

# Fracture Risks Related to Parity and Breastfeeding Effect in Post-Menopausal Women Aged Sixty and Over: Results from the “Quality of Bone in Lorraine” Register

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## Abstract

**Introduction:** The long term effect of accumulation of genital events as repeated pregnancy and longer breastfeeding in bone health later in women’s life is still disputed. The objective was to assess the impact of parity and cumulated duration of breastfeeding on fracture risk in post-menopausal women aged sixty and over. **Patients and Methods:** It was a leading study from the register “Quality of Bone in Lorraine (QBL)” achieved in the department of endocrinology and osteoporotic disease of Nancy (France). This register included all patients sent for an assessment of the bone mass density from January 1, 2006 to December 31, 2014 (9 years). It was about post-menopausal women aged sixty and over suffering or not from osteoporosis fracture or bone fragility just after the age of 45. The genital events of patients to their age (from puberty to menopause) as well as the existence of hormone replacement therapy use, parity, and breastfeeding duration were taken into account. The assessment of bone fracture was clinical, radiological or by using the vertebral fracture assessment method. **Results:** 861 post-menopausal women were included. In comparison to the control group, the fractured population had a mean age of (74.3 ± 9 vs. 72 ± 8 years), a family history of fracture (32.1% vs. 26%), and an average input of calcium (2.4 ± 1 vs. 2.3 ± 0 portions per day). The age at menarche was of 12.8 ± 1 years in each group, a mean genital activity duration of (36.8 ± 3 vs. 37.2 ± 3 years), a parity of (2.1 ± 1 vs. 1.8 ± 1 children), a cumulated breastfeeding duration (4.2 ± 16 vs. 3.1 ± 5 months) and an age of

menopause of ( $48.6 \pm 4$  vs.  $48.6 \pm 4$  years) were respectively found in fractured and witness population. Overall, an osteoporotic fracture has been re-discovered in 50.9%. In multivariate analysis, only a cumulative duration of breastfeeding of 6 months and over was associated with a higher fracture risk (OR = 1.5 [1.1 - 2.2]). The impact of parity was not significant (OR = 1.1 [0.7 - 1.8]). Association with obesity was quasi significant (OR = 1.3 [0.9 - 1.9]). There was no correlation between the fracture risk and the genital activity duration (OR = 0.7 [0.5 - 1.0]), hormone replacement therapy use (OR = 1.0 [0.8 - 1.4]), daily calcium input (OR = 0.8 [0.6 - 1.3]), and age of menarche (OR = 1.0 [0.9 - 1.1]). **Conclusion:** This work confirms a negative impact from 6 months of cumulative breastfeeding. The modest effects observed may be related to the selection of Caucasian patients who live in an economically developed country with a limited number of pregnancies and limited duration of breastfeeding.

### Keywords

Parity, Breastfeeding, Fracture Risk, Menopause

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## 1. Introduction

Osteoporosis is an increasingly important health problem with an estimation of more than 200 million people in the world. Osteoporosis is a disease essentially bound to menopause and ageing with fractures due to low energy traumas. It is known as the silent epidemic because it does not manifest until a fracture occurs. At least, 40% of osteoporotic women will suffer from one or several fragility fractures in their life. Post-menopausal osteoporosis represents 30% in the United States and in Europe. Despite advances in risk assessment and treatment, osteoporosis is still often either not recognized or untreated [1] [2] [3].

Pregnancy and breastfeeding cause in women an important calcic store loss favoring, in a temporal way, a negative calcic balance which is stabilized by bone resorption [4] [5]. The loss of bone mass during pregnancy and breastfeeding reaches up to 10% of total bone mass. This phenomenon is however reversible during the weaning [5] [6] [7]. The long term effect of accumulation of genital events as repeated pregnancy and longer breastfeeding in bone health later in women's life is still disputed [8] [9]. Findings sometimes seem contradictory depending on the series and the countries. According to the systematic review of Diédhiou *et al.* [10], pregnancy does not seem to be associated with an increased risk of osteoporotic fracture after menopause. The negative impact of  $\geq 5$  child-birth in Asiatic sub-population requires future investigations. The objective of this study was to assess the impact of parity and cumulated duration of breastfeeding on fracture risk in post-menopausal women aged sixty and over.

