

1 **Relationship of Breastfeeding Duration with Joint Pain and Knee Osteoarthritis in**
2 **Middle-aged Korean Women: A Cross-sectional Study using the Korea National Health**
3 **and Nutrition Examination Survey**

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18 **Highlights**

- 19 · We used Korea National Health and Nutrition Examination Survey data on Women age ≥ 50 .
- 20 · We surveyed lactation, joint pain, and we defined knee arthritis on X-ray images.
- 21 · Long-term breastfeeding is associated with joint pain and knee osteoarthritis.

22 **Abstract**

23 **Background**

24 The effect of joint health on quality of life in middle-aged and older women is becoming
25 more widely recognized with the aging of the world's population. However, the association
26 of long-term breastfeeding with joint pain and knee osteoarthritis has not been fully examined.
27 The aim of this study was to determine the association of long-term breastfeeding with joint
28 pain and knee osteoarthritis in middle-aged Korean women.

29 **Methods**

30 A cross-sectional study was conducted among 3,454 women aged ≥ 50 years who underwent
31 knee radiography and answered a questionnaire on breastfeeding and joint pain for the 5th
32 Korean National Health and Nutrition Examination Survey (2010–2011). After adjusting for
33 confounding sociodemographic, medical history, and obstetric and gynecologic variables,
34 logistic regression analysis was conducted to analyze the incidence of joint pain and knee
35 osteoarthritis according to breastfeeding and its duration. Among the 3,454 participants, 298
36 had not breastfed and 1,042, 815, and 1,299 had breastfed for 1–24, 25–48, and ≥ 49 months,
37 respectively. Of all participants, 1,731 had joint pain and 739 were diagnosed with knee
38 osteoarthritis after radiography.

39 **Results**

40 The odds ratio (OR) for joint pain among women who breastfed was 1.493 times higher than
41 that among women who did not ($p=0.044$). As breastfeeding duration increased, the OR of
42 joint pain incidence also increased (p for trend; $p=0.002$). For knee osteoarthritis, the OR was
43 significantly different between the 25–48 and ≥ 49 months groups (2.299 [$p=0.03$] and 2.166
44 [$p=0.047$], respectively). Reanalysis after selecting only participants aged ≥ 60 years showed
45 that the prevalence of joint pain and knee osteoarthritis was more positively correlated with
46 extended breastfeeding duration (joint pain, p for trend; $p=0.005$) (knee osteoarthritis, p for
47 trend; $p=0.012$).

48 **Conclusions**

49 Long-term feeding of more than 25 months was associated with an increased prevalence of
50 arthralgia and degenerative arthritis after menopause in Korean elderly women.

51 **Abbreviations**

52 BMI, body mass index; CI, confidence interval; KNHANES, Korea National Health and
53 Nutrition Examination Survey; OR, odds ratio

54 **Keywords**

55 KNHANES, Lactation, Menopause, Knee Osteoarthritis, Arthralgia

56 **Background**

57 Breast milk has species specificity and is superior to artificial compounds in providing
58 nutrition, promoting physical development, and boosting the immune system in neonates [1].
59 Breastfeeding also offers numerous benefits for mothers, preventing depression and stress,
60 promoting recovery to the prenatal state, and reducing the incidence of breast cancer, ovarian
61 cancer, and type 2 diabetes mellitus [2]. Thus, WHO and UNICEF recommend exclusively
62 breastfeeding during the first 6 months and continuing breastfeeding while providing a
63 supplemented diet up till 2 years after birth [3]. Worldwide, approximately 38% of newborns
64 are exclusively breastfed for 6 months [3].

65

66 Approximately one-third of the population aged ≥ 65 years has osteoarthritis, and this disease
67 affects approximately 5 million individuals in Korea [4] and 100 million worldwide [5].
68 Women are more susceptible to osteoarthritis. The risk of osteoarthritis in the hands, knees,
69 and hips increases after menopause [6, 7], likely owing to estrogen deficiency [8]. However,
70 long-term estrogen deficiency can occur not only after menopause but also during
71 breastfeeding [9]. Therefore, there may be an association between joint health in women and
72 breastfeeding duration.

73

74 Until recently, studies of the effects of breastfeeding on musculoskeletal systems in women
75 have focused on transient osteoporosis caused by changes in bone metabolism [10],
76 osteoporosis linked to menopause [11] and rheumatoid arthritis [12]. The effect of joint health
77 on quality of life in middle-aged and older women is becoming more widely recognized with
78 the aging of the world's population [13]. However, the association of long-term breastfeeding
79 with joint pain and knee osteoarthritis has not been fully examined.

80

81

82 **Methods**

83 **Aim**

84 To determine whether the risk of joint pain and knee osteoarthritis changes according to
85 breastfeeding and its duration, we conducted an analysis among Korean women using Korean
86 National Health and Nutrition Examination Survey (KNHANES) data.

87 **Study participants and examined variables**

88 **Participant selection**

89 KNHANES is a sample database representing health and nutrition-related behaviors of
90 Korean individuals nationwide. The number of subjects in the 5th KNHANES was 10,938 in
91 2010 and 10,589 in 2011, and the actual numbers of participants were 8,958 and 8,518,
92 respectively. For this study, we included women aged ≥ 50 years who underwent
93 osteoarthritis radiography examination and answered the self-administered questionnaire on
94 breastfeeding. Overall, 3,454 women were included (Figure 1).

