

Effects of Early and Premature Menopause on Women Health

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ABSTRACT

The families and communities health are no doubt depends on the health of women. Improvement in women health is very essential for achieving gender equality. As per the "World Economic Forum's Gender Gap Report" ranks out of 146 countries India ranked sexual hygiene, early marriages, poor nutritional intake, and prostitution. Certain factors contribute to abnormal ovarian functions which lead to an early and premature menopause in women. In fact, premature or an early menopause shows bad effect on women health, as women not taking these issues seriously, so authors are trying to help women to take concern about their health. As a result, this review is focused on various factors associated with premature menopause along with its preventions and management. Early menopause and premature menopause are linked to long-term health risks, including cardiovascular disease, neurological conditions, osteoporosis, whether they occur naturally or are caused by other factors. Hormone replacement therapy, increasing calcium intake, and regular exercise are a few ways to treat and manage the symptoms of early menopause.

Keywords: Menopause, Women's health, Risk factors, Prevention, Management.

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INTRODUCTION

The families and communities' health no doubt depends on the health of women. The improvement in women's health is very essential for achieving gender equality. Menopause means the end of reproductive stage. The normal period of menopause is the age of 45 to 55 in women. When women undergo menopause before 45 ages called early menopause and before at 135th in gender inequality in 2022.¹ As per the report it was found that the biggest challenges faced by women in India is gender-based violence and harassment, which will affect their sexual health and wellbeing. Some other important factors are family and work responsibilities due to number of pregnancies, insufficient gap between children, poor 40 ages called premature menopause. It can vary from region to region. As per the "World Economic Forum's Gender Gap Report" ranks out of 146 countries India ranked at 135th in gender inequality in 2022. In spite of advances in healthcare, women still face problems in their maternal and menstrual health.² Women in India are facing the biggest challenges having certain health issues like breast cancer, ovarian cancer, PCOS. Certain factors which affect women's health are insufficient gap between children, poor sexual hygiene, early marriages, poor nutritional intake, and

prostitution which affect their sexual health and well-being.³ In modern days women are self-dependent and use to work to look after the needs of their family. Working women contribute equal time to housework, office work, and child care and fail to think about themselves. Such overburden has an impact on their health status mentally, physically, and socially.⁴ Certain factors contribute to abnormal ovarian functions which leads to early and premature menopause in women.⁵ Menopause means the end of the reproductive stage. The normal period of menopause is the age of 45 to 55 in women. When women undergo menopause before 45 ages called early menopause and before 40 ages called premature menopause. It can vary from region to region. (Figure 1) Perimenopause, menopause, and postmenopause are the different stages of menopause.⁶

Stages of Menopause

Perimenopause

Perimenopause is also known as menopausal transition this is a stage in which our body make natural transition to menopause called as "around menopause".⁷ Perimenopause is an early stage of menopause where women notice some symptoms due to an abrupt change in the hormonal level. In this stage women experiences irregular period cycle followed by diminishing functioning of the ovaries, abnormalities in menstrual bleeding, heavy periods with bold clots, bleeding after sexual intercourse, very less gap between two periods. During these period ovaries stops the production of



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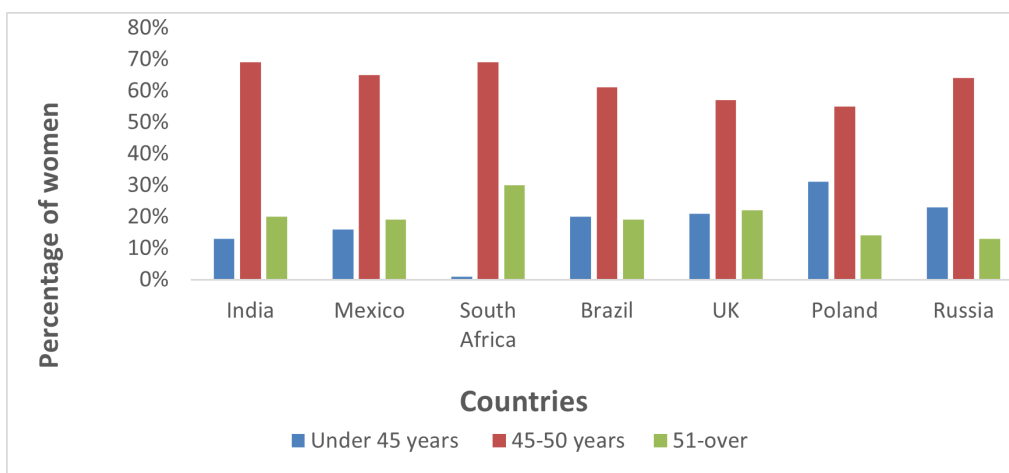


