

Artikel Penelitian

## *Gender and Hypertention (Data analysis of The Indonesia Basic Health Research 2007)*

### Gender dan Hipertensi (Analisis data Riset Kesehatan Dasar Indonesia 2007)

Krisnawati Bantas<sup>a\*</sup>, Dwi Gayatri<sup>a</sup><sup>a</sup>Departemen Epidemiologi, Fakultas Kesehatan Masyarakat, Universitas Indonesia

#### ABSTRAK

Tujuan penelitian ini adalah untuk melihat apakah terdapat perbedaan gender pada kejadian hipertensi pada orang-orang Indonesia, setelah dikontrol dengan faktor-faktor individu dan lingkungan. Data berasal dari Riset Kesehatan Dasar Indonesia 2007 dan rancangan potong lintang digunakan. Sampel terdiri dari 13.262 pria dan wanita berusia 15 tahun atau lebih. Regresi logistik regresi multilevel digunakan untuk menganalisis data. Terdapat hubungan yang signifikan secara statistik antara gender dan hipertensi. Wanita lebih kecil kemungkinannya mempunyai hipertensi dibanding pria (OR 0,86 nilai  $P < 0,0033$ ). Terdapat interaksi antara variabel gender dan umur. Hal tersebut mengindikasikan bahwa peluang untuk mempunyai hipertensi pada wanita dan pria bervariasi berdasarkan strata umur. Pada strata umur  $\geq 60$  tahun, wanita lebih besar kemungkinannya mempunyai hipertensi dibanding pria (OR 1,25, nilai  $P 0,0065$ ); pada strata umur 30-59 tahun, tidak terdapat perbedaan untuk mempunyai hipertensi antara wanita dan pria ( $P$  value  $> 0,05$ ); pada strata umur  $<30$  tahun, wanita lebih kecil kemungkinannya untuk mempunyai hipertensi dibanding pria (OR 0.67 Pvalue 0.0000). Diantara wanita, dengan bertambahnya umur terdapat peningkatan peluang mempunyai hipertensi. Umur  $\geq 60$  tahun merupakan risiko tertinggi untuk mempunyai hipertensi. Diantara pria, dengan bertambahnya umur terdapat peluang untuk mempunyai hipertensi, tetapi pada umur  $\geq 60$  tahun risiko untuk mempunyai hipertensi tidak setinggi pada wanita.

**Kata kunci:** Hipertensi, Gender, Analisis Multilevel, Indonesia

#### ABSTRACT

The objective of this study was to examine whether there was a gender difference in the occurrence of hypertension in Indonesian people, after controlling for individual and environment factors. Data were obtained from the Indonesia Basic Health Research 2007 and a cross-sectional design was used. Samples consisted of 13.262 men and women age 15 years or more. A multilevel logistic regression was used to analyze the data. There was a statistically significant association between gender and hypertension. Women were less likely to have hypertension than men (OR 0.86 P value  $< 0.0033$ ). There was an interaction between variable of gender and variable of age. It suggested that the probability of having hypertension in women and men was varied by the strata of age. In the strata of age more than 60 years, women were more likely to have hypertension than men (OR 1.25, P value 0.0065); in strata of age 30-59 years, there was no difference of having hypertension between women and men (P value  $> 0.05$ ); in strata of age  $<30$  years, women were less likely to have hypertension than men (OR 0.67 Pvalue 0.0000). Among women, there was an increased of having hypertension with age. Age of  $\geq 60$  years was the highest risk of having hypertension. Among men, there was an increased of having hypertension with age, but at in the age of  $\geq 60$  years the increased risk of having hypertension was not as high as in women.

**Keywords:** Hypertension, Gender, Multilevel Analysis, Indonesia

#### Background

According to The World Health Organization, hypertension is one of the most important causes of premature death worldwide. It is estimated that hypertension causes about 12.8% of the total of all deaths.<sup>1</sup> Hypertension is an independent risk factor for cardiovascular diseases (CVD) in both men and women, and the risk of CVD increases continuously as blood pressures rises from its normal values. For any increased of 20 mmHg of systolic blood pressure or 10 mmHg of diastolic blood pressure will increase 2 times the risk of death risk of CVD.<sup>2</sup> Hypertension can damage blood vessels along with organ function. The damage in blood vessels may lead to the risk for developing several dangerous health conditions including heart attack, stroke, chronic heart failure (CHF), and kidney disease.<sup>3</sup> Approximately 70% of people who have their first heart attack already have hypertension. About 80% of people who have their first stroke have high blood pressure.<sup>4</sup>

**The role of sex hormones in hypertension.** Glucose and lipid metabolism are modulated directly by estrogen and testosterone. Decreased of estrogen or increased of testosterone, relatively induces the occurrence of insulin resistance and atherogenic lipid profile which in turn induce atherosclerosis in blood vessels that result in hypertension. Hypertension is a strong risk factor for cardiovascular diseases in both of sexes, but the prevalence of hypertension, increases faster in older women than in men. Hypertension also carries a greater risk of cardiovascular diseases in women than in men.<sup>5</sup> The role of male and female steroid sex hormones in mediating or protecting cardiovascular diseases and hypertension is still controversial. Animal studies suggested a strong implication of androgen hormone as a mediator of hypertension,

\*Korespondensi: Krisnawati Bantas, Departemen Epidemiologi, Fakultas Kesehatan Masyarakat, Universitas Indonesia. 1st Floor Building A Kampus Baru UI Depok 16424, Indonesia. Email : Krisnabantas@yahoo.com

but epidemiological studies in human showed that blood testosterone levels appear to decrease in chronic diseases and hypertension.<sup>6</sup>

