

Original Article

Comparative Study of Hypertension With Increasing Age of Elderly Postmenopausal Punjabi Women With Cardiovascular Disease: A Cross-sectional Study

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Abstract

Background: The incidence of cardiovascular complications may increase after menopause. Hypertension (HTN) is one of the most remarkable causes leading to heart disease. The increased prevalence of HTN is associated with aging, causing adverse cardiovascular events in postmenopausal elderly women.

Objectives: The present study aimed to compare HTN with the increasing age of elderly postmenopausal women with cardiovascular disease (CVD) and then to find an association between estradiol (E2) levels and the increased prevalence of HTN in these women.

Methods: The present cross-sectional study recruited 265 cases of menopausal women suffering from CVD and 258 controls as menopausal women not suffering from CVD. Serum E2 and serum follicle-stimulating hormone (FSH) were estimated by enzyme-linked immunosorbent assay kits. HTN was assessed in accordance with the guidelines of the Joint National Committee (VII) of high blood pressure. Anthropometric measurements such as weight, height, hip circumference, waist circumference (WC), waist-hip ratio, and body mass index (BMI) for all menopausal women were recorded according to the World Health Organization (WHO) (WHO) 2000 protocol.

Results: Overall, cases of >45.1 years of the menopausal age group conferred more risk toward CVD as compared to cases of ≤45 years of the menopausal age group. A significant positive correlation ($P < 0.05$) was detected for E2 with HTN and obesity profile with increasing age at menopause.

Conclusion: High prevalence of HTN irrespective of the early onset of menopause is one of the crucial risk factors for CVD. Our findings revealed a significant positive correlation of HTN with age at menopause >45.1 years, along with increased levels of E2. Women in this age group were observed to be obese.

Keywords: Age, Cardiovascular disease, Estradiol, Hypertension, Menopause



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Background

The silent killer of the cardiovascular system, hypertension (HTN) can cause adverse outcomes such as myocardial infarction, coronary artery disease, and stroke. The incidence of cardiovascular complications mostly increases in women after menopause if left undiagnosed or inadequately treated. The increased prevalence of HTN in elderly women is mostly associated with aging and loss of endogenous estrogen production (1). According to the World Health Organization (WHO), HTN causes at least 45% and 51% of deaths from heart disease and stroke, respectively, resulting in 9.4 million deaths worldwide each year, which is expected to be an increase of 23.3 million deaths by 2030 (2-4). Engalgau et al reported that in India, the number of hypertensive women will rise from 118.2 million in 2000 to 213.5 million in 2025 (5).

Most people think that HTN is common in elderly people, thus the majority of people underestimate the disease, resulting in various complications such as heart failure and stroke (6).

Women, especially those who are menopausal, are at risk of HTN and cardiovascular disease (CVD) due to estrogen deficiency or imbalance. After age 40, women increasingly acquire atherosclerotic lesions with fibrous cap development as endogenous estrogen levels subside. Intima-media thickness measurements in women before menopause can detect the early signs of subclinical atherosclerosis, particularly when numerous risk factors of coronary heart disease are present (7).

The principal factor contributing to the great arteries' increased vascular stiffness with age is an increase in systolic blood pressure (SBP) in addition to atherosclerotic



changes in the vessel wall, and this abrupt increase in SBP in aging women than men may be due to changes in hormones per se during menopause (8).

Our study was designed with an objective in light of prior evidence regarding the relationship between HTN and age at menopause in postmenopausal women to compare HTN with the increasing age of elderly postmenopausal women of the North West Punjabi population of India with CVD. Further, the study sought to find an association between estradiol (E2) levels and the increased prevalence of HTN in these women. Postmenopausal women were further divided into two groups according to age at menopause (≤ 45 years and > 45.1 years) with a hypothesis on whether age at menopause has an impact on HTN and what can be the contributing factors for this association on the aforesaid population.

Materials and Methods

Design of the Study and Selection of Subjects

The current analytical cross-sectional study included 265 cases of menopausal women suffering from CVD and 258 controls of menopausal women not suffering from CVD. It was conducted at the Sri Guru Ram Das Institute of Medical Sciences and Research in Amritsar, Punjab, India. If necessary, angiography was performed to confirm the diagnosis of cardiovascular illness after taking into account the patient's history, clinical symptoms, and supporting electrocardiographic data. Menopausal women from the general community who had no signs of CVD or a history of the disease were recruited as controls.

