

## **Plasma atrial natriuretic peptide level and serum electrolyte status among patients with acute myocardial infarction complicated with cardiac arrhythmia**

**Prof. Abdul - Aziz Ahmed Aziz<sup>1</sup>, Dr. Abdul-Hassan M. S.<sup>2</sup>, Dr. Mohammed K. B.<sup>3</sup>**

<sup>1,3</sup>Ph.D. University of Telafer, Iraq.

<sup>2</sup>Ph.D. University of Thi-Qar, Iraq.

### **ABSTRACT**

**Objective:** Acute myocardial infarction is a leading cause of morbidity and mortality worldwide. Electrolyte imbalance among patients with acute myocardial infarction is not uncommon. The aim of the present study is to assess the status of serum sodium and potassium and plasma atrial natriuretic peptide level among patients with acute myocardial infarction complicated with cardiac arrhythmia.

**Design:** A case control study.

**Setting:** Ibn-Sena hospital/ Mosul-Iraq.

**Participants:** the study included 92 patients with acute myocardial infarction, divided into 2 group; Group I, included 44 patients with uncomplicated acute myocardial infarction; group II, included 48 AMI patients complicated with cardiac arrhythmia. The study also included 50 apparently healthy volunteers as a control group.

**Methods:** Plasma level of atrial natriuretic peptide, serum concentration of sodium, potassium were measured.

**Results:** The results of the study showed a significantly low serum sodium and potassium concentration in patients with AMI ( $p < 0.0001$  and  $p < 0.0001$ ) in comparison with control group. The means of plasma level of atrial natriuretic peptide was significantly higher in patient with acute myocardial infarction in comparison with control group ( $p < 0.0001$ ), atrial natriuretic peptide level was also higher in patient with complicated acute myocardial infarction in comparison with uncomplicated group ( $p < 0.0001$ ). A significant negative correlation was observed between plasma atrial natriuretic peptide and serum sodium concentration in patients with uncomplicated acute myocardial infarction ( $r = -0.825$ ,  $p < 0.0001$ ) and complicated acute myocardial infarction ( $r = -0.884$ ,  $p < 0.0001$ ).

**Conclusion:** In acute myocardial infarction, electrolytes imbalance is a common finding and usually associated with a variety of cardiac arrhythmia, plasma level of atrial natriuretic peptide significantly increased in patients with acute myocardial infarction and negatively correlated with serum sodium concentration.

**KEYWORDS:** Plasma atrial natriuretic peptide ; serum electrolyte status; acute myocardial infarction ; cardiac arrhythmia

### **INTRODUCTION**

Acute myocardial infarction (AMI) constitutes a big challenge facing health authority worldwide (Salim et al.,2020) . Despite a great advance in the diagnosis and treatment of AMI in the last few decades, it still one of the major killers with great impact on social and economic status of different communities (Oras et al.,2020). Acute myocardial infarction represents a great insult to body system regulatory mechanisms, one of the important systems involved is the humoral factor regulating body fluid and electrolyte specially those concerned with serum

sodium and potassium like sympathetic system (Ciarka et al.,2008) and natriuretic hormones (Xi-Ying et al.,2020; Guyton and Hall ,2020). These two ions play important role in maintaining the excitability of muscles and neuron (Tamagawa et al.,2019). Imbalance of these ions associated with distortion of excitable tissues functions. Cardiac myocyte is very sensitive for any alteration in serum sodium and potassium concentration; accordingly, we may challenge with a variety of cardiac rhythm disorder in patients with AMI who had electrolyte imbalance (Shubhangi et al.,2014).

Atrial natriuretic peptide (ANP) had a wide range of physiological activity, it acts as a counter-regulatory hormone in face of stress hormones like sympathetic nervous system hormones, and Renin-Angiotensin Aldosterone system. One of its main effects is shifting intravascular fluid into extravascular compartment and promoting diuresis and natriuresis that decreases extracellular fluid volume (Lugnier et al.,2019) with subsequent alteration in body fluid and electrolyte balance. The present study is an attempt to evaluate plasma level of ANP, body fluid electrolytes status and their relation to cardiac rhythm disorder among patients with AMI.