95

96 **Breastfeeding duration**

97 Participants who answered “no” to “(adult) presence of breastfeeding experience” in the
98 health survey were categorized into the non-breastfeeding group. Those who answered “yes”
99 were asked to provide their two-digit “(adult) breastfeeding duration” in months. The
100 participants were further divided into 1–24, 25–48, and ≥ 49 months breastfeeding groups.

101

102 **Joint pain**

103 The presence of perceived knee, hip, and lower back pain was determined in the survey.
104 Those who answered “yes” to “Have you experienced knee joint pain/hip joint pain/lumbar
105 pain for longer than 30 days in the past 3 months?” were classified into the knee joint, hip
106 joint, and lumbar pain joint groups. In the overall analysis, “joint pain” was defined as the
107 case where there was more than one joint pain in three sites.

108

109 **Knee osteoarthritis**

110 Radiography for osteoarthritis diagnosis was conducted for participants aged ≥ 50 years. The
111 radiological osteoarthritis diagnostic values for the knee joint were classified based on the
112 Kellgren-Lawrence Grading Scale, as follows: 0, normal; 1, suspicion of osteoarthritis; 2,
113 mild osteoarthritis; 3, moderate osteoarthritis; and 4, severe osteoarthritis [14]. Those
114 diagnosed with mild, moderate, and severe osteoarthritis were considered to have knee

115 osteoarthritis.

116

117 **Confounding variables**

118 **Sociodemographic variables**

119 Numerical variables were used to express participant ages. Income level was divided into
120 four categories (low, middle-low, middle-high, high) according to the average monthly
121 equivalized household income (monthly household income/ $\sqrt{\text{number of household members}}$).

122

123 **Lifestyle variables**

124 BMI (kg/m^2) was used to divide participants into three groups: underweight (<18.5), normal
125 ($18.5\text{--}24.9$), and overweight (≥ 25). Based on smoking status, participants were classified as
126 non-smokers (never smoked), ex-smokers, and current smokers. Second-hand smoke
127 exposure was defined as “exposure to indoor second-hand smoke at the workplace or in the
128 house for one hour or longer per day.” Based on alcohol consumption, participants were
129 divided into three groups: less than once a month, 1-4 times a month, and ≥ 5 times or more
130 per month.

131 The level of daily activities was classified into resting, light activities, moderate or intense
132 activities according to the amount of physical activities performed in the week before the
133 survey. Those who “performed walking and moderate physical activities for 30 minutes or
134 longer a day for 5 times or more per week” were categorized into the moderate or intense
135 activities group, and those who did neither were categorized into the resting group. The rest
136 of the participants were included in the light activities group. Occupational and physical
137 activities such as slow swimming, tennis doubles, badminton, table tennis, and carrying light
138 objects were considered moderate physical activities.

139

140 **Medical history**

141 Participants answered about their current dyslipidemia, diabetes, hypertension, and
142 osteoporosis status. In case of diabetes, impaired fasting glucose levels were also included.
143 Hypertension was defined as “the presence of systolic blood pressure of ≥ 140 mmHg or
144 diastolic blood pressure of ≥ 90 mmHg or treatment with medication for hypertension.”

145

146 **Obstetric and gynecological variables**

147 The numbers of natural birth, cesarean section, and preterm birth were combined to obtain the

148 total number of children, whereas the numbers of spontaneous and induced miscarriages were
149 combined to obtain the number of miscarriages. Participants were asked to provide a two-
150 digit number for age at menopause (in years). The length of postmenopause was measured by
151 subtracting this number from the age at the time of the survey. Women who took hormone
152 supplementation were checked, and the groups were categorized into 1-11 and ≥ 12 months.

153

154 **Data analysis**

155 KNHANES uses stratified cluster sampling and weighted values. In this study, complex
156 sampling design analysis was conducted using stratified, cluster, and weighted variables. All
157 data analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA).

158 The participants' sociodemographic, lifestyle, medical history, and obstetric and
159 gynecological characteristics were analyzed according to breastfeeding duration. The T-test
160 and Rao-Scott chi-squared test were conducted to compare continuous and categorical
161 variables among the non-breastfeeding (control) group and the 1–24, 25–48, and ≥ 49 months
162 breastfeeding groups. The missing values of the corrected confounding variables were
163 excluded in analysis.

164 To calculate the OR and 95% CI of joint pain and knee osteoarthritis, logistic regression
165 analysis was conducted with the non-breastfeeding group as the standard baseline, after
166 adjusting for confounders. As knee osteoarthritis is largely affected by age, and the
167 differences in mean age among the breastfeeding groups were fairly large, a secondary
168 analysis was conducted after re-selecting the participants aged ≥ 60 . The OR and 95% CIs of
169 knee osteoarthritis were calculated in groups aged ≥ 60 years after adjusting for the same
170 confounding variables. In all tests, $p < 0.05$ indicated statistical significance.