Prior to sampling, all the participants were interviewed for clinical history, including general, physical, and systemic examinations, along with written informed consent. The Institutional Ethics Committee approved the study. HTN was assessed according to the guidelines of the Joint National Committee (JNC) on the prevention, detection, evaluation, and treatment of high BP (JNC-VII) as reported by Chobanian et al (9). Those women who were on antihypertensive drugs or with SBP ≥ 140 mm Hg and/or with diastolic blood pressure (DBP) ≥ 90 mm Hg were considered clinically hypertensive. Anthropometric measurements such as height, weight, waist circumference (WC), hip circumference, waist-hip ratio, and body mass index (BMI) for all menopausal women were recorded twice according to the protocol of WHO (10). The normal values of E2 and follicle-stimulating hormone (FSH) were calculated according to the literature provided in the kits

Inclusion Criteria

Women undergoing surgical menopause and natural menopause were included in this study. The first step was to compare the levels of E2 and FSH in naturally menopausal women and surgically induced menopausal women in a pilot study with 50 participants. There was not much of a difference between the two groups' levels. The two groups were combined to emphasize the comparison only between menopausal women with CVD

and menopausal women without CVD. Both groups were matched for the age at menopause.

Exclusion Criteria

The study excluded those female participants who were taking antioxidant supplements or had a chronic illness, an acute infection, hormone therapy, or any of these conditions.

Sample Collection and Analysis

After a 12-hour overnight fast, all participants had their venous blood specimens collected under aseptic conditions. A clear serum sample was obtained after centrifuging the blood sample for 15 minutes at 3000 rpm. E2- a steroid hormone, was quantitatively estimated by an enzyme immunoassay (EIA) consuming commercially available enzyme-linked immunosorbent assay (ELISA) kits from Omega Diagnostic Ltd. (United Kingdom). FSH, a glycoprotein, was quantitatively estimated by an EIA using ELISA kits from ERBA Diagnostic Mannheim GmbH (Germany).

Statistical Analysis

The statistical analysis was performed using IBM SPSS 28.0 software. The continuous data are expressed as the mean \pm standard deviation (SD). In addition, the Student's *t* test was applied to work out the mean difference between the cases and controls. Bonferroni correction at $P < 0.006$ was considered statistically significant. Other than Bonferroni, $P < 0.05$ was considered significant. Frequencies for categorical factors were analyzed by 2×2 Chi-square (χ^2) tables. Further, the odds ratio (OR) at a 95% confidence interval (CI) was determined for the presence of CVD-related risk factors such as age at menopause and HTN. Karl Pearson's correlation was utilized to find the connection between E2, obesity, and HTN risk factors.

Results

Data in Table 1 revealed that SBP, DBP, and WC were statistically significant even after applying Bonferroni correction. The levels of E2 were found to be significantly lower in menopausal women suffering from CVD as compared to women not suffering from CVD. However, the difference was not significant after applying the Bonferroni correction. The levels of SBP ($P = 0.001$) and DBP ($P = 0.0001$), and WC ($P = 0.003$) were observed to be significantly high in cases than in controls.

The parameters of the HTN profile were further stratified into 2 groups according to age at menopause (≤ 45 years and > 45.1 years).

Table 2 represents an insignificant difference ($P = 0.361$ and $P = 0.079$) in the mean values of the HTN profile on comparing the groups for age at menopause ≤ 45 years, whereas a significant difference ($P = 0.001$) was observed between the two groups for all the HTN parameters for age at menopause > 45.1 years. For the hormonal profile,

Table 1. Comparison of Anthropometric and Clinical Characteristics Among Menopausal Women With and Without CVD

