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THE PROGNOSTIC VALUE OF HIGH LEVELS OF (BUN) IN ACUTE MYOCARDIAL INFARCTION PATIENTS

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ABSTRACT

Myocardial infarction is one of the most prevalent diseases around the world and is one of the most common diseases that cause mortality. Therefore, it was necessary to find markers that contribute to determining the prognosis in patients with acute coronary syndrome (ACS), hence the importance of cardiac troponine, ck, ck-mb, creatinine, electrolytes and blood urea nitrogen (BUN) in evaluating the prognosis and providing optimal treatment for patients. In this research, we will study the changes in BUN levels in patients with myocardial infarction and their impact on prognosis. This study included 80 patients and they were divided into two groups, a high-risk group and a low-risk group based on the global registry of acute cardiac events (GRACE score), and successive laboratory tests were made for BUN from admission to discharge. We found that the incidence of BUN elevation was 48.8% on the first day and 55% on the fourth day. We also noticed that a BUN level of more than 20 mg\dl was associated with bad prognosis in short-term follow-up (p-value = 0.001). We found a significant association between the development of cardiac shock and arrhythmias with BUN elevation (p-value = 0.001).

KEYWORDS: Myocardial infarction, BUN elevation.

I. INTRODUCTION

Myocardial infarction is one of the most common causes of death and morbidity around the world, and about 50% of patients with infarction die before reaching the hospital.[1]

Myocardial infarction is defined by the European Society of Cardiology as cardiomyocyte necrosis in a clinical setting consistent with acute myocardial ischemia.[2]

Cardiac ischemia is associated with many pathophysiological changes that can be summarized by three changes: acidosis, lack of energy, and hypoxia.

Myocardial infarction is a part of the acute coronary syndrome and it is divided into infarction with st-segment elevation (STEMI), infarction without st-segment elevation (NSTEMI).

The presentation of patients with ACS is quite varied, so it was important to determine risk factors in order to provide optimal care and treatment. Several models of risk stratifications have been developed such as Global Registry of acute coronary events (GRACE) which can be done when the patient is first admitted to the hospital. GRACE consist of several important risk factors such as blood pressure, heart failure, heart rate, serum creatinine, cardiac arrest during admission, st segment changes and cardiac enzymes,[3] but GRACE does not contain blood urea nitrogen.

The subject of our research is to study the changes in BUN levels and their role in determining the prognosis.

In addition to being used as a marker to assess renal function,[4] BUN can also be used in determining prognosis in patients with ischemia. The elevation of BUN in patients with ACS occurs independently of renal function and glomerular filtration rate as it is reabsorbed under the influence of the sympathetic nervous system from the proximal renal tubules,[5] and under the influence of the renin angiotensin aldosterone system. As a result of this process, angiotensin II stimulates the secretion of antidiuretic hormone (ADH), which in turn increases the reabsorption of BUN in the distal renal

tubules. Also, BUN reflects the oxidative stress condition associated with ischemia, as the increased cellular breakdown under the influence of free radicals increases the degradation of nucleus proteins, especially pyrimidine. This in turn increases ammonia secretion[6] which is converted by the liver into urea through the urea cycle,[7] thus increasing the level of BUN in the blood.

II. OBJECTIVES OF STUDY

There are many studies concerned with the role of cardiac markers (ck, ck-mb, troponin) in determining the prognosis in patients with acute coronary syndrome. However, because of the high cost of these laboratory tests, it was necessary to find a method which is less expensive but has the same prognostic importance. Hence, our goal in this research is to study the blood urea nitrogen changes that occur in patients with acute myocardial infarction and their role in determining the prognosis of myocardial infarction in order to provide them with the optimal care and treatment.

III. MATERIALS AND METHODS

Study Population

The sample of the study included 80 patients, who were admitted to the intensive care unit (ICU) at Tishreen University Hospital with a diagnosis of myocardial infarction, from December 2019 until December 2020. All patients agreed to informed consent to include their data in the research.

