Commentary



Early natural menopause – a marker of adverse life situations in women across the world: Not unique in Indian women

Premature or early menopause has been defined as the cessation of ovulation before the age of 40 years. and it is the result of primary ovarian insufficiency. Menopause marks the final step in ovarian ageing. Evidence from literature shows that the length of time between menarche and menopause, a crude indicator of lifetime oestrogen exposure has significant implications on women's health¹. Early menopause has been shown to be associated with cardiovascular diseases, osteoporosis-related bone fractures and earlier decline in cognitive function²⁻⁴. Women who had undergone bilateral oophorectomy before attaining the age 45 benefitted from hormone therapy in terms of lowering the risk of mortality from cardiovascular disease, whereas in women who have attained natural menopause before the age of 45, hormone therapy does not reduce the risk for ischaemic heart disease^{5,6}.

Thus, the timing of the final natural menstrual periods in women could have important clinical and public health implications. The increasing life expectancy and longevity will result in a greater proportion of women above the 50 years of age affected by chronic diseases including cardiovascular diseases, osteoporosis and poor cognitive function in India in future, if preventive measures are not incorporated into the existing public health services⁷.

Most of our knowledge and understanding of menopause have been based largely on studies done in the developed world, and many have been hospital-based studies rather than the population-based samples of women. The evidence from the existing studies shows that the physical and social environments in previous generations, and during the preconception to midlife, influence both reproductive health⁸ and later, chronic disease⁹. The studies conducted among women in the developed world have established that the age at natural menopause is probably determined by a combination

of genetic and environmental factors including age at menarche, maternal age at menopause¹⁰, physical activity¹¹⁻¹³, smoking and lower parity¹⁴⁻¹⁶. Women living in resource-poor countries experience natural menopause many years earlier than the women in resource sufficient countries¹⁷⁻¹⁹. Thus, there was a need to estimate the prevalence of menopause in women less than 40 yr of age and to explore the preventable risk factors that determine early natural menopause in India. Many of the published studies suffer from methodological flaws and lack power.

Pallikadavath et al²⁰ in this issue have done an analysis of secondary data collected as part of the Indian District Level Household Survey carried out during 2007-2008 covering 643,944 ever-married women aged 15-49 years. The objectives were to estimate the prevalence of natural menopause before 50 yr of age in India and its major States and to examine factors associated with early natural menopause. The data had population-based samples proportional to the actual rural-urban population ratio in India and also representing States with highest and lowest prevalence of natural menopause. The inclusion criteria for selection of data allowed separation of natural menopausal women from women who had undergone hysterectomy and that was the flaw noted in the National Family Health Survey-2 data, and it reported very high prevalence of early menopause in some States in India that raised concern and created panic²¹. The power to assess the significant association between potential risk factors and early natural menopause was slightly limited due to inability to gather the actual age at menopause from the data. The age of women reporting menopause at the time of survey was taken as age at menopause for analysis. However, since the data had large samples of women between the ages of 15-49 years, there was adequate

number of women below the age 40 in menopause to measure the associated risk factors. Furthermore, the authors have used less biased, robust Cox proportional hazard regression models rather than simple mean to obtain the median age of women reporting a natural menopause, and it took care of the duration to the event of interest, the age at menopause and dealt with censored observations from women who were still premenopausal at the time of the interview in the study population.

The authors were able to show that the prevalence of natural menopause in women below 40 years of age in India was comparable to estimates reported from developed countries²⁰. Further, the authors pointed out that the significant interstate variations of estimate could be attributed to the disparities found in the poverty-nutrition status in different States in India. More importantly, the authors were able to establish the negative association of prior surgical sterilization to early natural menopause. This finding will have an impact on family welfare programme in India where surgical sterilization has been the most popular contraceptive method. This study has addressed some of the misconceptions regarding the early menopause in women in India.

