

# N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE (NT-PROBNP) SERUM CONCENTRATIONS IN APPARENTLY HEALTHY BOSNIAN WOMEN

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## ABSTRACT

Brain natriuretic peptide (BNP) is a cardiac hormone secreted predominantly from the ventricles. This hormone is produced as pre-prohormone BNP (pro BNP), then cleaved by corine to biologically active 32-aminoacid BNP and non-biologically active N-terminal-pro brain natriuretic peptide (NTproBNP). NTproBNP has been found to be a useful marker for the diagnosis of heart failure and left ventricular systolic dysfunction. Recent studies showed that concentration of BNP and NTproBNP predict cardiovascular disease in apparently healthy individuals but their full screening characteristics are not firmly established. As NTproBNP serum concentration is altered by numerous factors there are also interindividual variations in NTproBNP values.

There are no previous results for Bosnian population so the aim of this study was to assess normal range of NTproBNP serum concentrations in apparently healthy women using electrochemiluminescence immunoassay (Elecsys, Roche Diagnostic). A group of 45, healthy females, aged 39,19 ( $\pm 6,62$ ), were enrolled in this study. Mean serum concentration of NTproBNP was 60,32 ( $\pm 36,25$ ) pg/ml, with the range of 112,60 pg/ml (minimum-maximum: 13,6-126,00 pg/ml).

We conclude that NTproBNP serum concentration in apparently healthy Bosnian women was not different from the average values of NTproBNP obtained on European population. Thus, we suggest that the NTproBNP serum upper cut off values measured by using electrochemiluminescence immunoassay "ECLIA" (Elecsys 2010, Roche Diagnostic) for Bosnian females, aged  $\leq 50$  years, should be 155 pg/ml as reported by Roche Diagnostic.

KEY WORDS: NTproBNP serum concentration, females, healthy subjects

## INTRODUCTION

Brain natriuretic peptide (BNP) is a cardiac hormone secreted predominantly from the ventricles. This hormone is produced as pre-prohormone BNP (pro BNP), processed to proBNP, and then cleaved by corine to mature, biologically active 32-aminoacid BNP and non-biologically active N-terminal-pro brain natriuretic peptide (NTproBNP) (1). The natriuretic peptides, especially NTproBNP are increased in conditions with cardiac ventricular volume and pressure overload. Both, plasma levels of brain natriuretic peptide and NTproBNP increase in a variety of cardiovascular conditions (2). Also, numerous studies have shown that concentration of BNP and NTproBNP predict cardiovascular disease in apparently healthy individuals although their full screening characteristics are yet to be firmly established (3). Pre-requisite for NTproBNP screening use is establishment of cut off values in clinical studies which include healthy subjects and also subjects with high risk for cardiovascular diseases. Recent studies showed variations in NTproBNP serum concentration in healthy subjects (3). Also, many subjects with raised natriuretic peptide levels had normal systolic function and no overt heart failure. Currently available commercial assays for NTproBNP are not standardized and consequently the results obtained with assays from different manufacturers may differ markedly (1). According to results of the clinical studies performed by Roche diagnostic group each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges (4). As there are no previous results for Bosnian population the aim of this study was to asses normal range of NTproBNP serum concentrations in healthy women, aged 50 years and less using electrochemiluminescence immunoassay "ECLIA" (Elecsys 2010, Roche Diagnostic).

## SUBJECTS AND METHODS

### Subjects

Subjects for this study, in total 45, were selected between persons who have performed regular control of hormonal status at Institute of Nuclear Medicine, University of Sarajevo Clinics Centre. Only women were included, aged 50 years and less. After an overnight fast, all patients underwent full medical assessment and laboratory examinations. The exclusion criteria were: clinically evident cardiovascular diseases, renal diseases, thyroid disorders, pituitary / hypothalamic disorders, diabetes mellitus, pregnan-

cy. The local ethics committee approved the study and the patients gave their written informed consent.

### NTproBNP measurement

Blood samples were collected in the fasting state, immediately put on ice and processed within 30 minutes. Thereafter, obtained serum samples were kept frozen at -70 °C. NTproBNP levels were determined using electrochemiluminescence immunoassay "ECLIA" on Elecsys 2010 (Roche Diagnostic). All measurements were performed at the Institute of Nuclear Medicine, University of Sarajevo Clinics Centre. This assay is an electrochemiluminescent sandwich immunoassay using two polyclonal antibodies directed at the NTproBNP molecule. The analytic range extends from 5-35000 pg/ml. Functional sensitivity was < 50 pg/ml, defined as the lowest analytic concentration that can be reproducibly measured with a between-run coefficient of variation 20%. Expected values for women, aged ≤ 50 years are 155 pg/ml.

### Statistical analysis

All data are expressed as means with standard deviation (SD) in table and median, interquartile range and ranges in Figure 1. Statistical analyses were performed using SPSS 12.0 statistical software system.

