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Prognostic Value of NT-proBNP Concentrations in Patients Attending a Hospital Cardiac Service

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Authors' contributions

This work was carried out in collaboration between all authors. Authors MA, AT and KB designed the study, wrote the protocol and wrote the first draft of the manuscript. Author ZZ performed the statistical analysis. Authors BN, HR and AB managed the analyses of the study. Author AK managed the literature writing and searches. Author IO performed surgical operations. All authors read and approved the final manuscript.

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ABSTRACT

Objective: Measurement of N-terminal pro-brain natriuretic peptide (NT-proBNP) in the assessment of patients with the acute coronary syndrome has appeared to be a useful prognostic marker of cardiovascular risk. The purpose of this study is to determine if the NTpro-BNP could be a biological marker in evaluating the severity of the disease in patients with the acute coronary syndrome (ACS).
Materials and Methods: This study has included 130 patients attending hospital cardiology department (Sétif Central University Hospital (Algeria)), 47 women and 83 men. All were affected by the coronary syndrome. This study was conducted for 5 months. Several tests were used, ECG,

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echocardiography, measurement of NT-proBNP, Homocysteine, C-reactive protein (CRP), Vitamin B9 in addition to biochemical and haematological profiles. Data were analysed using SPSS Version 21.0.

Results: The average age of coronary patients was 63.89 ± 12.68 years, with a high predominance of men (63.8%) compared to women (36.2%). There was a significant positive correlation between NT-proBNP and age, homocysteine, Hs-CRP, urea, creatinine, ASAT, ALAT, LDH, γGT, uric acid and fibrinogen. On the other side, NT-proBNP had a negative correlation with sodium, haemoglobin, creatinine clearance and LVEF. The statistical analysis a grouping patients according to NT-proBNP levels. They were separated into two groups (NT-proBNP ≤900 pg/ml, NT-proBNP>900 pg/ml). Then we correlated all parameters (biochemical, haematological, clinical signs) with the different risk factors).

Conclusion: NT-proBNP is a valuable marker for predicting the severity of coronary artery disease in patients with the acute coronary syndrome.

Keywords: Coronary syndrome; NT-proBNP; hemoglobin; anemia; heart failure.

ABBREVIATIONS

ALAT : Alanine aminotransferase.
ALP : Alkaline phosphatase.
ASAT : Aspartate aminotransferase.
ATP III : Adult Treatment Panel III.
CPK : Creatine Phosphokinase.
CRP HS : C reactive protein hypersensitive.
CBC : Complete blood count
HDL : High Density Lipid.
HGB : Hemoglobin.
HTA : Hypertension Arterial.
LAH : Left Atrial Hypertrophy.
LBBB : Left Bundle Branch Block.
LDH : Lactate Dehydrogenase.
LDL : Low Density Lipid.
LHD : Left Heart Decompensation.
LV : Left Ventricular.
LVEF : Left Ventricular Ejection Fraction.
LVF : Left Ventricle Failure.
LVH : Left Ventricular Hypertrophy.
NSTEMI : Non-ST-Elevation Myocardial Infarction.
RBBB : Right Bundle Branch Block.
RBC : Red Blood Cells.
RHD : Right Heart Decompensation.
RVF : Right Ventricle Failure.
RVH : Right Ventricular Hypertrophy.
STEMI : ST-Segment Elevation Myocardial Infarction.
UA : Uric Acid.

1. INTRODUCTION

According to the World Health Organization (WHO), coronary heart disease is the leading cause of death in developed countries and the second cause in middle and low-income countries. Lifestyle and environmental factors play an important role in coronary artery disease (CAD) development [1]. Coronary artery disease is common in general population and the single most common cause of death worldwide. Over 7 million people die annually, accounting for 13.2% of all deaths [2].

Acute coronary syndrome (ACS) is often the first presentation of coronary artery disease (CAD), and the leading cause of mortality and morbidity in many parts of the world [3]. Patients who survive after the acute phase of myocardial infarction remain at risk of recurrent cardiac events, including sudden death. In recent years, increased attention was focused on various circulating biologically active substances, collectively known as plasma biomarkers, and their utility in coronary artery disease (CAD) and heart failure (HF) prognosis.

