Special Invited Article: Review

Hypertension in Women: From Reproductive to Postmenopausal Phase

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Abstract

Globally, an estimated 1.28 billion adults aged 30–79 years have hypertension (HTN), most of them (two-thirds) living in low- and middle-income countries (WHO 2023 report). The demographic of blood pressure (BP) in both genders differs with aging. In people younger than 65 years of age, BP levels in men are higher compared to those of women. Conversely, at age 65 years and older, more women have been found to have elevated BP. Likewise, the cumulative incidence of increased adverse cardiovascular (CV) events in women has been reported as they age. Aside from aging, the influence of bio-social factors among women has been implicated in the development of HTN, such as health status—use of oral contraceptive pills (OCP), menopausal stage, obesity and having polycystic ovarian syndrome (PCOS) disease and socioeconomic condition—educational background, employment status and nuclear family setting. This paper will discuss how these factors affect the development of HTN and the approach of management among affected women from the reproductive to postmenopausal stage of life.

KEYWORDS: hypertension in women, vascular estrogen protection, blood pressure in women lifespan

INTRODUCTION

During their life span, the development of hypertension (HTN) among women varies and is markedly influenced by significant hormonal changes, lifestyle and aging.[1-9]

The prevalence of HTN among women during the reproductive age is lower when compared to men.[1-3] This is due to the protective effect of estrogen.[4] However, HTN in this age group develops due to some multifactorial health issues, such as polycystic ovarian syndrome (PCOS), obesity, development of metabolic syndrome, use of oral contraceptive pills (OCP), pregnancy-related and socioeconomic status.[3,5-7] On the other hand, the prevalence of HTN among women during menopause and the postmenopausal stage is comparable to that of men and increases thereafter with advanced aging.[1,2,8,9] HTN in this age group is primarily due to a decrease in estrogen and loss of its vasoprotective property.[4,8,9]

The diagnosis of HTN among women should be stratified according to the pathophysiologic/etiologic patterns.[9] Secondary cause of HTN (primary aldosteronism, pheochromocytoma, hyperthyroidism, hypothyroidism) must be considered among those in adolescence and early adulthood. In the reproductive years, pregnancy-related (gestational HTN, preeclampsia), PCOS and OCP use would be etiologic possibilities. During menopause, vasomotor symptoms and menopausal hormonal therapy (MHT)-associated causes must be entertained.[8,9] Lastly, in late adulthood, irrespective of age, a BP level above 130/80 is diagnosed as HTN, and vascular changes of aging are primary factors.[9]

Target BP and threshold for treatment in HTN among women are similar to the general population, with a combination of healthy lifestyle and pharmacologic management.[10,11]

Burden of HTN and Epidemiology in Women

The continuous increase in the aging population and prolonged life expectancy has affected disease burden, especially in the Asian region, such as India, China and Japan.[12-14] Global

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Table 1. Prevalence of hypertension among Filipinos according to age and sex in 2015 projected in 2050.

2015		
Age Group (yrs)	**Men**	**Women**
20-24	12.4	3.0
25-29	15.8	5.1
30-34	19.6	8.5
35-39	23.7	14.0
40-44	28.1	21.0
45-49	32.7	27.0
50-54	37.0	31.1
55-59	39.8	34.5
60-64	40.9	37.9
65-69	**41.0**	**41.1**
70-74	**40.8**	**43.4**
75-79	**40.5**	**44.5**
80 and older	**39.6**	**42.5**

2050		
Age Group	**Men**	**Women**
20-24	8.7	1.0
25-29	12.7	1.0
30-34	17.3	3.8
35-39	21.4	10.7
40-44	25.1	14.5
45-49	30.0	17.7
50-54	35.5	22.3
55-59	38.6	29.6
60-64	38.5	39.2
65-69	**37.0**	**48.4**
70-74	**35.6**	**55.3**
75-79	**34.8**	**59.1**
80 and older	**35.6**	**58.2**

Data from Mercado-Asis LB, Atilano AA, Ona DID, Bonzon DD, Vilela GA, Chua CL, et al. Prevalence of hypertension in the Philippines in the year 2050: confronting a major challenge. *J Clin Med Res.*2022;3:1–13.[2]

concern is escalating, specifically among affected hypertensive individuals with uncontrolled BP observed in the middle- and low-income countries with adverse cardiovascular consequences of ischemic heart disease, stroke and kidney disease.[12-19] The recent report by the NCD Risk Factor Collaboration (NCD RisC) [15] resonates with contributing factors that have been reported worldwide: unawareness, low rates of detection, high rates of untreated and low treatment and control rates. Only about 50% are diagnosed, and only two-thirds are treated. Of those treated, only half are controlled.[15-18] These factors lead to increased burden of disease, leading to high premature deaths worldwide.[16-19] Gender inequity and differences have recently been recognized as an equally significant burden and public health concern.[20]

