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Association between NT- pro BNP and Cardio-metabolic Risk Factors in Mongolians

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ABSTRACT

Objective of the study was to evaluate the association of NT-pro BNP to cardio-metabolic risk factors, including the metabolic syndrome. Research method: This study was included 194 participant s aged from 35- to 64 years, who were health checkup examinee's and had no clinical symptoms of heart failure. Cardio-metabolic risk factors were detected by clinical examinations and laboratory test. Metabolic syndrome was defined according to the International Diabetes Federation definition. NT-pro BNP determination was performed on an immunoassay analyzer (FIA8000, Getein Bio Medical Inc). The cut-off point for NT-pro BNP was 125pg/ml. We examined with multivariate linear regression of the relationship between NT-pro BNP and cardio-metabolic risk factors. A logistic regression analysis was also performed to assess the influence of cardio-metabolic risk factors and metabolic syndrome on NT-pro BNP values. Research results: A total of 194 participants included in the study of which, 75 (38.6%) were men and 119 (61.4%) were women. The mean age was 51.3±7.9 75 years. Thirty-two participant s (16.5%) showed elevated NT-pro BNP levels of ≥125 pg/ml. Sixty-one (31.4%) participants had metabolic syndrome. Multivariate linear regression analysis showed that age (β=0.140, P=0.049), systolic blood pressure (β=0.198, P=0.007) and diastolic blood pressure (β=0.174, P=0.018) were positively correlated with NT-pro BNP levels, while body mass index (β=-0.209, P=0.004) was negatively correlated with NT-pro BNP levels. Age (OR=1.07, P=0.011) and hypertension (OR=5.98, P=0.007) were the independent predictors of elevated NT-pro BNP levels. Conclusion: NT-pro BNP levels were significantly increased in participants with hypertension and metabolic syndrome and were lower in obesity.

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Keywords:
NT-pro BNP,
cardio-metabolic risk factor,
metabolic syndrome

1. INTRODUCTION

According to a Consensus Conference report published by the American Diabetes Association and the American College of Cardiology Foundation, cardio-metabolic risk factors include obesity (particularly central), hyperglycemia, hypertension, insulin resistance and dyslipidemia and are associated with a high lifetime risk for cardiovascular disease.

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Cardio-metabolic risk is similar to that of metabolic syndrome, but is more inclusive, as it also considers glucose in the diabetic range, not just pre diabetic range. Therefore, the cardio-metabolic risk population is a larger population than the population with metabolic syndrome alone [1].

Metabolic syndrome is a pathological condition with clustering of metabolic components, including glucose intolerance, elevated blood pressure, elevated triglycerides, low high-density lipoprotein cholesterol levels and obesity. Consistent with the epidemic of obesity and sedentary lifestyles, the prevalence of metabolic syndrome has been steadily increasing worldwide.

Brain natriuretic peptide and N-terminal pro-brain natriuretic peptide (NT-pro BNP) are cardiac hormones

secreted by ventricular myocardium in response to increased ventricular wall pressure and volume overload. Natriuretic peptides have natriuretic and vasodilatory properties and beneficial effects on cardiac remodeling. The inverse relationship between NT-pro BNP and BMI has been hypothesized to reflect a "natriuretic handicap" with a reduced response to cardiac wall stress contributing to the initiation and progression of cardiovascular complications [2]. Plasma concentrations of these hormones are powerful tools for the diagnosis and management of patients with acute or chronic heart failure in the routine clinical settings. Beleigoli AM et al. [3] suggested natriuretic peptides are potent lipolytic agents that act in adipose tissue.

Low levels of NT-pro BNP might lead to reduced lipolysis and excessive weight gain, which may be one of the biological alterations that contribute to the development of metabolic syndrome in the general population [4]. Epidemiological studies have shown that obese individuals have lower plasma levels of natriuretic peptides than those with normal weight, despite the higher prevalence of hypertension and left ventricular hypertrophy [5].

Despite the well-documented association between NT-pro BNP levels and obesity, the relationship between metabolic syndrome and natriuretic peptides are poorly understood and findings are controversial. Some studies have found no association between serum NT-pro BNP concentrations and metabolic syndrome [6], while others have shown an association of metabolic syndrome with lower levels of NT-pro BNP [7]. No data is currently available in Mongolians. The aim of the present study was to evaluate the association of NT-pro BNP with cardio-metabolic risk factors, including the metabolic syndrome.