Variables	Menopausal Women With CVD (n=265)		Menopausal Women Without CVD (n=258)		P Value
	Range	Mean (SD)	Range	Mean (SD)	
Age at menopause (y)	35-55	44.95 (4.39)	35-57	45.17 (4.65)	0.579
BMI (kg/m ²)	10-32.89	26.51 (5.02)	13.05-40.32	27.29 (4.80)	0.071
WC (cm)	65-124	96.96 (1.06)	67-128	94.12 (10.93)	0.003*
SBP (mm Hg)	90-224	146.34 (24.97)	90-208	139.88 (19.12)	0.001*
DBP (mm Hg)	40-140	86.43 (13.83)	54-110	82.49 (10.31)	0.0001*
PP (mm Hg)	10-119	60 (14.14)	20-101	74.50 (21.92)	0.514
Estradiol (pg/mL)	3.0-46.6	18.25 (9.18)	3.0-47.4	20.30 (9.78)	0.014
FSH (mIU/mL)	31.76-158.8	78.64 (19.35)	32.33-148	75.77 (21.48)	0.109

Note. * $P < 0.006$ was considered statistically significant after Bonferroni correction. Obesity, hypertension, and hormonal factors were compared considering an independent t-test (continuous variables), and the results are represented as mean levels and SD.

CVD: Cardiovascular disease; SD: Standard deviation; BMI: Body mass index; WC: Waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PP: Pulse pressure; FSH: Follicle-stimulating hormone.

Table 2. Comparison of Anthropometric and Clinical Characteristics Between Menopausal Women With and Without CVD Stratified According to Age at Menopause

Variables	Menopausal Women With Age at Menopause, ≤ 45 Years			Menopausal Women With Age at Menopause, > 45.1 Years		
	With CVD (n=151) (Mean Menopausal Age 41.96 Years)	Without CVD (n=120) (Mean Menopausal Age 41.12 Years)	P Value	With CVD (n=114) (Mean Menopausal Age 48.92 Years)	Without CVD (n=138) (Mean Menopausal Age 48.69 Years)	P Value
SBP (mm Hg)	142.83 \pm 23.78	140.35 \pm 19.93	0.361	151.00 \pm 25.83	139.48 \pm 18.46	0.001*
DBP (mm Hg)	85.39 \pm 13.01	82.79 \pm 10.75	0.079	87.82 \pm 14.80	82.22 \pm 9.94	0.001*
PP (mm Hg)	57.17 \pm 18.59	57.31 \pm 13.24	0.946	63.70 \pm 17.36	57.18 \pm 13.48	0.001*
Estradiol, pg/mL	16.71 \pm 7.55	20.43 \pm 9.19	0.001*	20.30 \pm 10.67	20.18 \pm 10.30	0.928
FSH, mIU/mL	80.49 \pm 19.51	73.72 \pm 20.03	0.005*	76.19 \pm 18.96	77.56 \pm 22.59	0.608

Note. * $P < 0.05$ is considered statistically significant. The results are expressed as the mean \pm SD.

SD: Standard deviation; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PP: Pulse pressure; FSH: Follicle-stimulating hormone.

significant ($P = 0.001$) low mean levels of E2 (16.71 ± 7.55) were found in cases with age at menopause ≤ 45 years than in controls (20.43 ± 9.19). The mean levels of FSH were also significantly ($P = 0.005$) high in cases (80.49 ± 19.51) than in controls (73.72 ± 20.03) for this group. On the contrary, an insignificant difference was noticed for both E2 ($P = 0.928$) and FSH ($P = 0.608$) among cases and control subjects with age at menopause > 45.1 years.

In Table 3, the comparison of clinical characteristics within the menopausal age groups of subjects with CVD demonstrated a significant difference in the average values of SBP ($P = 0.006$), pulse pressure (PP, $P = 0.004$), and E2 ($P = 0.002$) in the cases of > 45.1 years of age group as compared to women of ≤ 45 years of age group. With the increase in age at menopause, there is an increase in E2. In other words, women of ≤ 45 years of age group have less E2 value than women of the > 45 years age group.

Table 4 provides data on the prevalence of HTN in obese menopausal women with CVD. Obese women with age at menopause > 45.1 years had ~2-fold high risk toward HTN [$P = 0.023$, OR = 2.47 (1.111-5.462)] in comparison with obese women of ≤ 45 years of age group.

Pearson's correlation was analyzed to observe any association of obesity and HTN profile with E2 hormone in menopausal women with CVD with age at menopause > 5.1 years.