## 2. Patients and Methods

This case-control study was a survey achieved in the department of endocrinol-

ogy and osteoporotic diseases of Nancy University Hospital Center (France). This department has built up a long experience on diagnosis and treatment of metabolic and endocrine diseases. It includes a clinic for the diagnosis and treatment of osteoporosis and calcic diseases. This center disposes a Hologic Dual-Energy X-ray Absorptiometry in the service since 1996 and receives about 600 patients each year.

Our working base was established by the register “Quality of the Bone in Lorraine (QOL)” of bone mass density follow-up of the patients. This register included all patients sent for an assessment of the bone mass density from January 1, 2006 to December 31, 2014 (9 years). It is about patients received for a follow-up of an incidental or sentinel fracture, a persistent bone painful almost vertebral site, and for classic risk factors of osteoporosis [11]. The bone fracture assessment was clinical, radiological (such as x-ray standard, vertebral CT scan, magnetic resonance imaging and bone scintigraphy) or Dual-Energy X-ray Absorptiometry by the vertebral fracture assessment method. The vertebral fracture assessment results were used in case of vertebral settlement. The protocol was based on measurement of the anterior, middle, and posterior heights of each vertebra. A prevalent vertebral fracture was defined as a reduction of at least 20% in the height [12]. The bone mineral density expressed in T-Score was evaluated at the lumbar spine and femoral neck.

All the patients included in the register have systematically profited an assessment on the history of bone events, bone mass density with the vertebral fracture assessment method. In cases of bone fracture suspicion or any vertebral settlement, a targeted medical imaging was systematically performed. The reports of x-ray standard, ct-scan and magnetic resonance imaging were carried out in the radiology department by specialized radiologists. The medical records consisted of a systematic collection of clinical and densitometric data.

The cases concern all post-menopausal women aged sixty and over, suffering from an osteoporotic or fragility fracture broken out after the age of 45. The witnesses were recruited in the same population of post-menopausal women aged sixty and over, without any osteoporotic fracture, received for a bone mass density assessment. Osteoporosis was defined according to the World Health Organization criterions [13]. Osteoporosis was known as severe in associating one or many fragility fractures at the femoral neck, the humerus, the hip, and the spine or in the presence of three simultaneous costal fractures. The diagnosis of menopause was given by the full and final disappearance of the menstrual bleedings. It becomes premature when it occurred before the age 45 and later beyond the age of 55. The period of the genital activity corresponds to the passing time between menarche and menopause.

Being not concerned in the study, the men’s subjects, the women who have the following criteria such as ongoing corticoid therapy with a lengthy blocked dose, treatment by GnRH analogue, anti-cancer treatment by the aromatase inhibitory more than one year ago, metastatic fracture, genetics or metabolic bones’

disease, a metabolic disease (hyperthyroidism, hyperparathyroidism, and Cushing syndrome), anorexia nervosa including amenorrhea of more than 5 years old, vegetarian diet, early menopause, women who did not agree for an inclusion in the study and unexploited files. The study was designed in accordance with the Helsinki declaration and all participants were informed about the nature, purpose and procedures of the study, and gave their written informed consent.

A trained physician administered a questionnaire to all included participants to identify any history of clinical fractures, gynecological and obstetric history including history of abortions, number of pregnancies, the number of children, self-reported age at menarche and menopause, the existence of hormone replacement therapy use, and the cumulative duration of breastfeeding. The cumulated breastfeeding duration represented the total of breastfeeding durations of each fed child.

We also evaluated the age during the inclusion in the "QOL" register, the body weight, the height and the body Mass Index (BMI). The BMI was worked out on the ratio between the weight in kilogram and the square of height in meter. According to the BMI, the subjects were considered as normal between 18.5 and 24.9 kg/m<sup>2</sup>, in overweight between 25 and 29.9 kg/m<sup>2</sup>, in obesity beyond 30 kg/m<sup>2</sup> [14]. The other data were related to the lifestyle (cigarette smoking, chronic alcohol intake, physical activity level, daily calcium input) and the risk factors of osteoporosis. These parameters concern a first degree family history of osteoporosis or fracture of the upper extremity of the femur, age of menopause, existence of hormone replacement therapy (it was significant when it had lasted more than 2 years), metabolic disease (diabetes, hyperthyroidism, hyperparathyroidism, and Cushing syndrome), an undernourishment condition or a mental nervosa.

The concerned fracture sites were the lumbar spine, upper extremity of the femur, hip, ribs, wrist, ankle, and humerus. The data of the bone mass density during the first consultation were also recorded. The bone mineral density expressed in T-scores was recorded from the lumbar spine and the femoral neck. The two Dual-Energy X-ray Absorptiometry were from Hologic [QDR 4500 A (S/N 45328) and Discovery (S/N 83097)].

