

## SERUM ELECTROLYTE LEVELS AND CLINICAL FEATURES OF PATIENTS DIAGNOSED WITH ACUTE CORONARY SYNDROME

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### ABSTRACT

**Objective:** To evaluate electrolyte levels in patients diagnosed with Acute Coronary Syndrome (ACS) and to assess whether these levels can be used as a prognostic predictor.

**Study Design:** Cross-sectional study.

**Place and Duration of Study:** A total of 5 months at Cardiac Department of Civil Hospital Karachi, from Oct 2015 to Feb 2016.

**Methodology:** A cross-sectional study of 200 patients was conducted using Open EPI 3.03. After taking consent form, patient diagnosed by ACS. Demographic detail, laboratory test and electrolyte levels performed.

**Results:** Of the 200 patients included in the study, there was a male preponderance with 125 (62.5%) being male and 75 (37.5%) being female. 126 (63%) out of the 200 patients were aged over 50 at the time of presentation. The levels of potassium were significantly normal with only 50 (25%) of the values being abnormal. While sodium values showed a nearly equal divide with 90 (45%) of the values exhibiting derangement. In nearly half of the cases, Trop T levels were positive (53%) with 57% of the positive results skewed towards the greater than 50 years age group.

**Conclusion:** There was found to be no positive correlation between electrolyte levels and diagnosis of ACS. Potassium is a significantly poor prognostic marker in patients diagnosed with ACS, with sodium being, relatively, a more specific one.

**Keywords:** ACS, Electrolyte levels, Troponin T, Potassium, Prognostic marker, Sodium.

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### INTRODUCTION

Acute Coronary Syndrome (ACS) is a broad term used to define life-threatening conditions that result in an abrupt reduction of blood supply to viable myocardium. ACS is attributed to three disorders, Unstable Angina, ST Elevated Myocardial Infarction (STEMI) and Non-ST Elevated MI (NSTEMI), the hallmark of which is the rupture of a previously stable atherosclerotic plaque, thrombus formation and a compromised blood flow to the heart muscle. ACS is linked to more than 2.5 million hospitalizations worldwide each year and is estimated to be the cause of death of one person every 83 seconds in the United States<sup>1,2</sup>.

Electrolytes, mainly sodium (Na), potassium (K) and chloride (Cl), are measurable parameters in the blood which influence cardiovascular

health and cardiac function. The Na<sup>+</sup>-K<sup>+</sup> AT Pase pump is a key regulator of the cardiac action potential along side Ca<sup>2+</sup> levels. These serum electrolytes have been regarded as the major determinants of the electrophysiological properties of the myocardial membrane. Sodium and Chloride primarily regulate the fluid compartments of the body, and a reduction in cardiac output, can not only activate the renin-angiotensin system (leading to fluid overload), but may also cause renal dysfunction leading to decreased excretion of the electrolytes. Potassium regulates the resting potential phase of the cardiac cycle.

Electrolyte disturbance in the setting of congestive heart failure has been studied by Livio Deis Cas *et al*<sup>3</sup>. The influence of hypokalemia in a myocardial infarction event and its sequelae has been extensively researched. The efficacy of hyponatremia as an indicator of prognosis in patients suffering from myocardial infarction has also been considered<sup>4</sup>.

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There is, however, a scarcity of research concerning dyselectrolytemia in all three conditions that constitute the term Acute Coronary Syndrome. While the effectiveness of electrolytes plus cardiac markers playing a role in the diagnosis and treatment of Acute Coronary Syndrome has been proposed, there have been no conclusive studies regarding this topic.

Our objective is to assess the electrolyte disturbance amongst patients diagnosed with ACS in Civil Hospital, Karachi. Additionally, this study has been taken up to evaluate how the knowledge of electrolyte imbalance and cardiac biomarkers can be used to improve diagnostic and treatment plans of diagnosed patients in the future. This study also aims to correlate the development of an acute coronary syndrome event with age and gender in order to identify at risk populations.

