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Systematic Review (Pages: 8831-8843)

The Effect of Breastfeeding Duration on Bone Mineral Density (BMD): A Systematic Review and Meta-Analysis

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Abstract

Background: During lactation, metabolic changes in the bone in different areas of the body may affect the amount of bone mineral density. The aim of this study was to determine the relationship between breastfeeding and bone mineral density in women.

Materials and Methods: In this study, articles were searched at Cochran, Medline (via PubMed), Scopus, and Web of Science databases until June 2018. The search procedure was conducted with keywords related to breastfeeding and bone mineral density. The mean (SD) of bone mineral density was extracted in the lumbar spine and femoral neck. Funnel plot and Egger's test was used for publication bias assessing and I^2 index were used for heterogeneity.

***Results*:** In this study, 10 articles involving 3,613 healthy women included for Meta analyze. We observed the decreasing trend in mean bone mineral density (BMD) of lumbar spine, femur neck in non-breastfeeding subgroup to 24 months or more breastfeeding subgroup. BMD of lumbar spine in non-breastfeeding women were [M: 0.96, 95%confidence interval [CI]; 0.89-1.02, P=0.000], in subgroup with more than 24 months breastfeeding the BMD were [M: 0.87, 95%CI; 0.79-0.95, P=0.000]. The femoral neck BMD in non-breastfeeding were [M: 0.80 95%CI; 0.73-0.87, P=0.000], and in subgroup with more than 24 months breastfeeding the BMD were [M: 0.76, 95%CI; 0.71-0.81, P=0.000]. In subgroup analyze, the mean BMD in Asian and postmenopausal sub-group was lower than others.

***Conclusion*:** The results of this study showed that breastfeeding have reduced effect on bone mineral density in the lumbar spine and femoral neck of women, but there were high heterogeneity in sub-group analyze, so we recommended another studies in homogenous group of women.

Key Words: Breastfeeding, Bone mineral density, Children, Meta-analysis.

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1- INTRODUCTION

Estimated that the reduction in bone mineral density in the USA has occurred in almost 55 percent of women over 50 years of age (2). Osteoporosis is an important problem in all over world (3). Odén et al. in the year 2010 predicted that during the next 40 years, the number of people with the risk of bone fracture will be doubled (4). Along with the aging of the population it is estimated that until 2025 the annual cost of fractures will be $25.3 billion (5). Fractures caused by osteoporosis lead to increased mortality and reduced quality of life (6). The bone mineral density increases in childhood and reaches its peak at the age 20-30. In these years, bone mineral density are influenced by several factors such as genetics, nutrition, exercise and sex hormones (7). Estrogen, via inhibition of osteoclast activity has an anti-resorption impact on bone (8). The accompanying situations along with the changes in estrogen levels, such as pregnancy and lactation, affect the bone mineral density (9, 10).

During the breastfeeding period, changes occur in calcium homeostasis and bone metabolism and a large amount of maternal calcium flows to the baby via mother’s breast milk so in addition to supplying the baby's needs to calcium, it helps the continued development of its skeletal system as well (11). Also, during the breastfeeding period, stimulating the protein associated with parathyroid hormone (12), as well as increased levels of prolactin, reduce the amount of estrogen and this estrogen drop contributes to bone resorption (13). Too much breastfeeding reduces the amount of mother’s calcium and impairs mother’s bone mass (14). Although in many studies it has been shown that this decrease in the mother’s bone mass will be compensated for during 6-12 months after discontinuing breastfeeding, but the results of studies in relation with the factors associated with breastfeeding such as breastfeeding period are in conflict with bone density (15, 16). The results of some studies have shown longer breastfeeding reduces the bone mineral density even more (9, 17, 18); while this relationship is not observable in some other studies, in the study by Kyvernitakis et al. in a six-year follow-up there was no significant difference in the number of fractures and the length of the breastfeeding period (19). Therefore, due to the lack of a transparent relationship with the duration of breastfeeding with osteoporosis and reduction of bone mineral density in women in previous studies, we conducted the present meta-analysis to determine the relationship between the breastfeeding duration and bone mineral density in women.