As has been recently reported by us (Mercado-Asis, et al., 2023),[19] the impact of uncontrolled HTN among Filipinos has had a significant effect on days missing work (72%), loss of productivity (63%), suspended household work for up to six days (66%), eleven days of reduced household work (78%) and five days of affected social activity (60%). The paper projected the socioeconomic impact of uncontrolled HTN from 2020 to 2050 with an enormous, challenging and overwhelming impact. The productivity loss of premature mortality accounts for 17% in 2020 and will increase to 20% by 2050. In 2020, 70% of the total economic burden was accounted for by direct and indirect care. At its present value, the economic cost of HTN is expected to increase from US$1 billion in 2020 to US$1.9 billion by 2050.[19]

The aforementioned affected daily life functionality [19] has obviously been affecting the female gender most. Epidemiologically, it is interesting to note the gender differences in the prevalence of HTN in various age brackets.[2,3] In the report of Tyagi [3] and colleagues, the prevalence of HTN increased with age, from 7.3% among adults aged 18–39 to 32.2% among those aged 40–59 and 64.9% among those aged 60 and over. A similar pattern was found among both men (8.4% for those aged 18–39, 34.6% for 40–59 and 63.1% for 60 and over) and women (6.1% for those aged 18–39, 29.9% for 40–59 and 66.5% for 60 and over). Men had a higher prevalence of HTN than women among adults aged 18–39 (8.4% compared with 6.1%, respectively) and aged 40–59 (34.6% compared with 29.9%, respectively), but not among adults aged 60 and over (Figure 1).[3]

Our report (Mercado-Asis, et al., 2022) [2] on the prevalence of HTN among Filipinos projected in 2050 reflects the above study of Tyagi and his group.[2] If it remained uncontrolled by 2050, the prevalence of HTN will increase in the elderly Filipinos by two-fold, three-fold and more than five times among those in their 60s, 70s and 80s, respectively (Table 1). Conspicuously, there were more hypertensive males until equality in gender difference occurred at age 65 to 69 years, after which women dominate. A similar pattern was noted in the 2050 projection, but with a wider ratio of female predilection who will eventually suffer from HTN.[2]

Noteworthy is the burden of untreated HTN in our study.[19] There will be an increase in HTN-attributed deaths from 2015 to 2050 due to the over-doubling of affected individuals: ischemic heart disease (35,000 to 82,000 cases), stroke (26,000 to 60,000 cases), hypertensive heart disease (17,000 to 40,000 cases) and chronic kidney disease (12,000 to 29,000 cases). However, using a 4.70% decline in the prevalence of HTN, based on the 2018 Expanded National Nutrition Survey (ENNS) results,