## **METHODOLOGY**

This prospective cross sectional study was conducted after approval from the Institutional Review Board (IRB) of the Dow University of Health Sciences during the time bar beginning October 2015 to January 2016. We included two hundred patients diagnosed with acute coronary syndrome, who were admitted to the coronary care unit of Civil Hospital, Karachi. All the participants gave informed written and oral consent.

The inclusion criteria included patients who were older than 18 years of age, diagnosed with ACS and those with complete laboratory work up of serum electrolytes and cardiac enzymes. Patients meeting a minimum of two of the following criteria were considered in our study to have had ACS: (i) clinical features in accordance with ACS, (ii) elevated Troponin T concentration above the normality ( $>0.001$  ng/mL) and (iii) a coronary lesion consistent with the findings of ACS on coronary angiography. ACS patients were further categorized by using the following criteria: NSTEMI was confirmed if patients had raised cardiac enzymes without detectable ST-segment elevation in the ECG. STEMI was confirmed if the patient complained of typical chest

pain lasting more than 20 minutes along with any one of the following characteristics: ST-segment elevation of at least 1mm, formation of a new Q wave, left bundle branch block formation in two or more contiguous leads, and/or two times increase in the cardiac enzymes. Unstable angina was confirmed if the patient presented with ischemic symptoms in the absence of elevated cardiac enzymes.

Patients with non-ACS chest pain, severe liver disease, cancer, inflammatory diseases, bleeding disorders, autoimmune diseases, infectious diseases, and immunosuppression were excluded from the study. The study entailed taking a comprehensive medical history from the patients, especially focusing on the personal history, complaints and comorbidities.

## **Laboratory Analysis**

Patients' blood samples were taken on admission for the requisite laboratory investigations

including sodium, and potassium electrolyte levels and the cardiac marker troponin T while the patient was started on anti-ischemic therapy. The blood samples were normally taken from the patients' cubital vein and were relocated to the test tube with cautiousness and special care was taken to prevent the shaking of the tube while it was sent to the laboratory for accuracy. Electrolyte levels including serum sodium and potassium were measured by Roche Cobas c501 chemistry analyzer (Roche Diagnostics). Troponin T was also measured by Cobas c501.

## **Statistical Analysis**

Analysis was done using SPSS Statistics, version 17.0 (IBM SPSS Inc., Chicago, IL). The data was tested for normal distribution by the Shapiro-Wilk test. All the continuous variables were expressed as mean  $\pm$  standard deviation and median (interquartile range) and were scrutinized using the T-test and Mann Whitney U test, respectively. Categorical variables were expressed as frequencies (percentages) and were compared using the chi-square test or Fisher exact test. The possible correlations between

different variables were also investigated by Pearson's analysis.

## RESULTS

Out of 200 patients surveyed with ACS, only 3.5% of them were less than 35 years of age, 33.5% in the 35 years to 50 years age bracket and the majority 63% were older than 50 years old. This age group co-relation was found to be statistically significant ( $p=0.047$ ).

The study included both males and females

pain (16%). Chest pain, only on exertion, accounted for 13.5% of the complaints, palpitations with shortness of breath 10.5% whereas other complains like nausea, vomiting had a share of only 8%.

On further analysis, we sought to establish a link between the symptoms presented in different age groups (table-I).

In the study, we targeted to investigate the electrolyte imbalances present in ACS patients. In total, 45% of patients showed an abnormality

**Table-I: Association of complains with age distribution.**

		Crosstab Complains					
		SOB	Chest pain on exertion	SOB and chest pain	Others	Palpitation with SOB	Chest pain
Age Groups	<35 years	-	-	5 (71.4)	-	1 (14.3)	1 (14.3)
	35-50 years	11 (16.4)	11 (16.4)	28 (41.8)	2 (3)	5 (7.5)	10 (14.9)
	>50 years	28 (22.2)	16 (12.7)	32 (25.4)	14 (11.1)	15 (11.9)	21 (16.7)
Total		39 (19.5)	27 (13.5)	65 (32.5)	16 (8)	21 (10.5)	32 (16)