2- MATERIALS AND METHODS

2-1. Method

In this study search was performed by two blind investigators. Electronically search for this study conducted in June 2018 and without a time limit in the databases of Scopus, Medline (via PubMed), Web of Science and Cochran library. Search of articles was limited to English language. The search keyword include: "Bone Minera Density", "Bone Mineral Content", "Bone density", "Breastfeeding", Breast feeding", "Exclusive Breastfeeding", Exclusive Breast Feeding.
The details about the search strategy are displayed in **Table.1**. All searched articles were entered in Endnote software, then the duplicate articles were deleted, and the articles underwent an initial evaluation. After removal of irrelevant articles that were lacking in the assessment criteria of being included in the study, we checked the quality of the articles. To assess the quality of the articles we used a tool called Newcastle-Ottawa Scale adapted for cross-sectional studies. We measured 3 items such as Selection, Outcome, and Comparability in this tool (20).

In the next step, we prepared a check-list of the necessary information for the study (name of the researcher, study year, research location, age, number of samples, etc.) for all studies that passed the initial assessment in order to prepare the final evaluation. Finally, the ultimate checklist was reviewed and the relevant articles entered the meta-analysis. Following these steps, in the first search using the keywords, 25, 3437 articles became available and after evaluation, also manual search within the references of the extracted articles finally 10 suitable articles entered the meta-analysis phase. Also Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist to develop this systematic review (21). This checklist helps us to improve the reporting of systematic reviews and meta-analyses.

Table-1: Search keywords in PubMed database

A full electronic search strategy for PubMed database was applied using: (Bone Mineral Density [tiab] OR Bone Mineral Content [tiab] OR bone density[tiab] OR BMD [tiab] AND Breast feeding [tiab] OR Breastfeeding [tiab] OR Exclusive Breastfeeding [tiab] OR Exclusive Breast Feeding [tiab].

2-2. Articles inclusion criteria

Those articles were included in the study that: 1) Had reported one or more of these subgroups: nulliparous women or who have no breastfeeding, women with 1-24 months total breastfeeding and women with over 24 months total breastfeeding , 2) Had reported bone mineral density based on the unit g/cm^2 in the lumbar spine and femoral neck in women (it should be noted that we also extracted and analyzed the data in studies that reported total hip bone mineral density), 3) Measured bone mineral density with Dual-Energy X-ray Absorptiometry method (DXA) , 4) Study samples without a known disease and consumption of drugs affecting bone mineral density.

2-3. Data extraction and Statistical analyze

The Means and standard deviation of bone mineral density (BMD) (g /cm^2) at lumbar spine, femoral neck or total hip (if the study was reported) were extracted. Q-test and the I^2 index were used for heterogeneity, because of high heterogeneity (with I^2 >50%) the random effects model was used. A funnel plot and Egger's test be used for publication bias; data were analyzed using Stata Version 11.2.

3- RESULTS

This present study aimed to determine the relationship between the breastfeeding duration and bone mineral density in women. In this study 253, 437 articles identified through database searching; 275 articles removed because of duplicate, 253, 141 removed because of irrelevant topics, absence of full text and Due to the non-relevance and 11 removed because studies participants without inclusion criteria, after exclusion of articles without inclusion criteria finally 10 studies were included in this review (**Figure.1**). **Table.2** shows mean [95% confidence interval [CI] in BMD of the femoral neck, spine, between non breastfeeding and breastfeeding women in subgroups of studies defined by study characteristics. **Table.3** shows the characteristics of included studies (*please see the tables in the end of paper*).

Considering all the included studies, the total sample size of studies was 3,613 healthy women. The location of study was: Turkey (3 study), Moroccan (2 study), Sir Lanka (1 study), USA (1 study), Iran (1 study), Korea (1 study), Spain (1 study). The mean age of participants were [Mean (M) :54.48 , 95% CI;48.49-60.47, I^2=99.9, $P_{hetrogeneity}$ =0.000], the mean menarche age were [M:13.68 95%CI;13.2-14.16,

I^2=98.9%, $P_{hetrogeneity}$ =0.000], and the mean BMI (kg/cm^2) were [M:27.07 95%CI;25.55-28.59,I^2=99.7%, $P_{hetrogeneity}$ =0.000].