Men have a relatively higher blood pressure than women for most of their life and cardiovascular disease developed at an earlier age than women.<sup>7</sup> Those data support the role of androgen in mediating cardiovascular diseases in men. However, epidemiological studies in men with chronic cardiovascular diseases such as hypertension showed that testosterone levels were lower in healthy men with equal of age, these findings resulted in many researchers to assume that androgen is not responsible in mediating the occurrence of cardiovascular diseases. Nevertheless, some studies demonstrated the role of androgen on cardiovascular diseases, but the mechanism of how androgen may mediate cardiovascular disease and hypertension was not yet clear. One of the most important recent finding was a study of<sup>8</sup> which reported that testosterone can directly stimulate sodium absorption via the proximal renal tubules. Other researcher had shown previously that androgen receptors were in proximal renal tubules, and because of androgen may influence the components of *renin-angiotensin system* (RAS), it was hypothesized that androgen was able to mediate the sodium reabsorption indirectly via RAS.<sup>9</sup> This information becomes important because it provides evidence that androgen may influence the sodium reabsorption and therefore may influence blood pressures with various mechanisms. One of mechanisms where androgen may cause cardiovascular disease and hypertension is via its effect on vasoconstrictor production. The plasma rennin activity is higher in men than in premenopausal women.<sup>10</sup> Androgen may increase blood pressure and endothelial dysfunction that lead to cardiovascular diseases by increasing vasoconstrictor. It was reported that there was an increase in blood pressure in younger and older men with a low or high dose of androgen therapy.<sup>11</sup> Meanwhile with aging, blood levels of testosterone and other androgens are decreased.<sup>12</sup> Many of in vitro studies showed that estradiol was a cardio-protective.<sup>[13]</sup> However, estradiol also causes the release of hepatic angiotensinogen substrates.<sup>14</sup> The rennin activity increased with the increase of angiotensinogen substrates, and lead to the increase of angiotensin II. Endothelin was another vasoconstrictor affected by estradiol.<sup>15</sup> In animal studies, estradiol or its metabolites.<sup>16</sup> inhibited endothelin synthesis and improved endothelial dysfunction in the experimental female rat.<sup>17</sup> Therefore, estrogen should be a protector against cardiovascular disease due to its positive effect in endothelin inhibition. Estradiol should also be a protector for cardiovascular disease

due to its mitogenic effect. Mori in the year of 2000 reported that estradiol inhibited the neointimal proliferation in female rats with balloon dilatation in their carotid artery.<sup>18</sup> Furthermore, in 2002, Dubey et al.<sup>19</sup> Had reported that estradiol and some of its metabolites were anti mitogenic for smooth muscle cells and heart fibroblast or human aorta.<sup>20</sup> Estradiol was also antioxidants and it protected the occurrence of oxidative stress.<sup>21</sup> which was suspected as a causing factor of endothelial dysfunction related to the presence of hypertension.<sup>22</sup>

### Gender influence on health status.

Gender is different from sexuality. Sexuality is more emphasized in physical and biological differences that differentiate between female and male. Gender is a combination measurement of biological and social differences. It seems that the health inequality between male and female reflects the inequality of biological factors (which relates to sexuality) and social factors, and the interaction of both factors.<sup>[23]</sup> Gender inequality in the health sector can be attributed by the social differences between men and women, such as the differences in exposure to risk factors, resources, lifestyle, such as men are more likely to smoke and consume alcohol than women, while women are more likely physically inactive than men.<sup>24</sup> Women may have greater health problems than men because of lack of access to materials and social condition that support health.<sup>25</sup> Women's social positions are different from men, for example, women have fewer job opportunities due to limited job variations than men, women often earn lower income and more often become a domestic laborer than men.<sup>26</sup> Based on different exposures, gender inequality in health can be determined by conditions where men and women occupy different socioeconomic status. The emphasis of this issue is focused on the inequality of resources that are usually measured by socioeconomic status. Therefore it is expected that gender inequalities in health can occur due to the presence of individual socioeconomic status, and household resources. Further more there are vulnerability differences, which indicates that women undergo health problems with higher rates due to different reactions to social determinant of health than men.<sup>27</sup> As indicated by the literature, variables that related to women's health are more complex, and in addition to socioeconomic status, the different effects of family characteristic on women and men are important. Responsibility and the role of women at home and socioeconomic resources, both are important elements in women's life, and it is crucial for understanding how this condition can affect health. Stress and anxiety are more common among women who claim that they care the elderly or sick individual.<sup>28</sup>

Cardiovascular diseases including hypertension are influenced by sedentary activity patterns; consumptive lifestyle; inequality in the distribution of socioeconomic benefit; and atmosphere pollution. The mechanism in which socioeconomic status and air pollution influences the chronic non-communicable diseases including hypertension mortality can be described by using interconnection of elements of population, behaviour, and habitat. The elements of population include the age, sex and genetic characteristics of population. The behavioral elements accommodate the way of human interacts each other and with their environment. These include smoke, physical activity and diet. Cultural differences among community groups will lead to different behavioral pattern and therefore exposures and susceptibility of individuals to cardiovascular disease including hypertension are also different. In the habitat elements, there are many environmental factors that have implication for cardiovascular disease including hypertension, which include; socioeconomic status, air pollution, meteorology system, water quality, and geochemistry aspects.<sup>29</sup> Individuals from the same population have more similarities each other, than individuals who come from another population, because of individuals who come from the same community share the same amount of conditions such as socioeconomic condition, health care, genetic and lifestyle factors, in the same level over individual level variations. Most of comparative studies which studied the determinant of blood pressure typically use a pure ecological design study<sup>30</sup> or perform a separate analysis of individual and ecological, in the same study. Contrast with multilevel analysis, although the focus of the study in the population level, ecological analysis and combination between individual analysis and ecological analysis, may not allow to determine whether population characteristics affect blood pressure stronger than individual factors or whether blood pressure variations among population because of difference in individual composition in population. Ecological analysis also cannot detect individual characteristics in influencing blood pressure differently among different populations.<sup>31,32</sup> From social epidemiology literatures focusing on health inequality due to differences in poverty status indicates that there is often a negative association between morbidity and mortality with increasing socioeconomic status. This may be due to variation in risk factors at individual level such as, diet or smoking that is affected by socioeconomic status.<sup>33</sup> Other explanation may refer to contextual influences from the environment study in Australia found that there were mortality differences due to cardiovascular disease or other diseases among socioeconomic status groups.<sup>34</sup> The mechanism by which socioeconomic status may affect hypertension is complex and may involve matters such as: social

relationships; access to health resources; harmful behavior such as smoking; inadequate or improper diet; physical inactivity, stress and conditions that may affect individual health. These mechanisms particularly were investigated by epidemiologist looking at individual level risk factors, and comparison between groups in aggregate level studies, and recently with multilevel model which involving individual and aggregate level data.<sup>35</sup> The objective of this study was to examine whether there was a gender difference in the occurrence of hypertension, and whether the likelihood of gender difference in the occurrence of hypertension was influenced by household environment and neighbourhood environment.