**Table-II: Frequency of Trop T in gender.**

		Trop T		<i>p</i> -value
		Negative	Positive	
Gender	Male	60 (48)	65 (52)	<0.001
	Female	34 (45.3)	41 (54.7)	
Total		94 (47)	106 (53)	

**Table-III: Association of complains with gender.**

		Complains					
		SOB	Chest pain on exertion	SOB and chest pain	Others	Palpitation with SOB	Chest pain
Gender	Male	23 (18.4)	20 (16)	37 (29.6)	7 (5.6)	13 (10.4)	25 (20)
	Female	16 (21.3)	7 (9.3)	28 (37.3)	9 (12)	8 (10.7)	7 (9.3)
Total		39 (19.5)	27 (13.5)	65 (32.5)	16 (8)	21 (10.5)	32 (16)

but the bulk of patients were males (62.5%).

All of these patients were investigated for their Troponin T levels. Our study revealed that the ratio of troponin T being positive to negative was almost equal; 48% of patients were negative and 52% were positive. These troponin T values were statistically significant ( $p<0.01$ ).

This study also delved into the major clinical complaints of patients with acute coronary syndrome. Majority of the patients presented with shortness of breath and chest pain (32.5%), some had only shortness of breath (19.5%) or only chest

in sodium levels whereas only 25% showed a deviation in potassium levels, indicating that sodium disproportion is more likely to result in this syndrome. The results also demonstrated the percentage of population testing positive and negative for Troponin T with respect to gender (table-II).

Shortness of breath and chest pain, the most common of the presenting complains, were from 29.6% male patients and 37.3% female patients. The other complains according to their presentation in males and females (table-III).

According to our findings, unstable angina was the common diagnosis with 41.5% of the patients being diagnosed with it. This was followed by NSTEMI (31.5%) and STEMI (27%).

In both genders, the order of frequency of diagnosis was similar with males having an overall greater propensity to be diagnosed with

**Table-IV: Comparison of PDX with Na and K.**

PDX	Na			p-value
	Low	Normal	High	
ACS (USA)	35	62	18	0.01
STEMI	14	22	2	
NSTEMI	11	31	5	
Total	60	115	25	
PDX	K			p-value
	Low	Normal	High	
ACS (USA)	9	88	18	0.41
STEMI	2	32	4	
NSTEMI	9	31	7	
Total	20	151	29	

**Table-V: Frequency of PDX with gender.**

PDX	PDX	Gender		Total
		Male	Female	
	USA	49	34	83
	MI	29	25	54
	NSTEMI	34	29	63
Total		112	88	200

**Table-VI: Association between PDX\_Original and Trop T.**

PDX_ ORIGINAL		Trop T	
		Negative	Positive
	Unstable Angina	35 (50)	35 (50)
	NSTEMI	15 (32.6)	31 (67.4)
	STEMI	44 (52.4)	40 (47.6)
Total		94 (47)	106 (53)

unstable angina (73.1% of all USA patients and 24.5% of all ACS patients).

There was an equal divide of patients, diagnosed with USA and testing positive for Troponin T. The diagnosis of STEMI followed a similar pattern with Troponin T testing positive in 47.6% of these patients. NSTEMI, however, exhibited a divergent configuration with the results of the Troponin T tests skewed towards positivity (67.4% of NSTEMI diagnosed patients tested).

There were significant positive co-relations between serum sodium [Na] ( $p=0.01$ ) and complaints ( $p=0.049$ ) with Troponin T in ACS patients. The levels of serum potassium [K] were not significantly co related with Troponin T values ( $p=0.1410$ ) (table-IV).

## DISCUSSION

Cardiovascular disease remains the largest burden on health globally, with a mortality rate upwards of 17.3 million according to the WHO<sup>5</sup>. The number of deaths due to cardiovascular disease in Pakistan has approached approximately 200,000 per year with 40% of all deaths being attributed to CVD, according to a survey performed in 2011<sup>6</sup>.

