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Original Article

The associations between parity, other reproductive factors, and osteoarthritis in women aged over 50 years; data from the Korean National Health and Nutrition Examination Survey V (2010–2012)

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ABSTRACT

Objective: To evaluate the relationships between sociodemographic factors, reproductive history, and subsequent risk of osteoarthritis (OA) or pain of the hip, knee, and back in Korean women.
Materials and Methods: This study included data of 5101 women aged over 50 years, taken from the Korean National Health and Nutritional Examination Survey V from 2010 to 2012. Women were stratified according to parity, as well as delivery mode. Multivariate logistic regression analysis was conducted to evaluate relationships between radiographic OA or symptomatically possible OA (back, knee, or hip), and historical factors.
Results: Vaginal delivery was associated with an increased risk of symptomatic back OA [odds ratio (OR) 1.75, 95% confidence interval (CI) 1.062, 2.881] but was not associated with symptomatic knee and hip OA in adjusted analysis. Radiographically, vaginal delivery was not associated with risks of back and knee OA, but was negatively associated with hip OA (OR 0.184, 95% CI 0.039, 0.863), compared to cesarean delivery. High parity (over 5) was associated with radiographic knee OA (OR 1.328, 95% CI 1.006, 1.754) in adjusted analysis. High parity (over 3) was associated with symptomatic back OA.
Conclusion: Parity was associated with higher risk of radiographic knee OA. Vaginal delivery was positively associated with symptomatic back OA, but negatively associated with radiographic knee OA. Further study is required to evaluate the mechanism between delivery mode and subsequent OA.

Introduction

Osteoarthritis (OA) is the most common form of arthritis and is associated with disability and substantial cost to the individual and to society [1,2]. The pathophysiologic mechanisms of OA are under debate, but biological and lifestyle-related risk factors for OA, e.g., genetic factors, congenital joint deformities, joint injury, occupational physical activity, obesity, and ageing are considered as the risk factors [1,2]. It has also been suggested that women have a higher prevalence of OA than men, particularly after 50 years of age [3,4]. This may be due to differences between males and females associated with reproductive history and several studies have reported that reproductive history might be associated with risk of OA and that childbirth increases the risk of OA due to pregnancy-induced weight gain and joint laxity [5–8]. As the body mass index (BMI) increases during and after pregnancy [9], prevalence of OA can be related to parity and the main joints that are affected by mechanical loading could be typical sites of OA (knee, pelvis, and lower back area). Pelvic pain during and after pregnancy is widely known and there have been many efforts to investigate pain according to the mode of delivery [10,11]. Since pelvic pain can result from other problems such as fracture and sacral plexus injury, radiographic diagnosis of OA needs to be included [12].

Therefore, in this study, we attempted to determine the relationships between sociodemographic factors, reproductive history, and subsequent risk of OA in hip, knee, and back.

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Materials and methods

Data source and participants

Data were obtained from the Korean National Health and Nutrition Examination Survey (KNHANES), which was conducted by the Korea Centers for Disease Control and Prevention to examine the general health and nutritional status of Koreans. To select a representative sample of the Korean population, they used a stratified three-stage clustered probability design (local district → enumeration district → household). To date, five surveys have been completed as follows: I (1998), II (2001), III (2005), IV (2007–2009), and V (2010–2012). This study utilized data from the KNHANES V. Because radiographic evaluation for OA was performed in individuals with an age of more than 50 years, 11,616 male individuals and 8142 female individuals with an age of less than 50 years were excluded. In addition, 675 female individuals who did not respond to the questions of "Have you had back pain during the recent 3 months for more than 30 days?", "Have you had knee pain during the recent 3 months for more than 30 days?", and "Have you had pelvic pain during the recent 3 months for more than 30 days?", and who had no results of radiographic evaluation for OA (back, knee, and hip), and who did not respond to the questions of delivery frequency and mode, were excluded. The final study cohort included 5101 women (Figure 1). Written informed consent was obtained from all participants, and ethical approval for the survey was granted by the research ethics committee of the Korea CDC (approval numbers: 2010: 2010-02CON-21-C; 2011: 2011-02CON-06-C; and 2012: 2012-01EXP-01-2C).

Covariates

Data concerning clinical characteristics were collected by history taking, physical examinations, and radiographic analyses. History taking included basic demographics, income, and lifestyle habits of smoking, alcohol consumption, and exercise. Smoking status was examined by asking whether participants were never smokers, past smokers, or current smokers. Alcohol consumption was examined by asking about the frequency of drinking and the amount of alcoholic beverage per episode of drinking. Heavy drinking was defined as alcohol consumption of more than 30 g a day. Physical activity was quantified as the metabolic equivalent of task minutes per week (MET-minutes per week), which was calculated using the scoring protocol of the Korean version of the International Physical Activity Questionnaire short form [13]. Accordingly, physical activity levels were classified as low (< 600 MET-minutes per week), moderate (≥ 600 to < 3000 MET-minutes per week), or high (≥ 3000 MET-minutes per week). Exercise was defined as moderate or high physical activity.

