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The Pre-Heart Failure in Hypertension

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ABSTRACT

The objectives of this study were to detect pre-heart failure based on NT-proBNP in subjects with hypertension and to identify the risk factors for pre-heart failure. Research methods: We conducted a cross -sectional study between August and December 2022. This study was included 526 subjects with hypertension aged from 35- to 64 years, who had no clinical symptoms of heart failure. Cardiovascular risk factors were detected by clinical examinations and laboratory test. Hypertension was defined as systolic BP ≥ 130 mm Hg, diastolic BP ≥ 80 mm Hg, and/or receiving treatment with anti-hypertensive agents. NT-pro BNP determination was performed on an immunoassay analyzer (Getein 1100). An elevated NT-pro BNP was defined as a NT-pro BNP ≥ 125pg/ml. Pre-heart failure was based on elevated NT-pro BNPlevel. Ethical statement Research ethical permission was obtained from the Biomedical Ethics Committee of Mongolian National University of Medical Sciences. Research results: In total, 526 hypertensive subjects s aged 35-64 year enrolled in this study, of which, 243 (46.2%) were men and mean age was 52.5±7.7 years.

The prevalence of pre-heart failure based on NT-pro BNP in women was non-significantly higher than in men(17.3% vs 14.0%, p= 0.297). The prevalence of pre-heart failure increased from 4.0% for men aged 35-44 years to 20.9% for men aged 55-64 years. Based on our logistic regression analysis, the likelihood of elevated NT-pro BNP in hypertensive subjects was independently associated with age(OR 2.18, 95%CI 1.51-3.14) and poor blood pressure control(OR 2.41, 95%CI 1.29-4.50). Conclusion: The present study showed that the overall prevalence of pre-heart failure in hypertensive subjects was 15.8% and increased with age. The poor blood pressure control and ageing were significant risk factors in the development pre-heart failure in subjects with hypertension.

ARTICLE DETAILS

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1. INTRODUCTION

The prevalence of cardiovascular diseases (CVD) among Mongolian population has increased 2.5-fold during past decade [1]. In Mongolia uncontrolled hypertension was detected in 84.7% of all hypertensive subjects [2]. High blood pressure is associated with an increased risk of developing chronic heart failure [3]. Heart failure (HF) is a major public health issue and a leading cause of global morbidity and mortality [4]. The prevalence of heart failure (HF) and its associated morbidity and mortality have increased exponentially over recent decades. The increasing prevalence of HF remains a major public health concern underlining the need for an effective prevention strategy [5].

The universal definition and classification of heart failure was launched in 2021 [6] and included the concept of pre-heart failure. Individuals with pre-heart failure do not present any current or previous symptoms or signs of heart failure but do present evidence of at least one of the following: structural heart disease, abnormal cardiac function, elevated natriuretic peptide, or cardiac troponin levels [6]. Measurement of BNP (B-type natriuretic peptide) or NT-pro BNP (N-terminal pro-B-type natriuretic peptide) is now a cornerstone of many clinical guidelines in the diagnosis of heart failure. Recently updated guidelines from the European Society of Cardiology also specify the rule out heart failure thresholds of NT-pro BNP at 125 pg/mL in the nonacute setting [7].

Brain natriuretic peptide and N-terminal pro-brain natriuretic peptide (NT-pro BNP) are cardiac hormones which 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. N-terminal pro-B-type natriuretic peptide (NT-pro BNP) has been used as a biomarker for detecting and monitoring heart

failure. The importance of biomarkers that can be used to detect early-stage heart failure is increasing because biomarkers contribute to identification of risk and the presence of asymptomatic heart failure and help to provide a treatment strategy for the prevention of symptomatic heart failure [8].

The use of NT-pro BNP as a biomarker in the diagnosis of HF has been included in HF guidelines, including in the diagnosis of asymptomatic HF [4,9-12] and pre-HF [6]. Asymptomatic HF includes patients at risk for HF and patients with pre-HF [13]. According to ACC/AHA definition for stages of HF, Stage B is considered pre-heart failure. Many hypertensive subjects without symptoms or physical signs of CHF should thus be considered for screening of pre-heart failure. In patients with essential hypertension, serum concentrations of NT-pro BNP are mildly higher than in normotensive subjects. 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 [14]. Prevalence estimates of pre-HF ranged from 11 to 42.7% with higher estimates found in the elderly, in patients with hypertension, and in men [15]. The aims of this study were to detect pre-heart failure based on NT-pro BNP in subjects with hypertension and to identify the risk factors for pre-heart failure.