In our study, we aimed to investigate the electrolyte imbalances present in patients diagnosed with acute coronary syndrome and the correlation with their presenting clinical symptoms. This is of key significance as variations in electrolyte levels can be associated with life threatening arrhythmias<sup>7</sup>. Our study included 200 patients, with 63% belonging to an elderly populace (i.e. greater than 50 years old). Our study did not include subjects younger than 20 years old as the diagnosis of acute coronary syndrome is often marred by an increased incidence of smoking and cocaine use amongst this population<sup>8</sup>. Elderly patients form a greater part of studies conducted on acute coronary syndrome as recognized in a study conducted by Delahaye *et al*<sup>9</sup>. This is owing to the fact that with increasing age, the risk for cardiovascular events increases especially if other comorbidities such as hypertension, diabetes mellitus, or hyperlipidemia are present. Elderly patients often already have had transient ischemia, previous angina attacks and sometimes, revascularization procedures performed and hence, most of the patients in our study were of this age bracket<sup>10</sup>.

Gender is another important predisposing factor in acute coronary syndrome, with males being prone to developing it. Our study confirmed this finding as 62.5% patients were males. As noted in a previous study, this gender dis-

parity is attributed to women's tendency to smoke less<sup>11</sup>. Additionally, they are less likely than men to have a prior history of myocardial infarction, coronary artery bypass grafting, or percutaneous coronary intervention.

Cardiac biomarkers such as troponin T act as important prognosis predictors, and help identify the presence of myocardial necrosis. As such, 53% of the patients in our setup were Trop T positive, indicating that they had a greater risk of myocardial necrosis<sup>12</sup>.

Although several researches, including that of Patel *et al*, have stated that chest pain was the most frequently reported symptom, our findings show that patients in our setup were more likely to suffer from shortness of breath or a combination of chest pain and shortness of breath<sup>13</sup>.

Some patients, especially women, also presented with atypical symptoms (8%) like nausea and vomiting highlighting that acute coronary syndrome should be a differential diagnosis even in such cases that tend to diverge from the ordinary and more common complains.

The large burden on health that cardiovascular disease poses reflects a critical need to improve diagnostic and prognostic procedures to enhance patient stability and avoid further preventable damage. In addition, statistics reveal the pressing necessity to educate the masses to be able to identify symptoms of an acute coronary syndrome and to not delay providing the patient with adequate medical attention as there is a significant chance of mortality.

Our research explores the varied presentations of patients diagnosed with acute coronary syndrome and the age variation at the time of diagnosis. Additionally our research also correlates Troponin T Values with gender and the disparity in presenting complaints between the two genders.

Our research has also correlated gender with presenting complaints which can help better understand how underlying pathologies intrinsic to men or women for example, menopause, can

alter presenting complaints. Several researches have been conducted with similar correlations but results still remain inconclusive. In our study we have found that women are more likely than men to present with symptoms such as nausea, vomiting, back pain and cough, which parallels Meshack *et al's* findings<sup>14</sup>. Overall women are more likely to suffer from atypical symptoms at the time of presentation while the incidence of chest pain and of both chest pain and dyspnea is higher in men. In our findings although the occurrence of dyspnea is higher in men, in contrast to other researches women were more likely to suffer from dyspnea than chest pain<sup>15,16</sup>.

Troponin T values were positive by a small margin in 53% of the patients. In both males and females, the positive outcome of Troponin T outweighed negative by a narrow margin. This correlates with other researches where the troponin T values have been nonspecifically raised as its value may be dependent on other chronic conditions<sup>17</sup>. This prompts more research into the area to assess the value of Troponin T as a marker for the diagnosis of ACS.

While published data is present regarding age correlation with acute coronary syndrome, there is a dearth of research comparing age groups with presenting symptoms<sup>18,19</sup>. In our research the overwhelming majority of patients presenting with dyspnea and chest pain was in the less than 35 year old age group. While in the older than 50 year age group, dyspnea was a relatively more common occurrence. Overall atypical symptoms were a fairly common occurrence in those older than 50 years.