Table 5 presents a significant positive correlation of E2 with BMI ($P = 0.001$, $r = 0.384$), WC ($P = 0.001$, $r = 0.354$), SBP ($P = 0.008$, $r = 0.164$), DBP ($P = 0.011$, $r = 0.157$), and PP ($P = 0.042$, $r = 0.106$) among women with CVD in this age group.

Discussion

The onset of menopause marks the end of a woman's fertile period, including a course of perplexing changes that happen in the body with aging. Although the molecular mechanism underlying the beginning of menopause is not fully known, ovarian failure followed by hormonal imbalance and ovarian depletion may be one of the significant factors. The decline in follicles leads to the production of less estrogen, causing irregularity in menstruation and a combination of other physical discomforts (11).

Risk factors of coronary heart disease become more evident with a decrease in estrogen levels, particularly HTN. HTN management, mainly in the postmenopausal stage, is imperative to preserve the quality of life. CVD risk increases by an increase in the period of time since menopause (12).

The results of the present study revealed a significant increase in the mean values of SBP and DBP in menopausal women with CVD as compared to women without CVD

Table 3. Comparison of Anthropometric and Clinical Characteristics Among Menopausal Women With and Without CVD Within the Menopausal Age Groups

Variables	Menopausal Women With CVD Age at Menopause			Menopausal Women Without CVD Age at Menopause		
	≤45 Years, (n=151)	>45.1 Years, (n=114)	P Value	≤45 Years, (n=120)	>45.1 Years, (n=138)	P Value
SBP (mm Hg)	142.83±23.78	151.00±25.83	0.008*	140.35±19.93	139.48±18.46	0.716
DBP (mm Hg)	85.39±13.01	87.82±14.80	0.158	82.79±10.75	82.22±9.94	0.660
PP (mm Hg)	57.17±18.59	63.70±17.36	0.004*	57.31±13.24	57.18±13.48	0.939
Estradiol (pg/mL)	16.71±7.55	20.30±10.67	0.002*	20.43±9.19	20.18±10.30	0.834
FSH (mIU/mL)	80.49±19.51	76.19±18.96	0.073	73.72±20.03	77.56±22.59	0.153

Note. CVD: Cardiovascular disease; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FSH: Follicle-stimulating hormone

Table 4. Prevalence of HTN in Obese Menopausal Women With CVD According to Age at Menopause ≤45 and >45.1 Years

	Obese Menopausal Women With CVD With Age at Menopause ≤45 Years (n=83, %)	Obese Menopausal Women With CVD With Age at Menopause >45.1 Years (n=59, %)	Chi-square	P Value	OR (95% CI)
HTN present	53 (64)	48 (81)	5.14	0.023*	2.47 (1.111-5.462)
HTN absent	30 (36)	11 (19)			

Note. HTN: Hypertension; CVD: Cardiovascular disease; OR: Odds ratio; CI: Confidence interval.

Table 5. Association of Hypertension and Obesity Profile With Estradiol in Women With CVD

Variables	Women With CVD With Age at Menopause >45.1 Years Estradiol (pg/mL)	
	r	P Value
BMI (kg/m ²)	0.384	0.001*
WC (cm)	0.354	0.001*
SBP (mm Hg)	0.164	0.008*
DBP (mm Hg)	0.157	0.011*
PP (mm Hg)	0.106	0.042*

Note. r: Pearson correlation; CVD: Cardiovascular disease; BMI: Body mass index; WC: Waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PP: Pulse pressure.

(Table 1). Similarly, Coylewright et al observed that both SBP and DBP were related to menopause regardless of age, BMI, pulse rate, and hormonal therapy (13).

According to Conen et al, hypertensive women with high-normal BP (2.92/1000 person-years) had a high rate of cardiovascular events as compared with normotensive women (1.62/1000 person-years). (14).

Endogenous estrogens play a complex function in the development of HTN. It supports a baseline vasodilatory state. As a result, postmenopausal women's development of HTN is facilitated by the loss of endogenous estrogens (1). Dowling et al (15) enrolled menopausal women in the Kronos Early Estrogen Preventive Study and reported that BP was the only factor linked with carotid intimal media thickening prior to randomization to hormonal treatments.

