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Relationship between reproductive factors and bone mineral density in postmenopausal women

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A – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

Summary **Background.** Many studies have assessed the protective factors and risk factors of osteoporosis in postmenopausal women. Considering the uncertainty about the effects of reproductive factors on bone density and the scarcity of information about postmenopausal women in Iran, the present study was conducted.
Objectives. This study aimed to investigate the relationship between reproductive factors and bone density in postmenopausal women.
Material and methods. In this cross-sectional study, 600 postmenopausal women without any known condition affecting bone mineral density were selected through convenience sampling from among the women referred to the densitometry center of Golestan Hospital in Ahwaz, Iran. The data were collected through questionnaires on demographics and reproduction. Bone mineral density was measured by the DEXA method using a Hologic machine in the L1–L4 region and the femoral neck. The demographic and reproductive variables were compared in 3 groups (osteoporosis, osteopenia and normal BMD).
Results. The frequencies of osteoporosis and osteopenia were 15.16% and 57.33%, respectively. All reproductive factors were significantly different in the 3 groups. Multinomial logistic regression revealed later menarche to be a significant risk factor for osteopenia (OR = 4.36, CI = 3.38–5.63, p = 0.001) and osteoporosis (OR = 2.63, CI = 2.00–3.46, p = 0.001). A higher number of parity and longer breastfeeding were also revealed to be other risk factors; older age at first pregnancy is a protective factor. A higher BMI was found to be a protective factor only for osteoporosis.
Conclusions. Our results suggest that later menarche, multiparity and longer breastfeeding act as risk factors, while higher BMI and older age at first pregnancy act as protective factors for bone density disorders in postmenopausal women.
Key words: bone density, reproductive history, postmenopausal osteoporosis.

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Background

As defined by the World Health Organization, the loss of bone tissues and the breakdown of the skeletal structure are defined by bone mineral density (BMD) being reduced to more than 2.5 standard deviations below the mean value in adults [1]. In women, 90% of the maximum bone mass is reached by the age of 18 and then BMD reaches its peak by age 30. After that, minimal changes occur in BMD until the age of menopause; after menopause, a very progressive reduction of BMD occurs [2]. Women are exposed to osteoporosis four times as much as men [3].

According to the International Osteoporosis Foundation, it is estimated that 34% of Iran's population is affected by osteopenia and about two million people experience fractures due to osteoporosis. By 2050, about 34% of Iran's population will be over 50 years of age, so the rate of fractures due to osteoporosis will increase [4].

Several risk factors or protective factors have been reported in relation to BMD. The rate of decline in BMD is associated with aging. Other risk factors include smoking, drinking alcohol, calcium and vitamin D deficiency, a sedentary lifestyle, amenorrhea, low estrogen levels in women, prolonged use of corticosteroids, a family history of osteoporosis, low body mass index, rheumatoid arthritis and thyroid and parathyroid disorders [4]. Some protective factors are physical activity [5], vitamin D, [6] oral contraceptive pills, hormone therapy [7] and lactation [8].

Several epidemiological and clinical studies have shown that reproductive factors in women are important factors affecting BMD; however, the role of reproductive factors is currently controversial due to contradictory findings [9]. Various reproductive factors have been associated with decreased BMD, including delayed menarche [10], anovulation [11], duration of breastfeeding [12], number of pregnancies [13], menstrual disorders [14] and an age at menopause of under 50 years [15].

Estrogen prevents bone mass loss and osteoporosis by decreasing osteoclastic activity in bones, increasing bone matrix and increasing calcium and phosphate deposition in bones. Menopause is associated with hormonal, biological and clinical changes. The reduction of estrogen after menopause results in a rapid reduction in bone mass and osteoporosis [16]. Due to the importance of estrogen in the formation and development of bone and, in turn, the effect of reproductive factors on estrogen levels, these factors have been evaluated in investigations into the process of osteoporosis [17].