For the statistic analysis, the parameters taken into account from the matching were the age (by 5 years age group), gynecological and obstetric history, body mass index (BMI). The existence of a first degree family history of osteoporosis or fracture of the upper extremity of the femur was also taken into account. The analysis of the data was carried out with "SPSS version 8.0 and Epi Info version 6 for Windows". Quantitative general characteristics of the study were expressed as mean  $\pm$  standard deviation, using a t-test for mean comparisons. Qualitative characteristics were expressed in number and frequency, using the chi-square test to analyze the differences between subjects with and without fractures. The previously mentioned risk factors that showed associations between subjects with and without fractures in the univariate analysis were included in a multiple

logistic regression analysis (age, gynecological and obstetric history, and body mass index, family history of osteoporosis or fracture, lifestyle). The risk was expressed as odd ratio (OR) with 95% confidence interval (CI) and a *p* value.

### 3. Results

#### 3.1. Epidemiological Data

In total, 861 postmenopausal women were included with a mean age of  $73.09 \pm 8.8$  years (extreme of 60 and 100 years). A first degree family history of osteoporosis and fracture was found in respectively 169 cases (19.6%) and 251 cases (29.2%). Other associated pathologies were diabetes mellitus (9.6%), active smoking (19.9%), chronic alcoholism (15.3%), overweight (23.2%) and obesity (17.6%). The physical activity level was slight (26%), moderate (38.2%), average (29.2%), and intense (6.5%). The average input of calcium was higher than 2 portions per day in 384 cases (44.5%). **Table 1** shows the epidemiological characteristics of the population taken into account.

#### 3.2. Reproductive Events of Women

The mean age of menarche was of  $12.8 \pm 1$  years (extreme to 10 and 18). The average duration of genital activity was of  $37 \pm 3$  years (extreme of 22 and 46 years). This duration was  $\geq 40$  years in 207 cases (24%). The average parity was of  $1.9 \pm 1$  child (extreme of 0 and 13 children). The patients were nulliparous (20.4%), mothers with 1 or 2 children (47%), and with more than 2 children (32.6%). Only 11 abortions were found. The average duration of cumulated breastfeeding was of  $3.6 \pm 6$  months (extreme of 0 and 46 months). No breastfeeding was found in 44.9% of the cases. The other cases concerned cumulated

**Table 1.** Epidemiological characteristics of the population taken into account.

Characteristics of patients on admission	Global size	Fracture statut	
		Yes	No
Sample size	861	439	422
Mean age (years)	$73.1 \pm 8$	$74.3 \pm 9$	$72 \pm 8$
Mean weight (kg)	$65.8 \pm 13$	$66.6 \pm 13$	$65 \pm 13$
Mean BMI (kg/m <sup>2</sup> )	$25.9 \pm 5$	$26.3 \pm 5$	$25.5 \pm 5$
Active smoking	163 (19.9%)	86 (19.6%)	77 (18.2%)
Chronic alcoholism	131 (15.2%)	67 (15.3%)	64 (15.1%)
Family history of fracture	251 (29.2%)	141 (32.1%)	110 (26%)
Family history of osteoporosis	169 (19.6%)	86 (19.5%)	83 (19.6%)
Diabetes mellitus	83 (9.6%)	46 (10.4%)	37 (8.7%)
Hormone replacement therapy	408 (47.3%)	210 (47.8%)	198 (46.9%)
Physical activity practise	638 (74%)	304 (69.2%)	334 (79.1%)
Mean calcium input (portions)	$2.3 \pm 1$	$2.4 \pm 1$	$2.3 \pm 0$

breastfeeding duration from 1 to 6 months (39.1%), from 7 to 12 months (9.7%), of more than 12 months (6.3%). The mean age of menopause was of  $48.6 \pm 4$  years (extreme of 43 and 59 years). This age of menopause was  $\geq 50$  years in 423 cases (49.1%). The hormone replacement therapy concerned 408 women (47.3%). **Table 2** shows the reproductive characteristics of the population.

### 3.3. Fracture Status

Osteoporotic fracture has been found in 439 cases (50.9%). It concerned a fracture of lumbar spine in 130 cases (15%), femoral neck in 75 cases (8.7%), wrist in 197 cases (22.8%), humerus in 48 cases (5.5%) and of ribs in 42 cases (4.8%). **Table 3** shows the gynecological characteristics and the antecedent of subjects according to fracture profile.

