

Risk Factors of Hypertension in Menopausal Women in Rejomulyo, Madiun

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Abstract

Hypertension is a state of blood pressure ≥ 140 mmHg (systolic) or ≥ 90 mmHg (diastolic). Incidence of women hypertension in Rejomulyo from January to November 2013 reached 28.4%, in which 87% were menopausal. Risk factors increased since early menopausal period. The aim of the study was to analyze risk factors of hypertension in menopausal women in Rejomulyo, Madiun. An observational analysis was conducted with cross-sectional study design. Samples were 90 menopausal women aged 50-80 years using stratified random sampling. Bivariate analysis showed association between obesity ($p=0.023$; CI: 1.4-116.8), abdominal obesity ($p=0.002$; CI: 1.8-24.9), family history suffering of hypertension ($p=0.018$; CI: 1.2-7.1), elderly age ($p=0.028$; CI: 1.2-12.9), high stress level ($p=0.001$; CI: 2.9-19.4) and often sodium consumption ($p=0.001$; CI: 2.4-15.2). Multivariate analysis showed that risk factors of hypertension were abdominal obesity (POR adj=9.2 CI: 1.7-50.9), elderly age or >65 years old (POR adj=8.6; CI: 1.6-45.1), high stress level (POR adj=8.6; CI: 2.6-28.3) and often sodium consumption (POR adj=6.4; CI: 1.9-20.5). This study found that risk factors of hypertension were abdominal obesity, elderly age (>65 years old), high stress level, and high sodium consumption. Tawangrejo Health Center should be in collaboration with relevant sectors such as the PKK and health cadres.

Abstrak

Faktor Risiko Hipertensi pada Wanita Menopause di Rejomulyo, Madiun. Hipertensi merupakan keadaan dimana tekanan darah ≥ 140 mmHg (sistolik) atau ≥ 90 mmHg (diastolik). Kejadian hipertensi pada wanita di Rejomulyo pada bulan Januari-November 2013 mencapai 28,4%, dimana 87% dari jumlah tersebut merupakan wanita menopause. Faktor risiko meningkat sejak periode awal menopause. Tujuan dari penelitian ini adalah untuk menganalisis faktor-faktor risiko hipertensi pada wanita menopause di Rejomulyo, Madiun. Analisis pengamatan dilakukan dengan desain studi *cross-sectional*. Sampel studi adalah 90 wanita menopause berusia 50-80 tahun yang dipilih dengan *stratified random sampling*. Analisis bivariat menunjukkan adanya hubungan antara obesitas ($p=0,023$; CI: 1,4-116,8), obesitas abdominal ($p=0,002$; CI: 1,8-24,9), riwayat keluarga dengan hipertensi ($p=0,018$; CI: 1,2-7,1), usia lanjut ($p=0,028$; CI: 1,2-12,9), tingkat stres yang tinggi ($p=0,001$; CI: 2,9-19,4), dan konsumsi natrium yang tinggi ($p=0,001$ CI: 2,4-15,2). Analisis multivariat menunjukkan bahwa faktor risiko hipertensi adalah obesitas abdominal (POR adj=9,2; CI: 1,7-50,9), usia tua atau >65 tahun (POR adj=8,6; CI: 1,6-45,1), tingkat stres tinggi (POR adj=8,6; CI: 2,6-28,3) dan konsumsi natrium yang tinggi (POR adj=6,4; CI: 1,9-20,5). Studi ini menemukan bahwa faktor risiko hipertensi adalah obesitas abdominal, usia tua (>65 tahun), tingkat stres yang tinggi, dan konsumsi natrium yang tinggi. Pusat Kesehatan Tawangrejo harus bekerja sama dengan berbagai sektor relevan seperti PKK dan kader kesehatan.