Identifying the risk factors of osteoporosis can be useful in preventing the onset of the disease and reducing the costs of treatment and disability. Information about the factors associated with osteoporosis in postmenopausal women is inconclusive and contradictory.

Objectives

This study aimed to investigate the relationship between reproductive factors and BMD in postmenopausal women.

Material and methods

This cross-sectional study was conducted in 2016, enrolling a total of 600 postmenopausal women who were selected according to eligibility criteria from among women who were referred to the densitometry center of Golestan Hospital in Ahvaz by physicians across the city. This is the only state densitometry center in an educational hospital that people at a low or medium socioeconomic level are main customers. The study participants were postmenopausal women who had passed at least 1 and at most 5 years of menopause. Other inclusion criteria were normal menopause (not induced by surgery or drugs) and a history of pregnancy and breastfeeding. The exclusion criteria were a history of hysterectomy or oophorectomy, diseases affecting bone density – such as autoimmune diseases (rheumatoid arthritis, lupus, Behçet's disease, etc.), parathyroid or thyroid diseases, diabetes, chronic kidney, lung, or heart diseases – cancer, corticosteroid or anticonvulsant drug use and post-menopausal hormone therapy. Women who could not remember the required information (i.e., their age at menarche, at their first pregnancy or at menopause) were also excluded from the study.

To arrive at the sample size of 600, we assessed 703 women through the convenience sampling method over a four-month period. One hundred and three women were not eligible because of diabetes (46), hysterectomy (20), thyroid disorders (15), corticosteroid consumption (12) and lack of anamnesis (10).

The data collection tools consisted of a demographic information questionnaire and a checklist for reproductive factors, including age at menarche and first pregnancy, gynecological age (chronological age at the time of first pregnancy minus age at menarche), number of pregnancies, parity and duration of lactation. The data were collected through face-to-face interviews with the participants. A scale (Beure Bs50) with a precision of one kilogram was used to measure their weight, and a wall-mounted height gauge with a precision of 1 cm was used to measure their height. BMD in the women was measured in the lumbar vertebrae L1–L4 and the femoral neck non-invasively by a Hologic machine and the DEXA method (Dual-energy X-ray absorptiometry). All measurements related to bone density assessment were taken by a technician working at the densitometry center of Golestan Hospital. Technical points regarding the position of the patients and the determination of the area to be measured were carefully observed. A rheumatologist interpreted all of the bone density assessments.

The study plan was approved by the Committee of Ethics in Research of Ahvaz Jundishapur University of Medical Sciences (Ethics code: IR.AJUMS.REC.1395.174). All participants were required to sign an informed consent form after the objectives of the study were explained to them. The identity and information of the patients were encoded and kept confidential. They were allowed to leave the study if they did not wish to cooperate.

The data were analyzed using SPSS version 21 by descriptive and analytical tests (Kruskal–Wallis, chi-squared, Mann––Whitney and multinomial logistic regression). The significance level of α was set at < 0.05.

Results

The frequencies of osteopenia and osteoporosis were 57.33% and 15.16%, respectively. The demographic and reproductive variables were compared in 3 groups (osteoporosis, osteopenia and normal) and are presented in Tables 1 and 2. Age, BMI, education and economic status were significantly different among the 3 groups ($p < 0.001$). The women with normal BMD had significantly higher levels of education and economic status. After examining normality with the Kolmogorov–Smirnov test, the Mann–Whitney non-parametric test was used to examine the reproductive variables. All reproductive factors were significantly different in the 3 groups ($p < 0.001$). In women with abnormal BMD, their age at menarche, number of pregnancies, parity and duration of breastfeeding were all higher, whereas age at first pregnancy and gynecological age were lower than in women with normal BMD (Table 2). Pearson's correlation coefficient showed a significant correlation between education and breastfeeding ($r = -0.353$), age at first pregnancy ($r = 0.565$) and parity ($r = -0.588$). Therefore, we did not enter education into the regression model. Gynecological age and the number of pregnancies were also not included in the regression analysis because of overlap with age at menarche and parity, respectively.