Figure 1: Worldwide Percentage of Women age of premenopausal period.

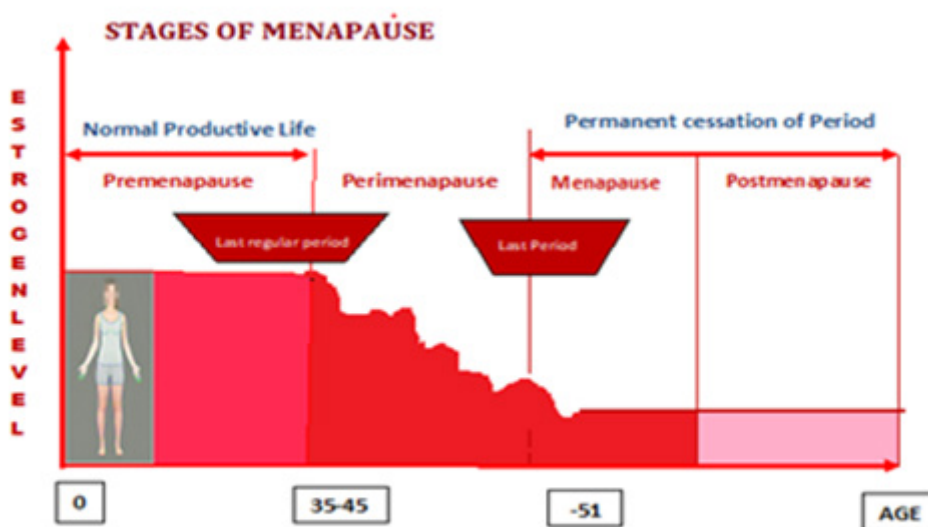


Figure 2: Stages of menopause.

estrogen and progesterone hormone which leads with following symptoms [Figure 2].⁸

- Insomnia (loss of sleep),
- Sweats at night (Body temperature increases at night),
- Sign of ending of periods or frequency of period increases,
- Sudden feeling of warmth felt on the face and neck,
- Palpitation (heart rate increases),
- Vaginal dryness,
- Painful intercourse,
- Low libido (sex drive),
- Frequent urinary tract infection,
- Urinary incontinence,
- Irritability, mood swings and inability to concentrate.

Menopause: End of reproductive age

This is a stage in which women do not get menstrual periods for 12 successive months in which they don't have any reason like

pregnancy, illness, medications, breastfeeding etc. These stages have a no chance of getting pregnant. The normal age for the women to undergo menopause is from 50 to 52 years,⁹ this age may vary from women to women depending on their life style. Those women who use to smoke are more likely get to menopause earlier than nonsmoking women.¹⁰ (Table 1) Women experience following symptoms in this stage.¹⁰ Frequent urge to pee. Breast tenderness. Joint and muscle aches and pains. More forgetful or unable to concentrate. Loss or gain of weight Loss or thinning of hairs.

Post-menopause: Life after menopause

The period after menopause is called as post-menopause, during this stage women not experience anxiety or mood swing but women are most commonly getting to be associated with problems like breast cancer, osteoporosis, cardiovascular disorders, kidney

Table 1: Symptoms associated at different stages of menopause.