Neurohormonal activation of N-terminal pro-B-type natriuretic peptides (NT-proBNP) remains one of the established markers for the detection and evaluation of the heart failure severity and is considered as a prognostic factor of disease progression in coronary artery disease patients. NT-pro-BNP is an essential biomarker in patients with the acute coronary syndrome (ACS) as it is a marker of myocardial cell necrosis and a strong predictor of morbidity and mortality [4].

The purpose of this study is to determine the usefulness of NT pro-BNP as a biological marker, in morbidity severity assessment in patients with the acute coronary syndrome (ACS).

2. MATERIALS AND METHODS

2.1 Study Population

A number of 130 patients were enrolled in this study. They were divided into 47 women and 83

men, aged from 26 to 93 years old, attending the Heart Disease Clinic at Sétif CHU hospital, within 5 months (from 12/2015 to 05/2016). 130 patients with the acute coronary syndrome who attended set if CHU hospital from Dec 2015 to May 2016 were enrolled in this study. Of these 83 (63.84%) were males and 46 (36.16%) were females. Their ages ranged from 26 to 93 years. All patients were examined by expert cardiologists, their clinical features.

Age, length, weight, body mass index (BMI), waist size, and classical coronary risk factors (smoking, diabetes, hypertension, dyslipidaemia, obesity, alcohol, faintness, presence or absence of metabolic syndrome NCEP/ATP IIIclassifications, and activity) and CAD family history were obtained in an interview using a structured questionnaire. Echocardiography was done in all patients.

2.2 Samples Collection

Peripheral blood was sampled from patients in a fasting state the morning following the admission day, then collected in 4 tubes: EDTA, heparin, citrate and dry tube. The samples were centrifuged in the cold (speed = 3000 r/min) to perform the appropriate analysis for each tube:

- EDTA: HbA1c, blood count formula.
- Heparin for biochemical tests: blood sugar, HDL cholesterol, LDL cholesterol, Triglycerides, Total Cholesterol, urea, creatinine, GGT, ASAT, ALAT, ALP, Bilirubin, Na, Ca, Cl, Iron, LDH, CPK, Uric Acid.
- Dry tube for: NT-pro BNP, troponin I, CRP hs, vitamin B9.
- Citrate tube for: fibrinogen.

2.3 Methods

2.3.1 Determination of NT-proBNP

We used automata to do analyses. IMMULITE 2000 allowed quantification of NT-proBNPin serum and determination of troponin I, Vitamin B9, CRP hs and homocysteine. ADVIA® type auto analyser and MEDONIC 16 were used to determine the other biochemical and haematological parameters.

2.3.2 Cardiac tests

The electrocardiogram permitted to classify the patients into 9 groups: NSTEMI, STEMI, LVH, RVH, LAH, LBBB, RBBB, LHD, RHD. The Echocardiography was performed for all patients, by a professional sonographer in a quiet room at constant temperature. M-dimensional echocardiography was recorded for the left ventricular ejection fraction (LVEF).

2.4 Statistical Analysis

Data were processed by the EXCEL® 2007 and using the SPSS V.21.0.softwares. Results were expressed as mean ± standard deviation for continuous variables, and percentages for discrete variables. The correlation between NT-proBNP and different other parameters were calculated. The normality test verified the normal distribution of continuous variables. Confidence intervals were fixed at 5% risk. Comparison of discrete variables percentage and continuous variables mean was performed with the using chi-square test and t-test respectively. The results are considered statistically significant from a value of $p < 0.05$.

3. RESULTS

The different biochemical and haematological parameters varied considerably between patients (Table 1).

The significance of the data shown above was analysed by Pearson correlation statistics to explain the different discrepancies (Table 2).

The association of the NT-proBNP with the different clinic signs was somewhat discordant (Table 3).