A multinomial logistic regression of the significant variables revealed later menarche to be a significant risk factor for the chance of both osteopenia (OR = 4.36, CI = 3.38–5.63, $p = 0.001$) and osteoporosis (OR = 2.63, CI = 2.00–3.46, $p = 0.001$). The number of parity was found to increase the likelihood of osteopenia (OR = 1.82, CI = 1.31–2.53, $p = 0.001$) and osteoporosis (OR = 1.43, CI = 1.00–2.04, $p = 0.049$). Longer breastfeeding was also shown to be a risk factor for both osteopenia and osteoporosis. Being older at first pregnancy and (only in the osteoporosis group) having higher values of BMI were found to have a protective effect (Table 3).

Table 1. Comparison of qualitative variables in the 3 groups

Variable \ Group		Normal *n* = 165	Osteopenia *n* = 344	Osteoporosis *n* = 91	*p*
		Number (percent)	Number (percent)	Number (percent)	
Occupation	housewife	124 (28.1)	258 (58.5)	59 (13.4)	0.126
	employed	41 (25.8)	86 (54.1)	32 (20.1)	
Marital status	married	121 (30)	218 (54)	65 (16.1)	0.067
	widowed/ divorced	44 (22.7)	124 (69.2)	26 (13.4)	
Residency	urban	132 (27.4)	269 (55.9)	80 (16.6)	0.139
	rural	33 (28.2)	73 (62.4)	11 (9.4)	
Economic condition	good	162 (30.8)	289 (54.9)	75 (14.3)	**< 0.001**
	weak	2 (2.8)	53 (74.6)	16 (22.5)	

Chi-squared test.

Table 2. Comparison of quantitative variables in the 3 groups				
Variable	Normal *n* = 165	Osteopenia *n* = 344	Osteoporosis *n* = 91	*p*
	M ± SD	M ± SD	M ± SD	
Age (years)	54.69 ± 3.3**	55.77 ± 3.34**	56.74 ± 3.01**	< 0.001
BMI	30.8 ± 4.51**	29.3 ± 4.96**	28.2 ± 4.42**	< 0.001
Education (years)	10.88 ± 4.03*	8.86 ± 4.44*	9.76 ± 4.13*	< 0.001
Age at menarche (years)	12.39 ± 0.97	14.52 ± 1.31	13.58 ± 1.6	< 0.001
Age at first pregnancy (years)	22.2 ± 3.23	20.43 ± 4.63	19.14 ± 3.72	< 0.001
Gynecological age (years)	9.88 ± 3.4	5.92 ± 4.3	5.6 ± 3·61	< 0.001
Number of pregnancies	3.26 ± 1·55	4.49 ± 1.61	4.49 ± 1.73	< 0.001
Number of parity	3.08 ± 0·78	4.14 ± 1.44	4.22 ± 1.71	< 0.001
Breastfeeding duration (months)	50.84 ± 19·76	66.64 ± 21.31	69.65 ± 22.53	< 0.001

* ANOVA; ** Kruskal–Wallis Test.

Table 3. Results of multinomial logistic regression					
BMD[a]		B	OR	95% CI	*p*
Osteopenia	age	-0.066	0.936	0.854–1.026	0.160
	BMI	-0.001	0.999	0.995–1.002	0.501
	age at first pregnancy	-0.124	0.883	0.813–0.959	**0.003**
	age at menarche	1.473	4.363	3.380–5.632	**0.001**
	parity	0.601	1.823	1.314–2.530	**0.001**
	breastfeeding	0.021	1.021	1.004–1.038	**0.014**
Osteoporosis	age	0.030	1·030	0.926–1.146	0.582
	BMI	-0.067	0.935	0.890–0.982	**0.007**
	age at first pregnancy	-0.172	0.842	0.760–0.933	**0.001**
	age at menarche	0.970	2.637	2.005–3.468	**0.001**
	parity	0.358	1.430	1.000–2.046	**0.049**
	breastfeeding	0.029	1.029	1.010–1.048	**0.002**

[a] The reference category is women with normal BMD.