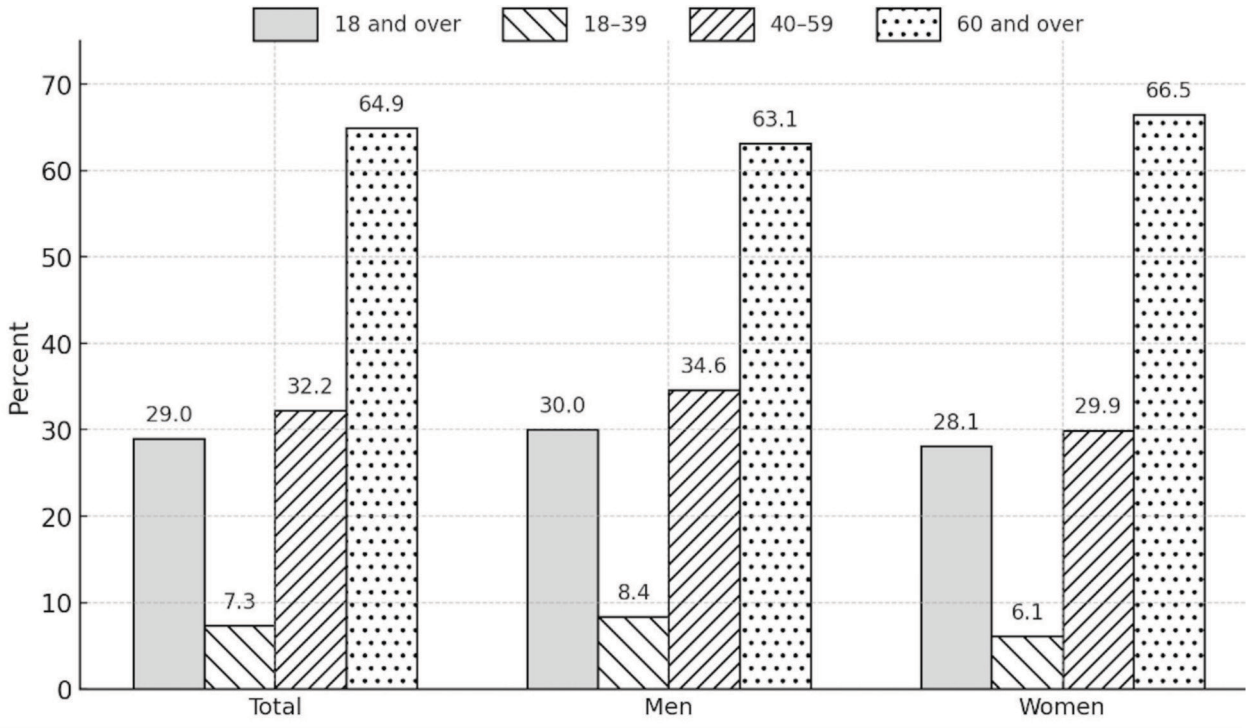

Figure 1. Prevalence of hypertension among adults aged 18 and over, by sex and age: United States, 2001-2014. Adapted with modifications from Yoon SS, Fryar CD, Carroll MD. Hypertension prevalence and control among adults: United States, 2011-2014. *NCHS Data Brief*. 2015 Nov;(220):1-8.[1]

the eventual prevalence of HTN in the Philippines by 2050 is projected to decrease to 15.60%, providing a significant total reduction of 8.30% in HTN prevalence from 2015.[18] The decrease in the prevalence was more observable among females (31.38%) than among males (17.00%). Moreover, a more significant decline in prevalence rate was noted in extreme age groups (the 20s to 30s and 60s to 80s), regardless of sex. If deceleration continues until 2050, the projected mortality will decrease from 210,272 to 137,685. This decline will result in an estimated reduction of 72,587 deaths.[19]

Multifactorial Issues in the Development of Hypertension in Women

There is an intricate network of pathophysiological mechanisms that defines the development of HTN in women from the premenopausal to postmenopausal stage.[3-10]

As the female body transforms through different stages, each of them characterized by specific physiological features and disposition to particular pathological conditions,[3-10] and that is exactly what makes the understanding of the genesis of diagnosis and adequate treatment of HTN in women so challenging.[3,14-20]

Predictors and Contributory Factors in the Development of Hypertension Among Premenopausal and Postmenopausal Women

In a cross-sectional study, the contribution of various biological (hormonal, obesity) and lifestyle factors towards progression of HTN across life phases in females has been elucidated by Tyagi and colleagues.[3] Among 245 women aged 20-65 years, measurements of BP, fat percentage using bio-electric impedance analyzer and adiposity indices such as body mass index (BMI), waist–hip ratio (WHR) and waist–height ratio was performed. As has been previously reported, among both premenopausal and postmenopausal women,[20] the study by Tyagi, et al., showed significant differences with the normotensive women for body weight, regional obesity and general obesity among the prehypertensive and hypertensive groups.[21,22] Furthermore, their findings showed low educational level, working status of women, socioeconomic status and nuclear family setup that were found to be significant risk factors among the female population to develop HTN.[3] This observation has been reflected in the earlier reports of the groups of Mendez (2003) and Minh (2006), specifically in the low-income countries.[23,24] HTN is the highest among the wealthiest women in Jamaica,[23] and, in Vietnam,[24] more women with lower occupational and economic status have elevated BP.

Hormonal and Pathophysiologic Changes in a Woman's Reproductive Life Cycle

Estrogen and Its Cardiovascular Disease (CVD) Protective Advantages

The contribution of estrogen to the gender differences in risk factors, epidemiology and clinical characteristics of HTN between men and women has long been established.[25,26] Reckelhoff recently further elucidated gender differences in the pathophysiologic influence of sex steroids on BP control.[26]