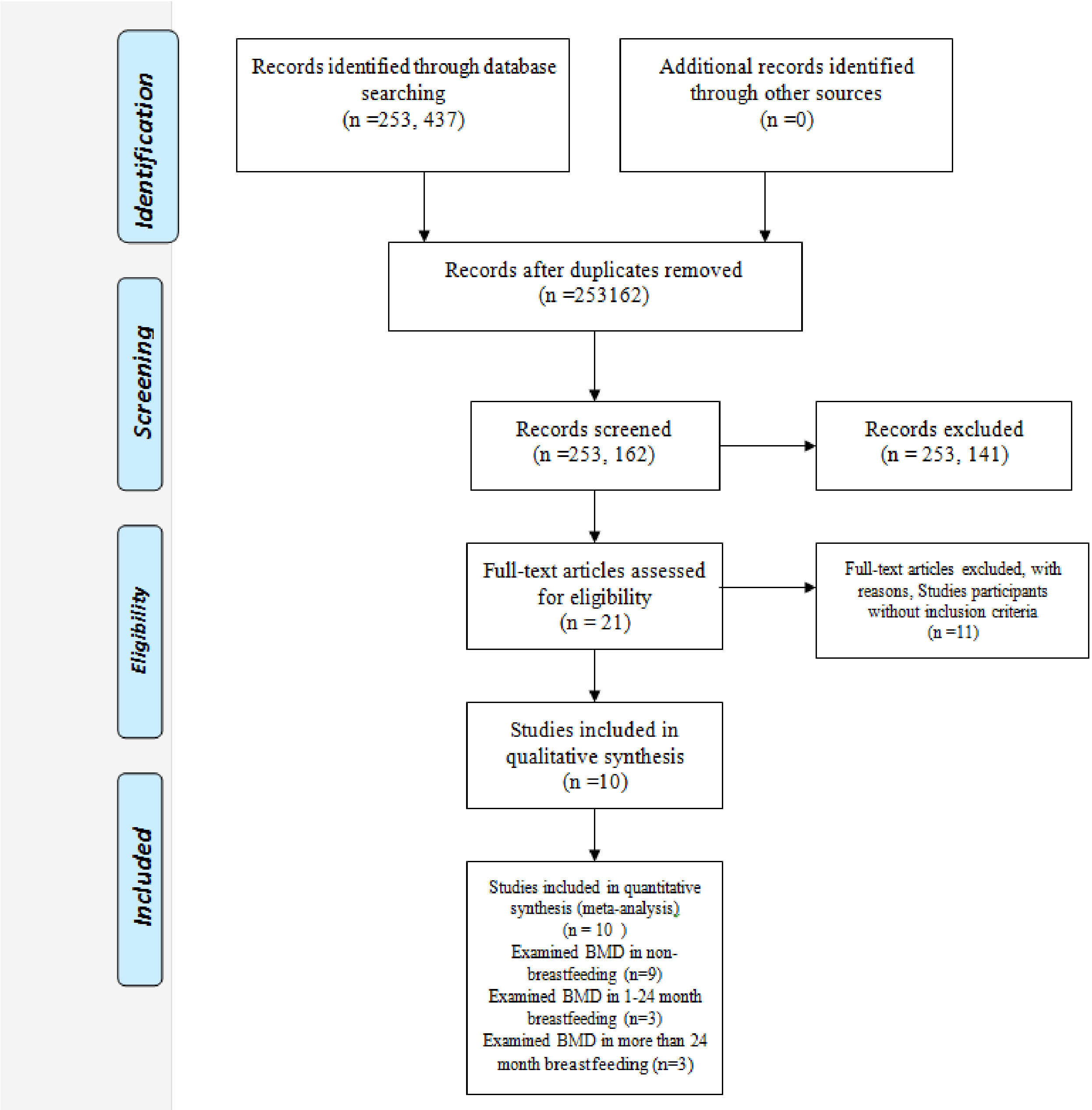

Fig.1: PRISMA flowchart of present study.