Women's reproductive history was assessed by self-administered questionnaires. Parity was defined based on the women's live or still births and then categorized as follows (1 = nulliparous, 1–2 children, 2 = 3–4 children, and 3 = 5 or more) to ensure similar proportions in each group. Delivery mode, gravity, age of menarche, and age of menopause were assessed. Women with more than one vaginal delivery were counted as the vaginal delivery group. Ever use of oral contraceptives and hormone replacement therapy were also assessed by questionnaires. Physical examinations included measurements of blood pressure and measures of body mass. Weight was measured on a calibrated balance-beam scale and height was measured in an upright position using a stadiometer. BMI was calculated by dividing weight (kg) by height^2 (square meters). Waist circumference (WC) was measured at the midpoint between the bottom of the rib cage and the top of the lateral border of the iliac crest with full expiration.

Radiographic examination of the knee and definition of radiographic knee OA

Bilateral anteroposterior, lateral (30° of flexion), and weight-bearing anteroposterior plain radiographs of the knees were taken using a SD3000 Synchro Stand (Accele Ray, SYFM Co., Seoul, Korea). Radiographic changes relating to OA were assessed, ranging from Grade 0 to Grade 4, using the Kellgren-Lawrence grading system [14]. The radiographic digital images were stored on a web hard disk drive and were graded by two radiographic musculoskeletal specialists, with concordant grades accepted. When there was a difference of one grade between the two radiologists, the higher grade was accepted. If the

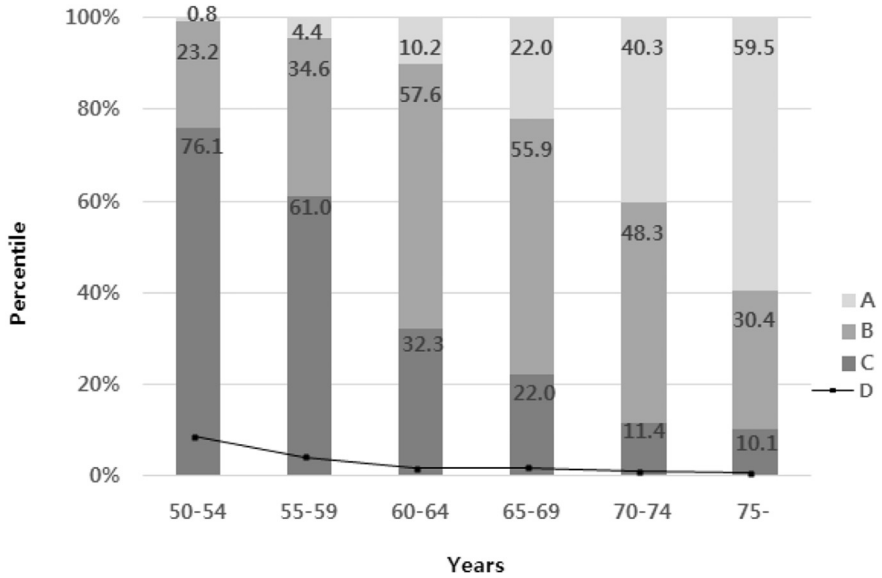

Figure 1. Distribution of the number of parity depending on age: (A) parity ≥ 5, (B) parity 3 or 4, (C) parity ≤ 2. The solid line shows the percentile of cesarean section depending on age.

discrepancy was more than one grade, a third radiologist was consulted, and the grade concordant with the third grade was accepted. Weighted Cohen's kappa coefficient was 0.66 (agreement 89.62%, expected agreement 69.46%). Participants with radiographic knee OA were defined as those who had a Kellgren/Lawrence grade > 2 in both knees.

Radiographic examination of the hip and definition of radiographic hip OA

Anteroposterior pelvis and upper femoral, anteroposterior and oblique hip joint plain radiographs were taken. Radiographic change was assessed as Grade 0 to Grade 3 by the Kellgren-Lawrence grading system. Weighted Cohen's kappa coefficient was 0.31 (agreement 95.98%, expected agreement 94.16%). Participants with radiographic hip OA were defined as those who had a Kellgren/Lawrence grade > 2.