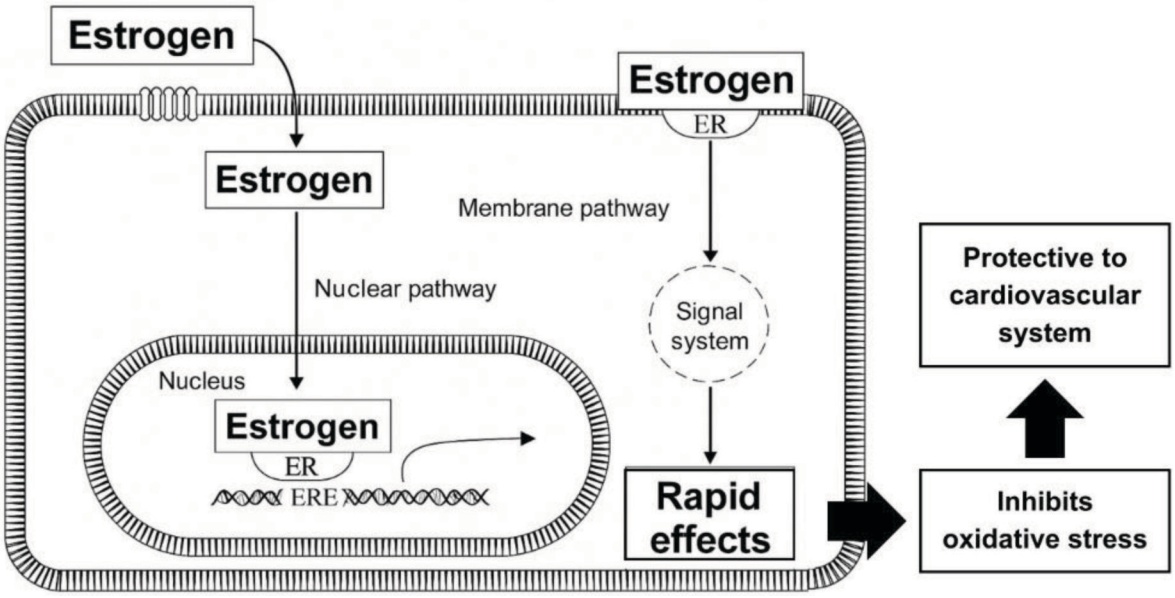

Figure 2. Estrogen genomic effect mediated by nuclear estrogen receptors (ERs) through estrogen response element (ERE) and the nongenomic effect (rapid effects) mediated by membrane ERs. Adapted with modifications from Xiang D, Liu Y, Zhou S, et al. Oxidative Medicine and Cellular Longevity. *Hindawi*. 2021; Article ID 5523516. https://doi.org/10.1155/2021/5523516.[4]

Of note, in females, estrogen is protective of adiposity, which is the reverse in males. On the other hand, androgen protects males against adiposity, favoring increases in lean mass, but in females, androgen causes increase in food intake and eventual adiposity.[26] Although further investigations need to be performed, estrogen has been implicated in two other associated mechanisms of HTN among women, that is, directly affecting major BP controlling pathways like sympathetic nervous system activation and increased sodium reabsorption via the renin-angiotensin system.[26-28]

Foremost among its CV actions, estrogens influence the vascular system, inducing vasodilatation, leading to a protective effect on arterial stiffness during reproductive age that is dramatically reversed after menopause.[3,4,26] Of its types, estradiol (E2) is the most important biological form, and has two classic modes of action, that is, genomic and nongenomic. The genomic effect is a slower mechanism that regulates gene expression and triggers a series of cascade reaction events. The nongenomic, a faster mechanism, relies on coupling with estrogen receptor (G-protein couples estrogen receptor (GPER) distributed in various tissues like the cardiovascular system.[4]

As depicted in Figure 2, one of the important preventive CVD mechanisms of estrogen is the inhibition of oxidative stress (OS), an important risk factor for the development of HTN.[4] Estrogen decreases the risk of CVD by downregulating inflammatory markers, such as chemokines and cell adhesion molecules, to fight atherosclerosis.[29] Moreover, high concentrations of estrogen promote vasodilation by producing prostacyclin, inhibiting endothelin synthesis and blocking calcium channels.[30] In addition, estrogen also has an effect on biomarkers of vascular activity.[31]

Combined Oral Contraceptive Pill-Induced Hypertension (OCPIH) and Hypertensive Disorders of Pregnancy (HDP): Similarities and Shared Mechanisms

Guranatne and colleagues recently elucidated the association of OCPHI and HDP (gestational HTN, preeclampsia, eclampsia) and compared them to oral contraceptive pill (OCP) non-users and normotensive pregnant subjects, respectively (Figure 3).[32] OCPIH and HDP are reported to have common risk factors, such as preexisting metabolic derangements (eg, insulin resistance) [33,34] and genetic predispositions (positive family history).[35,36] In the case of OCPIH, abnormal preexisting conditions can be aggravated by the inherent effects of OCPs, including alterations in lipid and carbohydrate metabolism, insulin resistance, HTN and altered hemostasis.[37,38] These abnormalities can be carried into pregnancy, as has been demonstrated among recent OCP users.[39] Family history is an important risk factor for both OCPIH and HDP, further supporting the role of genetic predisposition.[35,36]

Several studies have demonstrated a positive correlation between having a previous history of HDP/toxemia and OCPIH.[40-42] The development of diastolic HTN while on OCPs was observed to be higher in those who had histories of HDP.[42] Similarly, those with prior histories of elevated BP associated with OCPs, preeclampsia or any history of HTN without an identifiable etiology were found to be at a higher risk of developing OCPIH.[40] These findings are consistent with the group of Pritchard,[43] who found that among 180 women

