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Relation of serum of N-terminal pro-brain natriuretic peptide and echocardiographic parameters with age in *acute coronary syndrome* patients

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***Abstract*---**Background: B-type natriuretic peptide has been used as a biological marker for prognosis in patients with acute coronary syndrome (ACS). *Acute Coronary* Syndrome is one of the commonly diagnosed life threatening condition as of now. *Aim:* To estimate the serum level of N-terminal pro-Brain natriuretic peptide levels in Acute coronary syndrome. Also to find the association of serum *NT-pro-BNP* levels *and echocardiographic parameter* in *ACS* patients with age. *Materials and Methods:* 70 patients of age group between 25 to 84 of both sexes who got admitted within 24 hours after onset of symptoms and diagnosed as Acute Coronary at Baghdad Hospital medical city during the period of November 2020 to August 2021). *The study patients were divided into four quartiles ages.* The levels of NT-Pro BNP was measure in the *blood with NT-Pro BNP Elisa Assay kit.* Results: This study included 70 patients with means of age was (59.77±11.45) years the control group included 20 healthy persons with mean age (34.47±12.58) years and ranged from (20-58) years. Patients mean age was significantly higher than control group mean age (P-value =0.0149). There were non-significant difference in mean (±SEM)value of serum NT-PRO BNP concentrations, diameter of left atrium, deceleration time and ejection fraction among quartile groups, (P-value >0.5). There were significant difference in mean (± SEM) values of E/e among quartile groups, (P-value=0.041). There was highly significant difference in mean (± SEM) values of isovolumic relaxation time among quartile groups, (P-value=0.011). Conclusion: NT-PRO BNP was a useful biochemical marker in the diagnosis`of ischemia, age-related differences in natriuretic peptides may include both increased secretion secondary to structural changes in the heart, and decreased clearance.

***Keywords*---**Acute Coronary Syndromes, *NT-pro BNP, Age.*

Introduction

B-type natriuretic peptide (BNP) is a peptide consisting of 32 amino acids produced by the myocytes as a prohormone. It is released in response to ventricular dilatation and pressure overload, in its active form after peptidase degradation, into the cardiovascular system.[1] BNP levels are increased after myocardial infarction and high levels are related to an increased risk of adverse events. [2]. Atherosclerosis is the ongoing process of plaque formation that involves primarily the intima of large and medium-sized arteries; the condition progresses relentlessly throughout a person's lifetime, before finally manifesting itself as an acute ischemic event. Several coronary risk factors influence this process, including hypercholesterolemia, hypertension, diabetes, and smoking.[2-4]

Materials and Methodology

This study is conducted among 70 patients of age group between 30 to 84 of both sexes who got admitted within 12 hours after onset of symptoms and diagnosed as Acute Coronary Syndrome (STEMI, NSTEMI & Unstable Angina) in Baghdad Medical College &medical city Hospital, during the period of November 2019 to August 2021 Laboratory Investigations includes blood urea serum creatinine to rule out frank renal failure. Other investigations include serial ECG monitoring, Echocardiography, blood levels of Troponin T Within 12 hours of the onset of symptoms, the levels of NT-Pro BNP were measure in blood with Rapid NT-Pro BNP Assay kit. Description of the NT-pro BNP Rapid Assay Kit: The strips are coated with canine antibodies to human NT pro terminal end of brain Natriuretic peptide. It is a semi quantitative assay and it gives the measurement as 500pg/ml. Values below 100pg/ml was considered as minimal or insignificant and values above 100 pg/ml considered significant. Significant values in the range of 100-500pg/ml is taken as moderately elevated and values above 500pg/ml were taken as moderately elevated.