The results were further stratified according to menopausal age. Many epidemiological studies proved that the early onset of menopause may act as one of the reasons for early progression to CVD. It is usually accepted that the normal age at menopause is around 51 years in industrialized nations. However, in non-industrial nations, it goes from 43 to 49 years (16). The average menopausal age in India is 44.3 years. According to Gayathri Devi et al, in their study among the population of Tamil Nadu,

the mean age at menopause was 46.72±2.12 years (17). In a cross-sectional study, Poomalar and Arounassalami (18) reported that the lower income group of women in South India reached menopause at 43.3 years. According to Mahajan et al, the mean age at menopause was 44.54 years in North India (19).

According to the present study of North Western Punjabi females, the mean age at menopause for women with and without CVD was 44.95 and 45.17 years, respectively (Table 1). In Punjab, the incidence of menopause increases mostly after the age of 40. By the age of 40-43 years, 21% of women are affected by menopause. The percentage of menopausal women increases to 53 and 63 among women of age between 46-47 years and between 48-49 years, respectively. A higher proportion of rural than urban women is menopausal at all ages between 30-49 years, especially at younger ages (16). Kaur and Talwar (20) studied rural and urban Punjabi females and reported the mean age as 48.22 and 49.30 years in these groups of females, respectively. In Chandigarh women, the mean age at menopause was 47.91 years as observed by Pathak and Prashar (21). Khokhar et al (22) also concluded that the mean age at menopause was 46.55 years in working women of Jalandhar. Based on the results of Randhawa and Sidhu (23), 49.95 years was the mean age at menopause among the rural women of Amritsar.

Aging has been considered one of the significant determinants of postmenopausal HTN. Daugherty et al proposed that age influences the management of BP (24). Both early onset of menopause and a long postmenopausal period are related to increased BP levels (25). BP is recognized to play a crucial role in the manifestation and progression of atherosclerosis (26).

In the present study, it was represented that as the period of time since menopause increases, the risk of HTN increases as well. Interestingly, when menopausal women were stratified according to age at menopause into two groups, namely, ≤45 years and >45.1 years; hypertensive women with CVD with age at menopause >45.1 years

were at more risk as compared to hypertensive women with age at menopause ≤ 45 years. Significant high mean values were observed for HTN indices (SBP, DBP, and PP) in women with age at menopause > 45.1 years (Table 2). Similarly, Johnson et al (27) found an increased risk of CVD among women in the > 45 years menopausal age group. According to Bhatia et al, the prevalence of HTN over the age of 45 years was found to be 45.2% (28). Chen et al (29) reported a remarkable increase in SBP with age but not with DBP in the Taiwan population. However, Peters et al (30) concluded that SBP was not related to the increased risks of IHD and stroke in a gender-specific associated comparison.

In women of ≤ 45 years of the menopausal age group, a significant difference was found between the mean levels of hormones (E2 and FSH), representing that both E2 and FSH levels were disarranged in women suffering from CVD as compared to women not suffering from CVD with the early onset of the menopausal period (≤ 45 years). Based on the comparison within the menopausal age groups, significantly lower mean levels of E2 were detected for women with CVD in this group when compared to the age groups (Table 3), which adds strength to this observation.

Contrarily, no such difference was observed in the group with a menopausal period of above 45 years. This may imply that the early onset of menopause can be one of the reasons for the manifestation of CVD in these women, along with other factors.

PP acts as a surrogate marker for arterial stiffness which might act as a sign of preclinical atherosclerosis. Many studies have shown that age at menopause and PP are associated with each other. Luoto et al (31) found a small increase in PP in postmenopausal women with early age at menopause. Furthermore, the findings of Liu et al (26) suggested that to decrease the prevalence of atherosclerosis and the burden of CVD, there is a need for controlling BP and monitoring PP levels. Our findings confirmed significantly high levels of PP in the CVD women of > 45.1 years of menopausal age group in comparison to the CVD women of ≤ 45 years of menopausal age group, highlighting that HTN acts as a remarkable risk factor for cardiovascular illness and risk increases with advancing age.