4. DISCUSSION

NT-proBNP predicts mortality in patients with heart failure, as high levels of it reflects left ventricular dysfunction. Also, it predicts mortality in STEMI patients. In patients with a stable CAD, NT-proBNP provides better prognostic information that obtained from clinical risk markers and degree of left ventricular dysfunction. The prognostic value of NT-proBNP has also been investigated in several NSTE-ACS cohorts. They show a consistent association between biomarker levels and the risk of death [5]. In unstable angina, NT-proBNP is considered as an effective marker of the damage produced by cardiac ischaemia. The coronary disease is as severe as the levels of NT-proBNP are high. In addition, in the case of acute coronary syndromes, NT-proBNP had an immuno-modulating role and offered important information for the prognosis of the disease [6].

Table 1. Epidemiological association between NT-proBNPthresholds and other biochemical parameters

Biochemical parameters	Global	NT-proBNP ≤ 900 (pg/ml) N = 42	NT-proBNP> 900 (pg/ml) N = 88	ki-square P value
Age (years)	63.89± 12.68	59.9 ± 12.40	65.7 ± 12.44	0.014*
BMI (kg/m^2)	26.46± 4.74	27.49 ± 4.38	25.96 ± 4.84	0.038*
Troponin I (ng/ml)	17.20± 58.46	6.51 ± 15.94	22.29 ± 69.75	0.077
Homocysteine (µmol/l)	20.97± 10.34	19.70 ± 8.78	21.57 ± 11.00	0.473
Vitamin B9 (ng/ml)	14.24 ± 4.83	14.31 ± 5.13	14.20 ± 4.71	0.841
Hs-CRP (mg/l)	39.52± 37.83	27.20 ± 31.89	45.40 ± 39.17	0.003*
Glycemia (g/l)	1.58 ± 0.70	1.59 ± 0.59	1.57 ± 0.74	0.663
LDL (g/l)	0.94 ± 0.40	0.95 ± 0.37	0.93 ± 0.40	0.790
HDL (g/l)	0.36 ± 0.14	0.34 ± 0.11	0.37 ± 0.14	0.767
Cholesterol (g/l)	1.60 ± 0.42	1.62 ± 0.39	1.58 ± 0.43	0.542
Triglyceride (g/l)	1.49 ± 0.78	1.62 ± 0.72	1.42 ± 0.80	0.067
Urea (g/l)	0.59 ± 0.50	0.48 ± 0.32	0.63 ± 0.55	0.160
Creatinine (mg/l)	12.39± 16.23	7.67 ± 5.36	14.64 ± 19.00	0.007*
Creatinin clearance (ml/min)	174.33±248.36	200.48 ± 261.91	161.84 ± 242.15	0.009*
ASAT (U/l)	101.67±259.40	42.03 ± 37.85	130.12 ± 310.74	0.002*
ALAT (U/l)	47.89±151.96	25.12 ± 16.04	58.76 ± 183.70	0.039*
ALP(U/l)	78.83± 49.53	73.33 ± 36.12	81.44 ± 54.78	0.253
Gamma GT (U/l)	44.12± 40.96	33.71 ± 36.33	49.08 ± 42.29	0.015*
Total Bilirubin (mg/l)	6.33 ± 4.19	5.49 ± 2.55	6.72 ± 4.74	0.463
Na (mEq/l)	137.07± 5.36	138.77 ± 3.94	136.25 ± 5.75	0.014*
K (mEq/l)	4.41 ± 3.56	5.01 ± 6.17	4.12 ± 0.73	0.848
Cl (mEq/l)	1.93 ± 0.50	100.80 ± 4.86	100.95 ± 10.27	0.537
Iron (mg/l)	0.67 ± 0.47	0.74 ± 0.43	0.64 ± 0.48	0.130
Phosphor (mg/l)	39.54± 15.09	37.17 ± 13.79	40.67 ± 15.62	0.170
LDH (U/l)	426.59±354.88	267.95 ± 153.08	502.30 ± 397.17	0.000**
CPK (U/)	380.81±795.85	189.88 ± 328.10	471.93 ± 928.66	0.001*
Uric Acid (mg/l)	73.84± 52.52	63.71 ± 23.38	78.67 ± 61.31	0.196
HGB (g/dl)	13.50 ± 2.19	13.96 ± 1.90	13.27 ± 2.29	0.126
Fibrinogen (g/l)		3.24 ± 0.90	3.91 ± 1.21	0.003*
LVEF %		> 50 % 29 (22.3)	31(23.8)	
		< 50 ù 13 (10.0)	57(43.8)	0.000**