## **SUBJECTS, MATERIALS and METHODS**

### **patients**

Ninety-two (51 males and 41 females) patients with AMI admitted to the Coronary Care Unit, at Ibn-Sena teaching hospital/ Mosul were included in this study. Inclusion criteria were patients diagnosed as AMI on the basis of clinical, ECG and biochemical study. Exclusion criteria were AMI with other co morbidity like cerebrovascular attack, malignancy, patients who received diuretic, angiotensin receptor blocked or angiotensin converting enzyme inhibitor before AMI. Diagnosis of AMI was according to European Society of Cardiology (ESC), the American College of Cardiology (ACC), the American Heart Association (AHA) and the World Heart Federation (WHF) jointly (Thygesen et al.,2007):

1. History suggestive of ischemic chest pain for more than 30 minutes
2. Typical ECG pattern
3. serum biomarker consistent with myonecrosis.

The group of AMI patients are further subdivided into two subgroups

group I: Patients with uncomplicated AMI, included 44 patients (24 males and 20 females), their age range from 29 to 66 years ( $48.14 \pm 9.5$ ).

group II: Patients with AMI complicated with arrhythmia and included 48 patients (27 males and 21 females), their age range from 27 to 68 years ( $51.43 \pm 8.68$ ).

### **Control**

The study also included 50 (26 males and 24 females) apparently healthy subjects with age and sex matched as control group, their age range from 27 to 65 years ( $48.68 \pm 10.16$ ).

Informed consent was taken from both study and control group subjects after explaining the purpose and procedure of the study.

### **Biochemical analysis**

Ten ml of blood was taken from every subject participated in this study, 5ml placed in EDTA tube and other 5 ml was placed in plain tube. After centrifuging, samples were stored at  $-20^{\circ}\text{C}$

until the time of analysis. Serum potassium and sodium levels were measured using an emission flame photometer (Corning 400, England). Plasma atrial natriuretic peptide concentration was determined by Enzyme Linked Immunosorbent Assay (ELISA) utilizing kits provided by DRG International Inc., USA (Cat. No.: Eia-1524).

### statistical analysis

statistical analysis was done by SPSS software, version 22.0 (SPSS, Inc., Chicago, IL, USA). Data are represented as the mean  $\pm$  SD. Comparison between two groups used a t-test. Comparison between three groups used one-factor analysis of variance(ANOVA). Correlations of serum sodium and potassium concentration with plasma ANP was determined by Pearson Correlation. For all analysis 'p' value  $< 0.05$  was defined as significant.

### RESULTS

The study included 142 subjects, they are divided into three groups, control group include 50 (26 males and 24 females) apparently healthy subjects, 44 (24 males and 20 females) patients with uncomplicated AMI, and 48(27 males and 21 females) AMI patients complicated with cardiac rhythm disorder ( Table-1).

**Table 1: Age distribution of different studied groups.**

Groups	N	Mean	SD	ANOVA	P value
control	50	48.7	10.2	1.566	0.212
complicated AMI	48	48.1	9.5		
uncomplicated AMI	44	51.4	8.7		

The results of the study revealed significantly lower serum sodium concentration, and serum potassium concentration in patient with AMI in comparison with the control group ( $p < 0.0001$ , and  $p < 0.0001$ ) respectively (Table -2) and (figure 1).