Discussion

This study revealed that later menarche, multiparity and longer breastfeeding significantly increase the risk of abnormal BMD in postmenopausal women, whereas a higher BMI and being older at first pregnancy decrease the risk.

Age at menarche was found to be a significant risk factor for osteopenia and osteoporosis in our study. Similarly, in a study in Mexico, a menarche age higher than 13 years was considered a risk factor (p = 0.035, OR = 4.46) for osteoporosis in postmenopausal women [18]. A recent Mendelian randomization study investigated the potential causal effect of menarche age as a risk factor for BMD loss and discovered that each additional year in menarche age is associated with some reduction in BMD of the femoral neck [19]. Parker et al. reported that menarche at age 11 or under reduces the incidence of osteoporosis. Early menarche is associated with excessive estrogen circulation both during and after menstruation [17]. Estrogen can stabilize the process of osteoporosis or prevent it. In addition to inhibiting the solubilizing activity of osteoclasts, estrogen increases intestinal calcium and 1,25-dihydroxyvitamin D absorption, increases calcium preservation in the kidney and supports the survival of osteoblasts [20]. Thus, it may have a protective effect against the development of osteoporosis.

The results of previous studies on the relationship between the age of first pregnancy and BMD in postmenopausal women are controversial. As with the results of our study, in a study on postmenopausal women, an older age at first pregnancy was found to be a protective factor for normal BMD at menopause [21]. However, other studies have shown that age at first pregnancy has no significant effect on postmenopausal BMD [22, 23]. The disparate results may be due to differences in lifestyle, menarche age, gynecological age or marriage age – and subsequently, pregnancy age. Similarly, our study indicated that the gynecological age of women with normal BMD was significantly higher than that of women with osteoporosis or osteopenia. It is assumed that a first pregnancy before the age of 27 years may negatively affect the acquisition of peak bone mass [21].

Our study indicated that a higher parity increases the risk of osteoporosis and osteopenia in postmenopausal women. Some other studies have also reported this finding. In another study in Iran, multiparity and multiple pregnancies were reported to be risk factors for lower BMD values in postmenopausal women [24]. Some previous studies, however, show contradictory results. A study in China noted that a higher parity correlates linearly with reduced hip fracture risks among women [13]. In the United States, Schnatz et al. reported multiparity as a protective factor for osteoporosis [21]. In a study in Turkey, there was no significant difference between nulliparous and multiparous (5 deliveries or more) postmenopausal women in terms of BMD [25]. Heidari et al. concluded that a parity of > 7 has an early detrimental effect on BMD in younger postmenopausal women, but later plays a protective role against the age-related risk of bone loss; it should therefore not be considered a risk factor for bone loss in postmenopausal women [26]. Although parity reflects the number of pregnancies and thus seems to have the same effect on BMD, a recent systematic review shows a positive effect of multiparity on BMD that is site-specific, as multipa-

rous women have higher hip BMD. This conclusion may describe some controversial findings [27]. Several biological mechanisms have been reported on pregnancy's effect on bone. The increase in maternal–fetal calcium transmission during pregnancy leads to a decrease in calcium [28]; the rate of bone turnover increases in pregnancy as well [29]. In addition, during pregnancy, the placenta produces inflammatory and growth factors that affect bone turnover. The increase of insulin-like growth factor (IGF-I) in pregnancy leads to decreased bone density by increasing bone turnover [30]. On the other hand, intestinal calcium absorption and increases in estradiol hormone level during pregnancy [31] both play a protective role for bones.