## Method

This study used secondary data of The Indonesia Basic Health Research 2007 (Riskesdas 2007). A cross-sectional design and a multilevel analysis had been used to examine the relationship between gender and hypertension. Variables in the study: the outcome variable was Hypertension and the mean exposure variable was Gender (level-1). Hypertension was defined as  $\geq 135/85$  mm Hg Systolic / Diastolic a home blood pressure monitoring (HBPM) diagnostic threshold, according to the American Society of Hypertension, 2014.<sup>36</sup>

The level-2 cluster variable was Household Income which consisted of 5 clusters (1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> quintile of household income). The level-3 cluster variable was Province which consisted of 4 clusters (Sumatera, Jawa-Bali-NTB, Kalimantan-Sulawesi-Maluku, NTT-Papua). The exposure covariate variables of level-1 were variables of: Age (< 30 years, 30-39 years, 40-49 years, 50-59 years and  $\geq 60$  years); Marital status (unmarried, married, widow/widower); Educational level (< high school, = high school, > high school); Emotional status (stress, no stress); Smoking habit (non smoker, light smoker, moderate smoker, heavy smoker); and Physical activity (amount of activity in minutes/week, divided into 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> quartile of the amount of the activity). The exposure covariate variables of the level-2 cluster were variables of Household fibers consumption services per week (1<sup>st</sup> quartile = 0-7 services, 2<sup>nd</sup> quartile = 8-10 services, 3<sup>rd</sup> quartile = 11-14 services, 4<sup>th</sup> quartile  $\geq 15$  services); Household members (1<sup>st</sup> quartile  $\leq 3$  persons, 2<sup>nd</sup> quartile = 4 persons, 3<sup>rd</sup> quartile = 5-6 persons, 4<sup>th</sup> quartile  $\geq 7$  persons); Toddler in household (yes, no). The exposure covariate variables of the level-3 cluster were variables of: Urban status (urban-district, urban-city); Human Development Index (1<sup>st</sup> quartile  $\leq 69.75$ , 2<sup>nd</sup> quartile = 69.76-72.38, 3<sup>rd</sup> quartile = 72.39-75.29, 4<sup>th</sup> quartile  $\geq 75.3$ ).

Population and sample of study: The study population consisted of subjects aged of e" 15 years, lived in urban, have been selected as the sample of Riskesdas 2007, who had blood pressure examinations at least 2 times, non pregnant women, and had complete data. A total sample of 13.262 subjects were included. The Riskesdas 2007 was conducted in 33 provinces, consisted of 438 districts/cities) of Indonesia.

Data analysis: A computer soft ware of Lisrel Liserl 87, LisWin32 was used to analyze data. Univariate analysis was performed to describe the frequency and the distribution of each variable in the study. Bivariate analysis was performed to examine the relationship between each exposure variable and the outcome variable. The aim of the bivariate analysis was to choose the potential confounding variables among exposure variables, that could interfere with the relationship between the mean exposure and the outcome variable. The exposure variables that become candidates in the multivariate analysis were variables with P value of < 0.25. In this bivariate analysis a multilevel logistic regression with only one exposure variable in the model was performed. In multivariate analysis, data were analyzed using multilevel logistic regression.

Multilevel logistic regression analysis is a method to examine the relationship between two or more variables for multilevel data. The dependent variable in this study was a dichotomous variable, while the independent variables were all categorical. The multilevel logistic regression, is similar to The "conventional logistic regression", except in addition to select single analysis unit (e.g. individual) two or three other analysis units (e.g. individual, household, neighborhood), were also selected, analysis unit in the one level relates to analysis unit in other levels, such as subjects who live in a household and household neighbors. Model was built in every level, and the coefficients in lower levels were treated as independent variables in the next higher level. Because of the independent variable of level-1 (individual level) was a dichotomous variable (hypertension yes/no), then the logistic modeling was used. Model in this study consisted of 3 level; level-1: individual, level-2: household, level-3: living area. In each level contained variables of exposures and outcomes. The independent variables of level-1, level-2 and level-3 were hypertension status. The exposure variables of level-1 were: variables of gender (as the mean exposure), age, marital status, educational level, smoking habit, physical activity, and psychological status. The exposure variables of level-2 included variables of household income (as the cluster variable of level-2), household average % calorie consumption of nutritional adequacy rate, househ old average %

protein consumption of nutritional adequacy rate, household fibers consumption, household members,household toddler. The exposure variables of level-3 included: variables of province (as the cluster variable of level-3), living area, and human development index (HDI). There were four types of model in the analysis. Model 0, was a multilevel logistic regression equation without covariate variables of level-1, or level-2, or level-3 (empty model). Model 1, was a multilevel logistic regression equation with independent variables of level-1. Model 2, was a multilevel logistic regression equation with variables of level-1 and level-2 and Model was a multilevel logistic regression equation with variables of level-1, level-2 and level-3.

The aim of this analysis is to estimate validly the assosiation between a mean exposure variable (gender) and the outcome variable (hypertension) by controlling for all measurable covariates variables, so that the association that occurs is not biased by the potential confounder. The strength of the association in this study was measured by odds ratio (OR), interval OR (IOR), population averaged OR (PaOR) and median OR (MOR).

## Results

### Descriptive analysis

Study samples consisted of 13.262 men and women age 15 years or more, who lived in urban area throughout the province in Indonesia.

**Tabel1: Respondent distribution based on hypertension status**

Variable Name	Frekquency	Percentage
Hypertension		
▪ Normal	6013	45.3
▪ Hypertension	7249	54.7

Table 1 showed that 54.7% of respondents are hypertension (hypertension was defined as 85/135 mmHg).

### Bivariate analysis

Bivariate analysis was performed to select candidate exposure variables that would be included in the multivariate analysis model. In their association with the outcome variable, every exposure variable which had a P value of < 0.25 was included in the multivariate model. These exposure variables are presented in Table 4.