We used random effect model because of heterogeneity (I^2> 50%). In cases where the studies were heterogeneous, random effects model were used. In this review all included study were reported the Mean and SD of BMD at lumbar and femur site in different subgroups, but only 2 studies (22, 23) were reported the Mean and SD of BMD at Hip site, BMD in hip site were [M:0.91, 95%CI;0.89-0.93, p=000]; generally the BMD in lumbar site were [M:0.94, 95%CI;0.89-0.98] and in femoral neck were [M:0.87, 95%CI;0.75-0.82]. Our results showed that the BMD (g/cm^2) in subgroup with never breastfeeding in lumbar spine site were [M:0.96 ,95%CI;0.89-1.02, $P_{hetrogeneity}$ =0.000], in subgroup with lower than 24 months total breastfeeding were [M:0.93, 95%CI;0.86-1.00, p=0.000], and in subgroup with more than 24 months total breastfeeding the BMD were [M:0.87, 95%CI;0.79-0.95, p=0.000]. We observed the decreasing trend of BMD in non-breastfeeding subgroup to more than 24 months total breastfeeding subgroup, but this trend have low slop between the non-breastfeeding group and subgroup with lower than 24 months breastfeeding (**Figure.2**).

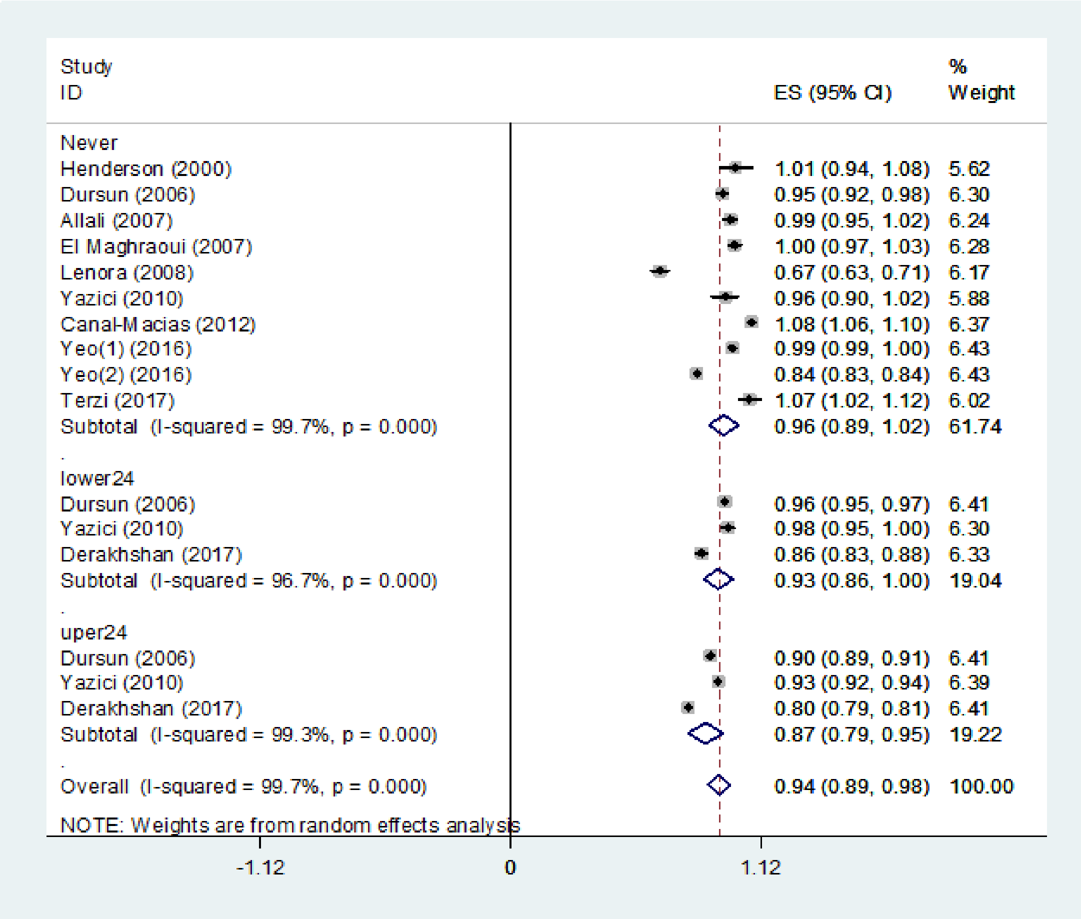

Fig.2: Evaluation of the mean bone mineral density at lumbar site according to random effects model, based the author's name and the year of study. Each line segment is indicating a confidence interval of 95%. CI: Confidence interval.

Also, the BMD (g/cm^2) in subgroup with never breastfeeding in femur site were [M:0.80 95%CI;0.73-0.87, $P_{hetrogeneity}$ =0.000], in subgroup with lower than 24 months total breastfeeding were [M:0.79 , 95%CI;0.74-0.84, $P_{hetrogeneity}$ =0.000] and in subgroup with more than 24 months total breastfeeding the BMD were [M:0.76, 95%CI;0.71-0.81, $P_{hetrogeneity}$ =0.000]. Also, we observed the decreasing trend in femur BMD in non-breastfeeding subgroup to more than 24 months breastfeeding subgroup, but this trend have low slop between the non-breastfeeding and lower than 24 months subgroup (**Figure.3**). The results of the subgroup analyses stratified by participant menopausal status, BMI state (mean) and study continent shows in **Table.1** (*Please see the table at the end of paper*). In this study there was no evidence of publication bias for BMD based on Begg's (p=0.126) funnel plot and Egger test (p=0.128) (**Figure.4**).

