Association of Serum Sodium, Potassium and High-Sensitivity C-Reactive Protein Levels With Mitral Regurgitation and Risk Factors in Patients With Acute Coronary Syndrome

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Abstract- Acute coronary syndrome (ACS) is a condition that manifests itself when there is a reduction in the amount of blood that flows to the coronary arteries. This can lead to damage to the heart muscle or possibly death of the heart muscle. The study was conducted with the intention of determining whether there were any alterations in the levels of sodium, potassium, and high-sensitivity C-reactive protein that were found in the serum of individuals who were diagnosed with acute coronary syndrome (ACS). In addition, the objective of this study was to evaluate the relationship between these levels and risk factors such as quitting smoking, having dyslipidemia, being overweight, and having mitral regurgitation. The study had a total of 133 participants, with 83 patients being assigned to the study group and 50 individuals being assigned to the control group. A specific group of people who had recently been diagnosed with ACS made comprised the members of the study group. Both groups' blood samples were taken and then flame photometry using the Bio-Lab Diagnostic kit was used to determine the levels of serum electrolytes (Na+ and K+). Furthermore, calorimetry was utilized in order to estimate the levels of the lipid profile. The levels of sodium, C-reactive protein, and potassium in the serum were shown to have significantly increased across all age groups when compared to the control group. Despite the fact that the female group had slightly higher mean±standard deviation values of serum sodium, potassium, and C-reactive protein concentrations compared to the male group, this difference did not meet the criteria for statistical significance. When comparing the mean±standard deviation levels of serum sodium, potassium, and C-reactive protein in the presence or absence of dyslipidemia, smoking, or obesity, the results of the T-tests revealed that there were no significant differences. There was a correlation between the severity of mitral regurgitation and the mean±standard deviation values of serum sodium, potassium, and C-reactive protein concentrations. The early evaluation of serum electrolyte levels is not only necessary for appropriate replenishment but also has the potential to assist in the diagnosis of acute coronary syndrome. C-reactive protein has been shown to be associated with the development of acute coronary syndrome. and we have also demonstrated that it has the potential to serve as a biomarker for both the risk and severity of ACS. It is possible to determine the severity of mitral regurgitation by observing the elevated levels of C-reactive protein, sodium and potassium in the serum.

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Introduction

Even though there have been substantial break throughs in the diagnosis and treatment of acute coronary syndrome, cardiovascular disease remains to be the leading cause of mortality across the continent. It is estimated that ischemic heart disease is responsible for over half of these premature fatalities (1). Through its pro- and anti-inflammatory properties, miR-155 facilitates the regulation of appropriate immuno-

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inflammatory responses. Miss regulation of the expression of microRNA-155 occurs when chronic inflammation is not under control, which ultimately results in diseases of periodontitis and atherosclerosis. Additionally, it is well known for the inflammatory qualities that it possesses (2,3).

The presence of single-nucleotide polymorphisms in the AIM2 and Pycard genes has been linked to an increased likelihood of developing periodontitis, either in conjunction with or independently of coronary heart disease that is present (4). Both the liver and adipocytes are responsible for the production of C-reactive protein, which is a plasma protein. A number of illnesses, such as systemic inflammation, infections, neoplasia like lymphoma, and immune-mediated rheumatic disorders like rheumatoid arthritis and vasculitis, are among those for which it is commonly acknowledged to be an essential biomarker (5).

The presence of elevated levels of prothrombotic autoantibodies, ACLA-IgG, and inflammatory mediators such hs-CRP and IL-6, which may be responsible for the enhanced inflammatory activity in atherosclerotic lesions, has the potential to increase the risk of cardiovascular events in individuals who have severe chronic periodontitis (6). On the other hand, it was discovered that both male and female secondary school students in the city of Sulaimani have a large prevalence of modifiable common risk factors that lead to in-hospital mortality rates (7). These risk factors include inadequate physical activity, smoking, hypertension, being overweight, and obesity.