Sl. No.	Symptoms	Stages of Menopause			
		Premature Menopause	Perimenopause	Postmenopausal	Menopause
1.	Burning flashes	√	√	√	-
2.	Infrequent periods	√	√	-	-
3.	Loss of bone	√	√	-	-
4.	Mood changes	√	√	√	√
5.	Vaginal aridity	√	√	√	
6.	Insomnia	√	√	√	
7.	Weight gain	-	-	√	√
8.	Breast Tenderness	√	-		
9.	Libido	-	-	√	√
10.	Hair loss	-	-		√
11.	Urinary tract infections	√	-	√	√
12.	Changes in cholesterol level	-	-	-	-

problems, vaginal infections due to imbalance level of estrogen and progesterone.¹¹

Factors responsible for Early/Premenopause

There are some biological and induced reasons to cause early menopause.

Cigarette Smoking

Cigarette is common causing factors of early menopause. In general, women who smoke are likely to get natural menopause about one year former than nonsmokers. In research, it was found that polycyclic hydrocarbons present in tobacco may affect ovarian germ cells and ovary decline to produce estrogen, nicotine and anabasine in tobacco also interfere with the aromatase enzyme which catalyzes the final step of estrogen synthesis which gives less active estrogen and cause the early menopause.¹²

Depression

Literature showed that depression is a possible indication of ovarian dysfunction, the most recent study observed that those women who are using oral contraceptives for a longer time experience depression and also undergo early menopause.¹³ Certain emotional factors are influenced by pituitary ovarian axis at the level of hypothalamus.¹⁴ Researchers have shown the link between deficiency of Gonadotropin Releasing Hormones and environmental and endogenous-generated stress causing hypothalamic amenorrhea.¹⁵ There are, however, few, if any, studies that link hypothalamic amenorrhea with the risk of

early menopause. The means by which depression causing early start of menopause is a bit complex, this mechanism has yet to be accomplished. It is reported that there is a strong association between early menopause and depression in the women.¹⁶

Chemotherapy and Radiation

Chemotherapy or radiation therapy can cause Premature Ovarian Insufficiency (POI) which occurs below a 40 years old age and early menopause between the ages of 40 and 45. Sometimes utilized in large dosages for diagnosing cancer, radiation treatment, and chemo is particularly hazardous to the ovaries.¹⁷ At inborn, ovaries comprise 1 million undeveloped eggs (primitive follicles). The number of eggs decreases naturally and less than 1000 eggs only remains after the treatment of cancer either by chemotherapy or radiation therapy. After this treatment, very few immature eggs remain and are unable to get mature and women can experience infertility. Following radiation or chemotherapy, menstrual period destruction may be temporary or long-lasting. It's certainly not a given that fertility will return just when the cycle of menstruation resumes.¹⁸

Surgery

Surgeries like hysterectomy and bilateral oophorectomy that remove your ovaries and uterus cause abrupt menopause. The menstruation stops after a hysterectomy. Ovaries remain the chief source of estrogen formation in the woman's body, elimination of ovaries produces instant menopause, warm flashes, mood changes, reduced libido, and vaginal aridity, and also sleep disturbances are the common symptoms of surgical menopause.¹⁹