Keywords: *hypertension, menopausal women, risk factors*

Introduction

Hypertension or high blood pressure is a state of systolic blood pressure ≥ 140 mmHg and a diastolic blood pressure ≥ 90 mmHg.¹ Symptoms of hypertension will continue in to organs causing more severe damage such as stroke (occurs in the brain and the impact of a high

death), heart failure, narrowing of the left ventricle of the heart muscle, dementia, kidney failure, encephalopathy, and retinal hemorrhage.²

After menopause, the prevalence of hypertension is higher in women than men with 41% of menopausal women suffering from hypertension. This is due to the

occurrence of significant changes in lifestyle, such as physical activity or work and those changes could trigger hypertension. In addition, hormonal changes also occur, namely estrogen decrease. Estrogen regulates the production of homocystein, endothelial, and components of the renin, angiotensin, and aldosterone system.³

According to the observation data of the Women's Health Initiative (WHI), prevalence of hypertension in postmenopausal women is 38%. The prevalence of hypertension in Indonesia in postmenopausal women aged 60-75 years is 58%.⁴ Based on the Annual Report of Hospitals in East Java in 2012, hypertension of outpatient in hospital type A ranked in the third place and ranked in the first place in type B, C, and D hospitals.⁵ One of the cities in East Java which had a high prevalence of hypertension in women was Madiun, which amounted to 14.8 per 1,000 population in January-June 2013.⁶ The highest incidence of hypertension in Madiun occurred in Rejomulyo Village, as it reached 28.4%, which 87% of them were menopausal women, in January-November 2013.⁷

The occurrence of hypertension may be caused several mechanisms that can influence each other. Mechanisms that can lead to hypertension, among others, are the renin and angiotensin system which cause the secretion of angiotensin II; increased cardiac output and peripheral resistance; autonomic nervous system activities; and structural and functional changes.⁸ According to White, the risk factors of hypertension in postmenopausal women can be divided into risk factors that cannot be controlled (such as family history of hypertension and age) and factors that can be controlled (such as obesity, abdominal obesity, lack of physical activity, smoking, alcohol consumption, fat, coffee and natrium consumption).⁹

This study was conducted because the occurrence of hypertension remains high, and incidence continues to rise, and complications occur. Studies on risk factors of hypertension in postmenopausal women have been done before, but variables such as physical activity, obesity and coffee consumption habits result remain controversial, and previous studies found no relationship of fat consumption habits with hypertension.^{10,11} In addition, no one has studied stress level variable using Perceived Stres Scale. The purpose of this study was to analyze risk factors associated with hypertension in postmenopausal women in Rejomulyo, Madiun.

Methods

The research was an observational study with quantitative methods using cross-sectional study design. The target population in this study was postmenopausal women who resided in Rejomulyo, Madiun. The sample of this study was women aged 50-80 years residing in the Rejomulyo who had not experienced menopause for

at least 12 months and had no surgery due. This study excluded those who had smoking habits and consumed alcohol. The respondents also had no history of heart disease, kidney, thyroid and diabetes mellitus. Minimum sample size was 90 respondents and used proportional stratified random sampling method. Data collection was performed by measuring blood pressure, weight, height, waist circumference, and respondent's interview using structured questionnaire. Obesity was measured using body mass index (BMI), while abdominal obesity was measured using waist circumference. Stress was measured using PSS (Perceived Stres Scale). There were 14 questions in the questionnaire prepared for stress level to know individual's perception of stressors in her life, for example, something that cannot be predicted, cannot be controlled as well as perceived burden. The question consists of two parts, namely question of negative responses to stressors with a value of 0-4, and then the second part of the positive responses to stressors with a value of 4-0. The criteria for assessment were often (≥ 1 a day), frequently (2-6 times a week), sometimes (≤ 1 time per week), rarely (≤ 1 time a month), and never. Then, all values were summed up to obtain the total value. An interviewer was present to measure stress level. Validity and reliability test were not conducted as the questionnaire PPS was already standardized. Data analysis used chi-square and logistic regression.

Results and Discussion

The study found that there was a relationship between obesity and hypertension in postmenopausal women. Menopausal women who were obese had 12.9 times higher risk of developing hypertension than lean postmenopausal women in the study, while menopausal women who were obese and had normal weight had no risk factor for hypertension when compared with lean postmenopausal women (Table 1).

Obesity had an association with hypertension in this study. If a person's weight increases, the body mass increases and the greater the volume of blood needed to supply oxygen and nourishment to all body tissues. This resulted in increased load for the heart to pump blood.¹² In addition, postmenopausal women also have atherosclerosis due to the older age and declining estrogen levels. This resulted in increased peripheral resistance that causes more friction volumes of blood into the blood vessels, which are also getting bigger. Increased fat cells result in increased production of angiotensinogen in adipose tissue. Angiotensinogen is important in the increase in blood pressure as it can be converted to angiotensin I by renin.