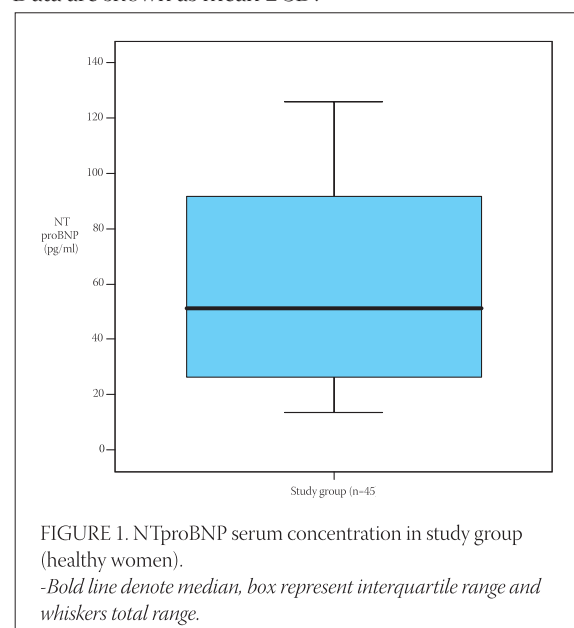
## RESULTS

Subject's physical characteristics are presented in Table 1.

Variable	Females (n=45)
Age (years)	39,19 ± 6,62
Body mass (kg)	70.96 ± 8,64
Height (cm)	168,96 ± 4,62
BMI	24,88 ± 3,04

TABLE 1. Subject's physical characteristics

Data are shown as mean ± SD.



## DISCUSSION

Natriuretic peptides are peptide hormones released into the circulation in response to increased myocardial stretch that leads to vasodilatation, natriuresis and inhibition of renin-angiotensin and sympathetic nervous system (5). NT proBNP has been found to be a useful marker for the diagnosis of heart failure and left ventricular systolic dysfunction (6). Brain natriuretic peptide (BNP) and NTproBNP as inactive but serum stabile component, have been shown to predict cardiovascular disease in apparently healthy individuals. Recent study by Kistrop et al. (7) showed that measurements of NT-proBNP provide prognostic information of mortality and first major cardiovascular events beyond traditional risk factors. NTproBNP was a stronger risk biomarker for cardiovascular disease than C-reactive protein (CRP) in nonhospitalized individuals aged 50 to 89 years. Serum concentration of NTproBNP is altered by different factors: age, gender, race, thyroid hormones, etc. (5). Screening characteristics of NTproBNP are yet to be established. There are few big clinical studies that resulted in establishing of upper cut off values for NTproBNP. According to data provided from the clinical studies on blood donors performed by Roche diagnostic group (4,8) upper cut-off values for the women aged 50 years and less is 155 pg/ml. Conversely, Raymond et al. (9) found higher values of NTproBNP serum concentration in women 50-59 years old, defined as normal subjects (no congestive

heart failure, no ischaemic heart disease, no history of hypertension, no diabetes, no lung disease, no cardiovascular drug treatment, left ventricular ejection fraction 60%, blood pressure <140/90, and a normal ECG). According to their results the average value of NT proBNP was 15,0 pmol/l (126,85 pg/ml) with the minimum-maximum range of 11,5-19,6 pmol/l (97,25-165,75 pg/ml).

Study of Leowattana et al.(10) which enrolled 243 healthy subjects from the checkup department of Bangkok showed that NTproBNP levels increase with aged and that females usually have higher NTproBNP than males (40,42±31,59 pg/ml vs. 27,51±37,40 pg/ml).

Shi et al. (11) have been found lower serum concentration of NTproBNP in apparently healthy Chinese people (< 131,6 ng/l for women aged < or=60 years) than those for western countries. They also concluded that NT-proBNP assay has a good clinical performance for the diagnosis of symptomatic heart failure (HF) but is not suitable as a screening test for HF.

Our results showed that mean serum concentration of NTproBNP in healthy females (Tab.1) was 60,32 (±36,25) pg/ml, with the range of 112,60 pg/ml (minimum-maximum:13,6-126,00 pg/ml) (Fig.1.). Our results are in accordance with previously mentioned results obtained from large studies performed on European's population (4,8).

## CONCLUSION

We conclude that NTproBNP serum concentration in apparently healthy Bosnian women was not different from the average values of NTproBNP obtained on European's population. Thus, we suggest that the normal NTproBNP serum upper cut off values measured by using electrochemiluminescence immunoassay "ECLIA" (Elecsys 2010, Roche Diagnostic) for Bosnian females, aged ≤ 50 years, should be 155 mg/ml as reported by Roche Diagnostic.

### List of abbreviations:

BNP	-	Brain natriuretic peptide
NTproBNP1	-	N-terminal pro brain natriuretic peptide
ProBNP	-	Pro- brain natriuretic peptide
BMI	-	Body mass index
HF	-	Heart failure
CRP	-	C-reactive protein

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