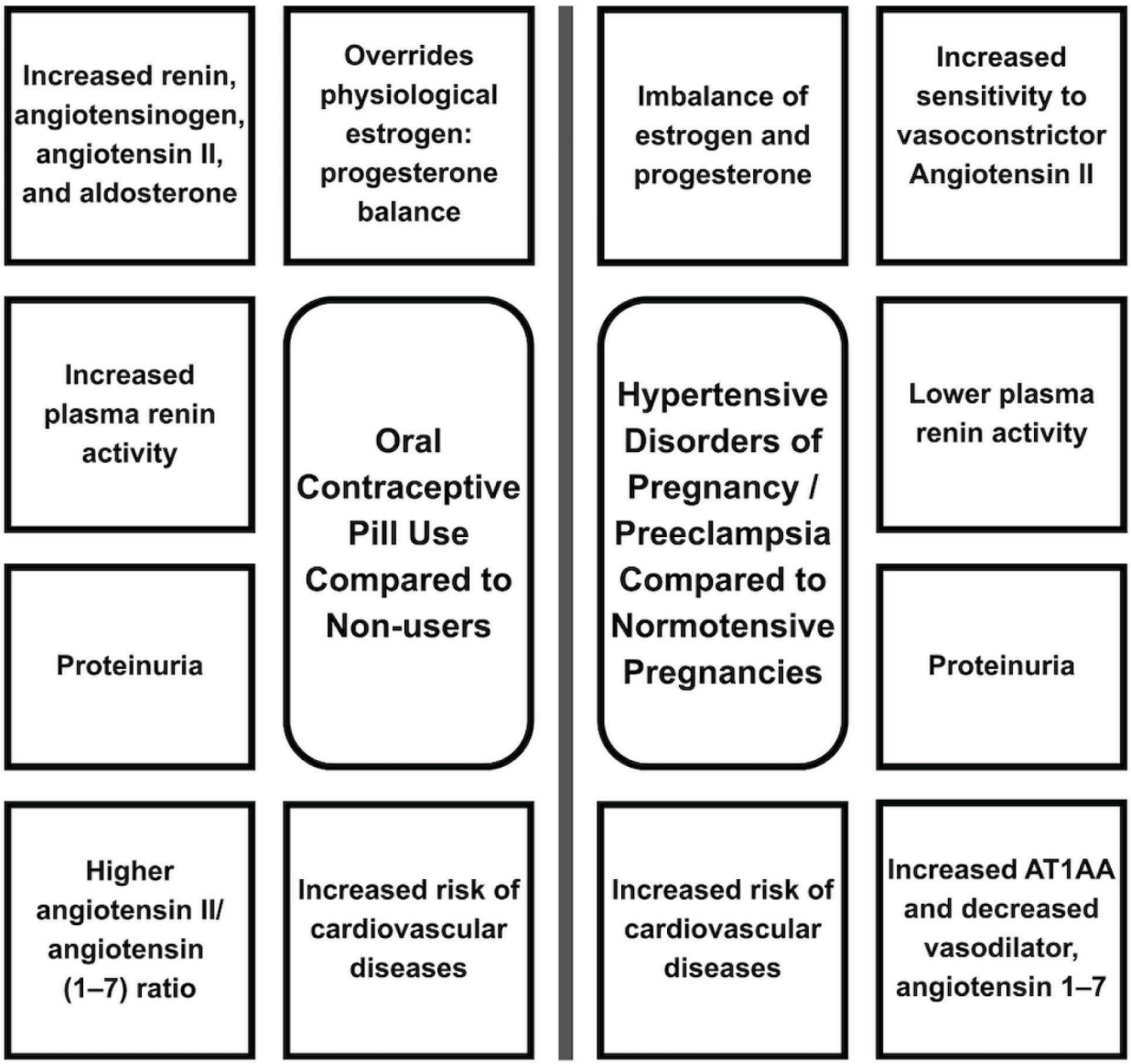

Figure 3. Comparison between physiological effects of oral contraceptive pill (OCP) use (versus non-users) (left) and HDP/ preeclampsia (versus normotensive pregnancies) (right). Adapted with modifications from Gunaratne, MDSK, Thorsteinsdottir, Garovic, VD. Combined oral contraceptive pill-induced hypertension and hypertensive disorders of pregnancy: Shared mechanisms and clinical similarities. *Curr Hypertens Rep*. 2021; 23:29. https://doi.org/10.1007/s11906-021-01147-4.31

following their first pregnancies complicated by HDP (including 26 with eclampsia), 5% developed OCPIH compared to 2.5% of 200 nulligravid women. This study further showed that among those who developed OCPIH, women who had HDP complicating their first pregnancies developed OCPIH within three months of initiation of OCPs, while none of the nulligravid women who developed OCPIH developed it within three months of starting OCPs, demonstrating an early onset in those who have had HDP.[43]

Alterations in the renin-angiotensin-aldosterone system (RAAS) have been implicated in the pathogenesis of both OCPIH [44] and HDP.[45] OCP users have increased angiotensinogen and plasma renin substrate,[46] regardless of the renin concentration.[47,48] In addition, increased levels of angiotensinogen, angiotensin II and aldosterone are also seen in OCP users.[47,49,50] Moreover, exogenous estrogens are better stimulants of angiotensinogen than endogenous estrogens.[51]