Results

Clinical data

This study included 70 patients with mean±SD of age was (59.77±11.45) years ranged from (25-84) years divided into two groups: Male group included 52(74.3%) patients, and female group included 18 (25.7%) patients. The control group included 20 healthy persons with mean age (34.47±12.58) years and ranged from (20-58) years, divided into two groups male group included 10 (50%) persons and female group included 10 (50%) persons, table(1),(2). patients mean age was significantly higher than control group mean age (P-value =0.0149). There was a significant increase in the frequency of ACS among males in comparison to females (P-value =0.0027).

Table (1) Frequency distribution of total study sample by age

	Control	patients	P-value
Mean± SD	34.47±12.58	59.77±11.45	0.0149 **
SE	1.49	1.36	--
Min	20	25	--
Max	58	84	--
C.V%	37.6089	19.48	--

Table (2) Frequency distribution of total study sample by gender

Sex	Control		patients	
	No.	%	No.	%
Male	10	50	52	74.3
Female	10	50	18	25.7
Total	20	100	70	100
P-value	---	1.00 NS	---	0.0027 **

Biochemical markers in Acute Coronary Syndrome (ACS) patients and control group

Serum level of NT-PRO Brain Natriuretic Peptide (NT-PROBNP), was compared between the patients group and the control group using analysis of variance (ANOVA) and t-test of significant as in table (3). The patients with ACS were found to have significantly higher mean (± SEM) value of serum NT-PROBNP concentrations (p=0.0144) as compared with mean (± SEM) value of serum control group,

Table (3) Comparison between patients & control according to biochemical marker.

Group	No.	NT-PROBNP (ng/L)
Patients	70	203.95 ± 21.43 203.95 ±179.22
Control	20	107.79 ± 4.24 107.79 ±18.92
T-test value P-value	--	34.782 ** 0.0144

- Results expressed as Mean (+ SEM).
- Results expressed as Mean (± SD).

Age

The table (4) shows effect of age grouping on biochemical parameters and echocardiographic findings, the study patients were divided into four quartiles. There were non-significant difference in mean (± SEM)value of serum NT-PRO BNP concentrations, diameter of left atrium, deceleration time and ejection

fraction among quartile groups, (P-value >0.5). There were significant difference in mean (± SEM) values of E/e among quartile groups, (P-value=0.041). There was highly significant difference in mean (± SEM) values of isovolumic relaxation time among quartile groups, (P-value=0.011).

Table (4) Effect of age grouping on biochemical markers & echocardiographic Finding.

Parameters	Age group (year) Mean ± SEM				P-value
	Quartile1 30-40 No.=3	Quartile2 41-50 No.=11	Quartile3 51-60 No.=26	Quartile4 >60 No.=29	
NT-PRO BNP(ng/L)	150.11± 43.54	203.69± 70.23	182.78± 25.57	225.51± 38.38	0.799 NS
LAD: Left atrium diameter (cm)	3.614± 0.24835	3.78± 0.15	3.49± 0.12	3.69± 0.12	0.514 NS
E/e	4.67± 0.66	11.53± 1.74	8.97± 0.51	9.79± 0.70	0.038*
IVRT:Isovolumic relaxation time (ms)	148.67± 40.71	73.46± 4.98	86.85± 4.90	89.69± 4.74	0.001**
DT: Deceleration time (ms)	219.01± 35.23	182.28± 28.80	174.24± 13.05	212.69± 11.47	0.193 NS
EF%:Ejection fraction	46.01± 6.65	48.72± 3.26	49.81± 2.36	50.28± 1.941	0.921 NS
* (P≤0.05), ** (P≤0.01), NS: Non-significant.					

Statistical Analyses

SPSS version 16 was used in analysis of the data. The cardiac markers were expressed as mean± standard errors. ANOVA tests were used to compare between different cardiac markers. A p-value less than 0.05 were considered statistically significant.