**Table 2 : Serum sodium concentration, serum potassium concentration and plasma level of ANP in patient with AMI in comparison with the control group.**

Blood Parameters	Mean $\pm$ S.D.		P value
	Control group (n=50)	Patients with AMI (n=92)	
sodium concentration mmol/L	140.5 $\pm$ 3.4	Un complicated (137.6 $\pm$ 3.6)	0.0001
		Complicated (137.5 $\pm$ 4.5 )	0.0001
potassium concentration mmol/L	4.2 $\pm$ 0.5	Un complicated (3.7 $\pm$ 0.3)	0.0001
		Complicated (3.9 $\pm$ 0.7)	0.0001
ANP pg/ ml	42.9 $\pm$ 9.5	Un complicated (79.316.8 $\pm$ )	0.0001
		Complicated (87.4 $\pm$ 20.1 )	0.0001

The serum concentration of sodium in patient with complicated AMI was slightly lower than that of uncomplicated cases. On the other hand serum potassium concentration in patient with complicated AMI was slightly higher than that of uncomplicated cases. However, these differences were non-significant( figure1 and 2).

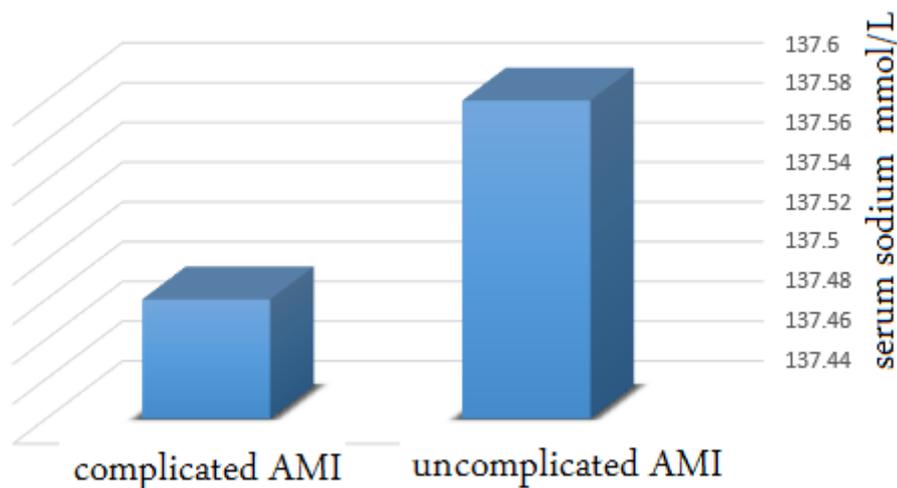


Figure 1: serum sodium concentration in the complicated and uncomplicated AMI group.

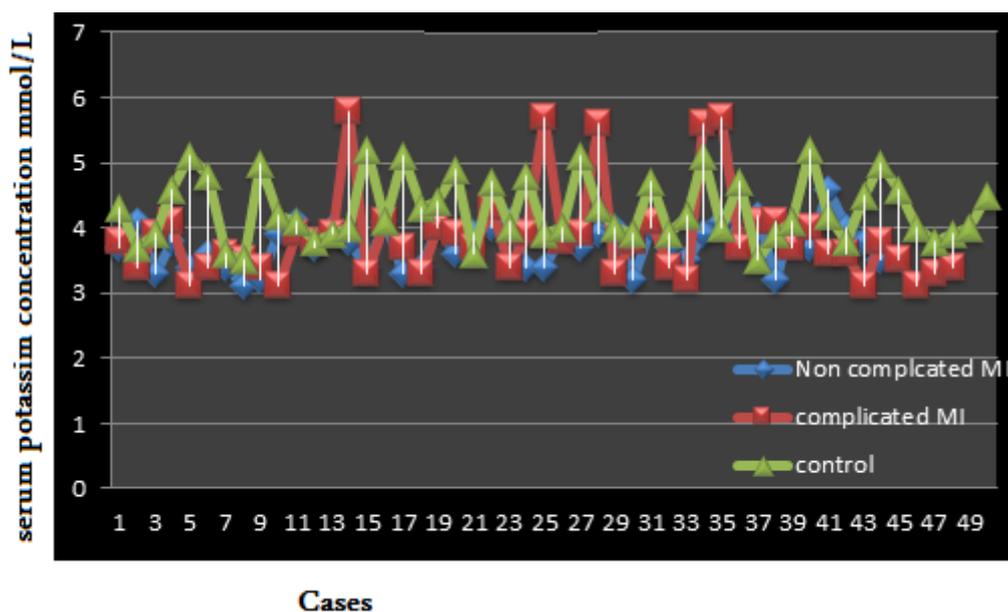


Figure 2: serum potassium concentration in the non-complicated, complicated AMI, and control groups.