2. MATERIALS AND METHODS

Study sample

The cross-sectional study was carried out for a period of five months (from August to December in 2022) in University hospital of Mongolian National University of Medical Sciences. 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 participants with clinical symptoms of chronic heart failure and with previous myocardial infarction. All participants had signed the informed consent to participate in this study.

Data collection

The questionnaire included participants' demographic characteristics, presence of risk factors for hypertension. Risk factors for arterial hypertension included excessive drinking of alcohol, smoking, family history of CVD, diabetes, obesity and hypercholesterolemia. Smoking was defined as current smoking status and excessive drinking of alcohol is defined as 15 or more standard drinks a week for men and; as 8 or more standard drinks a week for women. Family history of CVD as history of myocardial infarction or brain stroke or sudden cardiac death before the age of 55 years of the father or any other first-degree male relative or before the age of 65 years of the mother or any other first degree female relative. Diabetes mellitus was defined as self-reported physician-diagnosed diabetes and/or use of antidiabetic medication.

At the clinical examination, height, weight 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 of 30.0 kg/m2 or greater. 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 $\geq$ 130 mm Hg, diastolic BP $\geq$ 80 mm Hg, and/or receiving treatment with anti-hypertensive agents.

Hyperlipidemia, defined as elevated total cholesterol ($\geq$5.2mmol/l or triglycerides$\geq$2.3 mmol/l) according to national clinical guideline of dyslipidemia. A 10 ml venous blood sample was drawn into an EDTA tube. NT-pro BNP determination was performed on an immunoassay analyzer (Getein 1100**),** 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, 50-15000 pg/ml). An elevated NT-pro BNP was defined as a NT-pro BNP $\geq$ 125pg/ml. Pre-heart failure was based on elevated NT-pro BNP ($\geq$ 125pg/ml).

Ethical statement.

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

Statistical Analyses

Patients' demographic characteristics and clinical variables were analyzed in the whole sample using descriptive statistics. Continuous variables were expressed mean±standard deviation (for normal distribution). Categorical variables were shown as absolute numbers and percentages. Categorical data were compared using Chi-square test while continuous variables were compared using independent sample T-test. In addition, logistic regression analysis was performed to calculate the odds ratio to assess to identify the contribution of major risk factors for elevated NT-pro BNP levels. Statistical significance was considered for 2 sided p-value less than <0.05. SPSS 24.0 was used for data analysis.

3. RESULTS

In total, 526 hypertensive patients aged 35-64 years enrolled in this study. Of which, 243 (46.2%) were men and mean age was 52.5±7.7 years. Baseline characteristics of total participants weres summarized according to gender in table 1. Excessive alcohol consumption and smoking in male were significantly higher than in female. Obesity in female was significantly higher than in male.

Table 1. Baseline characteristics of the participants

Characteristics	Total participants (n=526)	Male (n=243)	Female (n=283)	p-value
Average years (SD)	52.5±7.7	52.5±7.8	52.5±7.7	0.971
35-44 years, n (%)	102(19.4)	50(20.6)	52(18.4)	
45-54 years, n (%)	212(40.3)	88(36.2)	124(43.8)	0.207
55-64 years, n (%)	212(40.3)	105(43.2)	107(37.8)	
Family history of CVD, n (%)	222(42.2)	92(37.9)	130(45.9)	0.062
Excessive alcohol consumption, n (%)	235(44.7)	160(65.8)	75(26.5)	**<0.0001**
Smoking, n (%)	199(37.8)	147(60.5)	52(18.4)	**<0.0001**
Diabetes mellitus, n (%)	199(37.8)	98(40.3)	101(35.7)	0.274
Obesity, n (%)	260(49.4)	104(42.8)	156(55.1)	**0.005**
Hypercholesterolemia, n (%)	251(47.8)	114(47.1)	137(48.4)	0.811
Systolic blood pressure, mmHg(SD)	140.5±20.7	142.4±19.4	138.9±21.6	0.052
Diastolic blood pressure, mmHg (SD)	91.4±12.0	91.6±11.5	91.2±12.5	0.691

Note: SD is standard deviation, CVD is cardiovascular disease

The overall prevalence of pre-HF in adults aged 35-64 years was 15.8%. The prevalence of pre-HF strongly increased with age and was 6.9 % in participants aged 35-44 years while its frequency was 24.0% among 55-64 years-old subjects (Figure 1).

