Age at natural menopause and factors affecting menopausal age: A cross-sectional study among postmenopausal female attendees of obstetrics and gynecology outpatient department

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ABSTRACT

Background: Menopause has now become a predominant subject of study as the life expectancy is globally on an increase. The average life expectancy at birth for females in India is 69.9 years. The average age at menopause ranges from 45 to 53 years both in the developed and developing countries. Age at natural menopause is determined by factors which influence the extent of dwindling of ovarian follicle reserve, and it includes both genetic and modifiable factors. **Objectives:** The present study was conducted to deduce the mean age at menopause and to find the factors affecting age at natural menopause among postmenopausal attendees of the Obstetrics and Gynaecology Outpatient Department at Sultania Zanana Hospital, Bhopal. **Materials and Methods:** A prospective cross-sectional study conducted for a period of 1 year starting from July 1st 2015, to June 30, 2016. Data were collected using Systematic Random Sampling from 232 cases of natural menopause and entered into MS Excel 2007. Analysis was performed with Epi-Info 7.2. Unpaired t-test was used to find the association between age at menarche and age at natural menopause. Chi-square applied as statistical test of significance for the association between age at natural menopause and qualitative variables. $P < 0.05$ was considered to be statistically significant. **Results:** The present study revealed a mean age of 46.77 ± 3.52 SD years at natural menopause. Association between age at menarche and age at natural menopause found not to be statistically significant (unpaired t-test). Statistically significant correlation was found between age at natural menopause and factors such as marital status, living alone, socioeconomic status, tobacco addiction, body mass index, psych-social problems, body mass index (BMI), psycho-social problems, OCP intake etc. **Conclusion:** Menopause whether occurring early or late in life, both are responsible for causing adverse health effects among women. Thus, it becomes utmost important to identify the factors influencing the onset of menopause.

KEY WORDS: Menopause; Post-menopausal Females; Cross-sectional Study; Bhopal.

INTRODUCTION

Menopause is a crucial stage in the life of a woman marked by her last menstrual period.[1] It is a normal physiological event where there is amenorrhea consecutively at least for 12 months and the main cause for this is deprivation of ovarian function that happens invariably to all women in their midlife.[2,3] The word "menopause" has Greek origins: "Meno" means month and "pause" means to end.[4] The permanent cessation of menstruation is not due to pathological or any other physiological cause,[5] and it signifies the end of reproductive phase of a woman's life where the ovaries gradually cease to function passing through the phase known as menopausal transition or perimenopause.[4] This ovarian function depletion causes

a variety of somatic, sexual, vasomotor, and psychological manifestations that are responsible for deteriorating the quality of life of women.[3,6,7] Menopause can also be surgically induced by hysterectomy with or without oophorectomy, and this is referred to as surgical menopause. Menopause can also happen due to treatment with cytotoxic chemotherapeutic agents and the gonadotrophic-releasing hormone agonist.[8]

Menopause has now become a predominant subject of study as the life expectancy is globally on an increase due to the provision of better nutrition and advancement of health-care systems,[9] which has led to a rise in the geriatric population including postmenopausal females. The global population of women in postmenopause period, in 1990, was approximately 476 million and 40% of those resided in the industrialized world. This figure is supposed to reach to a figure of around 1200 million by 2030, and 76% of these women will be living in the third world countries.[10] According to the World Health Statistics 2016, globally, the female life expectancy at birth is 73.8 years while that in developed countries such as the USA and Great Britain is 79.9 years and 80.2 years, respectively.[11] The average life expectancy at birth for females in India is 69.9 years.[11] The average age at natural menopause ranges from 45 to 53 years both in the developed and developing countries.[12-16] This implies that women now live approximately more than one-third of their life after ovarian failure.

There are some documentations to highlight that there has been a slight increase in the average age at natural menopause over the past few decades but not well supported. The influence of menopause can be very well seen in various domains of life such as physical, psychological, and sociocultural.[17] As the average length of life after menopause is increasing, it has become necessary for health-care personnels to pay a greater attention on the health issues of postmenopausal women so that they can relish these so-called "gloomy" years life optimally.

Age at natural menopause is determined by factors which influence the extent of dwindling of ovarian follicle reserve,[18] and it comprises of genetic and modifiable factors which can enhance or reduce the follicular atresia. The modifiable factors can be both intrinsic and extrinsic such as tobacco addiction, parity, age at menarche, socioeconomic class, and occupation.[19] These factors can be grouped into various categories such as sociodemographic factors, lifestyle factors, environmental/familial factors, menstrual/reproductive factors, and miscellaneous.