The impacts of hormonal changes after menopause are in many cases concealed by the presence of other cardiovascular risk factors such as age-dependent changes, obesity, and dyslipidemia. In the present study, it was revealed that E2 increased with the increase in the hypertensive profile. Our cases were further divided into obese and non-obese groups (Table 4); HTN was more prevalent in obese women of the menopausal age group of > 45.1 years as compared to obese women of ≤ 45 years of menopausal age group.

With the advancement of age, the vascular structure and functions get affected, resulting in an increase in peripheral vascular resistance and BP (29). Thus, the advancement of vascular illness in women may be affected by aging because

of the methylation of the estrogen receptor gene, which may cause changes in the receptor itself or the ligand for the receptor (32). The higher levels of estrogen in obese women after menopause, when the ovarian involvement of estrogen is extremely minimal, may be caused by aromatase in the adipose tissue, converting androgens to estrogens (33).

Endogenous E2 is related to the development of adiposity, while endogenous E2 itself results from the aromatization of androgens in adipocytes. In this way, the connection between E2 and adiposity is probably going to be bidirectional (34). This effectively explains why these women (> 45.1 years) with high levels of E2 were linked to an increased risk of HTN due to obesity.

Data attained in the study altogether suggest the coexistence of other cardiovascular risk factors such as obesity with increasing age of elderly postmenopausal Punjabi women along with HTN.

Conclusion

The findings of our study demonstrated increased mean values of SBP and PP in women of > 45.1 years of the menopausal age group. Though E2 levels decreased with an increase in age, E2 levels were observed to be more in women of > 45.1 years of the menopausal age group as compared to women in ≤ 45 years of the menopausal age group. Intervening for high levels of E2 observed in women in > 45.1 years of age group in comparison to ≤ 45 years, we observed a positive correlation of both HTN and obesity profile with E2 levels. Further analyses represented that the proportion of HTN was more in obese women of > 45.1 years of age group as compared to obese women of ≤ 45 years of age group. These women had ~ 2 -fold high risk of HTN. Although many studies reported that early menopause is one of the reasons for early HTN, our findings suggest that age at menopause is not necessarily a cause for HTN leading to CVD. The coexistence of other factors does play a vital role in the outcome of CVD complications. Timely screening, detection, treatment, and monitoring are important so that if obesity preceded HTN, it could be detected on time. Other strategies should also be promoted for postmenopausal women to lead a healthy life after their menopausal period.

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Authors' Contribution

Conceptualization: Jyot Amrita, Maninder Singh.

Formal analysis: Jyot Amrita.

Investigation: Jyot Amrita.

Methodology: Jyot Amrita.

Project administration: Jyot Amrita, Maninder Singh.

Resources: Jyot Amrita, Maninder Singh.

Validation: Jyot Amrita, Maninder Singh.

Writing – original draft: Jyot Amrita.

Writing – review & editing: Jyot Amrita, Maninder Singh.

Competing Interests

None.

Ethical Approval

The study was approved by the institute vide letter No. BFUHS/EX/PHD/11/9805 and 1070/Trust/15.