**Table 2: The Distribution of hypertension based on exposure variables**

Variable Name	Frequency	Percentage	Hypertension	Hypertension	
				Female	Male
<b>Sex</b>					
Female	7236	54.6	52.8%	-	-
Male	6026	45.4	56.9%		
<b>Age</b>					
≥ 60 years	1498	11.3	85.2%	86.4%	83.8%
50-59 years	1712	12.9	75.9%	77.9%	73.7%
40-49 years	2638	19.9	65.2%	64.3%	66.2%
30-39 years	3074	23.2	51.1%	51.0%	51.1%
< 30 years	4340	32.7	31.9%	25.7%	39.2%
<b>Educational Status</b>					
> High school	1113	8.4	49.7%	41.5%	58.6%
= High school	4018	30.3	47.1%	40.4%	53.7%
< High school	8131	61.3	59.1%	59.5%	58.5%
<b>Marital Status</b>					
Widow /widower	1138	8.6	31.8%	23.1%	39.2%
Married	9199	69.4	59.1%	56.2%	62.4%
Un married	2925	22.1	77.9%	78.0%	77.9%
<b>Smoking Habit</b>					
Nonsmoker	9243	69.7	53.7%	52.5%	57.5%
Light	1794	13.5	56.9%	62.1%	56.3%
Moderate	1926	14.5	56.6%	66.0%	56.3%
Heavy	299	2.3	58.2%	47.1%	58.9%
<b>Physical Activity (min/week)</b>					
4 <sup>th</sup> quartile (>1681)	3196	24.1	56.5%	53.4%	58.3%
3 <sup>rd</sup> quartile (3 841-1680)	2736	20.6	55.0%	53.8%	56.9%
2 <sup>nd</sup> quartile (241-840)	3888	29.3	53.5%	52.3%	55.9%
1 <sup>st</sup> quartile (<240)	3442	26.0	53.5%	52.3%	56.0%
<b>Stress</b>					
No stress	11825	89.2	54.0%	51.9%	56.5%
Stress	1437	10.8	59.8%	58.8%	61.5%
<b>Household income</b>					
1 <sup>st</sup> quintile	2413	18.2	52.5%	51.6%	53.7%
2 <sup>nd</sup> quintile	2689	20.3	55.2%	55.2%	55.2%
3 <sup>rd</sup> quintile	2630	19.8	54.0%	51.9%	56.5%
4 <sup>th</sup> quintile	2749	21.0	55.0%	52.9%	57.4%
5 <sup>th</sup> quintile	2780	20.7	56.3%	52.3%	61.1%
<b>Household average % calory consumption of nutritional adequacy rate</b>					
1 <sup>st</sup> quartile (0-52%)	2713	20.5	54.6%	54.1%	55.1%
2 <sup>nd</sup> quartile (53-69%)	2639	19.9	52.6%	49.8%	56.0%
3 <sup>rd</sup> quartile (70-93%)	5173	39.0	55.2%	52.6%	58.4%
4 <sup>th</sup> quartile (>94%)	2737	20.6	55.7%	54.7%	57.0%
<b>Household fibers consumption (service/week)</b>					
4 <sup>th</sup> quartile (> 15)	2862	21.6	54.6%	51.8%	58.2%
3 <sup>rd</sup> quartile (11-14)	2760	20.8	52.2%	49.4%	56.0%
2 <sup>nd</sup> quartile (8-10)	3970	29.9	54.2%	53.2%	55.2%
1 <sup>st</sup> quartile (0-7)	3670	27.7	57.1%	55.9%	58.3%
<b>Household average % protein consumption of nutritional adequacy rate</b>					
4 <sup>th</sup> quartile (>135%)	2712	20.4	53.6%	50.3%	57.7%
3 <sup>rd</sup> quartile (96-134%)	5020	37.9	54.3%	52.4%	56.8%
2 <sup>nd</sup> quartile (69-95%)	2769	20.9	54.6%	53.4%	56.0%
1 <sup>st</sup> quartile (0-68%)	2761	20.8	56.4%	55.6%	57.2%
<b>Household member</b>					
1 <sup>st</sup> quartile (0-3 people)	3933	29.7	62.4%	60.8%	64.4%
2 <sup>nd</sup> quartile (4 people)	3218	24.3	53.0%	50.7%	55.7%
3 <sup>rd</sup> quartile (5-6 people)	4350	32.8	52.4%	50.2%	54.9%
4 <sup>th</sup> quartile (=7 people)	1761	13.3	46.1%	44.7%	47.7%
<b>Toddler in household</b>					
No toddler	8947	67.5	57.2%	55.5%	59.1%
Toddler present	4315	32.5	49.5%	47.3%	52.2%

**Table 3: The frequency distribution of mean, median, mode, maximum-minimum values of systolic and diastolic blood pressure in men and women**

	Men		Women	
	Systolic BP	Diastolic BP	Systolic BP	Diastolic BP
Mean	133.44	81.73	132.81	82.44
Median	129.50	80.50	127.00	81.00
Mode	120.00	80.00	122.50	79.00
Minimum	114.00	63.00	118.00	59.00
Maximum	245.00	154.00	236.00	152.00

**Table 4 The ORs and P values for the association of each covariate variables with the outcome variable (hypertension)**