Concerning the plasma level of ANP, the results of this study showed a significantly higher values ( $p < 0.0001$ ) of ANP in patients with AMI in comparison with control group. Plasma level of ANP was significantly higher ( $p < 0.0001$ ) among complicated AMI patients in comparison with uncomplicated patients (Table-1) and (figure 3).

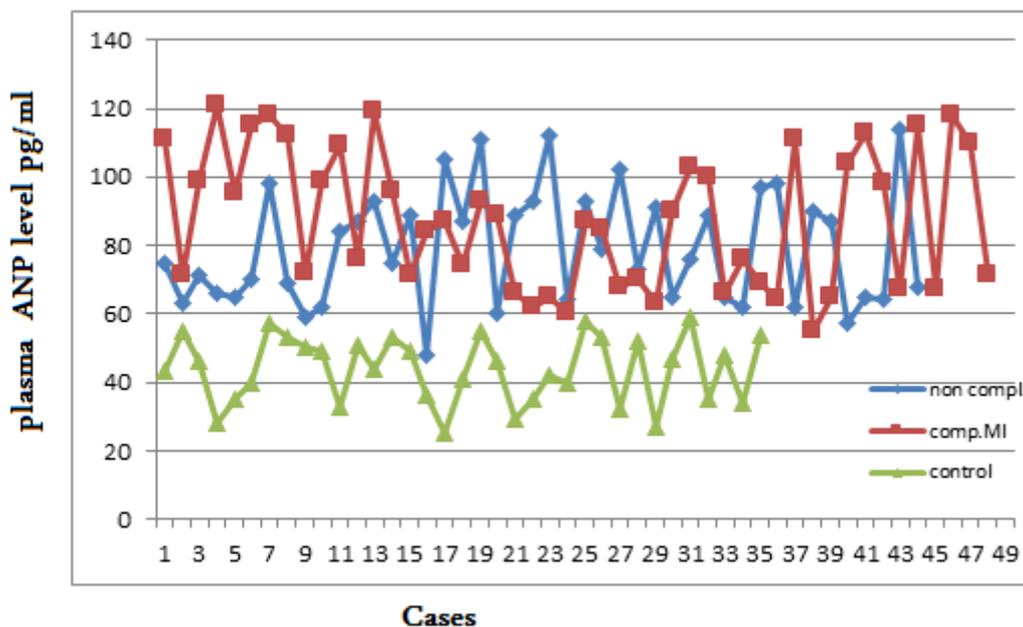


Figure 3: plasma ANP level in studied groups(patients and control).

The results of the present study also revealed strong negative correlation between plasma ANP and serum sodium concentration in patients with uncomplicated AMI ( $r = -0.825$ ,  $p < 0.0001$ ) and complicated AMI ( $r = -0.884$ ,  $p < 0.0001$ ) as shown in (Table- 3 and 4).

Table3: correlation of serum electrolyte concentration and plasma level of in uncomplicated AMI patients.

		Na	K	NAP
Na	Pearson Correlation	1	-.189-	-.825-*
	Sig. (1-tailed)		.110	.000
	N	44	44	44
K	Pearson Correlation	-.189-	1	.043
	Sig. (1-tailed)	.110		.390
	N	44	44	44
NAP	Pearson Correlation	-.825-*	.043	1
	Sig. (1-tailed)	.000	.390	
	N	44	44	44

\*\* . Correlation is significant at the 0.01 level (1-tailed).

Table4: correlation of serum electrolyte concentration and plasma level of in AMI patients with cardiac arrhythmia.