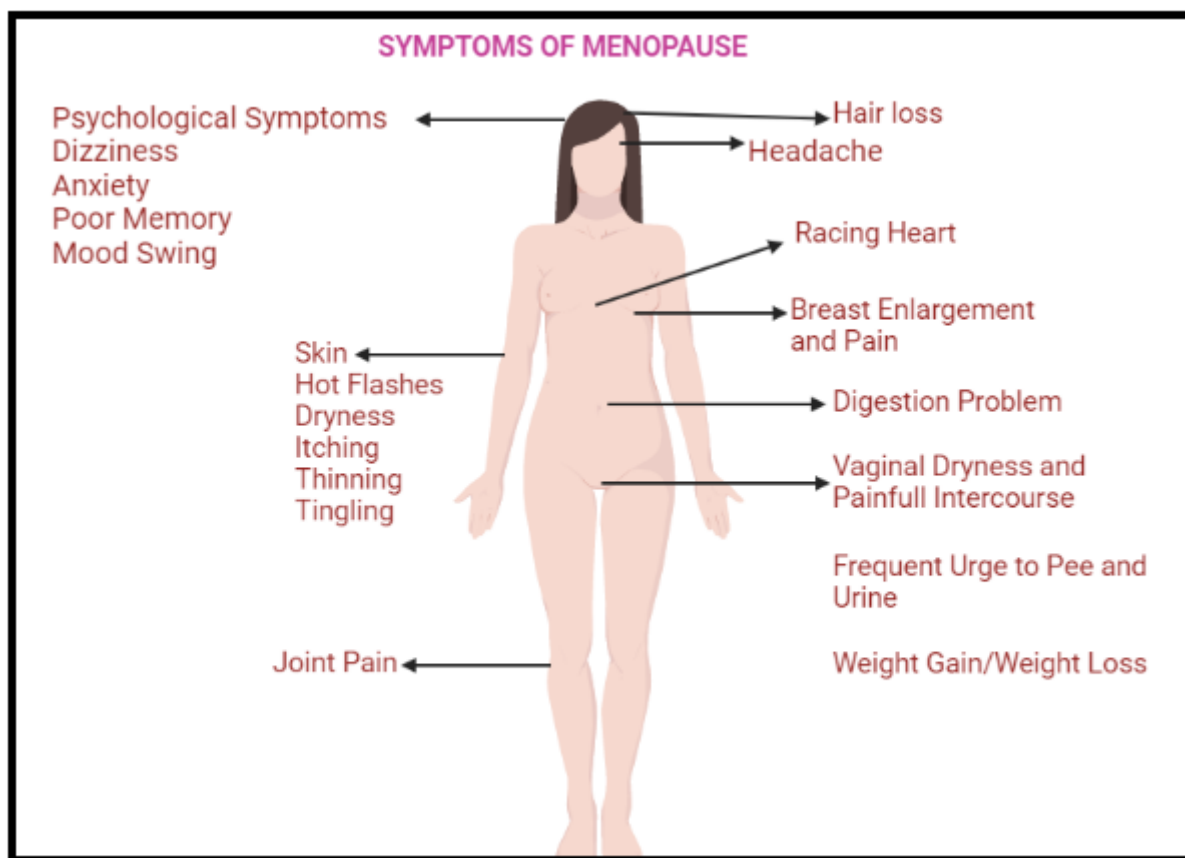


Figure 3: Symptoms of menopause.



Figure 4: Factors responsible for Early Menopause.

Genetics

Chromosomal Defects such as Fragile X or the most prevalent one is Turner syndrome cause a Primary Insufficiency of the Ovaries (POI) which results in early menopause in women. Turner syndrome is a condition where entirely or partially absent X Chromosomes, are characterized by stature, a lack of developing

breasts, as well as irregular periods.²⁰ Hormonal therapy is the best treatment for Turner syndrome. Autoimmune syndrome like rheumatoid arthritis. Thyroid disease also causes early menopause because the inflammation caused by some of these diseases' affects the ovaries and there is an ovarian function decline before the age of 40.²¹ It is believed that autoimmune illnesses account for 4–30% of occurrences. Ovaries are the main target site for autoimmune

attacks. Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED), commonly referred to simply as Autoimmune Polyglandular Syndrome (APS) type I, up to 60% of the cases develop in premature ovarian failure. Hypothyroidism, adrenal failure, mucocutaneous candidiasis, and mucocutaneous candidiasis hypoparathyroidism are the disorders associated with this syndrome. Single gene defect on chromosome results in APS type 1 is an autosomal recessive disease.²²

Mental Health

Women who visit themselves at hospitals as a result of early menopause suffer from psychological distress.²³ Certain percentage of women appear to continue to experience depression even after being diagnosed, however, this number might just decline gradually. Women experiencing psychological issues and needing specialists to care for them before they diagnosed with premature menopause, seem to have been particularly vulnerable to continuing to feel down. The offer of psychological care for these women, like for others who live intensely distressing lives, could maybe be a regular component of professional leadership²³ (Figures 3 and 4).