171

172 **Results**

173 Among the 3,454 women aged ≥ 50 years, 298 were included in the non-breastfeeding group,
174 and 1,042, 815, and 1,299 were included in the 1–24, 25–48, and ≥ 49 months breastfeeding
175 groups, respectively. Among those who answered the questionnaire, 1,731 participants had
176 joint pain and 739 had knee osteoarthritis diagnosed by radiography (Table 1).

177

178 The percentage of participants with a high income was high (approximately 31%) in the non-
179 breastfeeding group and 1–24 months breastfeeding group, and the percentage with a low
180 income was high in the 25–48 and ≥ 49 months breastfeeding groups. showing the likely
181 association between lower income and longer breastfeeding duration. The non-breastfeeding
182 group showed higher current and ex-smoking rates than the breastfeeding groups, and the no
183 alcohol consumption rate was 40% or higher in all groups. The long-term breastfeeding
184 groups (≥ 25 months) had high overweight rates (BMI > 25 kg/m²). The longer the lactation
185 period, the higher the average number of children.

186

187 The prevalence of hormone supplementation was low in the ≥ 49 months breastfeeding group,
188 and the duration was short. The percentage of those having experienced menopause was high
189 in the ≥ 25 months breastfeeding groups, and 99.3% of the ≥ 49 months breastfeeding group
190 had experienced menopause. The prevalence of diabetes and the percentage of joint pain
191 complaints also increased with breastfeeding duration (Table 1).

192

193 As a result of analyzing the incidence of joint pain in the non-breastfeeding group and
194 breastfeeding group over 1 month, the odds ratio among all women who breastfed was
195 significantly higher (OR 1.493; $p=0.044$). The longer lactation period, the higher the odds
196 ratio of joint pain (p for trend; $p=0.002$). (Table 2). When age and all other factors were
197 adjusted for, the ≥ 25 and ≥ 49 months breastfeeding groups showed a higher onset of knee
198 osteoarthritis than the non-breastfeeding group (OR 2.299 [$p=0.03$], OR 2.166 [$p=0.047$])
199 (Table 3).

200

201 Differences in the prevalence of joint pain between the non-breastfeeding group and
202 breastfeeding groups were more notable in women aged ≥ 60 years. After adjusting for all
203 confounding variables, the OR of joint pain was 2.614 times higher in the breastfeeding
204 groups than in the non-breastfeeding group (95% CI 1.417–4.821, $p=0.002$), and the OR
205 increased significantly with breastfeeding duration (p for trend; $p=0.005$) (Table 4). The
206 prevalence of knee osteoarthritis also increased in those aged ≥ 60 years in all breastfeeding
207 groups (OR 2.751, 95% CI 1.165–6.495) ($p=0.021$). The tendency of OR to increase with

208 breastfeeding duration was also significant (p for trend; p=0.012), and the OR of knee
209 osteoarthritis in the ≥ 49 months breastfeeding group was 3.18 (95% CI 1.349–7.498, p=0.008)
210 (Table 5).

211

212 **Discussion**

213 Taken together, our data showed that breastfeeding experience was associated with increases
214 in complaints of subjective joint pain and diagnostic rates (by radiography) of knee
215 osteoarthritis in Korean women aged ≥ 50 . In addition, we found that the prevalence of joint
216 pain significantly increased with a breastfeeding duration longer than 25 months.

217

218 In this study, longer breastfeeding duration was clearly associated with higher mean age.
219 Osteoarthritis is greatly influenced by age [15]. Hence, during logistic regression analysis,
220 age was the primary factor adjusted for, and participants aged ≥ 60 were separated and
221 included in a sub-analysis. The results showed more significant correlations between
222 breastfeeding duration and joint pain and knee osteoarthritis. When compared to the total
223 participants aged ≥ 50 years, the OR of knee osteoarthritis in the breastfeeding groups aged
224 ≥ 60 years increased from 1.493 to 2.614 (Tables 2, 4). The OR of knee osteoarthritis was 1.92
225 in the breastfeeding groups aged ≥ 50 and 2.751 in the breastfeeding groups aged ≥ 60 ,
226 showing a marked increase in older participants (Tables 3, 5).

227

228 The effects of breastfeeding on osteoarthritis have not been fully elucidated. Park's study
229 (2017) was the first investigation of the association between breastfeeding and osteoarthritis
230 [3]. It analyzed 6,783 women aged ≥ 50 years using 1999–2012 National Health and Nutrition
231 Examination Survey (NHANES) data, and showed an association between breastfeeding
232 experience >1 month and an increased risk of osteoarthritis in older women. In this study,
233 Park considered the “intensity of activities” that induces arthritis in detail. However, variables
234 related to exposure to female hormones that are considered risk factors of osteoarthritis in
235 women with breastfeeding experience, such as number of pregnancies and number of
236 children, did not show a significant association with the increased risk of osteoarthritis, and
237 breastfeeding duration could not be determined from the NHANES data.

238

239 Until recently, studies on the effects of accumulated breastfeeding duration on the
240 musculoskeletal system in women after menopause have mainly focused on changes in bone
241 density and rheumatoid arthritis. There is still controversy over the association of
242 breastfeeding with bone density [16]. Some studies reported that the bone density of women
243 who are breastfeeding or have just finished breastfeeding is higher than that of non-
244 breastfeeding women [17, 18]. However, other studies investigating bone density among
245 postmenopausal women showed a higher incidence of osteoporosis in those with long-term
246 breastfeeding experience [19]. In a cohort study on 500 women aged 35–55 years, long-term
247 breastfeeding showed significant associations with a decrease in spine bone mineral density
248 after menopause [20].

