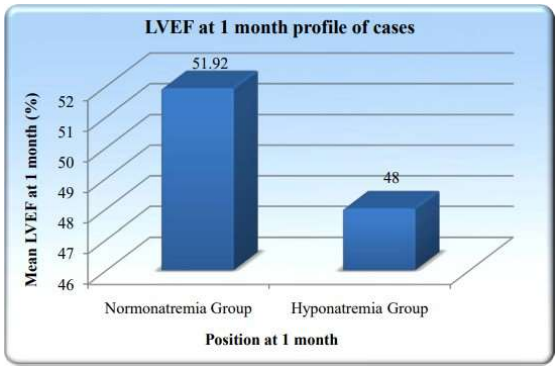


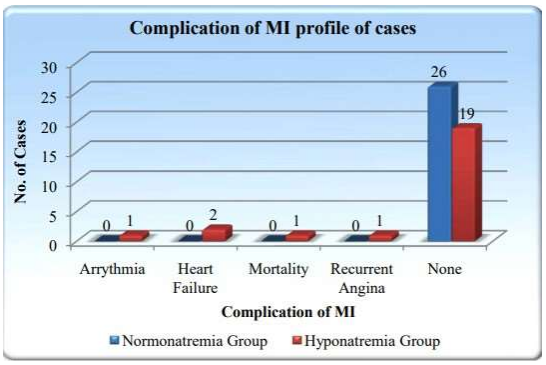
Table-7 Complication of MI profile of cases as per Hyponatremia at admission

Parameter		Normonatremia Group		Hyponatremia Group		Total		P Value
		No.	%	No.	%	No.	%	
Complication of MI	**Arrythmia**	0	0.0%	1	100.0%	1	2.0%	.198
	Heart Failure	0	0.0%	2	100.0%	2	4.0%	
	Mortality	0	0.0%	1	100.0%	1	2.0%	
	Recurrent Angina	0	0.0%	1	100.0%	1	2.0%	
	None	26	57.8%	19	42.2%	45	90.0%	
	Total	26	52.0%	24	48.0%	50	100.0%	

Out of 50 patients of ACS 45 patients have no complication and 5 patients have complication.None of the patients in Normonatremia Group have complications whereas out

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

of 24 patients of hyponatremia group Arrythmia, Heart Failure, Mortality, and Recurrent Angina were seen in 1, 2, 1 and 1 patient respectively.



DISCUSSION

Hyponatremia is a common electrolyte disorder in hospitalized patients, and it has been linked to increased morbidity and mortality in various clinical settings. Patients with Acute Coronary Syndrome(ACS) are at risk of developing hyponatremia due to a complex interplay of pathophysiological mechanisms. Several studies have the association between hyponatremia and outcomes in patients with STEMI, but the results have been conflicting. Various studies have found that hyponatremia is an independent predictor of mortality and morbidity in patients with STEMI.[22-23]

In present study the mean Trop-T at admission was significantly higher in the hyponatremia group as compared to normonatremia group . However Choi JS et al.[24] (2017) and Cordova Sanchez A et al.[25] (2022) in their study in ACS patients did not find significant differences on parameter of Trop-T at admission between hyponatremia group and normonatremia group which is in contrast with results of present study.

In present study the mean CPK-MB at admission was significantly higher in the hyponatremia group as compared to normonatremia group. However Choi JS et al.[24] (2017) and Cordova Sanchez A et al.[25] (2022) in their study in ACS patients did not find significant differences on parameter of CPK-MB at admission between hypoonatremia group and normonatremia group which is in contrast with results of present study.

In present study the mean Pro-BNP at admission was significantly higher in the hyponatremia group as compared to normonatremia group. Mohammed AA et al.[26](2010) and Cordova Sanchez A et al.[25](2022) in their study in ACS patients found significant differences on parameter of Pro-BNP at admission between hyponatremia group and normonatremia group (Pro-BNP was significantly higher in hyponatremia group than normonatremia group) which is consistent with results of present study.

In present study the mean LVEF at admission was significantly lower in the hyponatremia group as compared to normonatremia group. Mohammed AA et al.[26] (2010) and Cordova Sanchez et al.[25] (2022) in their study in ACS patients found that LVEF at admission was significantly lower in hyponatremia group than normonatremia group which

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

is consistent with results of present study. However Dai-Yin Lu et al. [28](2016) in their study in ACS patients found that LVEF at admission was not significantly different in hyponatremia group and normonatremia group which is in contrast with results of present study.