The severity of the underlying coronary artery disease (CAD) might be somewhat predicted by the clinical classification involved in acute coronary syndrome. It is possible, however, that the prediction might be significantly enhanced by considering the quantity and nature of risk factors, in addition to determining whether there was any previous instance of ischemia (8). In unstable angina, the clinical symptoms are consistent with acute coronary syndrome; however, there is no biochemical evidence of myocardial infarction (9). This condition is at the end of the spectrum of acute coronary syndrome for the least severe form of the condition.

Electrolytes are measurable parameters in the blood that influence the health of the circulatory system and the function of the heart. Some examples of electrolytes include sodium (Na), potassium (K), and chloride (Cl). Along with calcium (Ca2+) levels, the Na-K ATPase pump is an essential component in the process of controlling the action potential generated by the heart. For the most part, sodium and chloride are responsible for regulating the fluid compartments of the body, whereas potassium is responsible for regulating the resting potential phase of the cardiac cycle. An increase in the concentration of these electrolytes can lead to a decrease in the output of the heart (10). A significant amount of research has been carried out in order to investigate the effects of hypokalemia on myocardial infarction and the repercussions of this condition. In addition, hyponatremia has been investigated for its potential to act as a prognostic signal for patients who have suffered a myocardial infarction (11).

Objectives

Acute coronary syndrome patients will have their serum samples analyzed in order to determine the amounts of sodium, potassium, and C-reactive protein that are present in their bodies. In addition, it intends to explore the association between these levels and a variety of risk factors, including smoking, dyslipidemia, obesity, and mitral regurgitation, among others.

Materials and Methods

Study design

Inclusion criteria

In the current study, there were a total of eighty-three consecutive adult patients diagnosed with acute coronary syndrome who were hospitalized to the coronary care unit at Baghdad Teaching Hospital. Utilizing the G-Power program, the sample size was determined and calculated. In the control group, there were fifty individuals who did not have any history of cardiovascular illness. These individuals were recruited from the attendants or relatives of patients who did not have cardiovascular disease.

Exclusion criteria

Conditions such as advanced chronic renal disease (stage 4 or 5), advanced chronic coronary syndrome, pregnancy, cancer, thyroid illness, and liver disease are examples of chronic conditions. In addition, patients who were diagnosed with both diabetes mellitus and hypertension were recruited for the study.

Collection of data

Clinical data

In this particular study, the objective was to collect a detailed case sheet for each individual patient, which would include a complete medical history as well as a comprehensive examination. Individual demographic information as well as traditional risk factors for cardiovascular disease (CVD) were included in this

document. A comprehensive heart examination, an electrocardiogram (ECG), an echocardiogram, and a diagnostic coronary angiography were some of the other procedures that were performed on each patient. Acute myocardial infarction (AMI) and unstable angina (UA) were among the patients with unstable coronary artery disease (ACS) who participated in this investigation.

Risk factors

Among the clinical and laboratory data that are taken into consideration are smoking status (which is classified into three categories: current smokers, prior smokers, and patients who have never smoked), dyslipidemia (which is documented in patients if their Atherogenic Index is less than 3.2), and obesity (patients are deemed obese if their body mass index is greater than 25 kg/m2). A person's body mass index (BMI) was determined by dividing their weight in kilograms by their height in meters squared (BMI=weight/(height)2).

Laboratory data

Venipuncture was used to obtain blood samples from the study patients within twenty-four hours of their admission. The procedure was performed by hospital staff as part of their usual work. Aseptic procedures were used to collect the samples. It was promptly separated using a cool centrifuge on-site at a speed of 2000×g for a duration of 10 minutes at a temperature of 4° C. Finally, the samples were stored at a temperature of -70° C until they were analyzed. Immediately prior to beginning the analysis, serum samples were allowed to thaw at room temperature. A flame-photometry (Bio-Lab Diagnostic kit) was used to evaluate the electrolytes in the serum (Na+ and K+), an ELISA approach was used to assess the C-reactive protein, and a colorimetric method was used to measure the lipids.