Level-1 Covariate Variabels	Hypertension		OR	P value
	Yes	No		
<b>Age*</b>				
= 60 years	1276	222	3.78	0.0000
50-59 years	1299	413	2.27	0.0000
40-49 years	1799	835	1.86	0.0000
30-39 ears	1571	1503	1.18	0.0044
<30 years	1384	2956	1	
<b>Educational Status</b>				
> High school	553	560	1.10	0.1792
= High school	1892	2126	1.29	0.0000
< High school	4805	3326	1	
<b>Marital Status</b>				
Widow /widower	362	776	4.05	0.0000
Married	5437	3762	0.87	0.0056
Un married	2278	647	1	
<b>Smoking Habit *</b>				
Heavy	174	125	1.19	0.0130
moderate	1090	836	0.92	0.3947
mild	1021	773	0.98	0.8835
non smoker	4963	4285	1	
<b>Physical Activity (min/week)*</b>				
4 <sup>th</sup> qrtl (>1681)	1806	1390	0.89	0.0446
3 <sup>rd</sup> qrtl (3 841-1680)	1505	1231	0.98	0.8221
2 <sup>nd</sup> qrtl (241-840 )	2080	1808	1.14	0.0125
1 <sup>st</sup> qrtl (<240 )	1841	1601	1	
<b>Stress*</b>				
No stress	6385	5440	1.19	0.0003
Stress	859	578	1	1
<b>Level-2 Covariate Variables</b>			<b>OR</b>	<b>P value</b>
<b>Household average % caloric consumption of nutritional adequacy rate</b>				
1 <sup>st</sup> quartile (0-52%)	1481	1232	1.01	0.8313
2 <sup>nd</sup> quartile (53-69%)	1388	1251	1.06	0.2417
3 <sup>rd</sup> quartile (70-93%)	2855	2318	0.98	0.6469
4 <sup>th</sup> quartile (>94%)	1524	1213	1	
<b>Household average % protein consumption of nutritional requirement</b>				
4 <sup>th</sup> quartile (>135%)	1454	1258	1.05	0.3145
3 <sup>rd</sup> quartile (96-134%)	2728	2292	1.00	0.8430
2 <sup>nd</sup> quartile (69-95%)	1512	1257	0.99	0.8595
1 <sup>st</sup> quartile (0-68%)	1557	1204	1	
<b>Household fibers consumption* (service/week)</b>				
4 <sup>th</sup> quartile (> 15)				
3 <sup>rd</sup> quartile (11-14)	1563	1299	0.96	0.4922
2 <sup>nd</sup> quartile (8-10)	1441	1319	1.15	0.0111
1 <sup>st</sup> quartile (0-7)	2152	1818	1.03	0.5341
	2095	1575	1	
<b>Household member *</b>				
1 <sup>st</sup> qrtl (0-3 people)	2454	1479	0.64	0.0000
2 <sup>nd</sup> qrtl (4 people)	1705	1513	1.03	0.6150
3 <sup>rd</sup> qrtl (5-6 people)	2279	2071	1.05	0.3494
4 <sup>th</sup> qrtl (=7 people)	812	949	1	
<b>Toddler in household*</b>				
Toddler present	2136	2179	0.77	0.0000
No Toddler	5118	3829	1	
<b>Level-3 covariate Variables</b>			<b>OR</b>	<b>P value</b>
<b>Urban Status*</b>				
Urban-district	3841	2898	1.12	0.0007
Urban-city	3411	3112	1	
<b>Human Development Index (HDI)*</b>				
4 <sup>th</sup> qrtl (>75.3)	1877	1481	0.97	0.5957
3 <sup>rd</sup> qrtl (72.38-75.29)	1857	1384	0.85	0.0025
2 <sup>nd</sup> qrtl(69.76-72.38)	1731	1611	1.13	0.0172
1 <sup>st</sup> qrtl (<69.75)	1780	1541	1	

\*variables were included in the multivariate analysis with P value < 0.25

### Multivariate analysis for the association between gender and hypertension

Six models were developed in the analysis:

1. Model 0-1, there were only the mean exposure variable (Gender) and the outcome variable (Hypertension) in the model.
2. Model 0-2 there were only the mean exposure variable (Gender) and the mean level-2 cluster variable (Household income), with the mean level-3 cluster variable (Province)
3. Model1, all exposure covariate variables of level-1 which had P value of < 0.25 together with the random effect of level-2 (Household income) and the random effect of level-3 (Province) were included in the model;
4. Model 2, was the development of model 1 which included all covariate variables of level-2 cluster which had P value of < 0.25;
- 5) Model 3, was the development of model 2 which included all covariate variables of level-3 cluster;
5. Model 4, was the development of model 3 by excluding covariate variables that were not statistically significant associated with hypertension.

**Table 5: Model 0-1 and Model 0-2. Model 0-1: only consisted of mean exposure variable (gender). Model 0-2 consisted of mean exposure variable (gender) and "random effect" variables of level-2 (household income) and level-3 (province) for the occurrence of hypertension**

Fixed Effect Variabel	Model 0-1			Model 0-2		
	Estimate	OR	P value	Estimate	OR	P value
Gender						
▪ Woman	-0.165	0.85	0.0000	0.54307	0.87	0.00329
▪ Man		1	0.0000			
Random Effect Variabel	MOR		P value	MOR		P value
Level1	-		-			
Level 2				1.12		0.66614
House hold income						
Level3				1.53		0.00000
Province						

The heterogeneity of the occurrence of hypertension among provinces was relatively moderate, showed by the value of MOR of level-3 by 1.53. There was no heterogeneity of the occurrence of hypertension among household income (P value > 0.05)

### The relationship between gender and hypertension

Table 6 shows that the adjusted OR of the association between gender and hypertension in the last model (model 4) was 0.86, with P value < 0.05. There was significant association between gender and hypertension, where women were 0.86 times less likely to have hypertension than men, or with other words men were 1.16 times more likely to have hypertension

**Table 6 The model 1, model 2, model 3 and model 4 of the multilevel logistic regression equation for the association between gender and hypertension variables**