		Na	K	NAP
Na	Pearson Correlation	1	.060	-.884**
	Sig. (1-tailed)		.343	.000
	N	48	48	48
K	Pearson Correlation	.060	1	-.081-
	Sig. (1-tailed)	.343		.292
	N	48	48	48
NAP	Pearson Correlation	-.884**	-.081-	1
	Sig. (1-tailed)	.000	.292	
	N	48	48	48

\*\* . Correlation is significant at the 0.01 level (1-tailed).

Among the 48 AMI patients with cardiac arrhythmia 44 patients had developed single arrhythmia, and 4 developed double arrhythmias during the first 48 hours of admission. Sinus tachycardia observed in 16 patients followed by bradyarrhythmia's (sinus bradycardia and heart block) in 13 patient, premature ventricular beat in 12 patients, ventricular tachycardia in 9 patients and ventricular fibrillation in 2 patients. Cardiac arrhythmia was more common in male than females (Table-5).

**Table 5: Different types of arrhythmias documented in patients with AMI (n=48) in relation to gender.**

Cardiac rhythm disorder	Frequency	Percentage (%)	sex	
			male	female
Sinus tachycardia	16	30.76%	9	7
bradyarrhythmia's	13	25%	8	5
premature ventricular beat	12	23.07%	6	6
ventricular tachycardia	9	17.3%	6	3
ventricular fibrillation	2	3.24%	2	0

## DISCUSSION

Dyselectrolytemia are fairly common among patients with AMI, and early detection and proper interpretation is essential for adequate management and outcome of the disease. In the present study serum concentration of sodium was significantly lower among patients with AMI in comparison with control group. The decrease in serum concentration of sodium was more pronounced in complicated cases in comparison with uncomplicated cases. Twenty-five percent of uncomplicated AMI patients and 37.5% of AMI patients complicated with cardiac rhythm disorder were found to have hyponatremia. Shilpa Patil et al, founded that 27% of patients with AMI had hyponatremia and it is often associated with increased morbidity and mortality in AMI patients (Patil et al.,2016).

Hyponatremia could be due to increase secretion of antidiuretic hormone which impair water excretion causing dilutional hyponatremia(Singla et al.,2016). Flear et al had postulated that hyponatremia among patients with AMI could be due to increase cell membrane

permeability to sodium ions as a consequence of tissue hypoxia, activation of sympathetic nervous system and rennin-angiotensin system (Flear and Hilton,1979).

sodium regulation is achieved by a complex interaction between many systems. like, sympathetic nervous system, ANP, renin angiotensin aldosterone system and antidiuretic hormone (Kurtz et al.,1986) .However antidiuretic hormone, norepinephrine and angiotensin II all enhance the release of ANP(Cargill et al.,1994) .

The serum potassium concentration was significantly lower among patients with AMI in comparison with control group. Twelve (27.3%) patients with uncomplicated AMI manifest hypokalemia, while 15 (31.25%) of AMI patients complicated with arrhythmia had hypokalemia. Low serum potassium concentration is associated with an increased risk of ventricular tachycardia and ventricular fibrillation (Patel et al.,2017). The probable cause of hypokalemia is mostly due to the stress induced catecholamine response which lead to increase potassium uptake into cells (Kaltofen et al.,1990). Goyal A. etal. Found that admission hypokalemia and hyperkalemia in patients with AMI were associated with high mortality rate, on the other hand normal serum potassium coincidence with high survival rate (Goyal et al.,2012).

Mean plasma ANP level in patients with AMI included in this study was significantly higher than that in the control group. Furthermore, the mean plasma ANP was significantly higher in patients with complicated AMI compared with uncomplicated AMI. The result of the present study is comparable with many other studies done by Daniel Chan and Leong L Ng (Chan and Leong,2010) , and Hind T. Hamad etal(Hind et al.,2020). The natriuretic peptide family , consists of at least three structurally related polypeptides, they provide a counter-regulatory vasodilatation and natriuresis(Habib et al.,1994). Over the last few decades our understanding of natriuretic peptides role in body fluid and electrolyte hemostasis greatly increased. Recently the measurement of plasma natriuretic peptide levels is increasingly used to aid diagnosis, treatment and assess prognosis of heart diseases (Troughton et al.,2000).