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References

- Barton M, Meyer MR. Postmenopausal hypertension: mechanisms and therapy. *Hypertension*. 2009;54(1):11-8. doi: [10.1161/hypertensionaha.108.120022](https://doi.org/10.1161/hypertensionaha.108.120022).
- World Health Organization (WHO). Causes of Death 2008: Data Sources and Methods. WHO; 2011.
- Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):224-60. doi: [10.1016/s0140-6736\(12\)61766-8](https://doi.org/10.1016/s0140-6736(12)61766-8).
- Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med*. 2006;3(11):e442. doi: [10.1371/journal.pmed.0030442](https://doi.org/10.1371/journal.pmed.0030442).
- Engelgau MM, El-Saharty S, Kudesia P, Rajan V, Rosenhouse PS, Okamoto K. Capitalizing on the Demographic Transition: Tackling Non Communicable Diseases in South Asia. Washington, DC: World Bank; 2011.
- Pradani AD, Mudigdo A, Qadrijati I. Predictors of hypertension in post-menopausal women in Surakarta, Central Java. *J Epidemiol Public Health*. 2018;3(3):312-22. doi: [10.26911/jepublichealth.2018.03.03.02](https://doi.org/10.26911/jepublichealth.2018.03.03.02).
- Sutton-Tyrrell K, Lassila HC, Meilahn E, Bunker C, Matthews KA, Kuller LH. Carotid atherosclerosis in premenopausal and postmenopausal women and its association with risk factors measured after menopause. *Stroke*. 1998;29(6):1116-21. doi: [10.1161/01.str.29.6.1116](https://doi.org/10.1161/01.str.29.6.1116).
- Staessen JA, van der Heijden-Spek JJ, Safar ME, Den Hond E, Gasowski J, Fagard RH, et al. Menopause and the characteristics of the large arteries in a population study. *J Hum Hypertens*. 2001;15(8):511-8. doi: [10.1038/sj.jhh.1001226](https://doi.org/10.1038/sj.jhh.1001226).
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension*. 2003;42(6):1206-52. doi: [10.1161/01.HYP.0000107251.49515.c2](https://doi.org/10.1161/01.HYP.0000107251.49515.c2).
- World Health Organization (WHO). Obesity: Preventing and Managing the Global Epidemic: Report of a WHO Consultation. Vol 894. Geneva, Switzerland: WHO; 2000.
- Baghla N, Sharma S. Onset age of menopause among women in Kangra district of Himachal Pradesh. *The Anthropologist*. 2008;10(4):305-7. doi: [10.1080/09720073.2008.11891067](https://doi.org/10.1080/09720073.2008.11891067).
- Zhou H, Zhang C, Ni J, Han X. Prevalence of cardiovascular risk factors in non-menopausal and postmenopausal inpatients with type 2 diabetes mellitus in China. *BMC Endocr Disord*. 2019;19(1):98. doi: [10.1186/s12902-019-0427-7](https://doi.org/10.1186/s12902-019-0427-7).
- Coylewright M, Reckelhoff JF, Ouyang P. Menopause and hypertension: an age-old debate. *Hypertension*. 2008;51(4):952-9. doi: [10.1161/hypertensionaha.107.105742](https://doi.org/10.1161/hypertensionaha.107.105742).
- Conen D, Ridker PM, Buring JE, Glynn RJ. Risk of cardiovascular events among women with high normal blood pressure or blood pressure progression: prospective cohort study. *BMJ*. 2007;335(7617):432. doi: [10.1136/bmj.39269.672188.AE](https://doi.org/10.1136/bmj.39269.672188.AE).
- Dowling NM, Gleason CE, Manson JE, Hodis HN, Miller VM, Brinton EA, et al. Characterization of vascular disease risk in postmenopausal women and its association with cognitive performance. *PLoS One*. 2013;8(7):e68741. doi: [10.1371/journal.pone.0068741](https://doi.org/10.1371/journal.pone.0068741).
- Kaur K. Obesity in Pre-and Postmenopausal Women, and its Association with Hypertension and Type 2 Diabetes [thesis]. Amritsar: Guru Nanak Dev University; 2013.
- Gayathri Devi S, Ponne S. Health and nutritional status of postmenopausal women living in rural area of Tamil Nadu. *Indian J Res Food Sci Nutr*. 2021;8(1):7-13. doi: [10.15613/fijrfrn%2F2021%2Fv8i1%2F209121](https://doi.org/10.15613/fijrfrn%2F2021%2Fv8i1%2F209121).
- Poomalar GK, Arounassalame B. The quality of life during and after menopause among rural women. *J Clin Diagn Res*. 2013;7(1):135-9. doi: [10.7860/jcdr/2012/4910.2688](https://doi.org/10.7860/jcdr/2012/4910.2688).