The present study was carried out to deduce the mean age at menopause and to find the factors affecting age at natural menopause among post menopausal attendees of Obstetrics and Gynecology Outpatient Department (OPD) at Sultania Zanana Hospital, Bhopal.

MATERIALS AND METHODS

A prospective cross-sectional study was carried out over a period of 1 year starting from July 1, 2015, to June 30, 2016, among postmenopausal females attending the gynecology OPD of Obstetrics and Gynecology at Sultania Zanana Hospital, Bhopal, Madhya Pradesh, which is the teaching hospital of Gandhi Medical College, Bhopal, Madhya Pradesh. Those females who had amenorrhea continuously at least past 12 months and those females who had attained menopause surgically by means of Total Abdominal Hysterectomy with Bilateral Salpingo-oophorectomy or had documented exposure to cytotoxic chemotherapeutic agents at least 6 months back and willing to participate in the study were included in the study. Exclusion criteria included females already undergoing treatment for hypoestrogenic states and those who were severely ill. Ethical clearance was taken from the ethical committee of the institution.

The sample size for the present study was calculated on the basis of a pilot study which was done for 1 month. For the first fortnight of the month, a daily visit was made to gynecology OPD at Sultania Zanana Hospital, Bhopal, and all postmenopausal females who reported to OPD and fulfilled the criteria laid down for the study were interviewed. For the last fortnight of the month, visit was made for only 3 days in a week. In the 1st week of the last fortnight, Monday, Wednesday, and Friday were chosen for data collection, and in next week, other 3 days, i.e., Tuesday, Thursday, and Saturday were chosen. All patients on days of visit who fulfilled the study criteria were interviewed. The data collected from the pilot study were used for sample size calculation. Sample size was calculated on the basis of the following formula:

Sample size = $[Z_{1-\alpha/2}{}^2 p (1-p) \times DEFF]/d^2$

Here, $Z_{1-\alpha/2}$ = is standard normal variate (at 5 % type I error [$P < 0.05$] it is 1.96 and at 1% type error [$P < 0.001$] it is 2.58). As in majority of studies P values are considered significant <0.05, 1.96 is used in the formula.
p = Expected proportion in population based on previous studies or pilot study.
d = Absolute error or precision: it has to be decided by researcher. Precision chosen by us is 0.05.
DEFF = Design effect. It is calculated as cluster variance/SRS variance

The proportion of the least reported menopausal symptom, i.e., anxiety (inner restlessness and feeling panicky) in the pilot study was 0.08%. Hence, the sample size without DEFF was as follows:
Sample size = $[1.96 \times 1.96 \times 0.08 \times 0.92]/(0.05 \times 0.05) = 113.096$
Design effect (DEFF) was calculated to be 2.24
Thus, total sample size is $113 \times 2.24 = 253.12$
We took 255 cases.

Of 255 cases, 23 cases were those of surgical menopause. Hence, for determining the age at natural menopause, only 232 cases who underwent menopause naturally were considered. Data were collected using systematic random sampling technique. 3 alternating days in a week were decided to collect data. In 1st and 3rd weeks of every month, Monday, Wednesday, and Friday were chosen for data collection, and in the 2nd and 4th weeks, Tuesday, Thursday, and Saturday were chosen.

After obtaining consent from the study participants and ensuring confidentiality of the data provided by them, the data were collected by face-to-face interview of the participants using semi-structured questionnaire which included sociodemographic variables such as age, education, occupation, monthly income of family, type of family, number of family members, marital status, height (cm), and weight (kg). It also included variables related to personal history such as addiction, diet, exercise, and lifestyle. Detailed obstetric and gynecological history was taken along with past medical and surgical history. Menopausal symptoms were also assessed using Menopause Rating Scale.

Data were entered into MS Excel 2007, and the analysis was done with the help of Epi-Info 7.2 software. Frequency and percentages were calculated. Unpaired *t*-test was used to find the association between age at menarche and age at natural menopause. Chi-square was applied as statistical test of significance for the association between age at natural menopause and qualitative variables. $P < 0.05$ was considered to be statistically significant.