249

250 Numerous studies have reported a negative association between breastfeeding and
251 rheumatoid arthritis. A cohort study of 121,700 women from the Nurses' Health Study
252 showed that the relative risk of rheumatoid arthritis was significantly lower in those with
253 longer breastfeeding durations [12]. In a cohort study of 18,326 participants from Sweden,
254 the administration of oral birth control pills was not found to lower the risk of rheumatoid
255 arthritis, but breastfeeding did, in proportion to its duration [21].

256

257 There are various risk factors for knee osteoarthritis, such as old age, female sex, high level
258 of activities, consistent exercise, past knee joint injuries, and obesity [15]. In middle-aged or
259 older women in particular, age and female hormone deficiency can simultaneously act as risk
260 factors of joint degeneration [7]. Estrogen deficiency is also associated with osteoarthritis in
261 humans and animals [22]. Estrogen receptors are present in several cells in the joints,
262 including cartilage cells, subchondral bone cells, and synovial cells, and the expression of
263 estrogen receptors increases in osteoarthritis patients [22-24]. Experiments using
264 ovariectomized animal models showed that a continued state of low estrogen concentration
265 leads to decreased intra-articular subchondral bone mass, increased interface of the
266 subchondral cavity, and progression of severe cartilage degradation [25]. Altogether, women
267 experience rapid joint degeneration around the ages of 50–75 years after menopause, and
268 show higher prevalence, frequency, and severity of osteoarthritis than men [6, 15].

269

270 Changes in female hormones after childbirth are partially similar to the changes noted after
271 menopause. Estradiol, which is secreted from the placenta and increases up to 100-fold
272 during pregnancy, instantaneously decreases during childbirth along with placenta extraction,
273 and its concentration is maintained at a low level during breastfeeding as ovulation is delayed
274 [9]. Hence, extended breastfeeding leads to long-term estrogen deficiency [9]. The level of
275 female hormones increases during pregnancy, but breastfeeding can be associated with sex
276 hormone deficiency for several years after childbirth [26].

277

278 The long-term breastfeeding experience in a high percentage of Korean women aged ≥ 60 or
279 older can be attributed to historical and cultural circumstances in Korea. According to a
280 breastfeeding status survey conducted by the Korea Institute for Health and Social Affairs,
281 the breastfeeding rate was 95% in the 1960s and rapidly decreased to 46–68.9% in the 1970s
282 [27]. In the 1960s and 1970s, when women who are currently in their 60s and 70s were likely
283 experiencing childbirth and breastfeeding, Korea was going through rapid economic
284 development after the Korean war, and breast milk supplements were not yet widely
285 marketed [28]. Thus, the period before extensive economic development and the growth of

286 the formula market likely affected long-term breastfeeding among those aged ≥ 60 .
287 Furthermore, the rapid transition from an extended family to nuclear family and a declining
288 birthrate caused by rapid industrialization and modernization are also speculated to have
289 decreased the number of children and lifetime breastfeeding duration among this cohort [29].

290

291 In this study, economic factors, number of children, and level of physical activities including
292 occupational activities were considered confounding variables. However, residence type
293 (sedentary or stand-up) or lifestyle were not assessed in the survey. The residence type of
294 Korea was mainly sedentary in the past, and hence the population that is now elderly likely
295 spent a huge amount of time kneeling down on the floor rather than sitting down on the bed
296 or chairs [30] . It is possible that such a sedentary lifestyle became a risk factor for knee
297 osteoarthritis. As various sociocultural characteristics affect the prevalence of knee
298 osteoarthritis in the older population, the association between breastfeeding duration and knee
299 osteoarthritis can be different in different cultures and age groups.

300

301 This study has several strengths. To our knowledge, this study is the first to investigate the
302 association between breastfeeding duration and the prevalence of knee osteoarthritis. The
303 self-administered questionnaire answered by participants was systematically created by
304 skilled experts, and the study was conducted among a large-scale group representative of
305 Korea. Through the analysis of joint pain (a subjective symptom) as a dependent variable and
306 knee osteoarthritis diagnosed by radiography, the target condition was subdivided and the
307 accuracy of analysis was increased. In addition, various confounding variables that can affect
308 breastfeeding and the onset of osteoarthritis were adjusted for.

309

310 The study also has some limitations. This was a cross-sectional study collecting two data
311 variables from the same period. Thus, only the association between the two variables could
312 be determined and the cause-and-effect relationship could not, in principle, be deduced.
313 However, as breastfeeding is often experienced by women in their 20s and 30s and
314 osteoarthritis increases upon aging, it can be speculated that breastfeeding affects the onset of
315 osteoarthritis. The data used in this study were responses from self-administered
316 questionnaires, and there could be individual response errors due to the nature of the survey.
317 Additionally, as the study participants were women aged ≥ 50 years, their memory of
318 breastfeeding from decades ago might have been biased. Individual differences in the
319 subjective perception of joint pain may have also existed. Furthermore, interpretation of our
320 study results should take into account unique historical and cultural characteristics of Korea.