Then, it can be converted from angiotensin I to angiotensin II by angiotensin converting enzyme (ACE), which can enhance antidiuretic hormone (ADH) and aldosterone. ADH hormone is produced in the hypothalamus (pituitary

Table 1. Bivariate Analysis of Risk Factors of Hypertension in Postmenopausal Women in Rejomulyo, Madiun

Variable	p value	POR	CI 95%
Obesity and Hypertension	0.025*	-	-
Obese	0.023*	12.9	1.4-116.8
Overweight	0.104	7.0	0.7-72.9
Normal	0.189	4.4	0.5-40.6
		Control	
Abdominal obesity	0.002*	6.6	1.8-24.9
Family history of suffering hypertension	0.018*	2.9	1.2-7.1
Age	0.028*		
Elderly	0.028*	3.9	1.2-12.9
Late stage of elderly	0.856	1.1	0.4-3.2
Early elderly		Control	
Physical activity	0.203	1.8	0.7-4.4
Level of stress	0.001*	7.6	2.9-19.4
Sodium consumption	0.001*	6.1	2.4-15.2
High-fat food consumption	0.209	0.59	0.3-1.4
Coffee consumption	3.190	-	-

* $p < 0.05$

gland) and work in the kidney to regulate osmolality (viscosity) and urine volume.⁸ With the increase of ADH, very little urine is excreted out of the body, so that the urine becomes concentrated. To dilute the urine, extracellular fluid volume should be increased by pulling volume from the intracellular fluid. Blood pressure also increases as a result of increased blood volume. In addition, aldosterone hormone is secreted by the adrenal cortex. Aldosterone plays an important role in the kidney to regulate extracellular fluid volume. Aldosterone reduces the excretion of NaCl re-absorption from renal tubules. The increase in NaCl concentration is diluted again by increasing the extracellular fluid volume, which in turn increases the blood volume and pressure.¹³

These results were also consistent with previous studies that showed postmenopausal women who had BMI of 25-28 and ≥ 29 had 1.7 times (95% CI: 1.6 to 1.8) and 2.7 times (95% CI: 2.5-2.9) higher risk of developing hypertension than postmenopausal women who have a BMI < 25 .¹¹ The results also consistent with studies conducted in postmenopausal women in Italy, which found that menopausal women who had BMI of 24-26 had 1.48 (95% CI: 1.39 to 1.57) higher risk and those with BMI > 26 had 2.56 (95% CI 2.41 to 2.71) higher risk of developing hypertension compared to those with normal BMI.¹⁴

Estradiol is a form of estrogen that dramatically decreases in production in postmenopausal women, but estrone (estrogen is weaker than estradiol) is still produced in fat tissue, so it requires more fatty tissue in a postmenopausal woman's body. This causes increased appetite in meno-

pausal women.¹⁵ Thus, menopausal women are more at risk to suffer from obesity that can lead to hypertension.

Menopausal women who experienced abdominal obesity had greater risk 6.6 times of developing hypertension than those who did not experience abdominal obesity. While in the multivariate analysis abdominal obesity was the most influential variable on hypertension than other variables with POR adjusted=9.2. In abdominal obesity, the release of free fatty acids that can lead to excessive oxidative stress is a result of insulin resistance.¹⁶ Insulin resistance can reduce levels of nitric oxide (NO), increase salt sensitivity, or increase plasma volume and levels of catecholamines.¹⁷ This is consistent with a research conducted in 415 postmenopausal women in India aged 40 to 85 years whose results showed that waist circumference had the strongest association with hypertension. The risk of hypertension was the highest compared with lowest tertile of 2.55 (95% CI 1.07 to 6.06).¹⁸

According to Chang, after BMI control, postmenopausal women have higher android fat than gynoid fat than premenopausal women. After controlling for age, android fat in postmenopausal women remains higher than premenopausal women. This suggests that postmenopausal women are more at risk to suffer from abdominal obesity, and it can lead to hypertension.¹⁹

Hypertension tends to be a hereditary disease, particularly primary hypertension. Approximately 70-80% of patients with primary hypertension were found to have a family history of hypertension.