In univariate analysis, a cumulated lactation duration  $\geq 6$  months and a parity  $\geq 3$  children were associated with an increased fracture risk respectively with an (OR = 1.6 [1.1 - 2.2]) and (OR = 1.5 [1.0 - 2.3]). In a multiple logistic regression analysis, only a cumulated breastfeeding duration of 6 months or more was associated with a higher fracture risk (OR = 1.5 [1.1 - 2.2]). The impact of parity was not significant (OR = 1.1 [0.7 - 1.8]). The association with obesity significantly get closer (OR = 1.3 [0.9 - 1.9]). There was not any significant correlation between the fracture risk and the other following parameters: genital activity period (OR = 0.7 [0.5 - 1.0]), hormone replacement therapy (OR = 1.0 [0.8 - 1.4]), daily calcium input (OR = 0.8 [0.6 - 1.3]), chronic alcoholism (OR = 1.0 [0.7 - 1.5]), smoking (OR = 1.1 [0.8 - 1.6]), age at menarche (OR = 1.0 [0.9 - 1.1]). **Table 4** shows the level of correlation between the fracture risk and the gynecological factors.

## 4. Discussion

In the gestational period and during breastfeeding, the mother provides 200 to

**Table 2.** Reproductive characteristics of our population under consideration.

Characteristics of patients on admission	Global size	Fracture statut	
		Yes	No
Sample size	861	439	422
Mean age at menopause (year)	$48.6 \pm 4$	$48.6 \pm 4$	$48.6 \pm 4$
Age of menopausal $\geq 50$ years	423 (49.1%)	197 (44.8%)	226 (53.5%)
Mean age at menarche (years)	$12.8 \pm 1$	$12.8 \pm 1$	$12.8 \pm 1$
Mean duration of genital activity (years)	$37 \pm 3$	$36.8 \pm 3$	$37.2 \pm 3$
Duration of genital activity $\geq 40$ years	207 (24%)	91 (20.7%)	116 (27.5%)
Mean parity	$1.9 \pm 1$	$2.1 \pm 1$	$1.8 \pm 1$
Parity $\geq 2$ children	280 (32.6%)	152 (34.6%)	128 (30.3%)
Mean duration of breastfeeding (months)	$3.6 \pm 6$	$4.2 \pm 6$	$3.1 \pm 5$
Hormone replacement therapy	408 (47.3%)	210 (47.8%)	198 (46.9%)

**Table 3.** Gynecological profile and antecedent of subjects according to fracture profile.

Characteristics of patients on admission		All fractures	Vertebral fractures	Femoral fractures
Sample size		<b>439/861</b>	<b>130</b>	<b>75</b>
Femoral osteoporosis		86 (19.6%)	50 (38.5%)	10 (13.3%)
Family history of fracture		141 (32.1%)	50 (38.5%)	21 (28%)
Parity	<2 children	162 (37%)	51 (39.2%)	27 (36%)
	≥2 children	277 (63%)	79 (60.7%)	48 (64%)
Breastfeeding	<3 months	248 (56.5%)	78 (60%)	37 (49.3%)
	≥3 months	191 (43.5%)	52 (40%)	38 (50.7%)
Genital activity duration	<40 years	347 (79%)	105 (80.8%)	62 (82.7%)
	≥40 years	92 (21%)	25 (19.2%)	13 (17.3%)
Age at menopause	<50 years	333 (75.9%)	99 (76.1%)	59 (78.7%)
	≥50 years	106 (24.1%)	31 (23.8%)	16 (21.3%)
Without hormone replacement therapy	Non	229 (52.1%)	72 (55.4%)	49 (65.3%)
	Yes	210 (47.8%)	58 (44.6%)	26 (34.7%)
Diabetes mellitus	Yes	46 (10.5%)	11 (8.5%)	7 (9.3%)
	No	393 (89.5%)	119 (91.5%)	68 (90.7%)
Active smoking		88 (20%)	26 (20%)	8 (10.6%)
Chronic alcoholism		68 (15.5%)	17 (13%)	11 (14.6%)