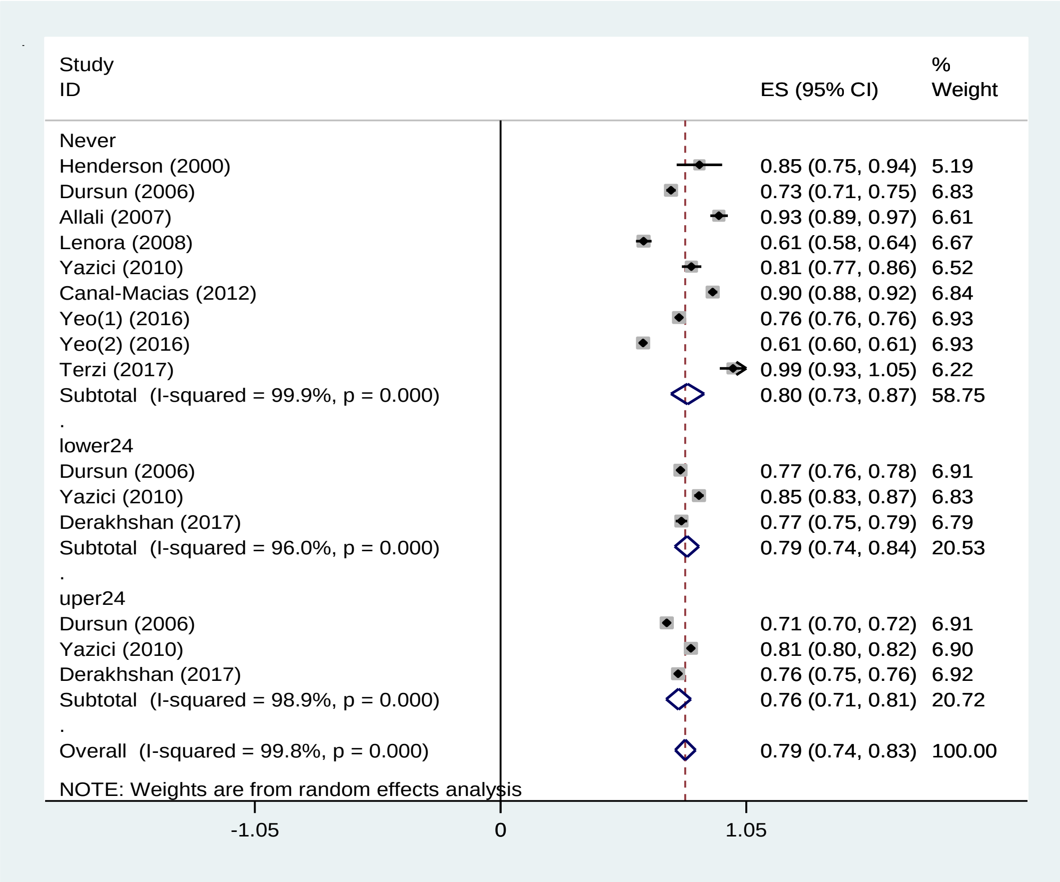

Fig.3: Evaluation of the mean bone mineral density at femur site according to random effects model, the author's name and the year of study. Each line segment is indicating a confidence interval of 95%.

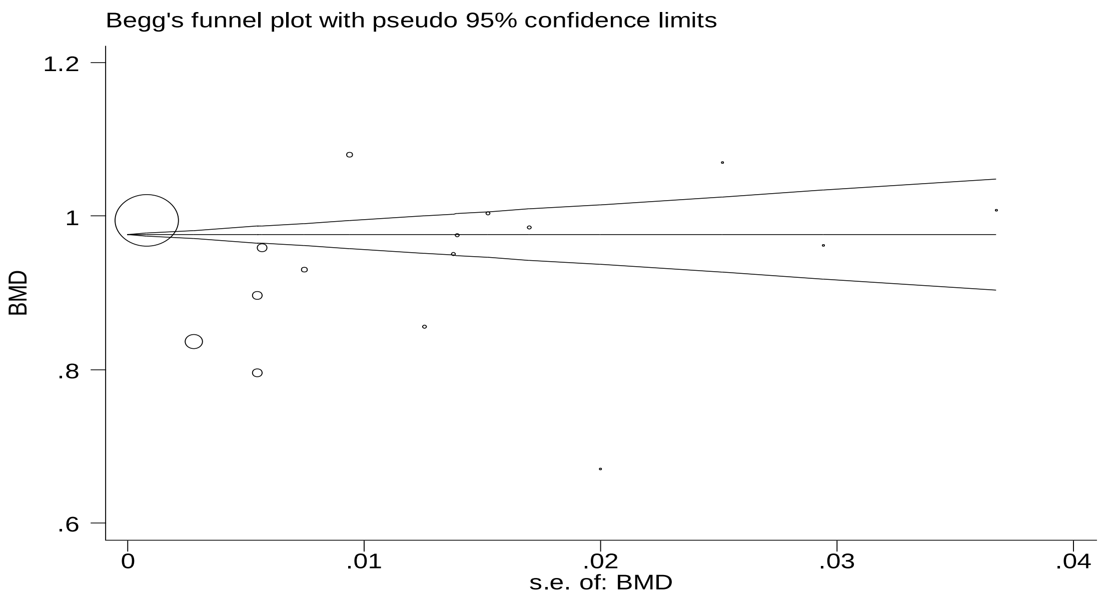

Fig.4: A. Funnel plot for checking publication bias.