- Mahajan N, Aggarwal M, Bagga A. Health issues of menopausal women in North India. *J Midlife Health*. 2012;3(2):84-7. doi: [10.4103/0976-7800.104467](https://doi.org/10.4103/0976-7800.104467).
- Kaur M, Talwar I. Age at natural menopause among rural and urban Punjabi Brahmin females. *Anthropologist*. 2009;11(4):255-8. doi: [10.1080/09720073.2009.11891112](https://doi.org/10.1080/09720073.2009.11891112).
- Pathak RK, Parashar P. Age at menopause and associated bio-social factors of health in Punjabi women. *Open Anthropol J*. 2010;3(1):172-80. doi: [10.2174/1874912701003010172](https://doi.org/10.2174/1874912701003010172).
- Khokhar KK, Kaur G, Sidhu S. Menopausal age in working Punjabi women of Jalandhar and trend in other Indian populations. *Hum Biol Rev*. 2012;1(3):292-305.
- Randhawa R, Sidhu S. Age at natural menopause and menopausal symptoms among rural women of Amritsar (Punjab). *Med Sci*. 2014;7(24):48-55.
- Daugherty SL, Masoudi FA, Ellis JL, Ho PM, Schmittiel JA, Tavel HM, et al. Age-dependent gender differences in hypertension management. *J Hypertens*. 2011;29(5):1005-11. doi: [10.1097/HJH.0b013e3283449512](https://doi.org/10.1097/HJH.0b013e3283449512).
- Izumi Y, Matsumoto K, Ozawa Y, Kasamaki Y, Shinndo A, Ohta M, et al. Effect of age at menopause on blood pressure in postmenopausal women. *Am J Hypertens*. 2007;20(10):1045-50. doi: [10.1016/j.amjhyper.2007.04.019](https://doi.org/10.1016/j.amjhyper.2007.04.019).
- Liu J, Lin Q, Guo D, Yang Y, Zhang X, Tu J, et al. Association between pulse pressure and carotid intima-media thickness among low-income adults aged 45 years and older: a population-based cross-sectional study in rural China. *Front Cardiovasc Med*. 2020;7:547365. doi: [10.3389/fcvm.2020.547365](https://doi.org/10.3389/fcvm.2020.547365).
- Johnson AR, Arasu S, Gnanaselvam NA. Cardiovascular Disease risk factors and 10 year risk of cardiovascular events among women over the age of 40 years in an urban underprivileged area of Bangalore city. *J Midlife Health*. 2021;12(3):225-31. doi: [10.4103/jmh.jmh_219_20](https://doi.org/10.4103/jmh.jmh_219_20).
- Bhatia M, Kumar M, Dixit P, Dwivedi LK. Diagnosis and treatment of hypertension among people aged 45 years and over in India: a sub-national analysis of the variation in performance of Indian states. *Front Public Health*. 2021;9:766458. doi: [10.3389/fpubh.2021.766458](https://doi.org/10.3389/fpubh.2021.766458).
- Chen SC, Lo TC, Chang JH, Kuo HW. Variations in aging, gender, menopause, and obesity and their effects on hypertension in taiwan. *Int J Hypertens*. 2014;2014:515297. doi: [10.1155/2014/515297](https://doi.org/10.1155/2014/515297).
- Peters SA, Huxley RR, Woodward M. Comparison of the sex-specific associations between systolic blood pressure and the risk of cardiovascular disease: a systematic review and meta-analysis of 124 cohort studies, including 1.2 million individuals. *Stroke*. 2013;44(9):2394-401. doi: [10.1161/strokeaha.113.001624](https://doi.org/10.1161/strokeaha.113.001624).

31. Luoto R, Sharrett AR, Eigenbrodt M, Arnett D. Pulse pressure and age at menopause. *BMC Womens Health*. 2002;2(1):6. doi: [10.1186/1472-6874-2-6](https://doi.org/10.1186/1472-6874-2-6).
32. Harvey RE, Coffman KE, Miller VM. Women-specific factors to consider in risk, diagnosis and treatment of cardiovascular disease. *Womens Health (Lond)*. 2015;11(2):239-57. doi: [10.2217/whe.14.64](https://doi.org/10.2217/whe.14.64).
33. Freeman EW, Sammel MD, Lin H, Gracia CR. Obesity and reproductive hormone levels in the transition to menopause. *Menopause*. 2010;17(4):718-26. doi: [10.1097/gme.0b013e3181cec85d](https://doi.org/10.1097/gme.0b013e3181cec85d).
34. Stefańska A, Odrowąż-Sypniewska G. Metabolic syndrome, adipokines and sex hormone concentrations in middle-aged women. *Med Res J*. 2014;2(3):77-83.