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Menopause: A hormone deficient state

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Abstract

Menopause or climacteric is a natural process marked by the end of the reproductive cycle in human females. It generally occurs between the ages of 45 to 55 years. It can be natural or artificial, where ovaries have been removed by surgery. Due to a decline in the level of estrogen and progesterone levels and dysregulation of the Hypothalamic -Pituitary- Gonadal Axis, many short-term and long-term symptoms disturb the quality of life of women. The objective of this study is to review the basics of menopause, its prevalence, mechanism, stages, and symptoms through relevant sources. Menopause can be divided into four stages, and approximately 80% of women experience the symptoms (Vasomotor, Physical and Somatic, Phycological, and Sexual) in their transition period. Hence, there should be the need to create awareness or nutritional interventions that may help increase knowledge, about the stages of menopause, and also their behaviour which will improve their general health and well-being and decrease the risk of various metabolic diseases.

Keywords: Climacteric, ovaries, transition period, symptoms

Introduction

Menopause is not a disease or disorder as it is a normal part of aging, can be marked by the end of reproductive years or it can be defined as the permanent cessation of menstruation resulting from loss of ovarian follicular activity (WHO Definition of Menopause - Google Search, n.d.) or 12 consecutive months without menstrual cycle or can be defined as a period when menstrual cycle and ovulation stops as a result of which ovaries no longer releases an egg. Possible causes can be due to naturally declining reproductive hormones (Estrogen and progesterone), oophorectomy, chemotherapy, radiation therapy, or primary ovarian insufficiency. Due to insufficiency in reproductive hormone levels there increases the risk of various mid-life diseases and problems.

2. Prevalence

The prevalence of natural and surgical menopause were found to be 9.5% and 6.2% (Mozumdar, 2021) ^[18] and about 50 million cases annually (Massart F, 2001) ^[14] and by 2030 increased the projection of menopausal women would be 1.2 billion worldwide. (K, 1996). The Natural menopause age of Indian women was found to be 46.2 ± 4.9 years (Ahuja, 2016) ^[1]

Table 1: Mean natural	age in	different	regions	of India.
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Region	Mean natural age of menopause
East	47.3±3.91
West	46.2 <u>±</u> 4.89
North	45.5 <u>±</u> 4.86
South	46.1±5.63
Center	47.8 <u>±</u> 4.41
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Source: A pan India survey by IMS (Ahuja, 2016)^[1]

Which is much less than in Western countries 51 years, moreover Indian women begin their Peri-menopausal stage by the age of 44.69±3.79 (Singh & Pradhan, 2014)^[24]. Large number of illiterate women, poor nutritional status with early childbearing, low age at marriage could be the problem of early menopause in India. (Syamala & Sivakami, 2005)^[25].

3. Mechanism

Female reproductive tract undergoes a series of changes that are basically meant to prepare the body for fertilization, pregnancy, and hence for the menstrual cycle. The length of the cycle varies but on average it is of 28 days, the cycle between 25 and 35 days(from the first day of menses in one cycle to the first day of menses of subsequent cycles) (Treloar: Variation of the Human Menstrual Cycle through. Google Scholar, n.d.).

At first during Follicular phase ,there increased the secretion of FSH from anterior pituitary under which primary follicles changes into Graafian follicle which secretes estrogens, which inhibits the secretion of FSH and stimulate the secretion of LH, then during Ovulatory phase Graffian follicles starts ovulating, this process is controlled by the level of LH in the blood ,and Graffian follicles changes into corpus luteum which starts secreting progesterone, there increases in the size of corpus luteum (Yellow body) and hence called as leuteal phase, decrease in the secretion of FSH and LH inhibits the process of ovulation ,when the ovum remains unfertilized there starts a degeneration of corpus luteum ,level of progesterone declines as a result of which there starts a menstrual flow or menstruation proceeded by menstrual phase this process is governed by positive feedback mechanism (decreased level of progesterone and estrogen stimulates hypothalamus and pituitary to release FSH-RF and FSH which starts the follicular phase of next menstrual cycle.

As the women reached their mid-thirties there starts a change in their hypothalamic-pituitary-gonadal axis and gradual attenuation of estrogen and inhibin occurs (Sherman *et al.*, 1976)^[23] Decreased level of inhibin accounts for an increase in FSH level induces rapid follicular development and shortening of cycles may be the first clinical sign of Perimenopause (Copeland & McGregor, 1993)^[7] After the age of 35 years their starts a gradual decrease in the weight and size of the ovary which contains much fewer oocytes and follicular structure and more atretic and degenerating follicles. (Block, 1952)^[5] Declining of ovarian functions due to exhaustion of the primary follicular pool results in menopause, and decreased inhibin and estradiol level may be responsible for an early rise in FSH level