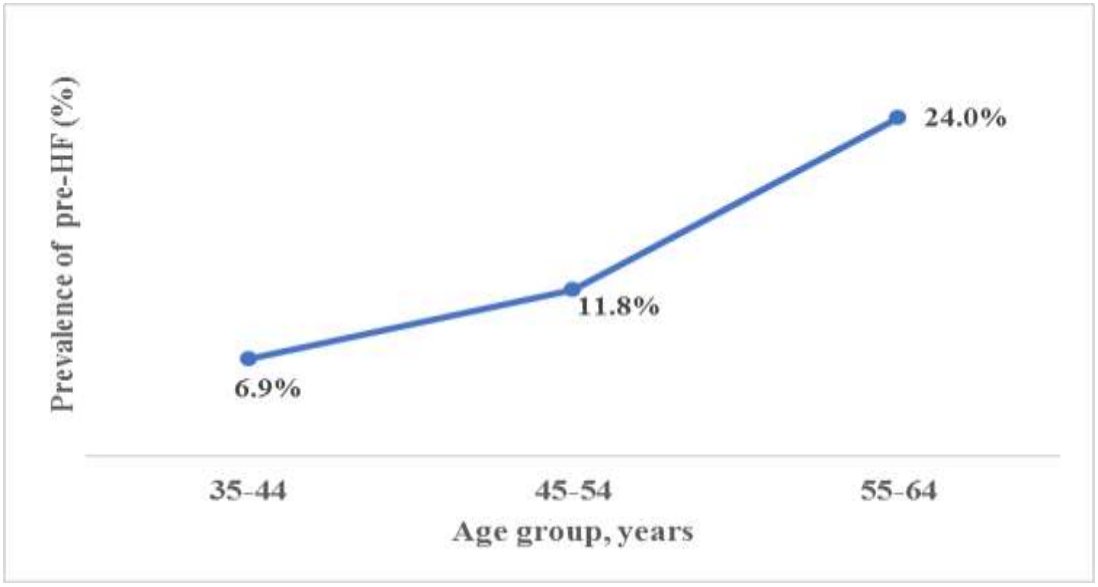

Figure 1. Age-specific prevalence of pre-HF in hypertensive subjects

Figure 2 shows the age-specific prevalence of overall pre-heart failure for 10-year age groups in men and women. The overall prevalence of pre-heart failure based on NT-pro BNP in women was non-significantly higher than in men (17.3% vs 14.0%, p= 0.297). The prevalence of pre-heart failure increased from 4.0% for men aged 35-44 years to 20.9% for men aged 55-64 years. For women, the prevalence rose from 9.6% years to 27.1% aged 55-64 years.