Plasma renin activity is increased in women with OCPIH compared to women with essential HTN, although a study did not distinguish differences in plasma renin activity according to phase of the menstrual cycle.[52] In HDP/preeclampsia, however, both de novo and superimposed on chronic HTN, the plasma renin activity was comparatively lower than in normotensive pregnancies.[53]

Another proposed mechanism for HTN that occurs in OCP users is reduced renal blood flow.[48,54] Treatment with

enalapril was shown to reduce the increase in plasma renin concentration, renin activity and angiotensin II that is due to ethinyl-estradiol.[55]

In the study by Ahmed, et al., they showed that non-diabetic OCP users have greater renal vasodilatory response to captopril than non-diabetic nonusers and that the vasodilatory effect was further apparent in diabetic OCP users.[56] They have speculated that the use of OCPs may trigger kidney injury in predisposed individuals.[57]

The identification of angiotensin II type 1 receptor autoantibodies (AT1AA) led to the discovery of a new mechanistic pathway in the pathogenesis of preeclampsia.[58] Studies have demonstrated that blocking the AT1 receptor in a rat model of preeclampsia improved preeclamptic symptoms such as HTN, impaired angiogenesis and preeclampsia-associated vasoconstriction.[59,60] AT1AA, furthermore, have been shown to enhance both renal angiotensin II vascular receptor sensitivity and vasoconstriction.[61]

Treatment for both OCPIH and HDP/preeclampsia mainly focuses on removal of stressors; discontinuation of OCPs and delivery, respectively, thereby reducing the underlying biochemical and biological stressors.[50,62,63] The use of aspirin has been recommended for select patients for the prevention of HDP/preeclampsia.[64] Varying time frames [50,62,65] have been observed for the reversal of increased BP in OCPIH patients, and improvements in both systolic and diastolic BP were noted.[66] However, similar to some preeclamptic pregnancies,[67] there was a susceptible group of individuals with OCPIH whose BP remained elevated [68] and progressed to chronic HTN, possibly prematurely triggered due to OCPs.[69] In multiple studies [41,70-72] and a meta- analysis [73] of OCP use, OCPIH [47] and HD [41,74,75] have been associated with long-term adverse cardiovascular effects, such as stroke and coronary artery disease. The increased risk of acute myocardial infarction (AMI) with OCP use was further increased in those with history of HDP compared to non-OCP users who had normotensive pregnancies.[72] This finding suggests that the adverse cardiovascular effects of OCPIH and HDP may be synergistic.[32]

Assistive Reproductive Technologies and Hypertension

The use of assisted reproductive technologies (ART) to help treat infertility is rising worldwide.[76] A recent systematic review found that there was significantly increased risk of preeclampsia in women who use ART (all types) for conception versus natural conception (relative risk [RR] = 1.71, 95% CI: 1.11–2.62).[77] Invasive ARTs, including intrauterine insemination, in vitro fertilization, intracytoplasmic sperm injection, oocyte donation, single or double embryo transfer and transfer after fresh and frozen cycles, are associated with increased risk of gestational HTN (RR = 1.79 [1.24, 2.57]), preeclampsia (RR = 1.75 [1.50, 2.03]) and all pregnancy related hypertensive disorders (RR= 1.54 [1.39–1.70]) regardless of gestation order.[78] A population-based cohort study from national health registries in Sweden, Denmark and Norway found that hypertensive disorders of pregnancy were found in 6% of ART singleton pregnancies and 13% of ART twin pregnancies.[79] For twin pregnancies, a higher risk of hypertensive disorders was only observed after frozen-thawed cycles compared to spontaneous twin pregnancies [OR = 1.57 (1.34, 1.85)]. The mechanism by which ART increases the risk of preeclampsia is unclear, especially given the multitude of potential confounders associated with infertility itself that may affect the association between ART and preeclampsia. However, a few hypotheses exist. First, recurrent spontaneous miscarriages, which are common with ART, are associated with an increased risk of preeclampsia.[80] Second, placental insufficiency, a hallmark of preeclampsia, may result upon transfer of the conceptus into the uterine cavity of the woman and altered hormonal environment in the endometrium.[81,82] Third, ART may contribute to oxidative stress, which increases the risk of preeclampsia.[77]

There have been conflicting results regarding the potential long-term effect of ART on HTN risk.[83,84] In one study of non-obese women aged 43 years and older who conceived by ART, mean systolic and diastolic BP was higher for up to three years after delivery and age at menopause was significantly earlier compared to women who conceived without ART.[85]

Metabolic Syndrome (MetS) and Increased Vascular Resistance

Within the microvascular network,[86] MetS involves structural changes of arterioles and capillary rarefaction, that in turn are associated with increase in vascular resistance and a resultant increase in mean arterial pressure (MAP). Within the microcirculation,[87] a similar process of vascular remodeling occurs and increases arterial stiffness, which favors increase in systolic BP but also a decrease in diastolic BP. Finally, in MetS, diastolic BP level is the result of two mechanisms: an increase of systemic vascular resistance, which tends to increase diastolic BP, and an increase of arterial stiffness, which is associated with low diastolic BP.[5]