Statistical analysis

The data that was acquired from both the patients and the controls was analyzed. When calculating the levels of serum electrolytes (Na+ and K+) and C-reactive protein, the means and standard deviations of these values were determined. In order to ascertain the values that were witnessed for the measurement data, cross tabulations were utilized. We used the straightforward 'Z' test with the standard error of difference between two proportions in order to determine whether or not the results were significant. In addition, the Duncan test was utilized in order to evaluate the squared means of different probability levels, specifically the one and the five.

Results

A total of 83 patients who had been diagnosed with Acute Coronary Syndrome (ACS) participated in this study. The patients' ages ranged from 25 to 84 years, with the mean age being 53.66 years with a standard deviation of 16.10 years. There were two groups: the male group included 53 patients, which accounted for 67.7% of the total, and the female group had 30 patients, which accounted for 32.3% of the total. Within the control group, there were fifty individuals who were in good health and had an average age of 34.16±12.17 years. All of the volunteers ranged in age from twenty to fifty-eight years old. Both boys and females made up an equal number of participants in the group, with 25 people (or fifty percent) belonging to each gender group. For further information, kindly refer to Table 1. After comparing the mean age of the patients to the mean age of the control group, the patients' mean age was found to be considerably higher (P=0.0149). In addition, there was a significant rise in the incidence of ACS among males in comparison to females (P=0.0027; see Table 2 for additional information).

Table 1. Frequency distribution of total study sample by age

	Control	Patients	*P*
Mean± SD	34.16±12.17	53.66±16.10	0.0149 *
SE	1.49	1.36	--
Min	20	25	--
Max	58	84	--
C.V%	37.6089	19.48	--

* significant (P<0.1)

It was shown that the patients who were diagnosed with acute coronary syndrome (ACS) had significantly higher mean±standard deviation (SD) values of serum concentrations of sodium (Na), potassium (K), and C-reactive protein (P=0.03,0.003, 0.0022) as compared to the mean±SD values experienced by the serum control

group (*P*=0.03, 0.003, 0.0022), (Table 3).

The table 4 illustrates the impact that gender and risk factors have on serum biochemical values in patients who have been diagnosed with acute coronary syndrome (ACS). The mean and standard deviation values of serum sodium, C-reactive protein, and potassium concentrations were found to be non-significantly higher in the female group compared to the male group, with a *P* of 0.3, 0.27, and 0.79 respectively. In a similar manner, the mean and standard deviation values of serum sodium, C-reactive protein, and potassium concentrations were shown to be substantially higher in patients with dyslipidemia compared to individuals who did not have dyslipidemia (*P*=0.85, 0.3, and 0.63, respectively). However, the mean and standard deviation of serum sodium and C-reactive protein concentrations were found to be slightly higher in obese individuals compared to non-obese patients. However, this difference did not meet the criteria for statistical significance (*P*=0.54, 0.64), indicating that it was not statistically significant. In contrast, the mean and standard deviation of serum potassium concentrations were found to be somewhat lower in obese individuals compared to non-obese patients. However, this difference was not statistically significant (*P*=0.12), indicating that it was not a meaningful difference. The mean±standard deviation value of blood sodium concentrations and C-reactive protein was found to be slightly higher in patients who smoked at least one cigarette compared to patients who did not smoke at all (*P*=0.21, 0.84), however the difference was not statistically significant. Alternatively, it was discovered that the mean±standard deviation of serum potassium concentrations was somewhat lower in patients who smoked compared to those who did not smoke, with a *P* of 0.19. This finding was not statistically significant.

The results are presented as the Mean plus minus the Standard Deviation. In the analysis of variance (ANOVA), the mean was found to be substantially different at a confidence level of 95%, with a *P* equal or less than 0.05

The distribution of biochemical markers that are based on the severity of mitral regurgitation (MR) when seen through the lens of echocardiography findings is presented in table 5. We found that there was no statistically significant difference in the mean±standard deviation values of serum sodium and potassium between the various MR severity groups, with a *P* of 0.6 and 0.2, respectively. While the mean±standard deviation (SD) value of serum C-reactive protein was significantly different across the MR severity groups, there was a significant difference in the mean value of the C-reactive protein. Furthermore, it was observed that the mean±standard deviation values of serum sodium, potassium, and C-reactive protein concentrations displayed an increase as the severity of the MR continued to grow.