FIXED EFFECT VARIABLES	OR							
	Model1		Model2		Model3		Model4	
Gender								
▪ Woman	0.91	0.87*	0.87*	0.87*	0.87*	0.87*	0.86*	0.86*
▪ Man	1	1	1	1	1	1	1	1
Age								
▪ Age (>60 years)	2.90*	2.95*	2.86*	2.86*	2.86*	2.86*	2.86*	2.86*
▪ Age (50-59 years)	1.55*	1.55*	1.53*	1.53*	1.53*	1.53*	1.53*	1.53*
▪ Age (40-49 years)	1.41*	1.42*	1.39*	1.39*	1.39*	1.39*	1.39*	1.39*
▪ Age (30-39 years)	1.15*	1.16*	1.16*	1.16*	1.16*	1.16*	1.16*	1.16*
▪ Age (<30 years)	1	1	1	1	1	1	1	1
Smoking habit								
▪ Smoking (heavy)	1.12	1.12	1.12	1.12	1.12	1.12	1.12	1.12
▪ Smoking (moderate)	0.88	0.88	0.87	0.87	0.87	0.87	0.87	0.87
▪ Smoking (mild)	0.94	0.94	0.94	0.94	0.94	0.94	0.94	0.94
▪ Smoking (no)	1	1	1	1	1	1	1	1
Marital status								
▪ Widowed	2.29*	2.40*	2.12*	2.12*	2.12*	2.12*	2.19*	2.19*
▪ Married	0.81*	0.81*	0.80*	0.80*	0.80*	0.80*	0.81*	0.81*
▪ Un married	1	1	1	1	1	1	1	1
Educational level								
▪ < High school	1.12	1.11	1.12	1.12	1.12	1.12	1.10	1.10
▪ = High school	1.17*	1.18*	1.16*	1.16*	1.16*	1.16*	1.18*	1.18*
▪ > High school	1	1	1	1	1	1	1	1
Emotional status								
▪ Stres (yes)	1.16*	1.01	0.99	0.99	0.99	0.99	-	-
▪ Stres (no)	1	1	1	1	1	1	1	1
Physical activity (min/wk)								
▪ 1 <sup>st</sup> qrtl (0-240)	0.90*	0.89*	0.89*	0.89*	0.89*	0.89*	0.89*	0.89*
▪ 2 <sup>nd</sup> qrtl (241-840)	1.01	1.00	1.00	1.00	1.00	1.00	1.02	1.02
▪ 3 <sup>rd</sup> qrtl (841-1680)	1.09*	1.09*	1.09*	1.09*	1.09*	1.09*	1.07	1.07
▪ 4 <sup>th</sup> qrtl (>1680)	1	1	1	1	1	1	1	1
Level-2 covariates								
		IOR	PaOR	IOR	PaOR	IOR	PaOR	PaOR
Household fiber consumption (service/wk)								
▪ 1 <sup>st</sup> qrtl (0-7)	-	0.74;1.32	0.99	0.81;1.21	0.99	-	-	-
▪ 2 <sup>nd</sup> qrtl (8-10)	-	0.83;1.48	1.11	0.91;1.34	1.10	-	-	-
▪ 3 <sup>rd</sup> qrtl (11-14)	-	0.76;1.35	1.01	0.83;1.23	1.01	-	-	-
▪ 4 <sup>th</sup> qrtl (>15)	-	1	1	1	1	-	-	-
Household members								
▪ 4 <sup>th</sup> qrtl (7persons)	-	0.51;0.90*	0.68*	0.57;0.84*	0.69*	0.42;0.99	0.64*	0.64*
▪ 3 <sup>rd</sup> qrtl (5-6 persons)	-	0.77;1.10	1.03	0.84;1.25	1.03	0.67;1.60	1.04	1.04
▪ 2 <sup>nd</sup> qrtl (3-4 persons)	-	0.78;1.40	1.05	0.86;1.28	1.05	0.71;1.66	1.08	1.08
▪ 1 <sup>st</sup> qrtl (<3 persons)	-	1	1	1	1	1	1	1
Household toddler								
▪ Yes	-	0.58;1.05*	0.78*	0.65;0.96*	0.79*	0.51;1.21	0.78*	0.78*
▪ No	-	1	1	1	1	1	1	1
Level -3 covariates								
		IOR	PaOR	IOR	PaOR	IOR	PaOR	PaOR
Human Development Index								
▪ 4 <sup>th</sup> qrtl (>753)	-	-	-	0.47;1.99	0.97	0.47;1.99	0.97	0.97
▪ 3 <sup>rd</sup> qrtl (72.38-75.29)	-	-	-	0.43;1.82	0.89*	0.42;2.05	0.87	0.87
▪ 2 <sup>nd</sup> qrtl (69.76-72.38)	-	-	-	0.54;2.29	1.11*	0.55;2.30	1.12	1.12
▪ 1 <sup>st</sup> qrtl (<69.75)	-	-	-	1	1	1	1	1
Urban Status								
▪ City	-	-	-	0.44;1.87*	0.92*	0.44;1.87*	0.91*	0.91*
▪ District	-	-	-	1	1	1	1	1
RANDOM EFFECT VARIABEL								
Level1	-	-	-	-	-	-	-	-
Level 2	-	-	-	-	-	-	-	-
House hold income	1.23	1.16	1.11	1.11	1.11	1.25	1.25	1.25
Level3	1.23	1.80	1.46	1.46	1.46	1.46	1.46	1.46
Province								

\*P value < 0.05, qrtl=quartile

than women. When it was compared to the crude OR of 0.85 (Model 0-1), it showed that after controlling for "random-effect" variables of level-2 and level-3 and all covariate variables of level-1, level-2 and level-3, there was only a small change of the OR value, (from 0.85 to 0.86)

## Modification Effect

To examine whether there was a modification effect of variable of age in the relationship between gender and hypertension, a stratified analysis was performed.

**Table 7: Modification effect test results of variable of gender with covariate variables of level-1 (variables of age)**

Fixed Effect Variabel	Estimate	SE	OR	95% Confidence Interval	P value
<b>Gender *Age</b>					
<b>Between women and man</b>					
▪ Women/men (=60 years)	0.2270	0.0835	1.25*	1.4779 - 1.0655	0.0065
▪ Women/men (50-59 years)	0.1244	0.0855	1.13	1.3389 - 0.9578	0.1455
▪ Women/men (40-49 years)	-0.0595	0.0652	0.94	1.0719 - 0.8282	0.3612
▪ Women/men (30-39 years)	0.0185	0.0656	1.02	1.1585 - 0.8958	0.7772
▪ Women/men (<30 years)	-0.4023	0.0539	0.67*	0.7433 - 0.6016	0.00000
<b>Among women</b>					
▪ Age (=60 years)	1.4482	0.0685	4.25	4.8669 - 3.7214	0.0000
▪ Age (50-59 years)	0.6343	0.0845	1.88	2.2252 - 1.5980	0.0000
▪ Age(40-49 years)	0.3423	0.0719	1.41	1.6214 - 1.2232	0.0000
▪ Age(30-39 years)	0.1706	0.0727	1.19	1.3678 - 1.0285	0.0189
▪ Age (<30 years)			1		
<b>Among men</b>					
▪ Age (=60 years)	0.7959	0.0676	2.22	2.5388 - 1.9414	0.0000
▪ Age (50-59 years)	0.2904	0.0825	1.34	1.5718 - 1.1374	0.0004
▪ Age(40-49 years)	0.3338	0.0751	1.40	1.6178 - 1.2052	0.0000
▪ Age(30-39 years)	0.1848	0.0768	1.20	1.3984 - 1.1141	0.0161
▪ Age (<30 years)			1		

Table 7 showed that the relationship between gender and hypertension was modified by age. **Between women and men:** In the age of e" 60 years, women were 1.25 times more likely to have hypertension than men (OR 1.25, P value 0.00653). In the age group of 50-59 years, 40-49 years, 30-39 years, women and men were likely to have no difference in the occurrence hypertension. In the age of < 30 years, women were 0.67 times less likely to have hypertension than men (OR 0.67, P value < 0.00001).