In present study there was significant association between Killip classification and hyponatremia. All the patients of normonatremia group belonged to Killip Classification Class I and Class II whereas patients of hyponatremia group belonged to Class II, Class III, and Class IV i.e. higher grade of Killip Classification is associated with Hyponatremia. Mohammed AA et al.[26] (2010) and Aravind, CL et al.[27] (2023) in their study in ACS patients found that patients with a higher Killip classification at admission were more likely to have hyponatremia compared to those with a lower Killip classification which is consistent with results of present study. Dai-Yin Lu et al.[28] (2016) in their study in ACS patients found no significant association of Killip classification with hyponatremia which is in contrast with results of present study.

Conclusion- Patients with acute coronary syndrome (ACS) who have hyponatremia experience significantly higher morbidity and mortality rates, as well as longer hospital stays, compared to those with normal sodium levels. The development of hyponatremia at admission and within the first 48 hours in acute myocardial infarction (MI) patients is an effective determinant of short-term outcomes. Therefore, serum sodium levels can serve as a simple and affordable marker to assess the risk status of patients with myocardial infarction. However, further studies are needed to investigate the effects of hyponatremia as a prognostic marker in patients with acute coronary syndrome (ACS)

BIBLIOGRAPHY

1. Chew NWS, Chong B, Kuo SM, Jayabaskaran J, Cai M, Zheng H, Goh R, Kong G, Chin YH, Imran SS, Liang M, Lim P, Yong TH, Liew BW, Chia PL, Ho HH, Foo D, Khoo D, Huang Z, Chua T, Tan JWC, Yeo KK, Hausenloy D, Sim HW, Kua J, Chan KH, Loh PH, Lim TW, Low AF, Chai P, Lee CH, Yeo TC, Yip J, Tan HC, Mamas MA, Nicholls SJ, Chan MY. Trends and predictions of metabolic risk factors for acute myocardial infarction: findings from a multiethnic nationwide cohort. Lancet Reg Health West Pac. 2023 May 31;37:100803. doi: 10.1016/j.lanwpc.2023.100803. PMID: 37693863; PMCID: PMC10485675
2. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD; Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. Fourth Universal Definition of Myocardial Infarction (2018).Circulation. 2018; 138:e618–e651.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

3. Overgaard-Steensen C. Initial approach to the hyponatremic patient. Acta Anaesthesiol Scand. 2011 Feb;55(2):139-48.
4. Overgaard-Steensen C, Larsson A, Bluhme H, Tønnesen E, Frøkiaer J, Ring T. Edelman's equation is valid in acute hyponatremia in a porcine model: plasma sodium concentration is determined by external balances of water and cations. Am J Physiol Regul Integr Comp Physiol. 2010 Jan;298(1):R120-9.
5. Upadhyay A., Jaber B.L., Madias N.E. Incidence and prevalence of hyponatremia. *Am. J. Med.* 2006;119:S30–S35. doi: 10.1016/j.amjmed.2006.05.005.
6. Mohan S., Gu S., Parikh A., Radhakrishnan J. Prevalence of hyponatremia and association with mortality: Results from NHANES. *Am. J. Med.* 2013;126:1127–1137.e1121.
7. Li Y., Chen X., Shen Z., Wang Y., Hu J., Xu J., Shen B., Ding X. Electrolyte and acid-base disorders in cancer patients and its impact on clinical outcomes: Evidence from a real-world study in China. *Ren. Fail.* 2020;42:234–243.
8. Castillo J.J., Glezerman I.G., Boklage S.H., Chiodo J., 3rd, Tidwell B.A., Lamerato L.E., Schulman K.L. The occurrence of hyponatremia and its importance as a prognostic factor in a cross-section of cancer patients. *BMC Cancer.* 2016;16:564.
9. Gill G, Huda B, Boyd A, Skagen K, Wile D, Watson I, et al Characteristics and mortality of severe hyponatraemia. A hospital-based study? Clin Endocrinol (Oxf). 2006;65:246–9.
10. Funk GC, Lindner G, Druml W, Metnitz B, Schwarz C, Bauer P, et al Incidence and prognosis of dysnatremias present on ICU admission Intensive Care Med. 2010;36:304–11.
11. Goldberg A, Hammerman H, Petcherski S, Zdorovyak A, Yalonetsky S, Kapeliovich M, et al. Prognostic importance of hyponatremia in acute ST-elevation myocardial infarction. *American Journal of Medicine*. 2004;117(4):242–8.
12. Wang LF, Li ZQ, Tang Q, Xu D, Sun XY, Li WM, et al. The prognostic value of hyponatremia in patients with acute myocardial infarction. *Zhonghua xin xue guan bing za zhi [Chinese journal of cardiovascular diseases]*. 2006;34(3):243–6.
13. Sigurdsson A, Swedberg K. The role of neurohormonal activation in chronic heart failure and postmyocardial infarction. Am Heart J. 1996;132:229–234.
14. Rodriguez M., Hernandez M., Cheungpasitporn W., Kashani K.B., Riaz I., Rangaswami J., Herzog E., Guglin M., Krittanawong C. Hyponatremia in Heart Failure: Pathogenesis and Management. *Curr. Cardiol. Rev.* 2019;15:252–261
15. Ma QQ, Fan XD, Li T, Hao YY, Ma F. Short- and long-term prognostic value of hyponatremia in patients with acute coronary syndrome: A systematic review and meta-analysis. PLoS One. 2018 Mar 2;13(3):e0193857.
16. Urso C, Brucculeri S, Caimi G. Acid-base and electrolyte abnormalities in heart failure: pathophysiology and implications. Heart Fail Rev. 2015 Jul;20(4):493-503. doi: 10.1007/s10741-015-9482-y. PMID: 25820346; PMCID: PMC4464645.
17. Oster JR, Preston RA, Materson BJ. Fluid and electrolyte disorders in congestive heart failure. *Semin Nephrol.* 1994;14:485–505.
18. Elisaf MS, Siamopoulos KC. Acid–base and electrolyte abnormalities in patients with congestive heart failure. *Exp Clin Cardiol.* 1997;2:140–144.
19. Islam MS. The Art and Science of Using Diuretics in the Treatment of Heart Failure in Diverse Clinical Settings. Adv Exp Med Biol. 2018;1067:47-65.
20. Kilburn H, Jr, Schoen L, Wang T. Acute myocardial infarction in New York State: 1996–2008. *J Community Health* 2012;37:473–9. [PubMed] [Google Scholar]