2. MATERIALS AND METHODS

Study sample

The study was conducted in clinic university of Mongolia during the September 1st to December 1st, 2018. The eligible participants were health checkup examinees, aged from 35 to 64 years, who had no symptoms of heart failure and agreed to participate in this study. We excluded participant s with clinical symptoms of chronic heart failure and history of myocardial infarction and brain stroke. All participants had signed the written informed consent to participate in this study.

Data collection

At the clinical examination, height, weight, waist circumference and blood pressure were measured. The body mass index (BMI) was calculated as weight (kilograms) divided by height squared (meters) and obesity was defined as a BMI level ≥30 kg/m^2. Waist circumference was measured midway between the lowest rib and the iliac crest using an anthropometric tape. Abdominal obesity is defined as values of waist circumference ≥90 cm for men and ≥80 cm for women. Blood pressure (BP) was measured twice using an automated sphygmomanometer in the sitting position after a few minutes' resting. The average value from two measurements was used, and hypertension was defined as systolic BP ≥ 130 mm Hg, diastolic BP ≥ 80 mm Hg, and/or receiving treatment with anti-hypertensive agents.

Serum levels of fasting glucose (FPG), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-cholesterol) and low-density lipoprotein cholesterol (LDL-cholesterol) were measured using a fully automatized analyzer BA200 (Bio Systems S.A, Barcelona, Spain). According to the national guideline for dyslipidemia, we used standard cutoff values for levels of total cholesterol (≥5.2 moll/L, triglycerides (≥1.7 mmol/L), LDL cholesterol (≥3.4 moll per liter) and HDL cholesterol (<1.0 mmol/L per liter) to define abnormal values.

We defined the following cardio-metabolic risk factors according to laboratory test results: impaired fasting glucose (≥6.1 mmol/l), dyslipidemia and insulin resistance. Dyslipidemia, defined as elevated total cholesterol or triglycerides or LDL cholesterol levels, or low levels of HDL cholesterol. The insulin resistance is defined as TG/HDL cholesterol ratio >2.1 as previously reported [8]. Metabolic syndrome was defined according to the International Diabetes Federation definition. Participants were classified as having metabolic syndrome if they had an abdominal obesity plus two or more of the following criteria: TG ≥1.7 mmol/l, HDL cholesterol <1.03 mmol/l, blood pressure ≥130/85 mmHg, and FBG ≥5.6 mmol/l. A 10 ml venous blood sample was drawn into an EDTA tube. NT-pro BNP determination was performed on an immunoassay analyzer (FIA8000, Getein Bio Medical Inc), which uses reagent strips to obtain quantitative NT-pro BNP results in whole blood or plasma. Plasma NT-pro BNP values are expressed in pg/ml (analytical range, 100-10000 pg/ml). An elevated NT-pro BNP was defined as a NT-pro BNP ≥ 125pg/ml.

Ethical statement

Research ethical permission was obtained from the Bio-medical Ethics Committee of Mongolian National University of Medical Sciences.

Statistical Analyses

Analysis was done with the SPSS 24 software. All quantitative values were presented as mean ± standard deviation. Differences between the study groups were analyzed with the chi-square test for categorical variables and with the Student t test. A p value of less than 0.05 was considered statistically significant. To compare baseline characteristics between men and women and between normal and elevated values, an independent two-tailed t-test and chi-square test were used for the analysis of continuous and categorical variables, respectively.

Pearson's correlation coefficient was used to correlate lipid profile values with NT-pro BNP levels. A logistic regression analysis was performed to identify the contribution of major cardio-metabolic risk factors for elevated NT-pro BNP levels. The statistical analysis was carried out using all the demographic and cardio-metabolic risk factors (age,

gender, hypertension, dyslipidemia, hyperglycemia, abdominal obesity, BMI ≥ 30 kg/m2, lipid profile, insulin resistance and metabolic syndrome) as independent variables and NT-pro BNP level as dependent variable. A multiple linear regression model with step-wise selection was used to estimate the association between cardio-metabolic risk factors and NT-pro BNP.

3. RESULTS

3.1. Participant characteristics.

The baseline characteristics of the 194 participants [75 (38.6%)men and 119 (61.4%) women) are shown in table 1.

The mean age and age ranges were 51.3 ± 7.9 and 35-64 years old. Abdominal obesity was the most common factor (82%), followed by hypertension (68%) and dyslipidemia (50%). In all participants, 61 (31.4%) met criteria for the metabolic syndrome. Women had less obesity, hypertension and metabolic syndrome and more dyslipidemia compared with men. The prevalence of elevated triglycerides (41.3% vs 24.4%, p=0.013) and insulin resistance (18.7 vs 3.4%, P<0.0001) was significantly higher in men than in women.