Table 2. Multivariate Analysis of Risk Factor of Hypertension in Menopausal Women at Rejomulyo, Madiun

Variable	B	P value	POR adj	95% CI
High level of stress	2.2	0.001*	8.6	2.6-28.3
High Natrium Consumption	1.8	0.002*	6.4	1.9-20.5
Abdominal obesity	2.2	0.011*	9.2	1.7-50.9
Age		0.036*		
Elderly	2.2	0.011*	8.6	1.6-45.1
Late stage of elderly	0.9	0.193	2.6	0.6-11.4

**p* < 0.05

Menopausal women who had a family history of hypertension had 2.9 times risk of developing hypertension compared with postmenopausal women who had no family history of hypertension in this study. This is consistent with research conducted in Italy, which showed that postmenopausal women who had a family history of hypertension had 1.41 times the risk of developing hypertension compared with postmenopausal women who had no family history of hypertension (95% CI 1.34 to 1.48).¹⁴

Elderly women had 3.9 times higher risk of developing hypertension compared with the initial elderly women in this study. Multivariate analysis showed that age of the elderly had a huge effect on elderly hypertension compared with baseline. It is also consistent with studies conducted Amigoni in Italy in menopausal women, in which women aged 51-55 years had a risk 1.4 times (95% CI 1.3-1.5) higher, while the age of 56-60 years have 2 times higher risk (95% CI 1.8 to 2.2) and those aged 61 years and older had 2.7 higher risk (95% CI 2.5 to 2.9) of having high blood pressure compared with age 40-50 year.¹¹ Variety of physiological changes occur in the body as the women get older such as the thickening of the arterial wall due to the buildup of collagen in the muscle layer. Stiffness of the blood vessels can also be accompanied with a narrowing and plaque that inhibit the possibility of enlarging the peripheral blood circulation. There is also an increase in peripheral resistance and sympathetic activity and lack of baroreceptor sensitivity and the role of the kidney in the rate of renal blood flow and glomerulus filtration rate decreases.²⁰ With older age, physical activity also decreases due to declining physical condition. People who are elderly tend to decrease their physical activity compared to when they were younger.

Lack of physical activity can increase the risk of hypertension because it increases the risk of overweight. People who are inactive are also likely to have higher heart rate that makes the heart muscle work harder at each contraction. The harder and more often heart muscle needs to pump, the greater the pressure imposed on the artery, thereby increasing blood pressure and, if it is persistent, it can lead to hypertension. In addition, the level of physical inactivity can lead to obesity and abdominal obesity.²¹ In this study, we found no correlation between physical activity in postmenopausal women

with hypertension (*p* = 0.203). It is also in line with research conducted by Sase in Semarang which found no association between physical activity in postmenopausal women with hypertension (*p* = 0.275).²² However, these results differ from studies in menopausal women in Italy who had 0.93 times (95% CI 0.87 to 0.99) high physical activity compared with menopausal women whose low physical activity.¹⁴ The difference results of this study may be due to the different criteria of moderate physical activity and weight in each country different and greatly influenced the respondents and the physical condition of the respondents.

Menopausal women experience physical and psychological changes. This occurs because estrogen production in the ovaries decreases, causing burning sensation in the body (hot flashes), and making the women sweaty and anxious, so easily depressed. Thus it is easier for menopausal women to experience stress.²³ Menopausal women who have high stress levels had 7.6 times higher risk of developing hypertension than those who had lower levels of stress. The multivariate analysis showed that high levels of stress had considerable influence on the rate of hypertension compared to low stress. Stress can increase the activity of the sympathetic nerve that regulates the function of nerves and hormones, so it can increase the heart rate, constricts blood vessels, and increased water and salt retention. In times of stress, catecholamine secretion increases.²⁴

Menopausal women who frequently consume foods high in natrium had 6.1 times the risk of developing hypertension than those who rarely consumed natrium consumption. The multivariate analysis revealed that women who had high natrium consumption have POR adjusted = 6.4. This is consistent with a research done by Siskarosi on menopausal women in Surabaya, which found that postmenopausal women who frequently consumed natrium have six times higher risk of developing hypertension than those who rarely consumed natrium.¹⁰ Increased natrium intake causes the body to retain fluid to dilute the natrium in the kidneys, which can ultimately increase blood volume. The heart must work harder to pump blood volume that increases throughout the body tissues via the blood vessels so that the width is fixed and cardiac output also increases. This causes the blood vessels to have blood friction and also

become larger which ultimately resulted in an increase in blood pressure. If this happens on an ongoing basis, it can lead to hypertension.¹³

Postmenopausal women are more sensitive to salt or natrium, compared to premenopausal women. Salt sensitivity in healthy post-menopausal women who do not get hormone replacement therapy (HRT) may be caused by reduced availability of NO. HRT of estradiol in postmenopausal women, lower salt sensitivity.⁴