In our study, breastfeeding increased the risk of osteopenia and osteoporosis by about 2% per month. The results of previous studies are somewhat contradictory. Long-term breastfeeding has been mentioned as a risk factor for osteoporosis [16] and it significantly correlated with lower BMD in the lumbar spine [32]. A significant difference in BMD has been observed with a duration of breastfeeding less than 4 years and more than 8 years (p = 0.001): with increasing lactation, BMD decreased [33]. Despite these findings, there is evidence that breastfeeding significantly decreases the incidence of postmenopausal osteoporosis [21] and increases premenopausal BMD [8]. However, in some studies, there was no significant correlation between the duration of lactation and BMD [22, 34]. Maternal adaptations differ between pregnancy and lactation to meet the mineral demands of the growing fetus. Increased intestinal absorption of calcium during pregnancy and skeletal resorption of calcium during lactation form the main maternal adaptive mechanisms to meet the increased requirements. In an otherwise healthy pregnant woman, the mild bone resorption which occurs during pregnancy and lactation is rapidly reversed after weaning, resulting in nearly no significant effect on the bones [35]. It may also be concluded that the relationship between lactation and bone density is mediated by the number of pregnancies and parity.

In this study, the women with normal BMD had a higher level of education and economic status than the women in the osteopenia and osteoporosis groups. This finding has also been reported by other studies [20, 36] and is consistent with the evidence that a low socioeconomic level is associated with later menarche [37], earlier age at first pregnancy and multiparity. Evidence about the relationship between socioeconomic status and physical activity, however, provides inconclusive results [38]. Moreover, there is some evidence that age at menarche is associated with age at menopause [39] and that earlier menopause is associated with an increased risk of postmenopausal osteoporosis [7]. Therefore, sociodemographic factors mediate or moderate the relationship between reproductive factors and BMD. The interaction between these influences needs further evaluation.

Limitations of the study

This study has some limitations. The use of convenience sampling may influence the generalizability of its findings. In addition, the effects of some confounding factors — such as nutrition status, exposure to sunlight, physical activity and contraceptive methods — are unclear due to the nature of the study design. Lastly, the veracity of the participants' responses about their age at menarche, age at first pregnancy or economic condition cannot be guaranteed.

Conclusions

Our findings add to evidence that later menarche increases the risk of postmenopausal osteopenia and osteoporosis. Our results also suggest that multiparity and longer breastfeeding are risk factors, while having a higher BMI and being older at first pregnancy are protective factors for abnormal BMD in postmenopausal women. Despite the uncertainty about the effect of other reproductive factors in the literature, age at menarche seems to be a strong risk factor for postmenopausal bone density disorders. It is unclear whether interventions can decrease the effect of later menarche. The interactions between effective factors need to be explored further. Future studies should focus on the mediator or moderator variables which affect this association.