2. Distribution of NT-pro BNP levels

Elevated NT-pro BNP levels (≥125 pg/ml) were detected in 16.5% (32) of participants. The proportion of individuals with an elevated NT-pro BNP level increased gradually with age (Figure 1).

The distribution of cardio-metabolic risk factors was different between the normal and elevated NT-pro BNP groups (Table 2). The percentage of participants with an elevated NT-pro BNP level was similar in males and females (18.7% vs 15.1%, p>0.05). Hypertension and metabolic syndrome differed significantly (p<0.05) between the normal and elevated NT-pro BNP level groups.

3. Risk factors associated with NT-pro BNP level.

Logistic regression analysis of the relationship between NT-pro BNP and cardo-metabolic risk factors showed that hypertension (p=0.007) and age (p=0.011) were independently associated with NT-pro BNP levels (Table 3). Based on odds ratio analysis, participants with hypertension had 6-times greater risk for elevated NT-pro BNP level than the participants with normal blood pressure.

4. Factors correlated with NT-pro BNP.

Correlations of NT-pro BNP levels with clinical and lipid parameters are shown in table 4. NT-pro BNP levels were positively correlated with age (r=0.16, p=0.04) and systolic blood pressure (r=0.15, p=0.037) and negatively with BMI (r=−0.16, p=0.023) and waist circumference (r=-0.14, p=0.04). The negative correlation between NT-pro BNP levels and lipid profile and positive correlation between NT-pro BNP levels and fasting plasma glucose was found, but they were non-significant.

The results of multivariate linear regression model of the relationship between NT-pro BNP level and cardio-metabolic parameters are shown in table 5.

A multivariate regression analysis considering age, body mass index, waist circumference, systolic and diastolic blood pressure, fasting plasma glucose, TC, triglyceride, HDL cholesterol, LDL cholesterol and triglyceride/high density lipoprotein cholesterol ratio as independent variables and NT-pro BNP level as dependent variable was applied. In multivariate regression analysis, a significant positive association was observed between NT-pro BNP levels and age (β=0.140, p=0.049), systolic (β=0.198, p=0.007) and diastolic (β=0.174, p=0.018) blood pressure. Body mass index was significantly negatively (β=-0.209, p=0.007) associated with NT-pro BNP level.

4. DISCUSSION

This study assessed the relationship between NT-pro BNP and cardio-metabolic risk factors, including metabolic syndrome in Mongolians. Overall, 16.5% of participant s had an elevated NT-pro BNT level, which was similar to''Shalnova et al a study'' [9]. Current study showed significant association between metabolic syndrome and NT-pro BNP levels. However, other studies noted serum NT-pro BNP was lower in the population with metabolic syndrome [4,10]. The relationship between NT-pro BNP and the metabolic syndrome have been conflicting, with studies showing either lower or similar natriuretic peptides values compared to people without metabolic syndrome. This is likely due to differences among examined populations in the relative frequencies of the metabolic syndrome components with opposite effects on NT-pro BNP, such as hypertension.

In the present study, the percentage of participants with elevated NT-pro BNP level was non significantly higher in males than in females (18.7% vs 15.1%, p>0.05). In previous studies, NT-pro BNP values were higher in women compared to men [9,11]. In our study, the age and hypertension were independently associated with elevated NT-pro BNP levels. The results are comparable with the results of the others studies [10,12,13]. Age has been shown to influence circulating natriuretic peptide. A possible explanation for increased NT-pro BNP levels with age may be increased age-related fibrosis, diastolic dysfunction. Previous studies reported that gender, BMI, waist circumference and triglycerides were independent predictors of NT-pro BNP levels [4,10].

The results of this study showed that age, systolic and diastolic blood pressure were all positively correlated with NT-pro BNP levels, whereas BMI, waist circumference and lipid profile were all inversely correlated with NT-pro BNP levels. These findings are similar to the results of the others studies [10,12,13]. Results of some studies showed significant positive correlation between fasting plasma glucose and NT-pro BNP levels [10,14] and significant negative correlation between level of triglycerides and NT-

pro BNP levels [10,13]. Stefano Baldassarre et al reported [15] that there were no significant correlations between NT-pro BNP and either BMI or waist circumference. The difference may be due to the differences in inclusion criteria between these studies.