Study Design

We performed a prognostic prospective study. A detailed history was taken from the patients, including the onset of chest pain, and cardiac risk factors (smoking, hypertension, and diabetes). Electrocardiograms, titration of cardiac enzymes, and determination of myocardial infarction pattern were done. Then the patients were divided into two groups: 1) Group A, which includes patients whose GRACE score is greater or equal to 128, and we will refer to them as high-risk patients, 2) Group B, which includes patients whose GRACE score is less than 128, and we will refer to them as low-risk patients. We took a blood sample during the first 12 hours of the onset of chest pain, a sample on the fourth day, and a sample on the seventh day. Then we performed a laboratory test of the BUN of each sample. We followed the patients during the hospitalization period and monitored the development of complications (arrhythmias, mechanical complications, cardiac shock).

Inclusion Criteria

STEMI and NSTEMI myocardial infarction patients as defined by the European Society of Cardiology.

Exclusion Criteria

1) Patients with renal insufficiency stage 3, 4, and 5.
2) Patients with severe hemorrhage.
3) Patients on diuretics.
4) Patients on ACE inhibitors and angiotensin receptor blockers before the infarction.
5) Patients who died during the hospitalization from a noncardiac cause.

Data Analysis

The data were analyzed using the Statistical Package of Social Sciences (SPSS) software, version 20. The values were expressed as mean and standard deviation. The independent T-test was performed to compare the mean values between the cases and the controls. A significant result means that the p-value test is < 0.05. The confidence intervals (CI) were reported as 95%.

IV. RESULTS

The sample included 80 patients (51 males, 29 females) of myocardial infarction admitted to ICU at Tishreen University Hospital. The number of patients with STEMI was (50) and the number of patients with NSTEMI was (30) (Table 1). The number of high-risk patients was (41) and the number of low-risk patients was (39). The patients' ages ranged from 37 to 85 years. The median average age is 62. Table 2 shows comparison of the demographic, clinical and biochemical characteristics between patients with high BUN (> 20 mg\dl for men & women) and patients with normal BUN (Table 2). For ease of expression, we will refer to the BUN value in the first 12 hours as BUN1, in the fourth day as BUN2, and in the seventh day as BUN3. The percentage of patients with elevation of BUN on admission was 48.8%, with a mean value of 30.8 ± 3.6, while on the fourth day it was 55%, with a mean value of 33.9 ± 4.1. (table 3)

In the sample population of men who experienced ACS, 32 were diagnosed with STEMI, while in the female group, fewer were diagnosed with STEMI than men, namely 18.

As shown below, 13.75% of the patients died, 27.5% had cardiogenic shock, and 45% had cardiac arrythmias.

Patients with high BUN were older (62 vs. 61, p=0.5) and were significantly more likely to present with hypertension (72.7% vs. 36.1%, P < 0.001) and diabetes (56.8 % vs 22.2 %, P=0.003) but not smoking (56.8% vs 66.7%, p=0.3).

Analysis of major adverse cardiovascular events (MACE) showed that in the high BUN group, a significantly greater proportion of patients experienced mortality (28.2% vs 0%, P=-), cardiogenic shock (51.3% VS 4.9%, P= 0.0001) cardiac arrhythmias (74.4% vs 17.1%, P= 0.0001) and mechanical complication (7.7 % vs 0 % p=-) compared with patients with normal BUN during the first day of follow-up (table 4). The analysis of MACE during follow-up on the fourth day showed that the number of patients who had arrhythmias increased to 33 compared to 29 on the first day. This is due to the occurrence of a second infarction within the hospital that occurred in two patients, and sepsis

acquired within the ICU that occurred in the remaining patients. We also observed an increase in the number of patients who had a cardiogenic shock on the fourth day (22 patients) compared to the first day (20 patients) (table 5).

We studied the correlation between BUN and GRACE risk scores and found that there is a significant positive correlation between BUN and GRACE risk score (P<0.0001).