RESULTS

Analysis of the study determined a mean age of 46.77 ± 3.52 (standard deviation [SD]) years at natural menopause, while the mean age at menarche was determined to be 13.56 ± 1.11 (SD) years. Table 1 shows that, in this study, the association between age at menarche and age at natural menopause is found not to be statistically significant (unpaired *t*-test). Table 2 shows the distribution of study participants according to relation between age at natural menopause and sociodemographic factors. Chi-square was used as the test of significance and $P < 0.05$ was taken to be statistically significant. It can be concluded that there is a correlation between marital status and age at menopause

Table 1: Comparison of age at menarche and age at natural menopause

Menopausal group (years)	Age at menarche mean (SD) (years)	*t*-value	*P*-value
≤45	13.49 (1.11)	1.2463	0.2139
>45	13.67 (1.12)		

SD: Standard deviation

as unmarried/widowed/divorced women had an earlier menopause than married women. The table also suggests that living alone may predispose to a later age at natural menopause. With regards to socioeconomic class, 62.86% of females in high socioeconomic class and 60.00% belonging to low socioeconomic class achieved menopause at age >45 years, and it was found to be statistically significant ($P < 0.05$). Residing locality, education of females, and occupation did not show statistically significant association with age at natural menopause. Table 3 shows the distribution of study participants according to the relationship between age at natural menopause and lifestyle factors, suggesting that women who were addicted to tobacco chewing attained menopause at a later age than women who were not addicted. Table 3 also suggests that females with higher body mass index (BMI) achieve menopause earlier than females having lower BMI. Tea/coffee intake, exercise, and dietary habits did not show statistically significant association with age at natural menopause. Table 4 shows the distribution of study participants according to the relationship between age at natural menopause and environmental/familial factors. Table 4 suggests that women who experience any psychosocial problems attain menopause earlier than women who do not experience such problems. Any untoward life incidence did not show statistically significant association with age at natural menopause. Table 5 shows the distribution of study participants according to the relationship between age at natural menopause and menstrual/reproductive factors. Table 5 suggests that women who took oral contraceptives in their reproductive span attain menopause earlier than women who do not. It can also be concluded that women having older age at last delivery attain menopause later. Parity did not show statistically significant association with age at natural menopause.

DISCUSSION

In the present study, statistically significant correlation was found between age at natural menopause and factors such as socioeconomic class, marital status, living alone, tobacco addiction, higher BMI, psychosocial problems, history of OCP intake, and age at last delivery. However, correlation between age at natural menopause and age at menarche was found not to be statistically significant.

Socioeconomic Factors

The present study revealed statistically significant correlation between socioeconomic class of the respondents and mean age at menopause since low socioeconomic class was supposedly found to be associated with early age at menopause. However, education and occupation did not show statistically significant association with age at menopause. Similar findings were reported by Luoto *et al.*,[20] where it was concluded that sociodemographic variables appear to be

Table 2: Distribution of study participants according to relation between age at natural menopause and sociodemographic factors

Sociodemographic factors	Group	Age at natural menopause (*n*=232)		Total (%)	Significance
		Up to 45 years (*n*=100) (%)	>45 years (*n*=132) (%)		
Residing locality	Urban	60 (45.45)	72 (54.55)	132 (100.00)	χ^2=0.6902; df=1; *P*=0.406
	Rural	40 (40.00)	60 (60.00)	100 (100.00)	
Marital status	Married	62 (38.27)	100 (61.73)	162 (100.00)	χ^2=5.111; df=1; *P*=0.02*
	Unmarried/ widowed/ divorced	38 (54.29)	32 (45.71)	70 (100.00)	
Education	Illiterate	70 (41.42)	99 (58.58)	169 (100.00)	χ^2=0.719; df=1; *P*=0.396
	Literate	30 (47.62)	33 (52.38)	63 (100.00)	
Occupation/working status	Housewife	58 (44.62)	72 (55.38)	130 (100.00)	$\chi^2$0.2756 =; df=1; *P*=0.599
	Employed/working	42 (41.18)	60 (58.82)	102 (100.00)	
Living with family or alone	Living with family	98 (44.75)	121 (55.25)	219 (100.00)	χ^2=4.314; df=1; P=0.03*
	Living alone	2 (15.38)	11 (84.62)	13 (100.00)	
Socioeconomic class	High (I and II)	13 (37.14)	22 (62.86)	35 (100.00)	χ^2=7.773; df=2; *P*=0.02*
	Middle (III)	21 (65.63)	11 (34.38)	32 (100.00)	
	Low (IV and V)	66 (40.00)	99 (60.00)	165 (100.00)	

*Statistically significant

Table 3: Distribution of study participants according to relation between age at natural menopause and lifestyle factors