**Table 4.** Factors associated with the probability of fracture.

Parameters Studied	Size	Fracture	Bivariate analysis	Multivariate analysis
	N	N (%)	OR (min-max)	OR (min-max)
<b>Genital activity periods (years)</b>				
≤35	269	146 (54.3%)	1	1
36 - 39	380	197 (51.9%)	0.9 (0.6 - 1.3)	0.9 (0.6 - 1.3)
≥40	207	91 (44.0%)	0.7 (0.5 - 1.0)	0.7 (0.5 - 1.0)
<b>Parity (children)</b>				
0	176	80 (45.5%)	1	1
1 - 3	578	291 (50.9%)	1.2 (0.8 - 1.8)	1.2 (0.8 - 1.8)
≥4	107	64 (59.8%)	<b>1.5 (1.0 - 2.3)*</b>	1.1 (0.7 - 1.8)
<b>Lactation (months)</b>				
0 - 1	438	212 (48.4%)	1	1
2 - 5	206	94 (45.6%)	0.9 (0.6 - 1.2)	0.9 (0.6 - 1.2)
≥6	217	129 (59.4%)	<b>1.6 (1.1 - 2.2)*</b>	<b>1.5 (1.0 - 2.1)*</b>
<b>Body mass index (Kg/m<sup>2</sup>)</b>				
≤25	439	207 (47.2%)	1	1

## Continued

>25	409	220 (53.9%)	1.3 (0.9 - 1.8)	1.3 (0.9 - 1.8)
<b>Hormone replacement therapy</b>				
Non	453	227 (50.1%)	1	
Oui	408	208 (51.0%)	1.0 (0.8 - 1.4)	
<b>Smoking</b>				
Yes	698	349 (50.0%)	1	
No	163	86 (52.8%)	1.1 (0.8 - 1.6)	
<b>Alcoholism</b>				
Yes	729	368 (50.5%)	1	
No	131	67 (51.1%)	1.0 (0.7 - 1.5)	
<b>Daily calcium intake (portion)</b>				
0 - 1	424	223 (52.6%)	1	
≥ 2	437	212 (48.4%)	0.9 (0.6 - 1.2)	

NB: univariate analysis was included in a multiple logistic regression analysis (age, gynecological and obstetric history, and body mass index, family history of osteoporosis or fracture, lifestyle).

300 mg of calcium daily for bone growth in the fetus and newborn. The supply of this calcium is provided by bone resorption [4] [5] [6] [7]. Fragility fractures have been reported in the peripartum and especially in primiparous women. This situation appears to be related to pre-existing fragility or excessive bone resorption in the mother [15] [16] [17]. However, this situation is reversible after weaning. Our study reports a risk of osteoporotic fracture proportionally increased with the cumulative duration of breastfeeding. Parity is deleterious but not significant in multivariate analysis.

The negative impact of breastfeeding on the risk of postmenopausal fracture was 50% (OR = 1.5 [1.1 - 2.1]). Clinically, some recent studies confirm our results in terms of increased postmenopausal fracture risk. In all these studies, the risk appears only after 6 months cumulative lactation. The impact was greater in trabecular bone [18] [19] [20]. In two Korean studies, the risk of vertebral and fragility fracture were respectively to 0.15% (OR = 1.015 [1.001 - 1.030]) at 6 months of lactation [18], up to 69% (HR = 1.69 [1.08 - 2.66]) beyond 8 months of lactation [19]. Bolzetta *et al.* [20], in a retrospective study of 752 Italian women, reported a doubling vertebral fracture risk (OR = 2.12 [1.14 - 5.38],  $p = 0.04$ ) after only 18 months of lactation.

From a physiopathological point of view, these effects are explained by a transient excess of resorption and bone loss secondary to hyper secretion of PTHrP and an estrogenic impregnation deficit that evolves in parallel with lactation [21] [22] [23]. We believe that extended or repeated periods of lactation may lead to transient and deep loss of bone mass with probably incomplete recovery.

This hypothesis is consistent with recent data from the case-control study of bone micro architecture before, during, and 2.6 years after weaning. In this study,



Bjørnerem *et al.* [24] reported an irreversible deterioration of micro architecture in relation to lactation. Exclusive breastfeeding for 5 months increased cortical porosity by 0.6%, reduced the matrix mineralization density by 0.26%, the trabecular number by 0.22/mm and increased trabecular separation by 0.07 mm (all  $p < 0.001$ ). Compared to the state before lactation, the 2.6 years after weaning found a high cortical porosity of 0.58 DS, a low matrix mineralization density of 1.28 DS, and a greater trabecular separation of 1.06 DS. On the other hand, the bone mineral density assessment in 1486 Turkish menopausal women reported both lower lumbar and femoral bone mass correlated with duration of breastfeeding [25].