Table 2. Frequency distribution of the total study sample by gender

Sex	Control		Patients	
	No.	%	No.	%
Male	25	50	53	67.7
Female	25	50	30	32.3
Total	50	100	83	100
P	---	1.00 NS	---	0.0027 ** HS

NS: Non-significant (*P*>0.05), HS: Highly significant (*P*<0.01)

Table 3. Comparison between patients & control according to biochemical markers.

Group	No.	Mean±SD		
		Sodium (Na) (mg/dl)	Potassium(K) (mg/dl)	CRP:C-Reactive protein(mg/l)
Patients	83	145.17±1.48	4.79± 0 .16	12.70±0.94
Control	50	141.18±0.72	4.02± 0.07	0.31±0.14
T-test value	--	2.9*	5.19 **	3.01**
P		0.03 S	0.003 HS	0.0022 HS

Results expressed as Mean (+ SD), S: significant* (*P*≤ 0.05) at 95% confidence limit. HS: Highly significant, **(*P*<0.01)

Table 4. Effect of Gender and Risk Factors on serum biochemical level in patients with ACS

Factors	Mean±SD of serum Na(mg/dl)	*P*	Mean± SD of serum K (mg/dl)	*P*	Mean± SD Serum C-Reactive protein(mg/l)	*P*
Gender						
Male	142.24±4.88	0.28	4.86±0.08	0.3	12.50±0.81	0.79 NS
Female	149± 1.59	NS	4.97±0.09	NS	13.12±0.90	
Dyslipidemia						
No	143.90±3.71	0.85	4.88±0.07	0.3	12.02±0.80	0.63NS
Yes	146.01±2.41	NS	5.07±.081	NS	12.80±1.00	
Obesity						
No	142.78±4.8	0.54	4.95±0.06	0.12	12.26±0.83	0.64 NS
Yes	147.34±0.99	NS	4.89±0.06	NS	12.92±1.31	
Smoking						
No	139.43±7.27	0.21	4.98±0.07	0.19	12.03±0.51	0.84 NS
Yes	147.95±1.05	NS	4.83±0.09	NS	13.65±0.81	

Results are expressed as Mean+SD. NS: Non-significant (P>0.05)

Table 5. Distribution of serum biochemical concentrations by mitral regurgitation (MR) echocardiographic Finding

MR severity	N	Mean± SD of serum Na(mg/dl)	Mean±SD of serum k(mg/dl)	Mean±SD of serum C-Reactive protein(mg/l)
Mild	47	142.96±5.48	4.81±0.07	8.77±0.07
Moderate	27	145.01±1.15	4.81±0.07	12.73±0.97
Sever	9	148.67±3.29	5.21±0.16	14.66±0.08
P		0.6 NS	0.2 NS	0.05 S

Results are expressed as Mean+SD. NS: Non-significant (P>0.05); (ANOVA) Mean was significantly different at $P \leq 0.05$ at 95% confidence limit

Discussion

According to the World Health Organization (12,13), cardiovascular disease continues to be the predominant cause of death around the world, with a mortality rate that exceeds 17.3 million. A substantial difference in the mean age was found between the patient group and the control group, as indicated by the findings of the study (P=0.0149). There are 6% of the world's population that is comprised of people who are above the age of 60. Thromboembolic events are more likely to occur because of endothelial dysfunction and dysregulated inflammation, both of which are connected with the advancement of age in the cardiovascular system. Furthermore, another substantial risk factor for bleeding is getting older (14). A large amount of structural and functional changes take place at the cellular and subcellular levels, which are the cause of the ageing of the cardiovascular system (CV). These variations have an effect on both the big and the small arteries, which result in changes in the systolic and diastolic functions of the myocardium as well as a heightened sensitivity to sympathetic sensations. It is ultimately the case that this process is a contributor to the development of cardiovascular disorders (15).