**: p < 0.05 / **: p < 0.01*

Table 2. NT pro-BNP pearson correlation with the different significant quantitative parameters of our population

Quantitative parameters	Corrélation NT-proBNP(pg/ml)	
Age (years)	r = 0.272**	p = 0.002
Homocysteine (µmol/L)	r = 0.281**	p = 0.001
Hs-CRP (mg/L)	r = 0.194*	p = 0.027
Triglyceride (g/L)	r = - 0.199*	p = 0.023
Urea (g/L)	r = 0.383**	p = 0.000
Creatinine (mg/L)	r = 0.426**	p = 0.000
ASAT (U/L)	r = 0.191*	p = 0.030
ALAT (U/L)	r = 0.222*	p = 0.011
Na (mEq/L)	r = -0.225*	p = 0.010
K (mEq/L)	r = 0.201*	p = 0.022
LDH (U/L)	r = 0.203*	p = 0.021
Uric Acid (mg/L)	r = 0.197*	p = 0.025
HGB (g/dL)	r = - 0.445**	p = 0.000

**: p < 0.05/ **: p < 0.01*

Table 3. Association of NT-pro-BNP and the different clinic signs, and cardiac results

Qualitative parameters		NT-proBNP ≤ 900 (pg/ml) N (%)	NT-proBNP> 900 (pg/ml) N (%)	chi-square P value
Dyspnea	Absence	28 (21.5)	55 (42.3)	0.644
	Presence	14 (10.8)	33 (25.4)	
Chest pain	Absence	4 (3.1)	16 (12.3)	0.201
	Presence	38 (29.2)	72 (55.4)	
Palpitations	Absence	38 (29.2)	74 (56.9)	0.324
	Presence	4 (3.1)	14 (10.8)	
syncope	Absence	40 (30.8)	84 (64.6)	1.000
	Presence	2 (1.5)	4 (3.1)	
Faintness	Absence	42 (32.3)	86 (66.2)	1.000
	Presence	0 (0.0)	2 (1.5)	
LVF signs	Absence	36 (27.7)	68 (52.3)	0.260
	Presence	6 (4.6)	20 (15.4)	
RVF signs	Absence	41 (31.5)	81 (62.3)	0.436
	Presence	1 (0.8)	7 (5.4)	
DVT signs	Absence	42 (32.3)	85 (65.4)	0.551
	presence	0 (0.0)	3 (2.3)	
Electrocardiogram data				
NSTEMI		14 (10.8)	25 (19.2)	0.939
STEMI		21 (16.2)	46 (35.4)	
LVH		3 (2.3)	4 (3.1)	
RVH		0 (0.0)	1 (0.8)	
LAH		0 (0.0)	1(0.8)	
LBBB		1 (0.8)	2 (1.5)	
RBBB		1 (0.8)	2 (1.5)	
DLH		2 (1.5)	57 (43.8)	
DRH		0 (0.0)	4 (3.1)	
Echocardiography data				
LVEF %	> 50	29 (22.3)	31 (23.8)	0.000**
	< 50	13 (10.0)	57 (43.8)	

***: p < 0.01*

Data are expressed as n (%), p values are from an independent-samples test ki-square

In patients with congestive heart failure, elevated levels of BNP and NT-proBNP have proved to be highly predictive for an adverse outcome. Recently, several clinical and experimental studies have shown that both neuro-hormones are also released in response to myocardial ischemia. Furthermore, other data showed that in patients with ACS, BNP and NT-proBNP provide independent prognostic information for mortality irrespective of the troponin status [7]. The potential for Natriuretic Peptides to guide therapy in HF patients is high due to the strong prognostic associations [8].