Lifestyle factors	Group	Age at natural menopause (*n*=232)		Total (%)	Significance
		Up to 45 years (*n*=100) (%)	Up to 45 years (*n*=100) (%)		
Exercise	Not doing any exercise	82 (42.71)	110 (57.29)	192 (100.00)	χ^2=0.0709; df=1; *P*=0.791
	Doing exercise	18 (45.00)	22 (55.00)	40 (100.00)	
Diet	Vegetarian	48 (42.11)	66 (57.89)	114 (100.00)	χ^2=0.091; df=1; *P*=0.763
	Non-vegetarian	52 (44.07)	66 (55.93)	118 (100.00)	
History of tobacco addiction	Yes	32 (33.33)	64 (66.67)	96 (100.00)	χ^2=6.374; df=1; *P*=0.01*
	No	68 (50.00)	68 (50.00)	136 (100.00)	
Tea/coffee intake	Yes	93 (42.27)	127 (57.73)	220 (100.00)	χ^2=2.562; df=1; *P*=0.278
	No	7 (58.33)	5 (41.67)	12 (100.00)	
BMI	Up to 29.99 Kg/m2	84 (40.58)	123 (59.42)	207 (100.00)	χ^2=4.989; df=1; *P*=0.02*
	≥30 Kg/m²	16 (64.00)	9 (36.00)	25 (100.00)	

*Statistically significant. BMI: Body mass index

associated with age at natural menopause. Similarly, Gold *et al.*[21] found that low levels of education and unemployment were significantly associated with early age at menopause. Similarly, a study conducted by Hardy *et al.*[13] advocates a similar finding that females whose fathers were working as manual laborers had an earlier age at menopause than those whose fathers were employed in other occupations. In India, Kapur *et al.*[22] found that females belonging from middle-class background had later onset of menopause (45.47 years)

than females from the lower socioeconomic background (42.13 years), and the difference was statistically significant. The most probable reason behind low socioeconomic status associated with early age at menopause could be lack of proper nutrition in families belonging to lower class, and the brunt of poor nutrition is suffered mainly by the females of the family. Furthermore, poor socioeconomic conditions predispose to stress and other psychological problems which might result in early menopause.

Table 4: Distribution of study participants according to relation between age at natural menopause and environmental/familial factors

Environmental/Familial factors	Group	Age at natural menopause (n=232)		Total (%)	Significance
		Up to 45 years (*n*=100) (%)	>45 years (*n*=132) (%)		
Unsolved relationship/familial problem	Yes	13 (65.00)	7 (35.00)	20 (100.00)	χ^2=4.279; df=1; P=0.03*
	No	87 (41.04)	125 (58.96)	212 (100.00)	
Any untoward life incidence	Yes	27 (35.06)	50 (64.94)	77 (100.00)	χ^2=3.037; df=1; P=0.082
	No	73 (47.10)	82 (52.90)	155 (100.00)	

*Statistically significant

Table 5: Distribution of study participants according to relation between age at natural menopause and menstrual/reproductive factors

Menstrual/Reproductive factors	Group	Age at natural menopause (*n*=232)		Total (%)	Significance
		Up to 45 years (*n*=100) (%)	>45 years (*n*=132) (%)		
History of oral contraceptive use	Yes	8 (72.73)	3 (27.27)	11 (100.00)	χ2=4.132; df=1; P=0.04*
	No	92 (41.63)	129 (58.37)	221 (100.00)	
Age at the last delivery (n=227)	Up to 30 years	48 (55.17)	39 (44.83)	87 (100.00)	χ2=7.667; df=1; P=0.005*
	>30 years	51 (36.43)	89 (63.57)	140 (100.00)	
Parity	Up to 2	10 (43.48)	13 (56.52)	23 (100.00)	χ2=0.247; df=2; P=0.884
	3–5	50 (44.64)	62 (55.36)	112 (100.00)	
	>5	40 (41.24)	57 (58.76)	97 (100.00)	

*Statistically significant

Geographical Factors

The present study did not reveal a statistically significant correlation between residing locality of the respondents and age at menopause. This finding was dissimilar to the findings of Dasgupta and Ray[23] since their study has clearly advocated the positive role of rural/urban locality in determining menopausal age. The mean age of menopause for rural participants was 53.9 ± 4.37 years while that for urban participants was 51.39 ± 4.6 years, and the difference was statistically significant.