**Among women:** Compared to women aged < 30 years, women aged e" 60 years were 4.25 times more likely to have hypertension (OR 4.25, P value < 0.00001), Women aged 50-59 years were 1.88 times more likely to have hypertension (OR 1.88, P value < 0.00001), women aged 40-49 years were 1.41 more likely to have hypertension (OR1.41, Pvalue <0.00001), and women aged 30-39 years were 1.19 times more likely to have hypertension (OR 1.19, P value 0.01895).

**Among men:** Compared to men aged < 30 years, men aged e" 60 years were 2.22 times more likely to have hypertension (OR 2.22, P value P< 0.00001), men aged 50-59 years were 1.34 times more likely to have hypertension (OR 2.22, Pvalue 0.00043), men aged 40-49 years were 1.40 times more likely to have hypertension (OR1.40, P value 0.00001), and men aged 30-39 years were 1.20 times more likely to have hypertension (OR 1.2, P value 0.01610)

## Discussion

### The prevalence of hypertension

Our study showed that the overall prevalence of hypertension was 54.7% (hypertension was defined as 135/85 mmHg) (Tabel1). Hajjar in 2006<sup>37</sup> revealed that in 1999-2002, 28.6 % of the USA population had hypertension. In the USA trend of the overall prevalence of hypertension from1988-1994 until 1999-2004 was increased particularly due to the increased of the prevalence of hypertension in women. It was in contrast with the goal of "the Health People 2010" which has a target to reduce the percentage of hypertension in adults by 14%.<sup>38</sup> The prevalence of hypertension (defined as 140/90 mmHg) in Eritrea was 15.9% in the general population, with 16.4 % in urban and 14.5% in rural. Leenen *et al.* in 2008<sup>39</sup> performed a study about the prevalence of hypertension (defined as 140/90 mmHg or taking anti-hypertension drugs) in the population aged 20-79 years in Ontario Canada, the result showed that the overall prevalence of hypertension was 21.3%. When compared to studies that have been mentioned above, the result of our study showed a very high rate of hypertension, which only similar with the prevalence rate of hypertension in India.<sup>40</sup> The difference of hypertension definition (hypertension was defined as 140/90 mmHg in some studies, while our study defined hypertension as 135/85 mmHg), may contribute why in our study the prevalence of hypertension was higher than in other studies.

### The prevalence of hypertension based on gender

Based on gender, the prevalence of hypertension in men was higher than in women (56.9% vs 52.8%) (Table 2) Our finding was in line with the finding of Mufunda et al. in 2006<sup>41</sup> and Sadfar et al. in 2004.<sup>42</sup> According to Mufunda *et al.*, the prevalence of hypertension (defined by 140/90 mmHg) was higher in men than in women. The prevalence of hypertension in Eritrea was 15.9% in general population, 17% in men and 5% in women. Sadfar et al. in 2004<sup>42</sup> performed a study in a lower socioeconomic area in Karachi Pakistan, results of the study showed that the overall prevalence of hypertension was 26%; 34% in men and 24% in women. A study of the prevalence of hypertension was conducted in the province of Ontario Canada in the population age of 20-79 year tahun. Hypertension was defined as 140/90 mmHg and/or taking anti-hypertension drug. Results of the study showed that the prevalence of hypertension was 23.8% in men and 19.0% in women.<sup>38,39</sup> Ibrahim et al., in 2008 a study in Saudi Arabia revealed that the overall prevalence of hypertension in adults (30-70 year) was 26.1%, 28.6 % in men and 23.6% in women.<sup>43</sup>

A study in Tirana Albania showed that the prevalence of hypertension (defined as 140/90 mmHg and/or taking anti-hypertension drug) was 30.2% in men and 22.7% in women.<sup>44</sup> Meanwhile the result of our study was in line with the finding of Gupta et al. in 2003<sup>40</sup> and Borges et al. in 2008<sup>45</sup> which revealed that the prevalence of hypertension was higher in women than in men. In 2003 Gupta et al.<sup>40</sup> reported that through 3 serial of epidemiological studies that observed the prevalence of hypertension in India in the year of 1994, 2001 and 2003. The results of the study showed that there was an increased of the prevalence of hypertension (30%, 36% and 51% in men, and 34%, 38% and 51% in women) from time to time. The study showed that the prevalence of hypertension was higher in women than in men. Borges et al. in 2008<sup>45</sup> conducted a cross-sectional in a country state of Brazil the study showed that the prevalence of hypertension was 16.2% in men and 18.3% in women.

### The relationship between gender and age in the occurrence of hypertension

The result of multivariate multilevel analysis in our study showed that there was an interaction between variables of gender and age in the occurrence of hypertension: Table 8 showed there was an interaction between variables of gender and age in the occurrence of hypertension. **Between women and men:** In the age of  $\geq$  60 years, women were 1.25 times more likely to have hypertension than men (OR 1.25, P value 0.0065); in the age group of 50-59 years, 40-49 years, 30-39 years, women and men were likely to have no difference in the occurrence hypertension; in the age of  $<$  30 years, women were 0.67 times less likely to have hypertension than men (OR 0.67 Pvalue nilai  $P < 0.00001$ ). These data showed that men under the age of 30 years were more likely to have hypertension than women, and ranging in age of 30-59 years there was no difference risk of having hypertension between men and women, it was only after the age of  $\geq$  60 years, women were more likely to have hypertension than men. The result of our study was in line with the finding of Gasse et al. in 2001.<sup>50</sup> Men have relatively higher blood pressures than women for most of their life and CVD developed at an earlier age than women. [7] Quan et al. in 2004<sup>8</sup> revealed that testosterone was able to stimulate directly the sodium absorption via renal proximal tubules. Androgen receptors were present in renal proximal tubules, and because androgens may affect the synthesis of RAS components, it had been hypothesized that androgen can indirectly mediate sodium reabsorption via RAS. This information was important because it provided evidence that androgen could affect sodium absorption and therefore affected blood pressure.<sup>47</sup> Another mechanism by which androgens may