Our study has some limitations. First, this study was of a cross-sectional study. We not know of any such longitudinal respective study in Mongolia. Second, our study enrolled participants aged 35 to 64 years. The findings cannot be extrapolated to younger age groups or elderly people.

CONCLUSION

The present study showed that age, systolic and diastolic blood pressure were significantly positively associated with NT- pro BNP levels and body mass index was significantly inversely correlated with NT-pro BNP levels. NT-pro BNP levels were significantly increased in participants with hypertension and metabolic syndrome and were lower in obesity.

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Conflict of interest is not declared.

TABLE AND FIGURE

Table 1. Participants' characteristics

Characteristics	All participants (n=194)	Men (n=75)	Women (n=119)	Chi-Square test	P- value*
Age group, n (%)				2.93	0.230
35-44 years	45(23.2)	21(28.0)	24(20.2)		
45-54 years	73(37.6)	23(30.7)	50(42.0)		
55-64 years	76(39.2)	31(41.3)	45(37.8)		
Hypertension, n (%)	132(68.0)	54(72.0)	78(65.5)	0.88	0.348
Dyslipidemia, n (%)	97(50.0)	36(48.0)	61(51.3)	0.19	0.658
IFG, n(%)	33(17.0)	16(21.6)	17(14.3)	1.619	0.203
Abdominal obesity, n (%)	159(82.0)	61(81.3)	98(82.3)	0.03	0.857
Insulin resistance, n (%)	18(9.2)	14(18.7)	4(3.4)	12.65	<0.001
BMI ≥30 kg/m^2), n (%)	71(36.6)	30(40.0)	41(34.4)	0.61	0.435
Metabolic syndrome, n (%)	61(31.4)	20(26.7)	41(34.4)	1.29	0.255

** For differences between men and women. BMI - body mass index, IFG – impaired fasting glucose*

Table 2. The distribution of risk factors between normal and elevated NT-pro BNP levels

Cardio-metabolic risk factors	Total (n=194)	NT-pro BNP <125 pg/ml (n=162)	NT-pro BNP ≥125 pg/ml (n=32)	P-value
Gender				0.518
Men	75(38.6)	61(37.7)	14(43.7)	
Women	119(61.4)	101(62.3)	18(56.3)	
Hypertension, n (%)	132(68.0)	103(63.6)	29(90.6)	0.003
Dyslipidemia, n (%)	97(50.0)	86(53.1)	11(34.4)	0.053
IFG , n (%)	33(17.0)	29(17.9)	4(12.5)	0.457
Abdominal obesity, n (%)	159(82.0)	135(83.3)	24(70.6)	0.263
Insulin resistance, n (%)	18(9.2)	16(9.9)	2(6.2)	0.152
BMI ≥30 kg/m^2), n (%)	71(36.6)	64(39.5)	7(21.9)	0.058
Metabolic syndrome, n (%)	61(31.4)	46(28.4)	15(46.9)	0.04

BMI - body mass index. NT-pro BNP – N-terminal pro-B type natriuretic peptide, IFG – impaired fasting glucose

Table 3. Logistic regression analysis of the relationship between NT-pro BNP and demographic and cardo-metabolic risk factors.

	OR(95% CI)	P - value
Gender	0.84(0.36-1.94)	0.683
Age	1.07(1.01-1.11)	0.011
Hypertension	5.98(1.62-22.01)	0.007
Dyslipidemia	0.55(0.23-1.31)	0.182
IFG	0.65(0.21-2.01)	0.460
Abdominal obesity	0.52(0.18-1.55)	0.247
Insulin resistance	0.60(0.13-2.76)	0.516
BMI ≥30 kg/m2	0.44(0.16-1.19)	0.107
Metabolic syndrome	1.78(0.77-4.11)	0.176
Hypercholesterolemia	0.60(0.11-3.11)	0.548
Hypertriglyceridemia	0.54(0.21-1.40)	0.208
High LDL cholesterol	0.69(0.13-3.67)	0.672

OR – odds ratio, CI - confidence interval

Table 4. Correlation analysis between NT-pro BNP levels and clinical and lipid profile parameters

Parameters	Mean ± SD	r coefficient (against NT-pro BNP levels)	P - value
Age, years	51.3±7.9	0.16	0.024*
BMI, kg/m2	29.0±5.3	-0.16	0.023*
Waist circumference, cm	95.7±13.1	-0.14	0.047*
SBP, mm Hg	133.3±20.6	0.15	0.037*
DBP, mm Hg	87.9±13.6	0.30	0.092
FPG, mmol/l	7.05±4.56	0.02	0.688
Total cholesterol, mmol/l	4.79±1.22	-0.14	0.050
Triglycerides, mmol/l	1.49± 1.22	-0.09	0.197
HDL cholesterol, mmol/l	1.56± 0.28	-0.09	0.181
LDL cholesterol, mmol/l	2.93 ±1.14	-0.11	0.122
Ratio TG/HDL	1.00± 0.67	0.06	0.389