Risks of Early Menopause

Ovarian Cancer

Women should know about the symptoms of ovarian cancer when they are nearing or in menopause, which includes weight loss, bloating, swelling, pelvic pain, vaginal bleeding or spotting, and constipation.²⁴ Menopause may affect the possibility of evolving ovarian cancer. Those females who enter menopause late usually after period 52, which means at the postmenopause stage, have more risk of developing ovarian cancer because those women have more ovulations.²⁵ This is the time when the cycle of menstruation causes female hormones to trigger egg release. Ovulation can be prevented by temporary birth control tablets and the chance of developing ovarian cancer. For women who take hormone therapy to get rid of symptoms of menopause like hot flushes, osteoporosis, and such therapy may raise the chance of getting cancer of the ovaries. When using hormonal therapy, patients often consume simply the hormone estrogen, estrogen, and progesterone, or estrogen and progestin, a chemically produced hormone that mimics progesterone. The American Cancer Society's research states that taking only estrogen (without progesterone) for at least 5 or 10 years seems to increase the risk.²⁶

Breast Cancer

Breast cancer risk increases in the case of those women who are exposed to estrogen for a longer period. Other factors are also

responsible for the development of breast cancer such as the use of contraceptive pills, hormonal therapy like treatment with diethyl stilbestrol after menopause, no breastfeeding, Consumption of alcohol, inactivity, and being overweight. The risk of developing breast cancer is higher for women who reach menopause beyond 55 years of age and is also higher among those who start menstruating before the age of 12.²⁷

About 70% of women are sensitive to estrogen, and the cells from breast cancer have receptor site to which estrogen bind and promote their growth and spread It is also known as estrogen receptor-positive cancer.²⁸

Neurological Disorder

Women who underwent hysterectomy and bilateral oophorectomy before menopause were at a higher risk of developing Parkinson's; however, those who received hysterectomy as well as isolated oophorectomy was not placed at a greater risk of developing the disease. The researchers of the present investigation also discovered that the menopause, whether biological or surgical, did not raise the risk of Parkinson's disease among women under the median age of 48.²⁹ Estrogen plays an important function in preventing dementia from damaging the nervous system, Once the levels of estrogen drop, this protective effect is eliminated. women with low levels of endogenous estradiol are found to be suffering from dementia as compared to those women who have high levels of estradiol.³⁰ It has been discovered that early menopause in females with Down syndrome women is linked to a greater possibility of dementia and fatality.³¹

Cognitive Impairment

Because of the decline in estrogen levels and the comorbidities of cardiovascular risk factors, autoimmune diseases, and aging, premature menopause has a direct and indirect impact on the Central Nervous System (CNS), both temporarily and permanently. This affects the CNS and results in cognitive impairment or even dementia.³² The sudden termination of exposure to ovarian hormones, which increase cognitive aging, is another reason for the effect of early menopause associated with oophorectomy on dementia. DNA methylation data from human saliva, blood and buccal epithelium also exhibit an epigenetic hallmark of aging, suggesting an earlier menopausal transition.³³ Estrogens appears to protect cognitive disorders arising from a cholinergic deficit in women and female animals in middle age. The key factor contributing to the adverse neurological effects of early menopause is the early and extended loss of ovarian-derived 17-estradiol (E2).³⁴ Experimental models have demonstrated that estradiol prevents emotional and cognitive issues resulting in a decrease in serotonin levels. In middle-aged women and female animals, estrogen also seems to be protective against cognitive issues caused by cholinergic deficit.³⁵