According to the data presented in Table 1, there was a statistically significant increase in the incidence of ACS among males in comparison to females (P=0.0027). The findings of this study agree with the findings of the research carried out by Villar *et al*., which demonstrated that the prevalence of cardiovascular disease is higher in men and postmenopausal women than it is in non-premenopausal women. A vasoprotective phenotype in females, which may be impacted by sex hormones, is suggested by this piece of evidence. Estrogen, in particular, has been discovered to have modulatory effects on the endothelium and circulating cells, both of which have been considered to be involved in the development of cardiovascular disease (16).

The mean±standard deviation values of serum concentrations of sodium (Na), potassium (K), and C-reactive protein were recorded to be substantially higher in patients diagnosed with acute coronary syndrome (ACS) (P=0.03, 0.003, 0.0022) when compared to the mean±SD values of the serum control group. Based on this result, it appears that the adrenergic mechanism may

be responsible for the increase in serum potassium concentration as well as the decrease in renal excretion levels of sodium (Na) and potassium that occurs as a result of ischemia. It has been found that there was a significant elevation in the levels of sodium during Acute Coronary Syndrome patients and the decrease in potassium (17). The hs-CRP level is a useful parameter for indicating the severity of CAD. It could also help with risk stratification and predicting prognosis (18).

The patients who participated in the study were separated into two groups: males (n=53) and females (n=30). Furthermore, the mean and standard deviation values of blood sodium and potassium concentrations were found to be non-significantly higher in the female group compared to the male group (*P*=0.3, 0.27), may be owing to differences in dietary habits. The mean and standard deviation of the amounts of C-reactive protein were found to be non-significantly higher in the female group compared to the male group. (*P* were 0.79, 0.27, and 0.31). There was a correlation between an increase in body mass index (BMI) and an increase in CRP levels across all racial and gender categories. On the other hand, it was found that the rise in CRP levels that was brought on by obesity was more pronounced in women than it was in men. The researcher's hypothesis that the observed variations in CRP levels may be due, at least in part, to the fact that there is a mismatch between the increase of CRP levels with increasing BMI between the sexes (19-21).

The mean±standard deviation values of blood sodium, C-reactive protein, and potassium concentrations were shown to be non-significantly higher in patients with dyslipidemia compared to those who did not have dyslipidemia (*P*=0.85, 0.3, and 0.63, respectively).Using the indirect ISE system, it has been reported that the lipid concentration exhibited an inverse relationship, not only with the concentration of sodium ions (Na+) (22), but also with the concentration of chloride ions (Cl−) and, to a lesser extent, potassium ions (K+) (23), despite the fact that there is no correlation between raised levels of CRP or LDL-Ch. alone and cardiovascular disease events, it has been determined that a contemporaneous rise in LDL-Ch. and hs-CRP levels is related with a higher risk of coronary heart.