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References

1. Nordin BEC, Morris HA, Anderson P. Definition, diagnosis and significance of osteoporosis [E-BOOK]. The Physiological basis of metabolic bone disease; 2014. Available from URL: https://www.taylorfrancis.com/books/9780429112324.
2. NIH (National Institutes of Health). Osteoporosis and related bone diseases. National Resource Center [cited 10.02.2013]. Available from URL: https://www.bones.nih.gov/health-info/bone/osteoporosis/bone-mass.
3. Suman V, Khalid P, Pratik KC. Risk factors associated with osteoporosis. *Int J Health Sci Res* 2013; 3(8): 85–89.
4. Middle East & Africa Audit, individual country reports, Iran. International Osteoporosis Foundation (2018). Available from URL: https://www.iofbonehealth.org/sites/default/files/PDFs/Audit%20Middle%20East_Africa/ME_Audit-Iran.pdf.
5. Englund U, Nordström P, Nilsson J, et al. Physical activity in middle-aged women and hip fracture risk: the UFO study. *Osteoporos Int* 2011; 22: 499–505, doi: 10.1007/s00198-010-1234-1.
6. Nair R, Maseeh A. Vitamin D: the "sunshine" vitamin. *J Pharmacol Pharmacother* 2012; 3: 118–126.
7. Yun BH, Choi YR, Choi YS, et al. Age at first delivery and osteoporosis risk in Korean postmenopausal women. The 2008–2011 Korea National Health and Nutrition Examination Survey (KNHANES). *PLoS ONE* 2015; 10(5): e0123665, doi: 10.1371/journal.pone.0123665.
8. Canal-Macias ML, Roncero-Martin R, Moran JM, et al. Increased bone mineral density is associated with breastfeeding history in premenopausal Spanish women. *Arch Med Sci* 2013; 9(4): 703–708.
9. Randolph JF, Sowers MR. *Premenopausal reproductive and hormonal characteristics and the risk for osteoporosis.* In: Marcus R, Feldman D, Dempster DW, et al., eds. *Osteoporosis.* 4th ed. San Diego: Academic Press; 2013: 721–744.
10. Pentyala S, Mysore P, Pentyala S, et al. Osteoporosis in female athletes. *Int J Clin Therap Diagnosis* 2013; 1(1): 1–9, doi: 10.19070/2332-2926-130002.
11. Berek JS. *Berek & Novak's Gynecology.* 15th ed. Philadelphia: Lippincott Williams & Wilkins; 2012.
12. Hosseinpanah F, Hosseinpanah F, Sorouri M, et al. Total duration of breastfeeding is associated with low bone mineral density in Iranian postmenopausal women. *Int J Endocrinol Metab* 2010; 8(3): 153–158.