Bone Mineral Density and Fractures

Earlier studies have reported that a deficiency of estrogen has a connection with bone loss resulting in the suppression in bone formation and uncoupling of bone formation from resorption.³⁶ Most studies also have reported that bone loss either will start or can increase during the menopausal period. If premenopause is caused by the agonist of gonadotropin-releasing hormone that affects estrogen levels in premenopausal women and induces rapid bone loss.³⁷ Before menopause spine density shows small changes in decrease in density but after menopause great changes can be seen. The most sensitive indicator of estrogen deficiency is spine. Because of the close connection between bone loss and menopause studies have shown that women who undergo an earlier menopause, either surgical or natural, compared with normal menopause would have lower bone density than someone of the same age.³⁸ Low bone mineral density is also connected with an increased rate of fracture at early menopause than the normal period of menopause. Several studies have found that women with early menopause had 50% more fractures than occurred in the higher age-at-menopause group. This was seen only in women younger than age 70 years but not in women older than 70 years, presumably because other age-related factors such as a decline in bone quality played a role in the older group.³⁹

Heart Disease

Recent research findings had shown that women may become more susceptible to cardiovascular diseases as a result of the cessation of menstruation and subsequent fall in estrogen levels.⁴⁰ The risk of incident heart failure raised as the age at menopause decreased. Women in the menopause age groups of 45 to 49, 40 to 44, and under 40 had, respectively, 11%, 23%, and 39% higher incident heart failure risks than women in the menopause age group of 50 years and above.⁴¹ The results of past research have demonstrated that a number of cardiovascular risks factors are related to menopause occurring earlier in life, with smoking history being the most frequently reproduced exposure. Kok *et al.* discovered that early natural menopause was linked to typical cardiac risk factors such higher blood pressure, cholesterol, and weight in the Framingham Heart Study. In the UK Biobank, early menopause especially surgical premature menopause was linked to an increased risk of incident hypertension, hyperlipidemia, and type 2 diabetes., providing further proof that premature menopause causally affects future cardio metabolic risk.⁴²

Sexual dysfunction or loss of intimacy

Due to their cancer-specific treatment, young women (45 years of age) with breast cancer have higher chances of developing sexual dysfunction. Chemotherapy-induced ovarian failure in young women with breast cancer may be accompanied by a

more significant loss of ovarian function than during natural menopause.⁴³ This is due to the fact that ovarian failure produced by chemotherapy causes a sudden reduction in both serum androgens and serum estrogen, whereas androgen levels in women progressively decline throughout adulthood and do not significantly decrease at the time of natural menopause. Premature menopause causes hypoestrogenism, which is associated with vulvovaginal atrophy, dyspareunia, a lowered libido, and negative effects on arousal and orgasm.⁴⁴

Treatment and Management of Early Menopause

The most important approach in the treatment of premenopause depends upon identifying the symptoms and causative factors. Depending on the cause of early or premature onset of menopause, different treatments are necessary.⁴⁵

Patient counseling

National self-support groups for POF exist, such as the Daisy Network in the UK (www.daisynetwork.org.uk), and these offers helpful psychological support for women. Women should be informed that ovulation can recur, frequently intermittently, and that this might lead to cyclical menstrual flow or even pregnancy.⁴⁶

Lifestyle Changes

Stress Management: The body reacts negatively to stress. Meditation, yoga, and aromatherapy are a few methods for handling stress.⁴⁷

Emotional assistance: Women are impacted emotionally as well as physiologically by changes in hormone levels. It's crucial to have relatives and friends, especially for young ladies.⁴⁸

Calcium Intake: When the estrogen levels decline in women, it is mainly associated with the increased risk of osteoporosis. It is advised to consume enough calcium to maintain bone health.⁴⁹

Healthy diet: One of the best methods for women to lessen the intensity and length of many menopause symptoms is by maintaining a balanced diet. Concentrate on consuming whole grains, lean meats, fish, nuts, beans, fresh fruits and vegetables, low-fat dairy products, and lean meats and seafood.⁵⁰

Regular exercise: Numerous areas of health, such as muscle flexibility, weight control, and increased blood flow and mental stability are all improved by exercise. Five days a week of physical activity for at least 30 min is advised.⁵¹