Rita Isaac

Department of RUHSA, Christian Medical College, Vellore 632 209, Tamil Nadu, India rita.isaac@cmcvellore.ac.in

Received March 17, 2016

References

- 1. Cooper GS, Sandler DP. Age at natural menopause and mortality. *Ann Epidemiol* 1998; 8 : 229-35.
- Kok HS, Kuh D, Cooper R, van der Schouw YT, Grobbee DE, Wadsworth ME, *et al.* Cognitive function across the life course and the menopausal transition in a British birth cohort. *Menopause* 2006; *13* : 19-27.
- Kivimäki M, Lawlor DA, Smith GD, Elovainio M, Jokela M, Keltikangas-Järvinen L, *et al.* Association of age at menarche with cardiovascular risk factors, vascular structure, and function in adulthood: the Cardiovascular Risk in Young Finns study. *Am J Clin Nutr* 2008; 87: 1876-82.
- 4. Mithal A, Kaur P. Osteoporosis in Asia: a call to action. *Curr Osteoporos Rep* 2012; *10* : 245-7.
- Rivera CM, Grossardt BR, Rhodes DJ, Brown RD Jr., Roger VL, Melton LJ 3rd, *et al.* Increased cardiovascular mortality after early bilateral oophorectomy. *Menopause* 2009; *16*: 15-23.

- Løkkegaard E, Jovanovic Z, Heitmann BL, Keiding N, Ottesen B, Pedersen AT. The association between early menopause and risk of ischaemic heart disease: influence of hormone therapy. *Maturitas* 2006; 53 : 226-33.
- Government of India: Ministry of Home Affairs. Office of the Registrar General and Census Commissioner, India; *Census* of India. 2011. Available from: http://www.censusindia.gov. in/, accessed on May 3, 2015.
- Rich-Edwards J. A life course approach to women's reproductive health. In: Kuh D, Hardy R, editors. *A life course approach to women's health*. Oxford, UK: Oxford University Press; 2002. p. 23-43.
- 9. Barker DJ. The fetal and infant origins of adult disease. *BMJ* 1990; *301* : 1111.
- Torgerson DJ, Avenell A, Russell IT, Reid DM. Factors associated with onset of menopause in women aged 45-49. *Maturitas* 1994; 19: 83-92.
- van Noord PA, Dubas JS, Dorland M, Boersma H, te Velde E. Age at natural menopause in a population-based screening cohort: the role of menarche, fecundity, and lifestyle factors. *Fertil Steril* 1997; 68: 95-102.
- de Bruin JP, Bovenhuis H, van Noord PA, Pearson PL, van Arendonk JA, te Velde ER, *et al.* The role of genetic factors in age at natural menopause. *Hum Reprod* 2001; *16*: 2014-8.
- Henderson KD, Bernstein L, Henderson B, Kolonel L, Pike MC. Predictors of the timing of natural menopause in the Multiethnic Cohort Study. *Am J Epidemiol* 2008; *167*: 1287-94.
- Jick H, Porter J. Relation between smoking and age of natural menopause. Report from the Boston Collaborative Drug Surveillance Program, Boston University Medical Center. *Lancet* 1977; 1: 1354-5.
- 15. Gold EB, Bromberger J, Crawford S, Samuels S, Greendale GA, Harlow SD, *et al.* Factors associated with age at natural menopause in a multiethnic sample of midlife women. *Am J Epidemiol* 2001; *153* : 865-74.
- Celentano E, Galasso R, Berrino F, Fusconi E, Giurdanella MC, Tumino R, *et al.* Correlates of age at natural menopause in the cohorts of EPIC-Italy. *Tumori* 2003; 89: 608-14.
- Castelo-Branco C, Blümel JE, Chedraui P, Calle A, Bocanera R, Depiano E, *et al.* Age at menopause in Latin America. *Menopause* 2006; *13* : 706-12.
- Gonzales GF, Villena A. Age at menopause in central Andean Peruvian women. *Menopause* 1997; 4: 32-8.
- McCarthy T. The prevalence of *symptoms* in menopausal women in the Far East: Singapore segment. *Maturitas* 1994; 19: 199-204.
- Pallikadavath S, Ogollah R, Singh A, Dean T, Dewey A, Stones W. Natural menopause among women below 50 years in India: A population-based study. *Indian J Med Res* 2016; *144* : 366-77.
- 21. International Institute for Population Sciences (IIPS) and Macro International. *National family health survey (NFHS-3)*, 2005-06: India. Vol. I. Mumbai: IIPS; 2007.