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

21. [16] Dzau VJ, Colucci WS, Hollenberg NK, et al. Relation of the renin–angiotensin–aldosterone system to clinical state in congestive heart failure. *Circulation* 1981;63:645–51.
22. Makrand B Mane. (2020). Assessing Acute St-Elevation Myocardial Infarction With Prognostic Significance Of The Hyponatramia. International Journal of Research in Pharmaceutical Sciences, 11(3), 3251–3260.
23. Bo, X., Liu, Y., Hao, C., Qian, H., Zhao, Y., Hu, Y., ... & Ma, G. (2023). Risk stratification and predictive value of serum sodium fluctuation for adverse prognosis in acute coronary syndrome patients. Clinica Chimica Acta, 548, 117491.
24. Choi JS, Kim CS, Bae EH, Ma SK, Ahn YK, Jeong MH, Kim SW. Prognostic impact of hyponatremia occurring at various time points during hospitalization on mortality in patients with acute myocardial infarction. Medicine (Baltimore). 2017 Jun;96(23):e7023. doi: 10.1097/MD.0000000000007023. PMID: 28591032; PMCID: PMC5466210.
25. Cordova Sanchez A, Bhuta K, Shmorgon G, Angeloni N, Murphy R, Chaudhuri D. The association of hyponatremia and clinical outcomes in patients with acute myocardial infarction: a cross-sectional study. BMC Cardiovasc Disord. 2022 Jun 18;22(1):276. doi: 10.1186/s12872-022-02700-y. PMID: 35717160; PMCID: PMC9206366.
26. Mohammed AA, van Kimmenade RR, Richards M, Bayes-Genis A, Pinto Y, Moore SA, Januzzi JL Jr. Hyponatremia, natriuretic peptides, and outcomes in acutely decompensated heart failure: results from the International Collaborative of NT-proBNP Study. Circ Heart Fail. 2010 May;3(3):354-61.
27. Aravind, CL; Ravikiran, R; Kumar, Amith; Ranjith Kumar, GK. Hyponatremiain Acute ST-elevation Myocardial Infarction – A Retrospective Observational Study. APIK Journal of Internal Medicine ():10.4103/ ajim.ajim_52_23, November 22, 2023. | DOI: 10.4103/ajim.ajim_52_23.
28. Lu DY, Cheng HM, Cheng YL, Hsu PF, Huang WM, Guo CY, Yu WC, Chen CH, Sung SH. Hyponatremia and Worsening Sodium Levels Are Associated With Long-Term Outcome in Patients Hospitalized for Acute Heart Failure. J Am Heart Assoc. 2016 Mar 23;5(3):e002668. doi: 10.1161/JAHA.115.002668. PMID: 27009619; PMCID: PMC4943243.