4- DISCUSSION

The results of the present meta-analysis showed that bone mineral density in lumbar spine and femoral area in women without the history of breastfeeding is significantly more than women breast feeder women. Generally, the mean BMD at lumbar 0.94 (g/cm^2) was more than the femoral area 0.87(g /cm^2). In this study, the results of analysis of the sub-groups showed that in Asian women and postmenopausal women the mean BMD was lower than other subgroups. A meta-analysis study in order to determine the effects of breastfeeding on health implications of the mother showed that breastfeeding impact on BMD was not clear (24). Salari et al. (2014) in their systematic study showed that the role of parity and breastfeeding may have a protective effect on bones but the number of parties and duration of lactation may affect this influence (25). In a study by Tsvetov et al. (2014) with controlling menopausal status, BMI, and number of births; prolonged breastfeeding was associated with decreased BMD (26).

The results of the study by Karlssen et al. (2001) showed that the reduction of lumbar BMD in lactating women was significantly more than non-lactating women (27). Impact of breastfeeding is different on the body's bones in every location. Trabecular bones are more sensitive to metabolic alterations (28). In this study, the rate of BMD decrease in lumbar area was higher such that the mean 0.96 (g/cm^2) in non-lactating women reached 0.87 in women with more than 24 months of total breastfeeding. But in the femoral area it 0.8 (g/cm^2) in non-lactating women and reached 0.76 in women with more than 24 months of total breastfeeding. Lumbar bone is more sensitive than the femur to hormonal changes and reduced calcium reserves (29). In a cohort study by Mori et al. (2015), the lumbar spine BMD was inversely correlated with the breastfeeding period (29). In a study by Bolzetta et al. (2014) women who had more than 18 months of experience in breastfeeding to a child compared with those who had less than 18 months, were twice more at risk of vertebral fractures (18).A study by Bjørnerem et al. (2011) showed that in women with a history of breastfeeding compared to women without breastfeeding, the risk of hip fracture was 50% lower (30). A study by Hwang et al. (2016) also showed a long breastfeeding period caused lower BMD at the lumbar area (31). According to some evidence, there is an inverse correlation between lumbar vertebrae BMD and femoral BMD with total lactation period in women (32, 33). The child in the first 6 months receives 200 mg of calcium daily and in the second 6 months, 120 mg of calcium daily from the breast milk and in case of twins, this value may be doubled (34).

A study by Okyay et al. (2013) showed in the group of women under 27 years of age, breastfeeding over one year to the child increased the risk of osteoporosis (35). In the lactation period, prolactin hormone restrains estrogen secretion and on the other hand, distribution of (PHTrp) hormone in the mother's blood circulation causes disorder of mineral recirculation (in particular, calcium and vitamin D) that affect the process of bone making (36). It is reported that the amount of calcium intake in North American women is inadequate (34), so some evidence implies that in women during prolonged breastfeeding, intake of nutritional supplements may be necessary (8). It is said that 6-12 months after breastfeeding the bone density returns to the initial base amount (31). In General, during breastfeeding, changes in hormones, body weight, nutrition, physical activity and lifestyle may affect BMD (37). A study showed that bone mineral content in lactating women in the lumbar and hip area during 24 months was reduced by 0.9% and recovered later but in non-lactating women the 0.8% figure increases and continues on (15). Although lactating women during breastfeeding are exposed to a significant hypo-estrogen with negative impact on the metabolism of calcium and phosphate (38, 39); but it is possible that progestin-only pills that are often used by lactating women might increase the BMD (40). Kalkwarf (2004) in his study reported that reduction of BMD during breastfeeding does not increase osteoporosis risk in these people at old age (41). Another study reported that by observing longer intervals between pregnancies, breastfeeding will decrease the risk of hip fracture (42). Reduced bone mineral density in lactation depends on the ovarian function and duration of amenorrhea in postpartum period (41).

Wiklund et al. (2012) in their study concluded that without considering the number of children; women who in their lifetime had more than 33 months breastfeeding had more bone strength in hip and tibia areas than women who had less than 12 months (43). The cohort study reported that 19 months after giving birth, BMD returned to the amount before pregnancy (44). One of the strengths of this study was that the healthy women without diseases affecting bone mineral density as well as women not taking drugs that affect bone metabolism were studied. In addition, 5 studies adjusted for various factors including age, body mass index, etc. Although, perhaps cohort studies from post-lactation period to postmenopausal period can perfectly show the effect of lactation on BMD.