The circulatory differences between men and women can be summarized as either hormonal or nonhormonal. Before menopause, high estrogen levels induce vascular relaxation through their influence on vascular cell membranes, endothelium and smooth muscle.[88] These effects lead to increased distensibility of the carotid arteries and aorta. With menopause, the reduction in estrogen levels and their associated effects help explain the accelerated CV risks in women when compared with men of the same age.[88]

Safar and colleagues have evaluated the effects of MetS on brachial central pulse pressure (PP), PP amplification, aortic stiffness and wave reflections.[5] Their findings have shown increased aortic stiffness, the progression of which is proportional to the number of risk factors involved in MetS. This has been demonstrated to be responsible for increased systolic BP and decreased diastolic BP with increasing age, the principal hallmarks of HTN in the elderly. However, only in patients with MetS were the mean values of PP significantly higher in women than in men.[5]

PCOS as a Risk for Hypertension

Polycystic ovary syndrome (PCOS), a prevalent endocrine and metabolic condition in reproductive age women,[89] is a heterogeneous disorder that is associated with increased cardiovascular risk. Previous studies have demonstrated that almost all CV risk factors, including obesity, insulin resistance, diabetes mellitus, atherogenic dyslipidemia, metabolic syndrome and C-reactive protein are elevated in patients with PCOS;[90-92] these risk factors are present even in young PCOS patients and predispose to the development of early atherosclerosis, cardiovascular morbidity and mortality.[93,94] Androgen excess in patients with PCOS is clearly associated with increased prevalence of cardio-metabolic disturbances.[95] Evidence demonstrated an increased prevalence of subclinical atherosclerosis, endothelial dysfunction, increased carotid intima media thickness and coronary artery calcification in PCOS patients.[92] Shroff and his group showed a 5-fold higher prevalence of subclinical coronary atherosclerosis in young obese women with PCOS compared to the general population.[96] The prevalence of coronary artery calcification is 4-fold higher than in the control population (39.0% vs. 9.9%).[97] It is well documented that PCOS in young women is associated with endothelial dysfunction.[90,98] Previous studies showed an atherogenic lipid profile and increased plasminogen activator type 1 (PAI-I) production in PCOS patients, suggesting that these risk factors are important for developing cardiovascular disease.[99,100]

Increased incidence of HTN has been reported among patients with PCOS.[8] This has been confirmed in a meta-analysis study by Amin and his colleagues, where there was a greater risk of developing HTN among females with PCOS observed only among those in the reproductive group. Interestingly, after menopause, having a history of PCOS may not be as important a predisposing factor for developing HTN.[8] Mechanisms determining the reduction of HTN risk by ageing are unclear, although the progressive decrease of androgens during adult reproductive ages may play a main role; a progressive decrease of serum testosterone in both general populations and in PCOS women was observed many years before the occurrence of menopause.[101] A follow-up study showed that approximately 50% of PCOS patients improve during the late reproductive age because of ovarian and adrenal aging that leads to decreasing androgen levels, which can result in a progressive decrease in cardiovascular risk factors.[102] Other longitudinal studies demonstrated that some cardiovascular risk factors in women with PCOS may be progressively decreased with aging.[103,104]

Menopausal and Postmenopausal Hypertension

During menopause, estradiol levels decrease, thus activating the RAAS and leading to vasoconstriction.[8] There is also increase in salt sensitivity.[8,105] Additionally, androgen production continues in postmenopausal women and may increase arterial stiffness and vascular inflammation, leading to endothelial dysfunction and increased BP.[8,106,107] The severity of menopausal symptoms should also be asked about. Studies have shown that women who experience vasomotor symptoms such as hot flashes have higher awake and asleep BP when compared to women without hot flashes.[108] It is important to note that it is difficult to separate the exact role of hormonal changes from aging on BP. Another mechanism contributing to HTN in postmenopausal women is an increase in sympathetic activation that could be due to increased body weight and redistribution of body fat as well as increased leptin levels.[106] Postmenopausal women are also more likely to have a non-dipping BP pattern which is associated with poorer cardiovascular outcomes and more target organ damage in women compared to men.[108,109]

Before menopause, BP is lower in women compared with age-matched men.[9,110,111] During the menstrual cycle, BP levels are inversely related to circulating estrogen concentrations and lower when 17-estradiol levels peak,[111] reflecting the vasodilator activity of endogenous 17-estradiol.[112] Similarly, increases in endogenous estrogen production during pregnancy contribute to the maintenance of normotension despite marked increases in plasma volume and cardiac output.[111,113] Barton and Meyer elucidated BP changes according to specific decades of a woman's life.[9] The first decade after menopause was accompanied by an increase in BP.[110,114] In the seventh decade of life, the prevalence of HTN among women was even higher than in men, regardless of ethnic background.[110,114] Specifically, there are pronounced increases in both systolic BP and PP in postmenopausal women, whereas diastolic BP remains at a similar level compared with age-matched men.[9]