321 **Conclusion**

322 This cross-sectional study examined breastfeeding experience, joint pain, and knee

323 osteoarthritis simultaneously. After adjusting for age variables, we showed significant
324 associations between joint pain symptoms and knee osteoarthritis, and long-term
325 breastfeeding (≥ 25 months). The risk of exposure to disease showed a tendency to increase
326 with breastfeeding duration. When all other confounding factors were adjusted for,
327 breastfeeding for 25 months or longer still showed a positive correlation with joint pain and
328 knee osteoarthritis.

329 Despite the findings of this study, breastfeeding has species-specific superiority as a source of
330 nutrients and immune factors that existing breastmilk substitutes cannot surpass, and it has
331 the effect of formation of attachment between mother and infants and preventing long-term
332 and short-term disease. Therefore, breastfeeding should not be excluded unconditionally as a
333 result of this study, and additional research should be taken carefully in other cultures and
334 races.

335

336 **Declarations**

337 **Ethics approval and consent to participate**

338 The KNHANES 5th was conducted by the Korea Center for Disease Control and Prevention
339 (KCDC). All survey protocols were approved by the institutional review board (IRB) of the
340 KCDC. Informed consent was obtained from all participants when the surveys were
341 conducted. Approval of IRB was not required because the study did not deal with any
342 sensitive information, but rather accessed only publicly available data from the KNHANES
343 (JASENG IRB File No. 2019-09-001).

344

345 **Availability of data and materials**

346 Original data are publicly available for free in the KNHANES website
347 (<http://knhanes.cdc.go.kr>) for purposes such as academic research. The data used in this
348 article are open access, available online at <https://knhanes.cdc.go.kr/knhanes/eng/index.do>.

349

350

351 **Competing interests**

352 The authors declare that they have no conflict of interest.

353

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357

358 **Authors' contributions**

359 MY Kim, SA Kim: Conceptualization, Methodology, Writing- Original draft preparation

360 HJ Kim, JH Noh: Data curation, Investigation

361 IH Ha: Project administration, Supervision, Writing- Reviewing and Editing

362 DS Hwang, CH Lee: Validation

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374 This article has undergone peer review.

375

376 **References**

377 [1] International Lactation Consultant Association, Core Curriculum for Lactation Consultant
378 Practice, Second ed., Jones and Bartlett Publishers, Massachusetts, (2010) 123-9, 156-166.

379 [2] Affairs, K.I.f.H.a.S., Trends in domestic and overseas breastfeeding and policy directions
380 for breastfeeding promotion, Health ·welfare Issue & Focus, 86 (2011) 1-8.

381 [3] C.Y. Park, Breastfeeding for one month or longer is associated with higher risk of
382 osteoarthritis in older adults: NHANES 1999-2012, Clinical nutrition research. 6 (4) (2017)
383 277-284.

- 384 [4] D.W. Shin, S. Nam, Y.S. Bang, J.-Y. Lee, Estimation of the prevalence of Korean adults
385 aged 50 years or more with knee osteoarthritis based on the data from fifth Korea National
386 Health and Nutrition Examination Survey, *Journal of the Korean Medical Association*. 56 (5)
387 (2013) 431-436.
- 388 [5] D. Bhatia, T. Bejarano, M. Novo, Current interventions in the management of knee
389 osteoarthritis, *J Pharm Bioallied Sci*. 5 (1) (2013) 30-38.
- 390 [6] V.K. Srikanth, J.L. Fryer, G. Zhai, T.M. Winzenberg, D. Hosmer, G. Jones, A meta-
391 analysis of sex differences prevalence, incidence and severity of osteoarthritis, *Osteoarthritis*
392 *and cartilage*. 13 (9) (2005) 769-81.
- 393 [7] A. Mahajan, R. Patni, Menopause and osteoarthritis: Any association ?, *J Midlife Health*. 9
394 (4) (2018) 171-172.
- 395 [8] F. Parazzini, Menopausal status, hormone replacement therapy use and risk of self-reported
396 physician-diagnosed osteoarthritis in women attending menopause clinics in Italy, *Maturitas*.
397 46 (3) (2003) 207-212.
- 398 [9] M.M. Shaaban, G.H. Sayed, S.A. Ghaneimah, The recovery of ovarian function during
399 breast-feeding, *Journal of Steroid Biochemistry*. 27 (4) (1987) 1043-1052.
- 400 [10] R. Terzi, H. Terzi, T. Özer, A. Kale, A rare cause of postpartum low back pain:
401 pregnancy- and lactation-associated osteoporosis, *BioMed research international*. 2014
402 (2014).
- 403 [11] F. Bolzetta, N. Veronese, M. De Rui, L. Berton, S. Carraro, S. Pizzato, G. Girotti, I. De
404 Ronch, E. Manzato, A. Coin, G. Sergi, Duration of breastfeeding as a risk factor for vertebral
405 fractures, *Bone*. 68 (2014) 41-45.
- 406 [12] E.W. Karlson, L.A. Mandl, S.E. Hankinson, F. Grodstein, Do breast-feeding and other
407 reproductive factors influence future risk of rheumatoid arthritis? Results from the Nurses'
408 Health Study, *Arthritis and rheumatism*. 50 (11) (2004) 3458-3467.
- 409 [13] Y.K. Jeon, W.J. Cho, Analysis of the metabolic syndrome factors and health-related
410 quality of life by menopausal status with physical activity level in middle-aged women, *The*
411 *Korea Journal of Sports Science*. 25 (5) (2016) 1173-1184.
- 412 [14] M.D. Kohn, A.A. Sassoon, N.D. Fernando, Classifications in brief: Kellgren-Lawrence
413 classification of osteoarthritis, *Clinical Orthopaedics and Related Research®*. 474 (8) (2016)
414 1886-1893.
- 415 [15] D. Prieto-Alhambra, A. Judge, M.K. Javaid, C. Cooper, A. Diez-Perez, N.K. Arden,
416 Incidence and risk factors for clinically diagnosed knee, hip and hand osteoarthritis:
417 influences of age, gender and osteoarthritis affecting other joints, *Annals of the rheumatic*
418 *diseases*. 73 (9) (2014) 1659-1664.