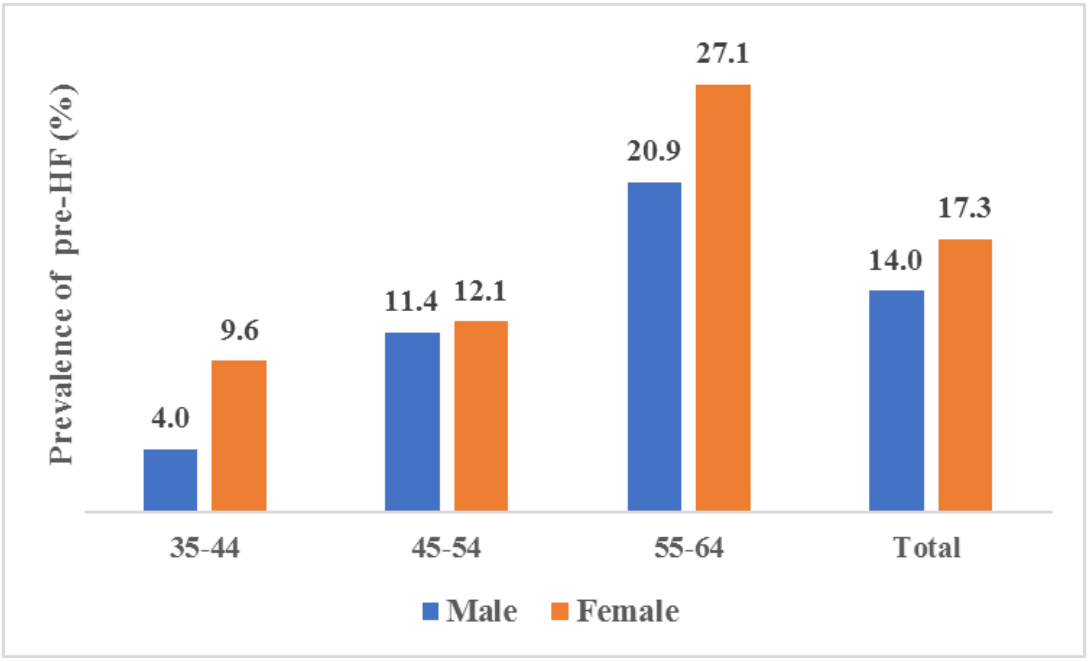

Figure 2. Age-specific prevalence of pre-HF by gender in hypertensive subjects

Comparison of risk factors between elevated and normal NT-pro BNP groups is shown in table 2.

The aging and percentage of diabetes, average systolic and diastolic blood pressure in elevated NT-pro BNP group were significantly higher than in normal NT-pro BNP group.

Table 2. The distribution of risk factors for pre-HF between normal and elevated NT-pro BNP groups

Variables	Group with increased NT-pro BNP (n=83)	Group with normal NT-pro BNP (n=443)	p-value
Average years (SD)	56.1±7.2	51.8±7.6	**<0.0001**
35-44 years, n (%)	7(8.4)	95(21.5)	
45-54 years, n (%)	25(30.1)	187(42.2)	**<0.0001**
55-64 years, n (%)	51(61.5)	161(36.3)	
Male, n (%)	34(41.0)	209(47.2)	0.297
Female, n (%)	49(51.0)	234(52.8)	
Family history of CVD, n (%)	32(38.5)	190(42.9)	0.463
Excessive alcohol consumption, n (%)	28(33.7)	207(46.7)	0.235
Smoking, n (%)	28(33.7)	171(38.6)	0.402
Diabetes mellitus, n (%)	23(27.7)	176(39.7)	**0.038**
Obesity, n (%)	40(48.2)	220(49.7)	0.806
Hypercholesterolemia, n (%)	37(41.7)	198(44.8)	0.36
Systolic blood pressure, mmHg (SD)	148.9±21.2	138.9±20.2	**<0.0001**
Diastolic blood pressure, mmHg (SD)	94.6±11.0	90.8±12.1	**0.008**

Note: SD is standard deviation, CVD is cardiovascular disease

Using logistic regression analysis (Table 3), the likelihood of elevated NT-pro BNP in hypertensive subjects was independently associated with age and poor blood pressure control.

Table 3. Risk factors for elevated NT-pro BNP levels (≥125 pg/ml)

Variable	OR	Min value	Max value	P value
Age ≥45 years	2.179	1.510	3.144	**<0.0001**
Female	1.124	0.842	1.752	0.229
Family history of CVD	0.836	0.517	1.351	0.463
Excess alcohol consumption	0.580	0.355	0.949	0.030
Smoking	0.810	0.494	1.327	0.402

Diabetes mellitus	0.582	0.347	0.975	0.040
Obesity	0.943	0.590	1.507	0.806
Hypercholesterolemia	0.749	0.404	1.387	0.358
Poor blood pressure control	2.411	1.290	4.505	**0.006**

Comparison of prevalence pre-HF between uncontrolled and controlled hypertension groups is shown in figure 3. The prevalence of pre-HF for all age groups in subjects with uncontrolled hypertension was significantly more than those in subjects with controlled hypertension