Alternative Medicine

Utilizing herbal therapies and natural alternative treatments control hormonal irregularities. Herbal treatments that assist regulate hormone levels fall into two categories based on the amount of estrogen they contain.⁵²

Phytoestrogenic herbs

Phytoestrogen, which some herbs contain, is similar to human estrogen. By ingesting these herbs through pills or herbal extracts, women can utilize them to balance their body's decrease levels of estrogen.⁵³

Hormone-regulating herbs

These plants don't have any estrogen. In the body, hormone-regulating herbs act as hormone stimulators, assisting the endocrine glands in their normal production of estrogen and other hormones.⁵⁴

Hormone Replacement Therapy (HRT)

Estrogen replacement therapy, which is recommended up until the normal age of natural menopause, is the mainstay of treatment for women with POE. Hormone Replacement Therapy (HRT) or the combined estrogen and progestogen contraceptive pill may be used.⁵⁵

Vaginal estrogen

Even if you are unable to use a skin patch or oral hormone therapy, you might be able to treat dryness by putting a small amount of estrogen in or near your vagina. These hormones are available as tablets, rings, gels, creams, and liquids.⁵⁶

Lubricants or moisturizers

These products can help make sex more comfortable if you have vaginal dryness. Look for a water-based lubricant, such as K-Y Jelly or Astroglide.⁵⁷

Protecting Your Bones and Heart

It is essential to maintain the health of your heart and bones because early menopause might negatively impact these conditions. Consuming adequate calcium and Vitamin D through salmon, eggs, and fortified milk. These nutrients support bone growth. Spinach, white beans, fat-free yogurt, and fat-free milk are examples of foods high in calcium.⁵⁸

CONCLUSION

Women of India are facing the biggest challenges having certain health issues like breast cancer, ovarian cancer, and PCOS. Certain factors which affect women's health are insufficient gap between children, poor sexual hygiene, early marriages, poor nutritional intake, and prostitution which affect their sexual health and well-being. Menopause means the end of the reproductive stage. When women undergo menopause before the age of 45 it is called as early menopause and before 40 ages known as premature menopause. During this time period women experience different symptoms like irregular periods, insomnia, vaginal dryness, mood swings. Early menopause and premature menopause are

linked to long-term health risks, including cardiovascular disease, neurological conditions, osteoporosis, whether they occur naturally or are caused by other factors. Hormone replacement therapy, increasing calcium intake, and regular exercise are a few ways to treat and manage the symptoms of early menopause.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

PCOS: Polycystic Ovarian Syndrome; **POI:** Premature ovarian insufficiency; **APS:** Autoimmune polyglandular syndrome; **DNA:** Deoxyribonucleic acid.

SUMMARY

The families and communities' health no doubt depends on the health of women. The improvement in women's health is very essential for achieving gender equality. Menopause means the end of reproductive stage. The normal period of menopause is the age of 45 to 55 in women. When women undergo menopause before 45 ages called early menopause and before at 135th in gender inequality in 2022. Perimenopause is also known as menopausal transition this is a stage in which our body make natural transition to menopause called as "around menopause". The normal age for the women to undergo menopause is from 50 to 52 years, this age may vary from women to women depending on their life style. Those women who use to smoke are more likely get to menopause earlier than nonsmoking women. The period after menopause is called as post-menopause, during this stage women not experience anxiety or mood swing but women are most commonly getting to be associated with problems like breast cancer, osteoporosis, cardiovascular disorders, kidney problems, vaginal infections due to imbalance level of estrogen and progesterone. Women should know about the symptoms of ovarian cancer when they are nearing or in menopause, which include weight loss, bloating, swelling, pelvic pain, vaginal bleeding or spotting, and constipation. Women of India are facing the biggest challenges having certain health issues like breast cancer, ovarian cancer, and PCOS. Certain factors which affect women's health are insufficient gap between children, poor sexual hygiene, early marriages, poor nutritional intake, and prostitution which affect their sexual health and well-being. Menopause means the end of the reproductive stage. When women undergo menopause before the age of 45 it is called as early menopause and before 40 ages known as premature menopause.

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