Our findings demonstrate that out of the 200 patients diagnosed with acute coronary syndrome, presented to our Cardiology Department, most of the patients presented with Unstable angina (41.5%) followed by NSTEMI patients (31.5%) and lastly STEMI (27%) as demonstrated in a similar study conducted by Study Group of Pakistan Aspirin Foundation<sup>20</sup>. Hence it can be said that overall in Pakistan, unstable angina

occurrence has been greater than the other two ACS components.

A similar prospective survey of ACS patients conducted in Europe and the Mediterranean basin in 2002 showed non-ST elevation ACS in 51 (2%), ST elevation ACS in 42 (3%) and undetermined electrocardiogram ACS in 6 (5%). Another conducted in Britain in 2006 concluded that more Asian patients had angina (51% v 37%), but more Caucasian patients had myocardial infarction (63% v 49%) and non-ST elevation infarcts (40% v 29%)<sup>21</sup>. In the light of these researches it can be said that Asians have greater prevalence for angina.

According to the findings in this research, males have greater overall prevalence of ACS, unstable angina being the most common (59.0% of all USA patients and 24.5% in all ACS patients). The order of ACS components' frequency is same in both gender i.e., unstable angina highest followed by NSTEMI then STEMI. It has been researched that women with acute ischemic syndromes tend to be older than men with such syndromes<sup>13</sup>. This has been linked to oestrogen performing a both cardioprotective and lipid-lowering effect, an effect that is lost post-menopausally, thereby equalizing the prevalence of heart disease between the two genders<sup>18</sup>.

On admission, 106 out of 200 patients with baseline serum samples had positive troponin T. The ratio of Troponin T being negative to positive was 1:1 in both unstable angina and STEMI patients. However it was 1:2 in NSTEMI patients. The cardiac troponin T level is a powerful marker in ACS patients, and measured within the first 24 hours, it provides independent and important prognostic information regardless of whether the patient is classified as having UA or non-Q-wave MI<sup>22</sup>. It can also allow further stratification of risk when combined with standard measures such as electrocardiography and the CK-MB level. People with positive troponin T are considered as high-risk patients for developing myocardial infarction and death<sup>23</sup>. However in accordance with this result,

Troponin T is inconclusive as per the separate ACS component.

In the present study, we found that approximately 57.5% have normal sodium levels and 75.5% have normal potassium levels. There has been no significant dip in sodium and potassium levels in the data collected. One theory to support this result can be found in a research which stated that serum potassium level is significantly decreased, albeit transiently, during ischemic attack compared to the stable phase in individual subjects with ACS<sup>24</sup>. Since only 27% of the patients had STEMI, it can be said that most of the patients, during their electrolyte assessment, were in stable phase of ACS. Hyponatremia is associated with increased mortality in ACS patients. However one research proved this relation, via p value, to be statistically insignificant (p-value 0.15), although only in patients with acute MI<sup>25</sup>.

## CONCLUSION

There was a higher propensity for males to be diagnosed with unstable angina, (our most common diagnosis). We can also conclude that in our setup older subjects are at a higher risk of developing acute coronary syndrome symptoms. Hence there needs to be a greater awareness, particularly in this age group, to correctly and promptly recognize symptoms to decrease chances of mortality.

Identification of symptoms, particularly dyspnea and chest pain, can be of extreme importance to medical staff as it can help in triage of patients requiring urgent attention. Since women are at a higher risk of developing atypical symptoms, prompt diagnosis can positively alter both morbidity and mortality.

Troponin T levels, inconsistent with prior researches, have been found to be an unreliable marker for diagnosis. In our setup there was no positive correlation between sodium, potassium levels and diagnosis of ACS. However, relative to potassium, sodium has been found to have a greater specificity for prognosis and should be a focal point for researches conducted in the future.

Therefore, there need to be more studies conducted to draw a more conclusive parallel between potassium and Troponin T.

### CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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