- 419 [16] M.S.G. Nazorcid, V. Ghasemiorcid, Z. Kianiorcid, F.R. Fakari,G. Ozgoli, The effect of
420 breastfeeding duration on bone mineral density (BMD): A systematic review and meta-
421 analysis, *Int J Pediatr.* 7 (1) (2019) 8831-8843.
- 422 [17] S. Cooke-Hubley, B.J. Kirby, J.E. Valcour, G. Mugford, J.D. Adachi,C.S. Kovacs, Spine
423 bone mineral density increases after 6 months of exclusive lactation, even in women who
424 keep breastfeeding, *Archives of osteoporosis.* 12 (1) (2017) 73.
- 425 [18] X. Duan, J. Wang,X. Jiang, A meta-analysis of breastfeeding and osteoporotic fracture
426 risk in the females, *Osteoporosis international : a journal established as result of cooperation*
427 *between the European Foundation for Osteoporosis and the National Osteoporosis*
428 *Foundation of the USA.* 28 (2) (2017) 495-503.
- 429 [19] E.N. Lee, Effects of parity and breastfeeding duration on bone density in
430 postmenopausal women, *Asian nursing research.* 13 (2) (2019) 161-167.
- 431 [20] G. Tsvetov, S. Levy, C. Benbassat, I. Shraga-Slutzky,D. Hirsch, Influence of number of
432 deliveries and total breast-feeding time on bone mineral density in premenopausal and young
433 postmenopausal women, *Maturitas.* 77 (3) (2014) 249-54.
- 434 [21] M. Pikwer, U. Bergstrom, J.A. Nilsson, L. Jacobsson, G. Berglund,C. Turesson, Breast
435 feeding, but not use of oral contraceptives, is associated with a reduced risk of rheumatoid
436 arthritis, *Annals of the rheumatic diseases.* 68 (4) (2009) 526-530.
- 437 [22] Y.H. Jung, J.-S. Shin, J. Lee, M.-r. Kim, K.B. Park, A. Choi, D. Shin,I.-H. Ha, Influence
438 of parity-related factors adjusted for abortion on knee osteoarthritis in Korean women aged
439 50 or older: A cross-sectional study, *Maturitas.* 82 (2) (2015) 176-183.
- 440 [23] B.J. Deroo,K.S. Korach, Estrogen receptors and human disease, *The Journal of Clinical*
441 *Investigation.* 116 (3) (2006) 561-570.
- 442 [24] P. Sciore, C.B. Frank,D.A. Hart, Identification of sex hormone receptors in human and
443 rabbit ligaments of the knee by reverse transcription- polymerase chain reaction: Evidence
444 that receptors are present in tissue from both male and female subjects, *Journal of*
445 *orthopaedic research.* 16 (5) (1998) 604-610.
- 446 [25] H. Chen, H. Zhu, K. Zhang, K. Chen,H. Yang, Estrogen deficiency accelerates lumbar
447 facet joints arthritis, *Scientific reports.* 7 (1) (2017) 1379.
- 448 [26] N.L. Petrakis, M.R. Wensch, V.L. Ernster, R. Midce, J. Murai, N. Simberg,P.K. Sirreri,
449 Influence of pregnancy and lactation on serum and breast fluid estrogen levels: implications
450 for breast cancer risk, *International Journal of Cancer.* 40 (5) (1987) 587-591.
- 451 [27] K. HR, Breastfeeding trends, affecting factors and policy options for breastfeeding
452 promotion in Korea, *Health and Welfare Policy Forum.* 201 (2013) 49-60.

453 [28] S.S. Choi, E.H. Lee, K.H. Youn, B.K. Sim, N.H. Choi, The study on the incidence of
454 breast feeding and related factors, Korean Journal of Women Health Nursing. 2 (2) (1996)
455 253-269.

456 [29] A. HY, K. HJ, Social implications of changes in Korean families, Journal of Korean
457 Society. 3 (2000) 89-132.