5- CONCLUSIONS

The results of this study showed that breastfeeding have reduced effect on bone mineral density in the lumbar spine and femoral neck of women, but there were high heterogeneity in subgroup analyze so we recommended another studies in homogenous group of women.

6- CONFLICT OF INTEREST

All the authors declare that they have no conflict of interest.

7- ACKNOWLEDGMENTS

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Table-2: Mean [95%CI] in BMD of the femoral neck, spine, between non breastfeeding and breastfeeding women in subgroups of studies defined by study characteristics.

Subgroup	Lumbar Spine				Femur Neck			
	Number	Mean (95%CI)	I^2	P-value	Number	Mean (95%CI)	I^2	P-value
Menopausal state								
1) Postmenopausal	7	0.91 [0.87-0.95]	98.9%	P=0.000	7	0.78 [0.72-0.83]	99.7%	0.000
2) Premenopausal	3	1.03 [0.96-1.10]	97.6%	P=0.000	3	0.84 [0.72-0.95]	99.1%	0.000
3) Pre- and postmenopausal	1	1.00 [0.97-1.03]	-	-	-	-	-	-
BMI state(mean)								
1) Normal	4	0.91 [0.81-1.00]	99.9%	P=0.000	4	0.72 [0.63-0.82]	99.9%	0.000
2) Upper than 25 (kg/m^2)	7	0.95 [0.90-0.99]	98.5%	P=0.000	6	0.82 [0.78-0.85]	97.80%	0.000
Study continent								
1) Africa	2	1.00 [0.97-1.02]	0%	P=0.405	1	0.93 [0.89-0.97]	-	-
2) Asia	6	0.91 [0.85-0.96]	99.8%	P=0.000	6	0.76 [0.71-0.81]	99.8%	0.000
3) Europe	1	1.08 [1.06-1.10]	-	-	1	0.90 [0.88-0.92]	-	-
4) America	1	1.01 [0.94-1.08]	-	-	1	0.85 [0.75-0.94]	-	-

CI: confidence intervals; BMI: Body mass index.

Table-3: Characteristics of included studies.

Author, year	Sample size Country	Menopausal status	Age, mean ± SD (range)	Adjusted for	Measurement
Yeo et al. (45)	229 non- breastfeed Korean women	Postmenopausal and premenopausal	Postmenopausal 55.8±1.3 Premenopausal 41.3 ± 0.3	Age and body mass index smoking status, alcohol consumption, physical activity, and serum 25-hydroxyvitamin D levels, calcium consumption and caloric intake.	Lumbar spine femur neck
Lenora et al. (46)	36 non- breastfeed Sri Lankan women	Postmenopausal	62.6±8.26 years	Age	Lumbar spine femur neck
Derakhsan et al. (47)	991 Iranian women	Post-menopausal	58.95 + 8.6 years	Age at menopause, BMI and weight between the groups.	Lumbar spine femur neck
Yazici et al. (48)	586 Turkish women	Postmenopausal	60.8 ±8.8 years	---------	Lumbar spine femur neck
Dursun et al. (17)	1,486 Turkish women	Postmenopausal	60.37±9.73 years	---------	Lumbar spine femur neck
Canal-Macias et al. (49)	138 non-breast-feeders spanian women	Premenopausal	39.92 ±8.30 years	--------	Lumbar spine femur neck
Allali et al. (23)	67 nulliparous Moroccan women	Postmenopausal	59.4±7.6 years	Age, and BMI	Lumbar Spine, femoral neck, Total hip
Maghraoui et al. (22)	43 Moroccan women	Premenopausal and postmenopausal	57.2±8.4 years	------	Lumbar Spine, Total hip
Terzi et al. (50)	31 nulliparous Turkish women	Postmenopausal	55.84 ± 7.51 years	-----	Spine, femur
Henderson et al. (51)	6 American women	Premenopausal	30.3 ± 8.8 years	------	Spine, femur

SD: Standard deviation; BMI: Body mass index.