Fig 1: The menstrual cycle



Fig 2: The hypothalamic-pituitary-gonadal axis

There is an effect of interaction at different levels of the hypothalamic-pituitary-ovarian axis(Santoro, 2005) ^[22] During the early menopausal transition, there is lower ovarian

inhibin secretion, which suppresses both hypothalamus and pituitary and hence increases in pituitary gonadotropins, follicular stimulating hormone secretion, elevation in ovarian oestradiol secretions have been found during the early menopausal transition(Santoro, 2005) ^[22] There is persistent

hypogonadism after five to ten years of menopause, and more stability in HPG axis (Hall & Gill, 2001) $^{[9]}\,$

Table 2: Major hormones of the HPG axis

Hormone	Source	Action		
GnRH	Hypothalamus	Stimulates release of LH and FSH		
FSH	Anterior pituitary	Stimulates E2 release		
LH	Anterior pituitary	Stimulates ovulation		
E2	Ovary	Follicular development, uterine lining		
Progesterone	Ovary (minor source), corpus luteum, placenta	Maintains uterine lining		

Source: (The Hypothalamic-Pituitary-Gonadal Axis and Women's Mental Health: PCOS, Premenstrual Dysphoric Disorder, and Perimenopause, n.d.)

4. Stages of menopause

For promoting the use of correct terminology of menopause, the first Congress of the International Menopause Society (IMS) in 1976 (Utian WH. The International Menopause Menopause-Related Terminology Definitions. C - Google Search, n.d.) After that World Health Organisation(WHO) Scientific Group on Research in Menopause was organized and given their general recommendations on the nomenclature perimenopause, for terms like menopause, and postmenopause (WHO Scientific Group on Research on Menopause in the 1990s (1994: Geneva & Organization, 1996)^[30]. The terminologies recommended by WHO1996 and Indian menopause society (IMS)-

- 1. **Premenopause:** The term premenopause could be used ambiguously either to refer to 1 to 2 years immediately before menopause or would be the whole reproductive period before a final menstrual period.
- 2. Perimenopause: The term perimenopause (or climatic)

could be the period immediately before menopause where there is a commencement of endocrinological, biological, and clinical features for approaching menopause

- 3. **Postmenopause**: The term post menopause is defined as the period of 12 months of spontaneous amenorrhea.
- 4. **Menopausal transition:** The period before the final menstrual period when variability in the menstrual cycle is usually increased.

Further, it was highly advocated the use of the word climatic interchangeably with Perimenopause which should be discarded to avoid confusion but as a widespread popularity, the word climacteric was restored by the Council of Affiliated Menopause Societies (CAMS) in 1999 and marked as a transition phase from reproductive to no reproductive phase. (Utian WH. The International Menopause Menopause-Related Terminol Ogy Definitions. C - Google Search, n.d.)



Source: (WHO Scientific Group on Research on the Menopause in the 1990s (1994 : Geneva & Organization, 1996) [30].

Fig 3: menopause timeline

The executive summary proposed by Stages of Reproductive Ageing Workshop; STRAW+10 on collaborations with ReSTAGE describes the female reproductive aging of adult females and divided it into mainly three phases namely the reproductive phase, menopausal transition phase, and post-menopause phase which itself gets subdivided into various sub-stages. According to STRAW+10, late reproductive stage(-3) can be further divided into -3b and -3a stages on the basis of FSH level and pattern of menstrual (Harlow SD, Gass M, Hall JE, Lobo R, Maki P, Rebar RW, *et al.* Executive

Summary of the Stages of Reproductive Aging Workshop + 10, n.d.), further early menopausal transition (stage-2) can be classified by elevated FSH level, and low AMH and AFC level, whereas in late menopausal transition (stage-1) there is increase in variance in cycle length ,alteration in FSH level with high estradiole level (Ambikairajah *et al.*, 2021) ^[3] furthermore there is an interval of amenorthea greater or equal to sixty days, with marked increase in FSH level of 25 IU/L (Evaluation of Four Proposed Bleeding Criteria for the Onset of Late Menopausal Transition Monash University,

n.d.), early postmenopause can be further subdivided into three stages (+1a, +1b, +1c) which is characterised by increase in the level of FSH and where in the level of estradiole continuously decreases for 2 years after the final menstrual period (FMP), +1a represents twelve months after FMP and +1b regarded as the year prior to stabilization of high FSH and low estradiole levels (+1c) (Harlow *et al.*, 2012)^[10]