cause CVD and hypertension was via its effect on the production of vasoconstrictors. Plasma rennin activity was higher in men than in premenopausal women.<sup>47</sup> Androgens could increase blood pressure and endothelial dysfunction that lead to CVD by increasing vasoconstrictors.<sup>11</sup> Allen et al. in 2004<sup>48</sup> reported that there was an increase of blood pressure in younger and older men with low or high doses of androgen therapy. A number of mechanisms by which testosterone can increase the blood pressure and damage the blood vessels have been clarified. Testosterone increases blood homocysteine levels. Homocysteine induces endothelial damage, therefore lead to the development of atherosclerosis, and adversely affects the renal function by damaging endothelial cells. In contrast to estradiol, testosterone increases endothelin-1 levels in subjects who undergoing sexual change, where it can increase blood pressure.<sup>47</sup>

According to Hancke in Reckelhoff, androgens affected vascular tone, vascular growth, and atherogenesis, there was evidence that testosterone can protect the response to vascular injury and the development of atherosclerosis.<sup>47</sup> Testosterone was an antisclerotic by a lipid change mechanism. Testosterone also protected the development of injury-induced plaques<sup>54</sup>, but did not inhibit smooth muscle cell proliferation.<sup>47</sup> Testosterone was ineffective in inhibiting mitogen-induced smooth muscle. According to Kolodgie et al. in Reckelhoff, these findings suggested that vasoprotective effect of testosterone was not mediated by the inhibition of the growth of vascular smooth muscle cells.<sup>47</sup> Premenopausal women have a lower tendency to have hypertension than men of her age. However with age the prevalence of hypertension increased sharper in women than in men, where in the age of 65-75 years the prevalence of hypertension was 69% in men and 72% in women.<sup>46</sup>

**Among women:** Compared to women aged  $<$  30 years, women aged  $\geq$  60 years were 4.25 times more likely to have hypertension (OR 4.25, P value  $<$  0.00001), Women aged 50-59 years were 1.88 times more likely to have hypertension (OR 1.88, P value  $<$  0.00001), women aged 40-49 years were 1.41 more likely to have hypertension (OR 1.41, P value  $P <$  0.00001), and women aged 30-39 years were 1.19 times more likely to have hypertension (OR 1.19, P value 0.01895) (Table 9). These data suggested that among women there was an increased risk of hypertension with age. Begin with the age of 30 years until 59 years, when compared to age of  $<$  30 years, women were about 2 times more likely to have hypertension than women aged  $<$  30 years, but after the age of  $\geq$  60 years women were more than 4 times likely to have hypertension than women aged  $<$  30 years. Results of our study were consistent with the finding of <sup>46</sup> which reported that there was an in



creased incidence of hypertension until 4 times in postmenopausal women than in premenopausal women (40% in postmenopausal women vs 10% in premenopausal women). Several cross sectional studies showed there was an increased of systolic and diastolic blood pressure after menopause.<sup>48</sup>

A prospective observation in premenopausal, perimenopausal, and postmenopausal women, showed that postmenopausal women had systolic blood pressure (4-5 mmHg) higher than premenopausal or perimenopausal women. Similarly there was an increase of systolic blood pressure per-decade of age, 5 mmHg higher in perimenopausal and postmenopausal women than in premenopausal women.<sup>47</sup> Because there was a relation with the decreased of estradiol synthesis, it was most likely that the changes in blood pressure was induced by menopause, partly may be due to the reduction of estradiol production. According to Chapman et al. in Reckelhoff, estradiol had an effect in lowering blood pressure, during menstrual cycle, blood pressure decreased in the luteal phase (at the peak of estradiol level) than in follicular phase. During pregnancy, estradiol level increased by 50-180 times and it was related to the decreased blood pressure.<sup>47</sup> Our finding seems to be in line with the findings of Reckelhoff et al. in 2005.<sup>47</sup> Increased of the incidence of postmenopausal hypertension may be mainly due to the activation of rennin-angiotensin-system (RAS) and the occurrence of obesity. The rennin-angiotensin-system is regulated differently in males and females, with the endogenous estrogens suppressing the type 1 prehypertensive angiotensin receptors and stimulating the type 2 protective angiotensin (AT2) receptors and angiotensinogen synthesis.<sup>50</sup> Activation of RAS may play a role in postmenopausal, and increase hypertension in females. RAS and sex hormones also affect natriuresis pressures, renal hemodynamic, and tubular response to salt.<sup>47</sup> This explains partially why females show a lower salt sensitivity in the regulation of their blood pressure before menopause and then salt sensitivity increases after menopause. **Among men:** Compared to men aged < 30 years, men aged e" 60 years were 2.22 times more likely to have hypertension (OR 2.22, P value < 0.00001), men aged 50-59 years were 1.34 times more likely to have hypertension (OR 2.22, P value 0.00043), men aged 40-49 years were 1.40 times more likely to have hypertension (OR 1.40, P value 0.00001), and men aged 30-39 years were 1.20 times more likely to have hypertension (OR 1.2, P value 0.01610) (Table 8). This data showed that among men there was an increased risk of hypertension with age. Compared to men aged < 30 years, men with age of > 30 -59 years were less than 1.5 times more likely to have hypertension, but

after the age of 60 years, until two folds the risk of having hypertension increased until 2 times when compared to men aged < 30 years

## Conclusion

The overall prevalence of hypertension in this study was 54.7%. The prevalence of hypertension was higher among men than women (56.9% vs. 52.8%). There was a statistically significant association between gender and the occurrence of hypertension, where women were less likely to have hypertension than men. There were interactions between variable of gender and variable of age. It suggested that the opportunity of having hypertension in women and men was varied by the strata of age .

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