In the current study sinus tachycardia was the common cardiac rhythm disorder, it observed in 30.8 % of cases, the result of this study is comparable with the studies done by Maturaju, N. & Chandrashekhar, H.M(Maturaju and Chandrashekhar,2016) and Mohammad K.I. A.(Alam et al.,2020). According to the result of this study the second commonest arrhythmia was bradyarrhythmia that seen in 25% of cases, this finding is in agreement with studies done by Rathod et al., (Rathod et al.,2014) and Nagabhushana et al, (Nagabhushana et al.,2015). In this study premature ventricular beat seen in 23%. This is in conformity with study by Chiwhane et al.( Chiwhane and Pradeep et al.,2018),.Ventricular tachycardia seen in 17.3%, which is comparable with the studies done by Maturaju, N. an Chandrashekhar, H.M.,( Maturaju and Chandrashekhar et al.,2016) and Sinha et al, ( Sinha et al.,2018) . cardiac rhythm disorder in AMI patients seems to be more common in male than females, a similar finding have been observed in other studies (Radhi et al.,2020).

## REFERENCES

---

- Agnieszka Ciarka, Philippe van de Borne, A. Pathak. (2008). Myocardial infarction, heart failure and sympathetic nervous system activity: New approaches that affect neurohumoral activation. *Expert Opinion on Investigational Drugs*.17(9):1315-1330.
- Cargill R.I, Coutie W.J, Lipworth B.J. (1994).The effects of angiotensin II on circulating levels of natriuretic peptides. *J. Clin. Pharmac*.38:139-142.
- Chiwhane, A. & Pradeep. (2018). Study of Rhythm Disturbances in Acute Myocardial Infarction. *Journal of The Association of Physician of India*. 66:54-58.
- Claire Lugnier, Alain Meyer, Anne Charloux. (2019). The Endocrine Function of the Heart: Physiology and Involvements of Natriuretic Peptides and Cyclic Nucleotide Phosphodiesterases in Heart Failure. *J. Clin. Med*.8: 1746 -1766.
- Daniel Chan and Leong L Ng. (2010).Biomarkers in acute myocardial infarction. Chan and Ng *BMC Medicine* 2010, 8:34-45.
- Flear C T G, Hilton P. (1979). Hyponatremia and severity and outcome of myocardial infarction. *BMJ*.1:1242-1246.
- Guyton and Hall. (2020). *Textbook of Medical Physiology (Guyton Physiology)*,14th Edition, Elsevier.
- Habib F., Dukta D., Crossman D. et al. (1994). Enhanced basal nitric oxide production in heart failure: another failed counter-regulatory vasodilator mechanism? *Lancet*.344 :371-377.
- Hind T. Hamad , Zaid M. M. Almahdawi , Zaidan J. Zaidan .(2020). Levels of some cardiac hormones in patients with heart diseases in Tikrit city . *Eurasian Journal of Biosciences*.14 (2): 2911-2915.
- K Thygesen, JS Alpert, HD White, AS Jaffe, FS Apple, M Galvani, et al. (2007). Universal definition of myocardial infarction Kristian Thygesen, Joseph S. Alpert and Harvey D. White on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. *Eur Heart J*.28(20):2525–2538.
- Kaltofen A, Lindner K H, Ensinger H, et al. (1990). The modification of the potassium concentration in blood by catecholamines. A literature review. *Anasth Intensiv ther Notfallmed*. 2:405-410.
- Kurtz A, Bruna R.D, Pfeilschifter J. et al. (1986). Atrial natriuretic peptide inhibits renin release from juxtaglomerular cells by a cGMP-mediated process. *Proc. Natl. Acad. Sci*. 83: 4769- 4773.
- Maturaju, N. & Chandrashekhar, H.M. (2016). The pattern of arrhythmias during first 48 hours of acute myocardial infarction’, *International Journal of Medical Research*.1(4):38-40.
- Maturaju, N. & Chandrashekhar, H.M. (2016). The pattern of arrhythmias during first 48 hours of acute myocardial infarction’, *International Journal of Medical Research*.1(4):38-40.
- Mohammad Khurshadul Alam, Manzoor Mahmood, Dipal Krishnaadhikary, et al. (2020). The Pattern of Cardiac Arrhythmias in Acute ST Elevated Myocardial Infarction and their in-hospital Outcome. *University Heart Journal*.16(1): 16-21.
- Nagabhushana, S., Ranjithkumar, G.K., Ranganatha, M. et al.(2015). ‘Study of Arrhythmias in Acute Myocardial Infarction. *International Journal of Medical Research and Review*.3(7):682-88.
- Oleg E. Osadchii. (2020). Mechanism of hypokalemia induced ventricular arrhythmogenicity. *Fundamental & Clinical Pharmacology*. 24: 547–559.