Discussion

Population-based investigations have reported age-related increases in BNP levels in individuals without cardiovascular, renal or pulmonary disease or diabetes as well as normal LV systolic and diastolic function.[6,7] In the present study, the majority of patients who developed UA and AMI were above the age of 40 years and there was a significant increase in the frequency of IHD with increasing age, the mean age (years) for patients was (59.77±11.45) table(1). This result agree with a study of Mackness et al. (2008) who stated that as you get older, your risk for atherosclerosis increases.[8] Atherogenesis was considered with distinct chronologic phases. The first phase, initiation occurs all too frequently during childhood or adolescence, then the nascent lesion which enters a phase of progression, that generally considered to occur during young adulthood through middle life. Ultimately, atherosclerotic disease becomes manifested with either

chronic, stable symptoms or thrombotic complications such as acute myocardial infarction or ischemic stroke. Traditionally, the latter phase of atherothrombosis, complication occurs in the middle-age or in elderly individuals .[9]

Patients mean age was higher than control mean age, theoretically patients mean age must be same as control mean age, but practically is impossible to find old age persons without thyroid disease, heart disease, kidney disease, pulmonary disease, diabetes, inflammatory disease, liver disease and arthritis together.

It's also found that the frequency of male patients group were (74.3%) patients, and female group were (25.7%) patients, table (2). So there was a significant increase in the frequency of MI and UA among males in comparison to females, these results agree with the study reported by Villar et al. (2008) who found greater incidence of CVD in men and postmenopausal women compared with premenopausal women implies a vasoprotective phenotype of females, which may be influenced by sex hormones. These hormones, particularly estrogen, have modulator effects on the endothelium and circulating cells that have been implicated in vascular inflammation and in the development of CVD. [10]

The present study result showed significant difference in mean±SE value of serum NT-PROBNP levels among quartiles age groups, explanations have been offered for this association, including a higher prevalence of subclinical cardiac dysfunction in the elderly,[11] this result agree with following studies:
Seon Gyu Choi et al.[12] reported that: NT-proBNP concentrations of older patients were significantly higher than those of young patients. Fazlinezhad et al.[13] reported that : slight positive relation between BNP levels of AMI patients and age (P = 0.01, r = 0.39). A striking increase in mean and upper centile values for NT-proBNP with age has been reported in healthy volunteers. After multivariate adjustment, a 10 year increase in age was associated with a 1.4-fold increase in pro-peptide concentration.[14] In animal studies, an increase in natriuretic peptide gene expression has been documented with advancing age.[15] Furthermore, the increase in natriuretic peptide concentrations with age may reflect a higher prevalence of subclinical cardiac disease in healthy older people. Of all the major clinical predictors such as age, admission symptoms of HF, parameters related to the infarct size, including biochemical measurements (maximal CK-MB activity, maximal creatinine and CRP concentrations) and echocardiographic assessments, the differences among three BNP groups were present only according to age, the time from the start of symptoms to admission, TIMI Risk Score and LVEF. Plasma BNP, serum creatinine concentration, LVEF and age were predictive only in univariate analysis. It is worth noting that even BNP was not an independent predictor of mortality. Based on the previous reports, these parameters are known to be strong and independent predictors of mortality in patients with HF and coronary artery disease, including acute phase of MI [16]. Agnieszka et al.[17] reported that only age finally became an independent risk factor: in multivariate analysis neither BNP, creatinine concentration, nor LVEF were predictive. The mechanisms for age-related differences in natriuretic peptides are also not fully understood, but may include both increased secretion secondary to structural changes in the heart, and decreased clearance.[18] decreased clearance of natriuretic peptides in elderly patients without underlying renal dysfunction,[19] and less effective no renal clearance mechanisms such as platelet-

associated clearance receptors.[20] Additionally, animal studies suggest an age-related increase in expression of genes coding for natriuretic peptides.[21]

Conclusion

N-terminal pro-Brain natriuretic peptide represents a biomarker for left ventricular dysfunction and enlargement as well as for myocardial ischemia, age-related differences in natriuretic peptides may include both increased secretion secondary to structural changes in the heart, and decreased clearance.

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