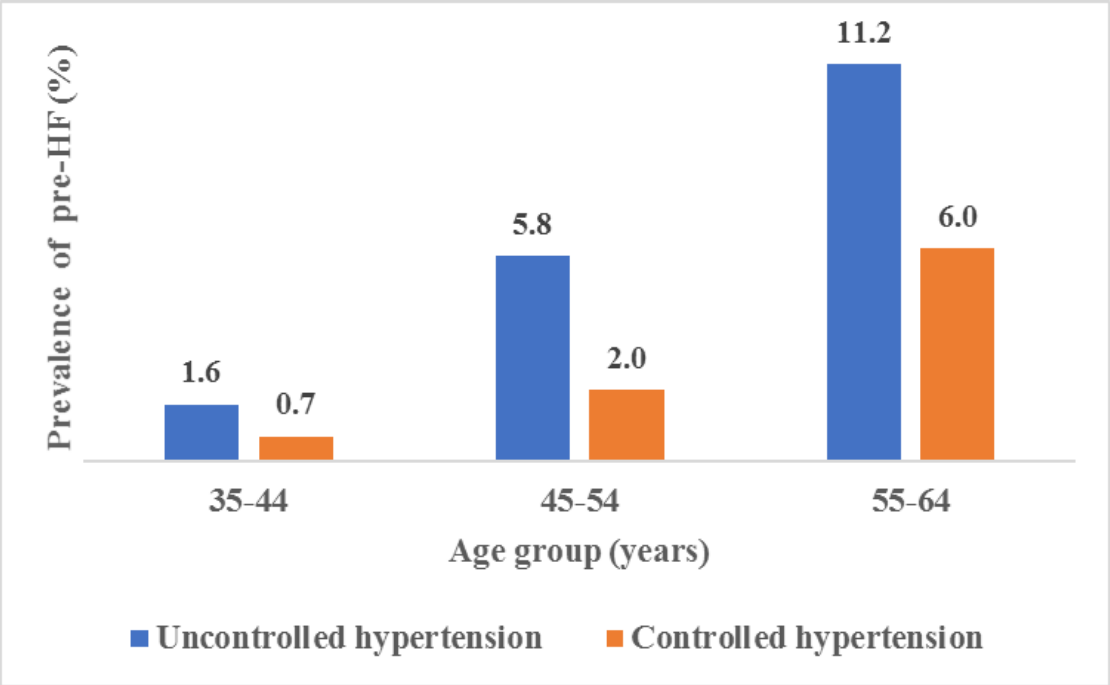

Figure 3. The prevalence of pre-HF in uncontrolled and controlled hypertension groups

4. DISCUSSION

In our study, NT-pro BNP levels were measured in 526 subjects with arterial hypertension. Approximately 15.8% of the participants had pre-HF (NT-pro BNP levels of ≥125 pg /ml). Some studies conducted in the general population aged ≥45 years revealed that the prevalence of pre-HF was 11-12.5% [16,17]. Based on our data, the prevalence of pre-HF increased with age. This finding similar to other studies conducted in Belgium, USA and UK [16,17,18]. The current study showed that prevalence of pre-HF was higher in females than in males. These finding is consistent with previous study from United Kingdom [18]. Another study showed the prevalence of pre-HF is increased in patients with hypertension [19,20]. Hypertension is slightly more common in women and conveys an increased risk of heart failure (3-fold) in comparison to men (2-fold). Women are more likely to have uncontrolled blood pressure [21].

We found the aging and high blood pressure were independently associated with elevated NT-pro BNP levels. These results were in line with former studies. The results are comparable with the other studies [22,23]. 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 [24]. Shoko Aoki, et al reported that high BMI, current smoking, diabetes mellitus, and hypertension in a general Japanese population were positively associated with risk of pre-heart failure or symptomatic heart failure [25]. The present study demonstrated that aging and poor blood pressure control are the strongest risk factors for pre-HF among other risk factors.

A modestly elevated BNP or NT-pro BNP in those without a symptomatic HF identifies patients at high risk for developing HF events; such events may be prevented [5]. Early identification of asymptomatic patients and implementation of targeted interventions aiming to reduce the risk of progression from asymptomatic pre-HF to symptomatic HF may help prevent premature death attributed to symptomatic HF. ACC/AHA and ESC guidelines recommend early identification of patients at risk for developing HF in order to prevent progression to clinical stages of HF [26,27]. The limitations of our study were the following: We involved in present study only subjects aged 35 to 64 years, several factors such as renal function and cardiac rhythm were not recorded in this study, which may have had some influence on the NT-pro BNP levels.

5. CONCLUSION

The present study showed that the overall prevalence of pre-heart failure in hypertensive subjects was 15.8% and has increased with age. The poor blood pressure control and

aging were significant risk factors in the development of pre-heart failure in subjects with hypertension.

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Conflict of interest is not declared.

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