Other studies found that the plasma NT-proBNP levels were significantly higher when ACS occurred, so plasma NT pro-BNP may contribute to the early diagnosis of ACS. However, at present, troponin was still commonly used in clinical ACS diagnosis, and it was not possible to achieve an early diagnosis of ACS. NT-proBNP levels are closely related to the severity of heart failure and became objective indicators in the diagnosis of heart failure and dyspnea. It has also been used in evaluating the effect of heart failure treatment [9].

Elder patients who are affected by acute coronary syndrome face higher risks, and this may be due to the greater extent of atherosclerosis in the coronary arteries and peripheral vessels, as well as many other diseases that patients may suffer from at the same time [10]. In the present study, the results showed that the plasma concentration of NT pro-BNP almost doubled per age decade despite sex or normality status. This probably reflects an increased myocardial mass, and a possible reduction in the renal clearance of natriuretic peptides with ageing which is not entirely reflected by the plasma creatinine concentration [11,12]. Moreover, aged people who are affected

by the relaxation of the ventricular heart muscle which leads to high pressure end-diastolic and increased secretion of NT-pro BNP symptoms are also affected by the degradation of renal function and fluid overload [10].

Inflammation of coronary arteries is probably a significant component which causes changes in vessel wall morphology. It has been proposed that inflammation of arteries results in the elevated production of cytokines, especially interleukin 6, and activation of clotting factors increased platelet aggregation, and smooth muscle cell proliferation. Recent work indicates that CRP can be produced within the vascular smooth muscle of coronary arteries. This production may lead to the expression of several mediators of the atherothrombotic process [13].

Nayak et al. (2015) claimed that NT-pro-BNP and hs-CRP from initial evidence, has started to emerge as a deciding element of diagnosis and therefore detection for cardiovascular outcomes. Several studies demonstrated an association between CRP and various cardiovascular diseases, namely atherosclerosis, hypertension, and chronic HF. The serum concentrations of CRP are increased primarily in patients with heart failure and those with severe acute heart failure (HF) [14].

In addition, low levels of BNP can also affect BMI through its effects on mitochondrial genesis. As a result, obesity can be both a cause and a consequence of low BNP levels. The actions of BNP in promoting mitochondrial biogenesis, increasing oxygen consumption, and fat oxidation explain how lower levels of BNP might lead to the variations in BMI and blood lipids, these physiological and biochemical pathways provide potential biological explanations for the associations between low levels of NT-pro-BNP with higher BMI and blood lipids.

Hypertension affects a billion individuals worldwide and represents a substantial risk factor for cardiovascular disease. Because the relationship between blood pressure and cardiovascular risk is continuous, even small increments in blood pressure could be at risk [15]. In the other side, plasma NT-pro-BNP appeared as a strong predictive marker in hypertensive patients. This study contributes to the use of NT-pro-BNP as an easy and powerful predictive marker that could be used in every hypertensive patient to enhance the risk stratification.

Identification of depressed left ventricular function may improve prevention and treatment of progression to symptomatic heart failure. Increased levels of the natriuretic peptide are linked with depressed LVEF in the general population including aged adults. Elevated N-terminal pro–B-type natriuretic peptide (NT-pro-BNP) levels are also linked with an increased risk of new-onset heart failure in general population studies [16]. NT-pro-BNP is a well-known marker of ventricular dysfunction and heart failure in patients with acquired heart disease.In contrast, the study of Corteville et al. (2007) indicates that NT-pro-BNP levels lower than 100 pg/ml effectively ruled out ventricular dysfunction in patients with coronary heart disease (CHD). Although elevated NT-pro-BNP levels do not necessarily identify ventricular dysfunction, They could identify patients with CHD with a probability of 47% to have a ventricular dysfunction. This may lead to choosing a specific management because Angiotensin-converting enzyme inhibitors and β-blockers should already treat patients with CHD. NT-pro-BNP levels higher than 500 pg/mL would encourage to prescribe these medications.