**P <0.05 was considered statistically significant. SD – standard deviation, r - coefficient of correlation, BMI- body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure, HDL – high density lipoprotein, LDL – low density lipoprotein, FPG – fasting plasma glucose, TG-triglycerides, BMI- body mass index, LDL – low density lipoprotein, IFG – impaired fasting glucose.*

Table5. Multivariate regression analysis of the relationship between NT-pro BNP and cardo-metabolic parameters.

Variables	β	B	(95%CI) for B		P-value
			Lower bound	Upper bound	
Age (years)	0.140	2.35	0.01	4.69	0.045*
BMI (kg/m2)	-0.209	-5.249	-8.82	-1.67	0.004*
SBP (mm Hg)	0.198	1.27	0.36	2.19	0.007*
DBP (mm Hg)	0.174	1.12	0.19	2.04	0.018*
Waist circumference (cm)	-0.213	-2.15	-4.98	0.67	0.135
Total cholesterol (mmol/l)	-0.023	-2.53	-19.54	14.48	0.770
Triglycerides (mmol/l)	-0.123	-18.70	-41.03	3.61	0.100
HDL cholesterol (mmol/l)	-0.116	-55.60	-126.53	15.32	0.124
LDL cholesterol (mmol/l)	-0.091	-10.59	-27.21	6.03	0.210
FPG (mmol/l)	0.158	4.61	-1.44	10.66	0.134
Ratio TG/HDL	-0.097	-19.15	-49.05	10.74	0.208

**P <0.05 was considered statistically significant. CI - confidence interval, β(beta) – standardized regression coefficient, B unstandardized regression coefficient. BMI- body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure, HDL – high density lipoprotein, LDL – low density lipoprotein, FPG – fasting plasma glucose, TG-triglycerides.*

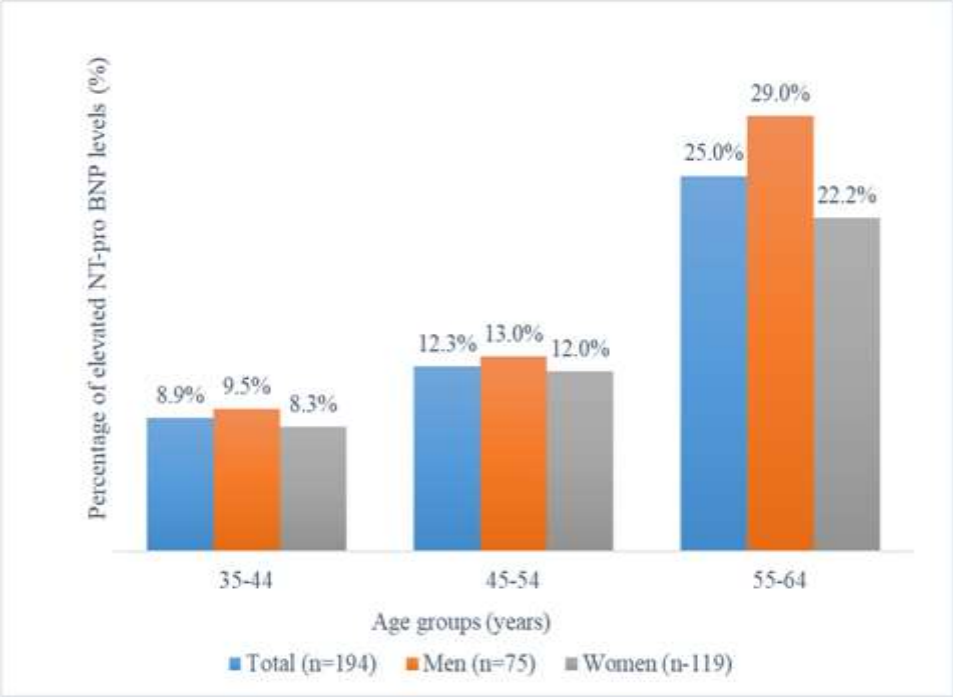

Figure 1. Distribution of elevated NT-pro BNP levels regarding to age groups and gender

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