13. Wang Q, Huang Q, Zeng Y, et al. Parity and osteoporotic fracture risk in postmenopausal women: a dose-response meta-analysis of prospective studies. *Osteoporos Int* 2016; 27(1): 319–330, doi: 10.1007/s00198-015-3351-3.
14. Sobaś K, Wądołowska L, Sowińska M, et al. Analysis of the occurrence of dietary and non-dietary factors of fracture risk in relation to bone mineral density in women. *Acta Sci Pol Technol Aliment* 2010; 9(3): 373–382.
15. Noale M, Maggi S, Crepaldi G. Osteoporosis among Italian women at risk: the OSTEOLAB study. *J Nutr Health Aging* 2012; 16(6): 529–533.
16. Ebrahim K, Ramezanpoor M, Rezaee Sahraee A. Effect of eight weeks of aerobic and progressive exercises on changes of estrogen hormone and effective factors on bone mass in menopaused sedentary women. *Iran J Endocrinol Metab* 2010; 12. Available from URL: https://www.researchgate.net/publication/287684663_Effect_of_eight_weeks_of_aerobic_and_progressive_exercises_on_changes_of_estrogen_hormone_and_effective_factors_on_bone_mass_in_menopaused_sedentary_women.
17. Parker SE, Troisi R, Wise LA, et al. Menarche, menopause, years of menstruation, and the incidence of osteoporosis: the influence of prenatal exposure to diethylstilbestrol. *J Clin Endocrinol Metab* 2014; 99(2): 594–601.
18. Mendoza-Romo MA, Ramírez-Arriola MC, Velasco-Chávez JF, et al. Parity and menarche as risk factors for osteoporosis in postmenopausal women. *Ginecol Obstet Mex* 2014; 82(2): 75–82.
19. Zhang Q, Greenbaum J, Zhang W-D, et al. Age at menarche and osteoporosis: a Mendelian randomization study. *Bone* 2018; 117: 91–97.
20. Berry SD, Kiel DP, Donaldson MG, et al. Application of the National Osteoporosis Foundation guidelines to postmenopausal women and men: the Framingham osteoporosis study. *Osteoporos Int* 2010; 21(1): 53–60.
21. Schnatz PF, Barker KG, Marakovits KA, et al. Effects of age at first pregnancy and breast-feeding on the development of postmenopausal osteoporosis. *Menopause* 2010; 17(6): 1161–1166.
22. Guler NS, Aydın GA, Gurgen I. Effects of lactation and age of first pregnancy on postmenopausal osteoporosis. *Anatolian Clinic J Medical Sciences* 2018; 23(1), doi: 10.21673/anadoluklin.348820.
23. Cavkaytar S, Seval MM, Atak Z, et al. Effect of reproductive history, lactation, first pregnancy age and habits on bone mineral density in natural postmenopausal women. *Aging Clin Exp Res* 2015; 27(5): 689–694, doi: 10.1007/s40520-015-0333-4.
24. Derakhshan S, Mahmoudi M, Shahsawari S. Effects of multiparity and duration of breast-feeding on maternal bone mineral density in post-menopausal Kurdish women: a retrospective study. *Iran J Nucl Med* 2017; 25(1): 43–50.
25. Terzi H, Terzi R, Kale E, et al. Effect of multiparity on bone mineral density, evaluated with bone turnover markers. *Rev Bras Reumatol Engl Ed* 2017; 57(5): 371–377.
26. Heidari B, Heidari P, Nourooddini HG, et al. Relationship between parity and bone mass in postmenopausal women according to number of parities and age. *J Reprod Med* 2013; 58(9–10): 389–394.
27. Song SY, Kim Y, Park H, et al. Effect of parity on bone mineral density: a systematic review and meta-analysis. *Bone* 2017; 101: 70–76.
28. Yılmaz H, Erkin G, Demir Polat H, et al. Effects of reproductive factors on bone mineral densitometry. *Turk J Osteoporosis* 2012; 18: 8–12.
29. Salles JP. Bone metabolism during pregnancy. *Ann Endocrinol* (Paris) 2016; 77(2): 163–168.
30. Naylor K, Iqbal P, Fledelius C, et al. The effect of pregnancy on bone density and bone turnover. *J Bone Mineral Res* 2000; 15(1): 129–137.
31. Gallagher JC. Effect of early menopause on bone mineral density and fractures. *Menopause* 2007; 14: 567–571.
32. Tsvetov G, Levy S, Benbassat C, et al. Influence of number of deliveries and total breast-feeding time on bone mineral density in premenopausal and young postmenopausal women. *Maturitas* 2014; 77(3): 249–254.
33. Singh R, Gupta S, Awasthi A. Differential effect of predictors of bone mineral density and hip geometry in postmenopausal women: a cross-sectional study. *Arch Osteoporos* 2015; 10: 39, doi: 10.1007/s11657-015-0246-z.
34. Lenora J, Lekamwasam S, Karlsson MK. Effects of multiparity and prolonged breast-feeding on maternal bone mineral density: a community-based cross-sectional study. *BMC Women's Health* 2009; 9: 19, doi: 10.1186/1472-6874-9-19.
35. Mahadevan S, Kumaravel V, Bharath R. Calcium and bone disorders in pregnancy. *Indian J Endocrinol Metab* 2012; 16(3): 358–363.
36. Maddah M, Sharami SH, Karandish M. Educational difference in the prevalence of osteoporosis in postmenopausal women: a study in northern Iran. *BMC Public Health* 2011; 11: 845, doi: 10.1186/1471-2458-11-845.
37. Karapanou O, Papadimitriou A. Determinants of menarche. *Reprod Biol Endocrinol* 2010; 8: 115, doi: 10.1186/1477-7827-8-115.
38. O'Donoghue G, Kennedy A, Puggina A, et al. Socio-economic determinants of physical activity across the life course: a „DEterminants of DIet and Physical ACtivity" (DEDIPAC) umbrella literature review. *PLoS ONE* 2018; 13(1): e0190737, doi: 10.1371/journal.pone.0190737.
39. Shahrani A, Faraj S, Alhargan A, et al. Factors affecting age at menopause among Saudi women in Riyadh, SA: a cross-sectional study. *Fam Med Prim Care Rev* 2018; 20(1): 55–60, doi: 10.5114/fmpcr.2018.73704.

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