Mohammed et al. (2013), noted that lower serum Na was more common among patients with severe HF and higher NT-proBNP levels, and they found a significant interaction between serum Na and NT-proBNP levels [17]. At last, they confirmed that hyponatremia is associated with adverse outcome in patients with acutely decompensating heart failure; however, the prognostic value of low Na is mainly clear in those with a more pronounced elevation of NT-proBNP concentrations. In addition, Lu et al. (2017) explained that hyponatremia is a common disorder in patients with either acute or chronic heart failure, which caused mainly by impaired water excretion instead of sodium depletion. The underlying pathophysiology may involve an increase of non-osmotic release of arginine vasopressin (AVP) attributed to baroreceptor activation and decreased distal renal tubular flow associated with compromised glomerular filtration.

Recently, a number of studies have reported an association between the uric acid (UA) level and cardiovascular risk factors or adverse cardiovascular outcomes. Elevated UA levels were also associated with HF. A high serum UA level was an independent prognostic marker in patients with moderate to severe chronic heart failure (CHF) [18].

In the present study, we found a positive correlation among NT-proBNP levels and uric acid concentrations. This may be explained by Park et al. (2017) study, which indicates that patients with a high UA or high NT-ProBNP level showed a poorer prognosis. The combination of the UA and NT-ProBNP levels provided incremental prognostic value than conventional risk factors. Therefore, the combination of UA and NT-ProBNP levels appears to be a more powerful prognostic indicator for short-term clinical outcome in the setting of AHF, and risk stratification of patients according to the UA and NT-proBNP levels is possible.

Anemia at admission and during hospitalisation is common in acute coronary syndrome (ACS) patients, and these patients are reported to have a poor prognosis. In addition, the need for a blood transfusion due to anaemia in the setting of ACS is associated with higher short-term mortality. Furthermore, a low baseline haemoglobin level in ACS patients has been found to be an independent predictor of the risk of in-hospital major bleeding and risk of death and myocardial infarction at 30 days [19]. In the absence of clinical HF, patients with anaemia have elevated levels of natriuretic peptides, suggesting that anaemia may lead to subclinical ventricular dysfunction [20]. In the present study, we found a profoundly negative correlation between NT-proBNP and haemoglobin concentrations. Sulaiman et al. (2012) study demonstrated that ACS patients with anaemia were more likely to be older, female, and associated with co-morbidities like diabetes, hypertension, chronic renal failure, and stroke, thus identifying a high-risk population with poor hematopoietic reserve. Moreover, Desai et al. (2017) confirmed our results. They found that anaemia was inversely associated with circulating levels of NT-proBNP in 809 outpatients with known coronary heart disease (CHD) and no clinical history of HF. The association between anaemia and elevated NT-pro BNP was considerably attenuated after accounting for greater systolic dysfunction, diastolic dysfunction, CHD severity, inflammation, and kidney dysfunction in patients with anaemia. Adjustment for these variables explained approximately 2/3 of the association. However, even after adjustment for all of these factors, anaemia remained independently predictive of NT-proBNP.

The relation between anaemia and HF may be caused by activation of the renin-angiotensin-aldosterone system, hyperactivity of the sympathetic nervous system, or poor oxygen carrying capacity, resulting in an increased workload on the heart. Three primary factors determine the amount of oxygen delivered to an organ: blood flow and its distribution, the blood's oxygen-carrying capacity, and oxygen extraction. When the oxygen-carrying capacity is diminished as in chronic anaemia, the primary hemodynamic mechanism that compensates is an increase in cardiac output, mediated by lower after-load and consequentially increased preload. Tissue hypoxia enhanced nitric oxide activity, and lower blood viscosity which caused vasodilation and decreased vascular resistance. In response, venous return, and left ventricular filling increase, this results in an increased left ventricular end-diastolic volume and maintenance of high stroke volume [19].