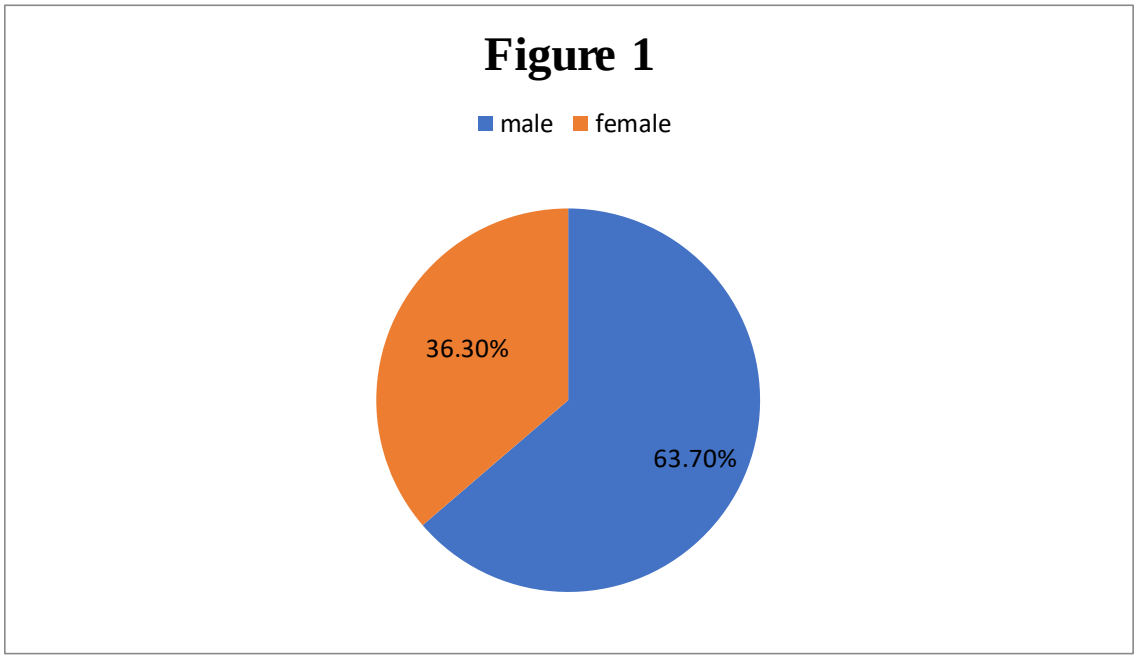

Table (1): Distribution of a sample of 80 patients according to the type of infarction among the acute myocardial infarction patients within the cardiac intensive care unit at Tishreen University Hospital in Lattakia 2019-2020.

MI type	Number	Percent
STEMI	50	62.5%
NSTEMI	30	37.5%
Total	80	100%

Table (2): Demographic differences upon admission between the two groups of acute myocardial infarction patients classified according to the value of BUN within the cardiac intensive care unit at Tishreen University Hospital in Lattakia 2019-2020.

Demographic variables	Blood Urea Nitrogen (BUN)		p-value
	>20mg/dl	<20mg/dl	
Sex (%) **male** **female**	 23(59%) 16(41%)	 28(68.3%) 13(31.7%)	 0.3
Age (year)	62[42 - 85]	61[37 - 82]	0.5
BUN	30.8 ± 3.6	16.1 ± 2.1	0.0001

Table (3): A sample of 80 patients distributed according to the increase in the BUN value according to the follow-up days of the acute myocardial infarction patients within the cardiac intensive care unit at Tishreen University Hospital in Lattakia 2019-2020.

BUN	Follow-up days		
	BUN1	BUN2	BUN3
>20mg/dl	39(48.8%)	44(55%)	44(55%)
<20mg/dl	41(51.3%)	36(45%)	36(45%)

Table (4): Distribution according to complications and deaths occurring between the two groups of acute myocardial infarction patients classified according to the value of BUN upon admission to the cardiac intensive care unit at Tishreen University Hospital in Lattakia 2019-2020.