Tasic and colleagues described the changes in heart morphology, function and compliance of arterial blood vessels that have all been recognized and described in postmenopausal HTN.[20] Postmenopausal women have a higher incidence of left ventricular hypertrophy and are at greater risk of developing diastolic dysfunction compared to young adult women.[114] Groban, et al.,[115] showed that female Lewis rats that underwent bilateral ovariectomy developed progressive diastolic dysfunction. Mori, et al., reported that ovariectomized hypertensive rats had cardiac hypertrophy, myocardial fibrosis and diastolic dysfunction, but 17β-estradiol replacement treatment prevented these changes.[116] The isolated systolic HTN in postmenopausal women was related to aortic stiffness, probably caused by smooth muscle cell proliferation, collagen accumulation and increased levels of vasoconstrictor molecules in the blood vessel wall due to the lack of estrogen's protective effect.[117] Maiello and his group showed that global pulse wave velocity, a reliable indicator of aortic stiffness, is highly increased in postmenopausal women with HTN.[118]

Hypertension in Elderly Women

HTN prevalence increases with age, and a steep rise in rates occurs in women starting as early as the third decade of life.[9] HTN rates are higher in women than in men aged 65 years and older.[119] The mechanism behind increasing BP in elderly women is linked to a decline in nitric oxide synthesis after menopause and a decline in endothelial function, thus leading to impaired endothelium-mediated vasodilation.[120,121] Other non-specific sex mechanisms related to aging contribute to a rise in BP with age, such as inflammation, oxidative stress, comorbidities,

and arterial stiffness.[122,123] NHANES data (2011–2014) showed that among individuals ≥75 years, 81.2% of women have HTN versus 73.4% of men. Compared to young and middle-aged women, elderly women also have more severe HTN and lower rates of BP control.[119]

Treatment of Hypertension in Women

Irrespective of sex and age, the current recommended BP goal is <130/80 mmHg for all adults, except for pregnant women, as previously discussed.[8,11,124] This is in line with the findings from the Systolic BP Intervention Trial (SPRINT) that showed intensive (systolic BP <120 mmHg) versus standard (<140 mmHg) BP lowering resulted in significantly lower rates of fatal and nonfatal cardiovascular events and all-cause mortality even in the prespecified subgroups of women and adults ≥75 years.[125,126] There was no difference in the number of participants who experienced injurious falls or prevalence of orthostatic hypotension in the SPRINT in the intensive versus standard group.[126] The Hypertension in the Very Elderly Trial (HYVET), which enrolled participants over the age of 80 (60% women), showed that hypertensive treatment versus no treatment significantly reduced cardiovascular and all-cause mortality, fatal and non-fatal stroke, and heart failure even after adjustment for sex.[127] Thus, it is important to treat HTN in elderly women and men. Not only that, but controlling BP as a way to optimize cardiovascular health may reduce cognitive decline and prevent dementia in the elderly, irrespective of sex.[128-131]

In a recent review by Carey and his group [10] the following observations were reported. First-line therapy for HTN is a lifestyle modification, including weight loss, a healthy dietary pattern that includes low sodium and high potassium intake, physical activity and moderation or elimination of alcohol consumption. The BP-lowering effects of individual lifestyle components are partially additive and enhance the efficacy of pharmacologic therapy. The decision to initiate antihypertensive medication should be based on the level of BP and presence of high atherosclerotic CVD risk. First-line drug therapy for HTN consists of a thiazide or thiazide-like diuretic such as hydrochlorothiazide or chlorthalidone, an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker such as enalapril or candesartan, and a calcium channel blocker such as amlodipine and should be titrated according to office and home systolic BP/diastolic BP levels to achieve in most people an systolic BP/diastolic BP target (<130/80 mmHg for adults <65 years and systolic BP 130 mmHg in adults ≥65 years). Randomized clinical trials have established the efficacy of BP lowering to reduce the risk of CVD morbidity and mortality. A systolic BP reduction of 10 mmHg decreases the risk of CVD events by approximately 20% to 30%.[10]

Summary and Insight

Prevalence of HTN among women during the reproductive age is lower when compared to men. HTN at this age group is due to lifestyle issues, obesity, PCOS and pregnancy-related. Prevalence of HTN among women during menopause and postmenopausal stage is comparable to men and increases thereafter with advanced aging. HTN at this age group is primarily due to decrease in estrogen and loss of its vasoprotective property and to aging. Target BP and threshold for treatment is around 130/80, with a combination of healthy lifestyle and pharmacologic management.

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