In the study of Hogenhuis et al. [21], which have studied the influence of both anemia and renal function on BNP and NT-proBNP levels in a large group of hospitalized HF patients, found that elevated levels of BNP were independently related to renal dysfunction, and, although not directly compared, this relation seemed less powerful than the relation between renal dysfunction and NT-proBNP. This difference may be explained by differences in kidney clearance. NT-proBNP is probably mainly cleared from the blood by the kidneys, while BNP is thought mainly cleared by neutral endopeptidases and natriuretic peptide clearance receptors. This implies that the influence of renal dysfunction should be more pronounced on NT-proBNP levels compared to BNP levels. The most obvious reason for the independent associations of anemia with BNP/NT-proBNP levels is that anemia results in elevated plasma volume independent of severity of HF. Since BNP and NT-proBNP are released in response to ventricular plasma overload it is conceivable that BNP and NT-proBNP levels are higher in anemic HF patients compared to non-anemic HF patients. Additionally, patients with anemia and renal dysfunction showed higher BNP and NT-proBNP levels, compared to anemic patients without renal dysfunction. This can be explained that renal dysfunction was found to be a major cause of anemia in HF patients, mediated by an erythropoietin production deficiency in the kidneys.

Liver enzymes γ-gamma-glutamyltransferase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline

phosphatase (ALP) are commonly used as markers of liver dysfunction. Over the past decade, these enzymes have gained great interest as emerging markers for cardiovascular risk. Despite a lack of obvious etiological relationships with cardiovascular disease (CVD) these remain unresolved. Several studies have observed associations of these markers of liver dysfunction with the risk of CVD, others have shown no association at all [22]. In the present study, we found a positive correlation between NT-proBNP and liver enzymes (ASAT, ALAT, GammaGT). Lee et al. in their review indicates that Aminotransferase (ASAT, ALAT) can be elevated in certain non-hepatic diseases. Obviously, ASAT is one of the cardiac enzymes whose elevation can be seen in cardiac conditions such as ischemic and congestive heart failure.Recently, several reports correlated elevated GGT with increased mortality. Compared with healthy populations with normal GGT, those with increased GGT had higher mortality from liver disease, cancer, and diabetes, as well as cardiac disease.

Many epidemiological studies and several meta-analyses have reported that elevated plasma fibrinogen level is associated with coronary artery disease, stroke and other adverse cardiovascular events [23]. In the present study, we found a highly significant among fibrinogen concentrations and NT-proBNP thresholds. Yan et al. study [22], explained the major role of fibrinogen, demonstrating that fibrinogen plays a vital role in various pathophysiological processes interrelated with inflammation and atherogenesis. Fibrinogen is a major acute phase reactant and a ligand for intercellular adhesion molecules controller that enhance monocyte and leukocyte adhesion to endothelial cells. On receptor binding of the integrin leukocyte, fibrinogen facilitates chemotaxis essential for inflammatory response. Fibrinogen also stimulates the mononuclear cell expression of pro-inflammatory cytokines, such as interleukin-1β and tumor necrosis factor-α, which induces nitric oxide-induced negative inotropic effects and apoptosis of cardiac myocytes in experimental animal models. Upon binding to endothelial cells, fibrinogen also causes the release of vasoactive mediators and modulates the permeability of endothelial cells and migration, in addition to promoting the proliferation of muscle smooth cells, foam cells and platelets atheroma formation.

5. CONCLUSION

According to our data and previous similar studies, it seems that the NT-proBNP is a valuable marker for predicting higher incidence of heart failure in acute coronary syndrome. It is highly correlated with the majority of parameters in patients with the acute coronary syndrome. However, it is important to note that this correlation may be influenced and suffered from interference by several other factors such as age, sex, obesity, anemia, hyponatremia, in addition to liver, renal and left ventricular dysfunction, which may affect its release to the bloodstream and elimination.

Further studies are needed to better define the clinical applications of BNP and NT-proBNP, to evaluate a strategy of making NT-proBNP results available to primary care physicians, in order to help for optimal clinical decision, which might predict severe complications including heart failure.

CONSENT

As per international standard or university standard, the patients' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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