However, the majority of studies in the literature did not report significant bone impact in relation to lactation [26]-[36]. Most of them did not adopt a gradual impact assessment methodology of the lactation according to its cumulative duration. This could lead to an underestimation of the fracture risk for extended periods of lactation. In the meta-analysis of Duan *et al.* [8], the authors reported a possible reduction in the risk of fracture with the duration of lactation. The cumulative relative risk of osteoporotic fracture, hip fracture and wrist fracture was respectively of 16% (OR = 0.84 [0.67 - 1.05]), 28% (OR = 0.72 [0.52 - 0.99]), and 18% (OR = 0.82 [0.56 - 1.19]). This risk decreased by 0.9% and 1.2% per month of breastfeed respectively for the osteoporotic and hip fracture.

Only three studies reported a significant reduction in fracture risk essentially on cortical bone. Bjørnerem *et al.* [37] found a reduction in the risk of hip and fragility fracture by 50% and 27% respectively. This reduction in the risk of hip fracture occurred only after 13 months of lactation (OR = 0.28 [0.10 - 0.82]) and decreased by 13% for every additional 6 months of lactation [38]. A 39% reduced risk of wrist fracture (OR = 0.61 [0.40 - 0.94]) was reported by Mallmin *et al.* [39]. The positive effect was already found by Wiklund *et al.* [40], who found an increase in hip and tibia bone strength in women with 33 cumulative months of lactation. This possible bone protection could be explained by already known mechanical phenomena. The permissive effect of lactation associated with estrogen deficiency plays an important role in increasing bone volume. This promotes an increase in bone diameter by increasing periosteal apposition and endosteal resorption [23] [40] [41] [42].

The torsional and flexural mechanical strength of a hollow cylinder increases exponentially with its diameter for a constant quantity of material. This applies to the diaphyseal bone that undergoes a beneficial transformation during pregnancy for a constant or even slightly diminished of bone mineral density [40] [43] [44]. This is consistent with the findings of Henderson *et al.* [45] on the post-menopausal densitometric outcome. The authors reported that in 30 multiparous mothers with 6 or more children, postmenopausal osteoporotic risk was unaffected by multiple new pregnancies that occurred during lactation and regardless of the length of lactation.

The effect of parity on the risk of osteoporotic fracture is not significant in

multivariate analysis (OR = 1.1 [0.7 - 1.8]). In the systematic review of Diédhiou *et al.* [10] the authors concluded a neutral or slightly positive impact of parity on fracture risk. In fact, only 3 out of 29 studies reported an increased risk [46] [47] [48]. In multivariate analysis, the risk of fracture was associated with parity  $\geq 5$  children in two studies with respectively a HR = 1.65 (1.06 - 2.56) [48] and RR = 2.53 (1.07 - 6.68) [48].

On the other hand, studies essentially reported a 6% to 50% reduction in the risk of vertebral and non-vertebral fractures and that this protection increased with parity [29] [30] [49]-[55]. A reduction in the risk of femoral neck fracture of 8% to 10% per child was reported by Michaelsson *et al.* [29] and Hillier *et al.* [52]. Honkanen *et al.* [50] in a large series of 1.1798 pre and postmenopausal women found 30% reduction (HR = 0.71 [0.52 - 0.97]) of the risk of wrist fracture. In the meta-analysis of Wang *et al.* [9], the risk of both osteoporotic and femoral neck fracture was reduced by 11% and 26%, respectively, in women with at least one child. At the femoral neck, the reduction was 12% for each additional birth.

## 5. Limitations of the Study

- 1) The study was conducted in university hospital. It may not represent the community situation which is important in terms of knowledge and practice.
- 2) This is a single center study. Large scale multicenter study is needed to represent the national situation.
- 3) This is a retrospective study conducted from patient's files. Only the complete files were included which makes a loss of data.
- 4) This kind of work doesn't require in our country the approval of ethic committee because it is a retrospective work on patient's file.

## 6. Conclusion

This work confirms the achievements of the literature. It shows the absence of a negative effect of parity and a negative impact from 6 months of cumulative breastfeeding. The modest effects observed may be related to the insufficient power of studies or the selection of Caucasian patients who live in an economically developed country with a limited number of pregnancies and limited duration of breastfeeding. The next step in this work will be its repetition in sub-Saharan Africa with large multiparous, where breastfeeding is often used as a contraceptive method.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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