- Oras A Alabas, Tomas Jernberg, Mar Pujades-Rodriguez, et al.(2020). Statistics on mortality following acute myocardial infarction in 842 897 Europeans. *Cardiovascular Research*.116(1): 149–157.
- Radhi F. Shlash, Sarah Abdul Kareem Abdul Jabbar. (2020). Frequency of Arrhythmia after Acute Myocardial Infarction During Admission to the Coronary Care Unit in Ad\_diwaniyah Teaching Hospital. *Indian Journal of Forensic Medicine & Toxicology*.149(1): 1286-1291.
- Rathod, S., Parmar, P., Rathod, G.B. & Parikh, A. (2014). Study of various cardiac arrhythmias in patients of acute myocardial infarction ', *International Archives of Integrated Medicine*.1(4):32-41.
- Ravi B Patel, Sara Tannenbaum, Ana Viana-Tejedor, et al. (2017). Serum potassium levels, cardiac arrhythmias, and mortality following non-ST-elevation myocardial infarction or unstable angina: insights from MERLIN-TIMI 36. *Eur Heart J Acute Cardiovasc Care*. 6(1): 18–25.
- Salim S. Virani, Alvaro Alonso, Emelia J. Benjamin, et al. (2020). Heart Disease and Stroke Statistics—2020 Update: A Report From the American Heart Association. *Circulation*.141: e139–e596.
- Shilpa Patil, Saurabh Gandhi, Piyush Prajapati, et al. (2016). A Study of Electrolyte Imbalance in Acute Myocardial Infarction Patients at A Tertiary Care Hospital in Western Maharashtra. *International Journal of Contemporary Medical Research*. 3 : 2454-7379.
- Singla I, Zahid M, Good C B, et al. (2007).Effect of hyponatremia on outcome of patients in non ST elevation acute coronary syndrome. *Am J Cardiol*. 100:406-408.
- Sinha, R.P., Agrawal, D. & Jain, A. (2018). Incidence of various arrhythmias and its prognosis in different type of ST segment elevation myocardial infarction in first 72 hours. *J. Evid. Based Med. Health c*. 5(39):2772-2777.
- Tamagawa H. (2019).Mathematical expression of membrane potential based on Ling's adsorption theory is approximately the same as the Goldman-Hodgkin-Katz equation. *J Biol Phys*.45(1):13-30.
- Troughton R.W., Frampton C.M., Yandle T.G. et al. (2000). Treatment of heart failure guided by plasma aminoterminal natriuretic peptide (N-BNP) concentrations .*Lancet*. 355: 1126-1130.
- Verma Shubhangi, Vikki, Sharma SK. (2014). A study of serum electrolytes sodium and potassium in relation to arrhythmias after acute myocardial infarction. *Int J Biol Med Res*.5(3): 4332-4335.
- Xi-Ying W., Fen Zhang, Chi Zhang. (2020). The Biomarkers for acute myocardial infarction and heart failure. *BioMed Research International*.5 :1-14.