Physical Activity and Body Mass Index (BMI)

The present study did not reveal a significant correlation between exercise and age at menopause, but on the other hand, it was found that females with higher BMI attain menopause early than females having lower BMI, and this difference was found to be statistically significant. Similar findings were reported by Bromberger *et al.*[12] In their study, it was found that the median age of menopause was 50.9 years for women with highest BMI, 51.5 years for the middle group, and 53.4 years for women with lowest BMI. Gold *et al.*,[21] however, reported a dissimilar finding that age at natural menopause was not related to BMI and physical activity. A few studies, however, have reported findings which are dissimilar to the findings of the present study like

Palmer *et al.*[24] who concluded an inverse association of BMI with early age at menopause. Likewise, Bansal *et al.*[25] concluded that heavier women had menopause at later age (46.13 years) than women with normal BMI (45.32). Maru *et al.*[26] conducted a cross-sectional study and reported trends which showed that, as the BMI increased, the age of menopause also increased. Thus, higher the BMI, higher was the age of menopause, and these values also showed a definite statistical correlation. The possible explanation for this could be that the reproductive span in obese women could be slightly longer than that in lean women due to greater production of estrogen in obese women on account of having more adipose tissue.

History of Tobacco Addiction

The present study revealed that women who were addicted to tobacco chewing attained menopause later than the females who were not addicted tobacco chewing, and this difference was found to be statistically significant. This finding is dissimilar to the finding of Midgette and Baron[27] who reported that smoking tobacco increases the risk of early menopause. Likewise, Luoto *et al.*[20] reported that the median menopausal age in women who smoked was 50 years and that of nonsmokers was 52 years. Similarly, in a prospective study conducted by Bromberger *et al.*,[12] it was reported that

the median age at menopause was earlier for women who were smokers. Gold et al.[21] showed that current smoking is associated with earlier age at menopause. Palmer et al.[24] also reported similar findings regarding the onset of menopause and smoking. The possible explanation for this observation could be that the toxic effects of polycyclic aromatic hydrocarbons present in cigarette smoke can lead to the depletion of ovarian follicles, resulting in early menopause.

Dietary Habits

In the present study, dietary habits of postmenopausal women along with tea/coffee intake did not show statistically significant association with age at natural menopause. The findings of this study were found to be dissimilar to the findings of Torgerson et al.[28] who concluded that meat consumption was independently associated with an early natural menopause. Nagata et al.[29] reported inverse and significant association between high intake of cholesterol, fat, and coffee with later age at menopause. Likewise, Nagata et al.[30] also found that consumption of green/yellow vegetables was significantly and inversely associated with menopausal age. Nagel et al.[31] reported that a variety of dietary factors such as high intake of vegetables, cereals, and carbohydrates are related in an inverse association to the age at natural menopause. Women with greater intake of fats and proteins were found to experience a delayed onset of menopause.

Menstrual/Reproductive Factors

The present study revealed that women who were married or living as married attained menopause later than women who were unmarried/widowed/divorcee, and the difference is statistically significant. Similar finding reported by Gold et al. that separated/ divorced/ widowed women had an earlier menopause than women who were married. Likewise, Reynolds and Obermeyer[32] also reported that marital status was found to be statistically associated with age at menopause.

The present study also revealed that women who gave a history of oral contraceptive use attained menopause earlier than women who did not used oral contraceptives, and this difference was found to be statistically significant. This finding was similar to the findings of Gold et al.[21] who reported that the use of OCPs during reproductive span was associated with an earlier age at natural menopause. This finding was dissimilar to the findings of Palmer et al.[24] who reported an inverse association between OCP use and age at menopause. The most probable reason behind parity and OCP use leading to later age at natural menopause might be that they reduce ovulatory cycles in earlier life, thereby preserving oocytes for longer duration, resulting in later age at menopause. Dissimilar to this finding, Reynolds and Obermeyer[32] reported that oral contraceptive use was not statistically associated with at age menopause.

The present study also reported that women who had their last delivery at age > 30 years attained menopause later as compared to women who had their last delivery at age ≤ 30 years, and this difference was also found to be statistically significant. Age at menarche and parity did not show statistically significant association with age at natural menopause. Palmer et al.[24] reported a similar finding as no association was found with parity. Reynolds and Obermeyer[32] also concluded that females with any number of children had a later age at menopause.

Strength and Limitations

The strength of this study is that it highlights the issues related to menopause, which has been neglected for long. It helps to identify the factors which could influence the age at natural menopause and thus can help in regulating women's health in a better way. This study has certain limitations also. This is a hospital-based study and cases are not representative of the community.

CONCLUSION

Age at natural menopause plays a critical role in women's health as it is a signal of declining ovarian function and thereby aging. Menopause whether occurring early or late in life, both are responsible for causing adverse health effects among women. Thus, it becomes utmost important to identify the factors influencing the onset of menopause.

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