458 [30] S.-Y.L. Seong-In Hong, A Study on the Change of the Housing Culture Koreans through
459 the First-generation Apartment in Korea, Asia-pacific Journal of Multimedia Services
460 Convergent with Art, Humanities, and Sociology. 8 (4) (2018) 985-998.

461

462 **Figure legends**

463 Figure 1. Flow chart for study population selection

464

465 Table 1. Characteristics of the study population according to duration of breastfeeding above 50 years (n=3,454)

Variables	All women (n=3,454)	Duration of breastfeeding (months)				P-value ^a
		None (n=298)	1-24 mths (n=1042)	25-48 mths (n=815)	≥49 mths (n=1299)	
Age(years) (mean±sd)	3454	57.5±7.6	56.5±6.5	61.6±7.5	70.7±8.4	<.001
Household income	3417					
Low	1184	67 (23)	199 (19.3)	241 (29.8)	677 (52.8)	<.001
Middle-low	850	75 (25.7)	262 (25.3)	226 (28)	287 (22.4)	
Middle- High	674	58 (19.9)	251 (24.3)	190 (23.5)	175 (13.6)	
High	709	92 (31.5)	322 (31.1)	151 (18.7)	144 (11.2)	
Smoking status	3453					
Never smoker	2668	217 (72.8)	757 (72.7)	639 (78.4)	1055 (81.3)	<.001
Ex-smoker	102	14 (4.7)	24 (2.3)	14 (1.7)	50 (3.9)	
Current smoker	131	21 (7.1)	49 (4.7)	20 (2.5)	41 (3.2)	
Indirect smoking	552	46 (15.4)	212 (20.4)	142 (17.4)	152 (11.7)	
Drinking	3438					
Non alcohol consumption	1789	149 (50.2)	447 (43.2)	399 (49.1)	794 (61.4)	<.001
< 1 drinking episode per month	794	79 (26.6)	252 (24.4)	224 (27.6)	239 (18.5)	
< 5 drinking episode per month	663	52 (17.5)	262 (25.3)	154 (18.9)	195 (15.1)	
≥ 5 drinking episodes per month	192	17 (5.7)	73 (7.1)	36 (4.4)	66 (5.1)	
BMI(kg/m²) (mean±sd)	3450	23.6±2.9	24±3.1	24.6±3.2	24.4±3.4	<.001
Underweight (<18.5)	92	8 (2.7)	16 (1.5)	15 (1.9)	53 (4.1)	<.001
Normal (18.5~24.9)	2052	197 (66.1)	688 (66.2)	443 (54.5)	724 (55.7)	
Obese (≥25)	1306	93 (31.2)	336 (32.3)	355 (43.7)	522 (40.2)	
Children(n) (mean±sd)	3451	1.7±1.2	2.2±0.9	3±0.9	4.7±1.7	<.001
None	79	75 (25.2)	2 (0.2)	1 (0.1)	1 (0.1)	<.001
1-2	1262	167 (56)	834 (80)	199 (24.5)	62 (4.8)	
3-4	1395	49 (16.4)	184 (17.7)	585 (71.9)	577 (44.5)	
≥5	715	7 (2.4)	22 (2.1)	29 (3.6)	657 (50.7)	
Abortion(n)	3445					

None	975	109 (36.8)	248 (23.9)	202 (24.8)	416 (32.1)	<.001
1-2	1664	132 (44.6)	572 (55.1)	383 (47.1)	577 (44.5)	
≥3	806	55 (18.6)	218 (21)	229 (28.1)	304 (23.4)	
Hormone replacement therapy(months)	3450					
None	2945	255 (85.9)	843 (80.9)	660 (81.1)	1187 (91.5)	<.001
<6	149	10 (3.4)	54 (5.2)	48 (5.9)	37 (2.9)	
<12	29	3 (1)	14 (1.3)	6 (0.7)	6 (0.5)	
≥13	327	29 (9.8)	131 (12.6)	100 (12.3)	67 (5.2)	
Menopause	3452					
No	216	37 (12.4)	133 (12.8)	37 (4.6)	9 (0.7)	<.001
Yes	3236	261 (87.6)	909 (87.2)	777 (95.5)	1289 (99.3)	
Dyslipidemia	3454					
No	2945	250 (83.9)	888 (85.2)	695 (85.3)	1112 (85.6)	0.592
Yes	509	48 (16.1)	154 (14.8)	120 (14.7)	187 (14.4)	
Diabetes	3152					
No	2047	199 (71.6)	708 (72.2)	498 (65)	642 (57)	<.001
Yes	1105	79 (28.4)	273 (27.8)	268 (35)	485 (43)	
Hypertension	3446					
No	1645	169 (56.9)	618 (59.5)	377 (46.4)	481 (37.1)	<.001
Yes	1801	128 (43.1)	421 (40.5)	436 (53.6)	816 (62.9)	
Knee joint pain	3454					
No	2365	241 (80.9)	826 (79.3)	574 (70.4)	724 (55.7)	<.001
Yes	1089	57 (19.1)	216 (20.7)	241 (29.6)	575 (44.3)	
Hip joint pain	3454					
No	2942	264 (88.6)	939 (90.1)	711 (87.2)	1028 (79.1)	<.001
Yes	512	34 (11.4)	103 (9.9)	104 (12.8)	271 (20.9)	
Low back pain	3454					
No	2247	236 (79.2)	797 (76.5)	541 (66.4)	673 (51.8)	<.001
Yes	1207	62 (20.8)	245 (23.5)	274 (33.6)	626 (48.2)	
Osteoarthritis	3454					

No	2715	264 (88.6)	934 (89.6)	649 (79.6)	868 (66.8)	<.001
Yes	739	34 (11.4)	108 (10.4)	166 (20.4)	431 (33.2)	

466

467 ^a. P-value from t-test or Rao-Scott chi-squared test for continuous or categorical variables.