Complications	Blood Urea Nitrogen (BUN)		p-value
	>20mg/dl	<20mg/dl	
Arrhythmias	29(74.4%)	7(17.1%)	0.0001
Mechanical complications	3(7.7%)	0(0%)	——
Cardiogenic shock	20(51.3%)	2(4.9%)	0.0001
Death	11(28.2%)	0(0%)	——

Table (5): Distribution according to complications and deaths occurring between the two groups of acute myocardial infarction patients classified according to the value of BUN on the fourth day of follow-up within the cardiac intensive care unit at Tishreen University Hospital in Lattakia 2019-2020.

Complications	Blood Urea Nitrogen (BUN)		p-value
	>20mg/dl	<20mg/dl	
Arrhythmias	33(75%)	3(8.3%)	0.0001
Mechanical complications	3(6.8%)	0(0%)	——
Cardiogenic shock	22(50%)	0(0%)	——
Death	11(25%)	0(0%)	——

V. DISCUSSION

Our study showed an important statistical relationship between high BUN and the occurrence of complications in ACS patients with normal renal function and normal glomerular filtration rate.

BUN is an indicator for assessing renal function. Its serum concentration is determined by the balance between elimination and reabsorption, and by the rate at which it is synthesized in the liver through the UREA cycle to eliminate ammonia.

The reabsorption of BUN in the context of cardiac ischemia is mainly the result of two mechanisms. The first mechanism: cardiac ischemia is associated with heart failure (relative or overt) and a decrease in cardiac output, which leads to the stimulation of baroreceptors in the aortic arch and carotid sinus. This in turn leads to the activation of the sympathetic nervous system and increased noradrenaline secretion through nerve endings, which leads to increased reabsorption of BUN with water and salt through the proximal renal tubules.[8]

The second mechanism: heart failure and the decrease in cardiac output are associated with renal hypoperfusion which results in the activation of the renin-angiotensin aldestron system. As a result of this process, the angiotensin II increases the secretion of ADH, which increases the reabsorption of BUN with water through the distal renal tubules and thus the BUN can be considered as a sign of poor Cardiorenal function (Cardiorenal syndrome type I).

The increase in serum BUN not only depends on increased reabsorption, but also on increased synthesis within the liver, as ischemia is associated with the occurrence of oxidative stress and an increase in the production of free radicals. This causes an increase in inflammation and an increase in cellular breakdown, all of which causes an increase in the synthesis of ammonia (by catabolism of pyrimidine). The liver then converts this ammonia into urea via the urea cycle to rid the body of toxic ammonia and thus increases the concentrations of BUN in the blood. This shows that in patients with ACS, BUN can be considered a more important indicator than creatinine in determining the prognosis and mortality.

In this study, we found that there are differences in the values of the BUN elevation between the first and fourth day, as the elevation values were greater on the fourth day. This reflects the accumulated increase in sympathetic secretion and reabsorption, in addition to the increase in urea formation in the liver to get rid of ammonia compared to the first day, while BUN values on day 7 were similar to day 1, and this reflects a progressive descent into sympathetic activation.

In this study we investigated AMI patients (STEMI or NSTEMI) who enrolled in a prospective observational study and found that increased BUN was associated with arrhythmias, cardiogenic shock, and mechanical complications. These hemodynamic disturbances are associated with more sympathetic activation and activation of the renin-angiotensin system and thus more BUN reabsorption. Hence, elevated BUN can be considered an important indicator in providing important information about the prognosis in patients with ACS, thus providing better treatment.

VI. CONCLUSION

Blood Urea Nitrogen (BUN) can be considered as an independent, cheap and effective prognostic indicator in patients with AMI during the in-hospital period, so it can be used in risk stratification in parallel with other biomarkers and scores. Moreover, patients with AMI with high BUN should be monitored closely for cardiovascular events (cardiac arrhythmias, death, cardiogenic shock and mechanical complication), during the in-hospital period.

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