When comparing patients who were obese to patients who were not fat, it was shown that the mean±standard deviation (SD) value of serum salt concentrations was higher in obese patients. The P-value for this difference was 0.54, which indicates that it did not fulfil the requirements for statistical significance. On the other hand, it was shown that the mean±standard deviation of serum potassium concentrations was lower in persons who were obese in comparison to patients who were not obese. The difference was not statistically significant (*P*=0.12), which indicates that it was not a meaningful difference. This was the case despite the realization that the difference was found. It is likely that these findings can be related to the difficulty that obese individuals have in effectively coping with stress, there was no previous research in this sector that could serve as a point of comparison. Furthermore, it was shown that the mean±standard deviation (SD) value of serum C-Reactive protein concentrations was higher in obese patients compared to non-obese persons. This was a significant finding. Having said that, it is important to point out that this difference did not satisfy the requirements for statistical significance (the *P* was equivalent to 0.64) (24), Female gender, high body mass index (BMI), the use of sex hormones, and low income are all chronic characteristics that have been shown to be associated with CRP levels that are more than 10 mg/L at a single cross-sectional time point, according to research that were conducted in the past. These findings imply that these factors may be responsible for CRP levels that continue to be significantly elevated over an extended period of time. According to the findings, the mean±standard deviation (SD) value of serum sodium concentrations was shown to be marginally higher in patients who smoked in comparison to people who did not smoke (*P*=0.21). Nevertheless, it was observed that the mean±standard deviation value of serum potassium concentrations was found to be marginally lower in patients who smoked in comparison to those who did not smoke (*P*=0.19). This conclusion is compatible with the findings of previous research (25) which showed that non-smokers had a serum potassium level that was not significantly higher than that of smokers. This conclusion is, therefore, in accord with those findings. It has been established that there is a direct connection between smoking and decreased potassium levels in the serum, as indicated by the data. It has been reported (26) that excessive salt intake was higher among Korean men who had a history of smoking and who also consumed alcohol. This finding implies that smoking and alcohol consumption have an effect that occurs simultaneously. Among the patients who smoked, there was a little rise in the mean±standard deviation (SD) of serum C-reactive protein when compared to patients who did not smoke. However, this difference did not reach the threshold for statistical significance, as indicated by the *P* of 0.84. The act of smoking can be a contributor to oxidative stress, which can then lead to inflammation in the blood vessels.

It was discovered in a study on cytokine-mediated inflammation that smoking is associated with a significant increase in levels of IL-6; however, the increase in CRP levels that was detected in smokers was not statistically significant (27). This was the conclusion reached by the researchers. The results of another study (28), which compared persons who were now smoking to those who had never smoked, revealed that the levels of CRP in individuals who had never smoked were significantly lower. The mean±standard deviation (SD) values of serum sodium and potassium were shown to be non-significantly different among the various severity groups of MR, with a *P* of 0.4 and 0.47, respectively. This found that the values were not statistically different from one another. It is hypothesized that ischemic impairment to the papillary muscle apparatus or dilatation of the left ventricle could be the driving force behind the development of mitral regurgitation (MR) in individuals who are suffering acute coronary syndrome (ACS). Both conditions are associated with an increased risk of developing mitral regurgitation. This syndrome has been associated with an increased risk of death and heart failure in persons who have experienced an acute myocardial infarction (MI). This is the case independent of the left ventricular ejection fraction (LVEF) or any other clinical factors that may be present (29). The mean and standard deviation of blood C-reactive protein levels were significantly different between the MR severity groups. This difference was statistically significant. Additionally, as the severity of the MR grew, there was a rise in the mean and standard deviation values of blood sodium, potassium, and C-reactive protein concentrations. There was also an increase in the ratio of sodium to potassium. Although CRP is most commonly regarded as a marker of inflammation, it is also capable of causing damage to tissue in diseases such as ischemic tissue injury and autoimmune illness. This is despite the fact that CRP is most commonly recognized as a marker of inflammation. The central reticulum protein, commonly known as CRP, is now regarded not just as a marker of inflammation but also as an active protein that promotes inflammation. Some people believe that selective CRP-apheresis could reduce the amount of myocardial necrosis that occurs in patients who have had an acute myocardial infarction (AMI), which in turn can improve the outcomes of these patients. There is evidence that hs-CRP levels can help in the identification of patients who are asymptomatic and have moderate or severe mitral regurgitation. This information was taken from the research that was conducted (30).

The early evaluation of serum electrolyte levels is not only necessary for appropriate replenishment but also has the potential to assist in the diagnosis of acute coronary syndrome (ACS). C-reactive protein has been shown to be associated with the development of acute coronary syndrome (ACS), and we have also demonstrated that it has the potential to serve as a biomarker for both the risk and severity of ACS. It is possible to determine the severity of mitral regurgitation (MR) by observing the elevated levels of C-reactive protein, sodium and potassium in the serum.

Limitations

There were no previous studies to compare the relationship between sodium, potassium, and CRP with MR severity, highlighting a lack of prior research on the topic. Citing previous research studies forms the basis of our literature review and helps lay a foundation for understanding the research problem we were investigating.

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