468

469 Table 2 Association between duration of breastfeeding and joint pain (n=3,454)

Factors	Unadjusted		Model 1		Model 2	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Breastfeeding history						
Non-Breastfeed	1		1		1	
Breastfeed ≥ 1 mth	2.255 (1.683, 3.021)	<.001	1.593 (1.175, 2.16)	0.003	1.493 (1.01, 2.206)	0.044
Breastfeeding history						
None	1		1		1	
1-24 mths	1.198 (0.865, 1.66)	0.276	1.29 (0.928, 1.792)	0.129	1.335 (0.891, 2.002)	0.161
25-48 mths	2.13 (1.51, 3.005)	<.001	1.75 (1.228, 2.493)	0.002	1.671 (1.069, 2.612)	0.025
≥49 mths	4.099 (3.076, 5.462)	<.001	2.078 (1.528, 2.827)	<.001	1.97 (1.286, 3.017)	0.002
p for trend		<.001		<.001		0.002

470 OR, odds ratio; 95% CI, 95% confidence interval

471 Model 1 was adjusted by age.

472 Model 2 was adjusted by age, BMI, household income, smoking, alcohol consumption, children, diabetes, hypertension, menopausal status, physical activity, abortion,
473 hormone replacement therapy.

474

475 Table 3 Association between duration of breastfeeding and knee osteoarthritis (OA) (n=3,454)

Factors	Unadjusted		Model 1		Model 2	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Breastfeeding history						
Non-Breastfeed	1		1		1	
Breastfeed ≥ 1 mth	2.412 (1.542, 3.771)	0.0001	1.443 (0.916, 2.274)	0.114	1.92 (0.942, 3.915)	0.072
Breastfeeding history						
None	1		1		1	
1-24 mths	0.929 (0.565, 1.526)	0.769	1.049 (0.647, 1.702)	0.845	1.598 (0.791, 3.227)	0.191
25-48 mths	2.176 (1.345, 3.521)	0.002	1.673 (1.033, 2.71)	0.037	2.299 (1.086, 4.864)	0.03
≥49 mths	4.374 (2.762, 6.925)	<.001	1.689 (1.028, 2.775)	0.039	2.166 (1.011, 4.642)	0.047
p for trend		<.001		0.004		0.062

476 OR, odds ratio; 95% CI, 95% confidence interval

477 Model 1 was adjusted by age

478 Model 2 was adjusted by age, BMI, household income, smoking, alcohol consumption, children, diabetes, hypertension, menopausal status, physical activity, abortion,
479 hormone replacement therapy

480

481 Table 4. Association between duration of breastfeeding and joint pain, above 60 years (n=2,102)

Factors	Unadjusted		Model 2	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Breastfeeding history				
Non-Breastfeed	1		1	
Breastfeed \geq 1 mth	1.912 (1.233, 2.963)	0.004	2.614 (1.417, 4.821)	0.002
Breastfeeding history				
None	1		1	
1-24 mths	1.275 (0.77, 2.109)	0.344	2.39 (1.231, 4.639)	0.01
25-48 mths	1.526 (0.941, 2.475)	0.086	2.352 (1.254, 4.409)	0.008
\geq 49 mths	2.331 (1.498, 3.628)	<.001	3.068 (1.625, 5.792)	0.001
p for trend		<.001		0.005

482 OR, odds ratio; 95% CI, 95% confidence interval

483 Model 2 was adjusted by age, BMI, household income, smoking, alcohol consumption, children, diabetes, hypertension, menopausal status, physical activity, abortion,
 484 hormone replacement therapy

485

486 Table 5. Association between duration of breastfeeding and knee osteoarthritis (OA), above 60 years (n=2,102)

Factors	Unadjusted		Model 2	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Breastfeeding history				
Non-Breastfeed	1		1	
Breastfeed \geq 1 mth	1.471 (0.853, 2.536)	0.165	2.751 (1.165, 6.495)	0.021
Breastfeeding history				
None	1		1	
1-24 mths	0.872 (0.464, 1.641)	0.671	2.14 (0.851, 5.385)	0.106
25-48 mths	1.215 (0.69, 2.137)	0.499	2.705 (1.147, 6.382)	0.023
\geq 49 mths	1.757 (1.004, 3.078)	0.049	3.18 (1.349, 7.498)	0.008
p for trend		<.001		0.012

487 OR, odds ratio; 95% CI, 95% confidence interval

488 Model 2 was adjusted by age, BMI, household income, smoking, alcohol consumption, children, diabetes, hypertension, menopausal status, physical activity, abortion,
 489 hormone replacement therapy.

490

491