Frequent fat consumption is closely associated with weight gain risk of hypertension. Fat consumption also increases the risk of atherosclerosis which is associated with increased blood pressure.²⁵ In this study there was no association between fat consumption habits with hypertension in postmenopausal women ($p = 0.209$). It is also consistent with a research in Albania which found that there was no association between habitual consumption of fatty foods in postmenopausal women with hypertension.²⁶ The absence of a relationship between the consumption of high-fat foods can be caused by instruments used, which were only concerned with the frequency of the FFQ. However, the size or quantity of food was also very influential on the calculation of food consumption habits. Therefore, semi-quantitative FFQ instrument is needed to calculate the frequency and size of food consumption that results of a calculation of food consumption habits more specific. By using a semi-quantitative FFQ edible fat content based on the type and size of food consumed can be known.

Caffeine is one component of coffee that has been proven to increase a person's blood pressure by increasing peripheral resistance and increases cardiac output by stimulating the sympathetic.²¹ The results of this study showed that there was no association between frequent coffee consumption and hypertension in postmenopausal women in this study ($p = 3.190$). This is consistent with research in menopausal women in Surabaya, which revealed no association between coffee consumption and hypertension.¹⁰ However, these results differ from studies conducted in New York which found that caffeine had a significant relationship ($p < 0.01$) in six groups of respondents, including postmenopausal women aged 50-64 years.²⁷ In addition, diastolic blood pressure was also significantly associated with coffee consumption. There is an association between coffee consumption and hypertension can be caused by drinking coffee assessment is only concerned with the frequency in one day, but do not pay attention to the type of coffee. Each type of coffee contains different types of caffeine with different resulting effect. For example, milk coffee has different caffeine content with black coffee. In addition, it should be noted that the size of cup of the coffee used and coffee spoon sizes when making coffee may vary.

The multivariate analysis did not find any confounding variables. However, information bias might happen when interviewer ask about family income per month, the perceived stress scale (PSS) and the food frequency questionnaire (FFQ) if during the interview process there is a neighbor or a friend or due to mostly respondents were elderly which less hearing. The study design was cross-sectional, in which the independent and dependent variables were measured at one time as well. As if it took a very long time so that risk factors can lead to hypertension. In addition, measurements were made at the time the woman had entered the postmenopausal period, and it was unknown whether the respondent suffered from hypertension since menopause or before menopause.

Conclusions

Obesity, abdominal obesity, family history of hypertension, age, level of stress, and natrium consumption were statistically associated with hypertension in postmenopausal women. While the level of physical activity, high-fat food consumption and coffee consumption habits were not associated with hypertension in postmenopausal women. Therefore, efforts to prevent hypertension are needed, and they can be done by increasing socialization of the young mothers, pregnant women, and adolescent girls to maintain their weight, so when they enter the menopausal age, their body weight can be controlled. In addition, increasing the development of monitoring sessions and the elderly in the form of Integrated Communicable Diseases is also necessary so that the target is not just the elderly, but also various age groups.

References

1. U.S. Department of Health and Human Service. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report. *NIH Publication* 2004; 4:5230.
2. Tambayong J. *Patofisiologi untuk Keperawatan*. Jakarta: EGC, 2000. [In Indonesia]
3. National Center for Health Statistics (US). *Health, United States, 2010, with Special Feature on Death and Dying*. Hyattsville MD: Data Tables, 2011.
4. Ethical Digest. *Hipertensi dan Menopause*. *Semijurnal Farmasi dan Kedokteran*, 2013;116. [In Indonesia]
5. East Province Health Office. *Profil Kesehatan Provinsi Jawa Timur Tahun 2012*. Surabaya: East PHO; 2013. [In Indonesia]
6. District Health Office Madiun. *Laporan Surveilans Terpadu Penyakit (STP) Puskesmas dan Rumah Sakit Sentinel Kota Madiun*. Madiun: DHO Madiun, 2013. [In Indonesia]
7. PHC Tawangrejo. *Laporan Surveilans Terpadu Penyakit (STP) Puskesmas Tawangrejo Kota Madiun*. Madiun: Puskesmas Tawangrejo, 2013. [In Indonesia]
8. Rusdi NI. *Awat! Anda Bisa Mati Cepat Akibat Hipertensi & Diabetes*. Yogyakarta: Power Books Publishing; 2009. [In Indonesia]