Stage	-5	-4	-3b	-3a	-2	1+ 1	+1 # +	1b +1c	+2
Terminology	REPRODUCTIVE			MENOPAUSAL		POSTMENOPAUSE			
	Early	Peak	Late		Early	Late	Early		Late
					Perimenopause				all the masterne
Duration	variable			variable	1-3 years	2 your (1+1)	s 3-6 years	Remaining Mespan	
PRINCIPAL C	RITERIA	587-51.55	2.625.025.2	1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-	Seconder 1	West States	0		normeren er
Menstrual Cycle	Variable to regular	Regular	Regular	Suble changes in Flow/ Length	Variable Length Persistent 27- day difference in length of consecutive cycles	Interval of amenorthes of >=60 days			
SUPPORTIVE	CRITERIA								
Endocrine FSH AMH Inhibin B			Low Low	Variable* Low Low	T Variable* Low Low	T 525 RAL" Low Low	† Variabi Low Low	e Stabilizes Very Low Very Low	
Antral Folicity Count			Low	Low	Low	Low	Very Low	Very Low	
DESCRIPTION	CHARAC	TEDIOTIO		C	č				
Samploms	CHARAC	ERISTIC	1			Vaacmobs	Vatemnt	or l	Increasing
ovinition	1. 1		0			symptoms Likety	sympton Most Like	B.	symptoms of

Source: STRAW+10 staging system (Harlow et al., 2012)^[10]

5. Symptoms

Menopausal symptoms can range from short-term-hot flushes, and night sweats (vasomotor symptoms), to long-term chronic symptoms like -osteoporosis, cardiovascular diseases (CVD), and cognitive impairment, which may affect the quality of life of women. However, VMS can be considered a biomarker of other chronic diseases. Symptoms have a direct effect on the well-being and health of the women. Individuals within the same populations may have variability in frequency and severity of symptoms, which may be of different stages of menopause(Randolph Jr *et al.*, 2005) ^[21] Women can experience a wide range of symptoms during the menopausal transition and after menopause ("Menopause," 2023)^[29] Some women's are having less severe while others are having frequent and severe symptoms. Menopausal symptoms vary geographically (Palacios S, 2010)^[20].

1. Vasomotor symptoms (VMS)

Also referred to as a cardinal symptom of menopause include hot flashes and night sweats. VMS can be defined as a period of profuse heat followed by sweating and flushing which occurs generally during the transition period. According to (SWAN) African Americans (46%) was having the highest prevalence of hot flashes, than by Hispanics (34%), Whites (31%), Chinese (21%), and Japanese (18%) (Menopause and Perceived Health Status among the Women of the French GAZEL Cohort - PubMed, n.d.) Some women experience hot flush daily, while some every hour whereas other experiences infrequently (North American Menopause Society, 2004)^[19]

2. Physical and Somatic symptoms

Which includes muscle or joint pain or discomfort decrease in strength and stamina making more mistakes than usual. According to the study in Riyadh about (83.9%) of women were having muscle and joint problems, (80.2%) suffering from physical and mental exhaustion, (73.1%) were having heart discomfort, (71.2%) sleep disorders, (71%) were having irritability, whereas (36.5%) experienced severe psychological distress, these symptoms were more

dominating in Perimenopausal stage as compared to Pre and Postmenopausal women. (AlQuaiz *et al.*, 2013)^[2]

3. Phycological symptoms

May include anxiety, irritability, dizziness, forgetfulness, poor concentration, and less self-esteem. It was found that the most commonest psychological symptom was irritability in perimenopausal women, while much lower in the postmenopausal group i.e 16% had irritability, 12% forgetfulness lethargy 10%, and 3% were having loss of libido (Inayat *et al.*, 2017)^[12].

4. Sexual symptoms

Include dryness of the vagina, low sex drive, sexual problems, vaginal discharge, or itching. According to (Singh & Pradhan, 2014)^[24] 32% of premenopausal and 54% of post-menopausal women were found to be sexually inactive while

6. Discussion

The Review systematically mentioned the various aspects of menopause literature: Introduction, Prevalence, Mechanism, Stages of menopause, and Symptoms. The problem of illiteracy, early marriages, and early childbearing with minimum nutritional status can be the reason for early menopause in Indians as compared to other Asian countries. Lower ovarian inhibin secretion results in early menopausal transition. There is the maximum loss of follicles from a woman's ovaries during foetal life (Block, 1952)^[5], followed by exponential loss of oocytes during the reproductive life span (Baker, 1963)^[4], and this loss is accelerated as women enter their menopausal transition (Faddy et al., 1992)^[8]. There may be some short-term (hot flushes, night sweats (vasomotor symptoms), to long-term chronic symptoms like osteoporosis, cardiovascular diseases (CVD), and cognitive impairment that could be experienced by the women. More prominent distressing symptoms are hot flashes, and vaginal dryness due to low levels of estrogen experienced by 70% of women (Bruce & Rymer, 2009)^[6] Fewer somatic symptoms are reported by physically active women (Moilanen et al.,

from

2010) ^[17]. Hence patient education and enhancing healthcare team outcomes can lower the morbidity of menopause.

7. Conclusion

The Menopause is a normal part of aging followed by permanent cessation of menstruation for 12 consecutive months. Due to insufficiency in reproductive hormone level which results in various mid-life diseases and problems, which would impact the quality of life of the women. There should be the need of creating awareness or nutritional interventions that may help increase knowledge, about the stages of menopause, and also their behaviour which will improve their general health and well-being and decrease the risk of various metabolic diseases.

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