9. White D, Matthew MDD. *The Hormone Makeover 7 Steps to Transform Your Life with Bioidentical Hormones*. US: Xulon Press; 2010.
10. Siskarosi ME. *Faktor yang berhubungan dengan kejadian hipertensi pada wanita menopause di puskesmas lidah kulon Surabaya* [Skripsi]. Surabaya: Universitas Airlangga; 2010. [In Indonesia]
11. Amigoni S, Morelli P, Parazzini F, Chatenoud L. Determinants of elevated blood pressure in women around menopause: results from a cross-sectional study in Italy. *Maturitas*. 2000;34(1):25-32.
12. Yogiantoro M. Hypertension and Insulin Resistance. Dalam: Makalah lengkap The 6th Jakarta nephrology and hypertension course and symposium on hypertension. *Pernefri*. 2006:103-115.
13. Sobel. *Hipertensi: Pedoman Klinis Diagnosis dan Terapi*. Jakarta: Hipokrates; 1999. [In Indonesia]
14. Progetto Menopausal Italia Study Group (AOGOI). Risk factors for high blood pressure in women attending menopause clinics in Italy. *Maturitas*. 2006;53:83-88.
15. Karyadi E. *Hidup bersama penyakit hipertensi, asam urat, jantung koroner*. Jakarta: PT. Intisari Mediatama; 2002. [In Indonesia]
16. WHO. *Regional action plan for the prevention and control of noncommunicable diseases (2013-2020)*. Geneva, Switzerland: WHO; 2013.
17. Dornfeld LP, Maxwell MH, Wals A, Tuck M. Mechanisms of hypertension in obesity. *Kidney Int*. 1987;22:254-258.
18. Ganguli D, Das N, Saha I, Chaudhuri D, Ghosh S, Dey S. Risk factors for hypertension in a population-based sample of postmenopausal women in Kolkata, West Bengal, India. (Online), *Asia Pac. J. Public Health*. 2013;25(5):388-389. doi: 10.1177/1010539511420703.
19. Chang CJ, Wu CH, Yao WJ, Yang YC, Wu JS, Lu FH. Relationships of age, menopause and central obesity on cardiovascular disease risk factors in chinese women. *Int. J. Obes*. 2000;24:1699-1704.
20. Kumar V, Abbas AK, Fausto N. *Hypertensive Vascular Disease*. In: *Robins and Cotran Pathologic Basis of Disease, 7th edition*. Philadelphia: Elsevier Saunders; 2005:528-529.
21. Hernelahti M, Kujala UM, Kaprio J, Karjalainen J, Sarna S. Hypertension in master endurance athletes. *J. Hypertens*. 1998;16(11):1573-1577.
22. Sase FA. *Hubungan durasi aktivitas fisik dan asupan natrium dengan tekanan darah pada wanita menopause*. [Skripsi]. Semarang: Universitas Diponegoro; 2013. [In Indonesia]
23. Palupi S. *Persoalan Psikologis Wanita Menopause*. Yogyakarta: Al-Risalah; 2012. [In Indonesia]
24. Gangwisch JE, Heymsfield SB, Boden-Albala B, Buijs RM, Kreier F, Pickering TG, Rundle AG, Zammit GK, Malaspina D. Short Sleep Duration as a Risk Factor for Hypertension, Analyses of the First National Health and Nutrition Examination Survey. *J. Hypertens*. 2006;47(5): 833-839.
25. Sheps SG. *Mayo Clinic Hipertensi, Mengatasi Tekanan Darah Tinggi*. Jakarta: PT Intisari Mediatama; 2005. [In Indonesia]
26. Haxhihyseni D, Mersini M, Tavo V, Haxhihyseni L, Haxhihyseni A, Spahiu E. *Hypertension and Its Risk Factors Among Women in Fertile and Postmenopausal Period*. COGI BCGI (internet) [cited 2013]. Available from: <http://www.bcgip.com/China/Uploads/Editor/PDF/Haxhihyseni%20%28Vercuni%29.pdf>.
27. Faraq NH, Whitsett TL, McKey BS, Wilson MF, Vincent AS, Everson-Rose SA, Lovallo WR. Caffeine and Blood Pressure Response: Sex, Age, and Hormonal Status. *J Womens Health (Larchmt)*. 2010;19(6):1171-1176.