Radiographic examination of the back and definition of back OA

Anteroposterior, oblique, and lateral lumbar spine plain radiographs were taken. Radiographic change was assessed as Grade 0 to Grade 2 by a scale developed by the Korean academy of family medicine according to the Kellgren-Lawrence grading system and the report of Yoshimura et al [15]. Participants with Grade 2 were defined as back OA

Definition and description of symptomatically possible knee, hip, and back OA

Participants who had replied "yes" to more than one of the following questions were defined as symptomatically possible OA; "Have you had back pain during the recent 3 months for more than 30 days?", "Have you had knee pain during the recent 3 months for more than 30 days?", and "Have you had pelvic pain during the recent 3 months for more than 30 days?". Also, symptomatically possible OA was described as symptomatic OA in this study

Statistical analysis

Clinical characteristics among the participants with OA (back, knee, or hip) and controls were compared by Student t test for continuous variables and Pearson's Chi-square test or Fisher's exact test for categorical variables. Multivariate logistic regression analysis was conducted to evaluate relationships between OA (back, knee, or hip) with delivery histories. Cesarean delivery among delivery modes and less than 2 of category 1 of delivery frequency were used as the reference category, respectively. Variables entered as either a factor or a covariate included age, WC, smoking, heavy drinking, exercise, income, and education. Statistical analysis was performed with the SPSS for Windows statistical package (version 20.0, SPSS Inc., Chicago, IL, USA), and all p values < 0.05 were considered significant.

Results

Clinical characteristics and delivery history

Clinical characteristics according to the presence or absence of back, knee, or hip OA diagnosed by symptom or radiography, are shown in Table 1. The prevalence of symptomatic or radiographic OA in this study was 72.8% ($n = 3711$) in women over 50 years old. Compared with individuals without back, knee, and hip OA, those with OA had higher mean age, BMI, WC, gravida, parity, number of vaginal deliveries, and urban residence, as well as a higher prevalence of alcohol intake; meanwhile, they showed lower educational status, income, history of oral pill or hormone replacement therapy, and lower number of cesarean sections and preterm deliveries. There was no significant difference of the age at menopause, exercise, and history of current smoking. As the age advanced, the number of parity increased but the rate of cesarean delivery decreased (Figure 2). The prevalence rate of parity over 3 was 24% in the group aged 50–54 years and 89.9% in those over 75 years of age. On the contrary, history of cesarean section was 11.6% among 50–54-year-old women and 0.1% in those over 75 years of age.

Table 1
Characteristics of study participants.

	OA		
	No ($n = 1390$)	Yes ($n = 3711$)	p
Age (y)	56.7 ± 0.2	65.6 ± 0.2	< 0.0001
BMI (kg/m^2)	23.5 ± 0.1	24.6 ± 0.1	< 0.0001
Waist circumference (cm)	79.5 ± 0.3	83.4 ± 0.2	< 0.0001
Gravida	3.9 ± 0.1	5.1 ± 0.1	< 0.0001
Parity	2.42 ± 0.04	3.52 ± 0.04	< 0.0001
Vaginal delivery (n)[a]	2.17 ± 0.04	3.42 ± 0.04	< 0.0001
Cesarean section (n)[a]	0.22 ± 0.02	0.07 ± 0.01	< 0.0001
Preterm delivery (n)[a]	0.15 ± 0.03	0.09 ± 0.02	0.0228
Menarche (y)	15.8 ± 0.1	16.3 ± 0	< 0.0001
Menopause age (y)	49.3 ± 0.2	49 ± 0.1	0.0522
Oral pill (%)	18.4 (1.2)	22.3 (0.8)	0.0118
Hormone therapy (%)	17.6 (1.2)	11.9 (0.7)	< 0.0001
Current-smoker (%)	5.3 (0.9)	4.2 (0.4)	0.2083
Heavy drinker (> 30 g/d) (%)	3.2 (0.6)	1.3 (0.3)	0.001
Exercise (≥ moderate)[b] (%)	15.2 (1.2)	15.4 (0.8)	1
Urban residence (%)	83.9 (1.9)	67 (2.6)	< 0.0001
Spouse (yes) (%)	80.4 (1.4)	62.8 (1.1)	< 0.0001
Education (to university) (%)	39.6 (1.7)	17 (0.9)	< 0.0001

BMI = body mass index; OA = osteoarthritis.
Values are presented with mean ± standard deviations or number (s) or percentile (s).
[a] Number of delivery history.
[b] Exercise: high – a strenuous physical activity > 20 min/d, > 3 d/wk, moderate – moderate physical activity > 30 min/d, > 5 d/wk.

The relation between delivery history and OA

As seen in Table 2, the history of vaginal delivery was associated with an increased risk of radiographic back and knee OA, but was not associated with radiographic hip OA. By symptomatic diagnosis, the history of vaginal delivery was positively associated with increased risks of back, knee, and hip OA. As parity increased, back and knee OA diagnosed by radiography were significantly increased, but in the parity 3–4 group, hip OA prevalence was lower than in the parity below 2 group ($p < 0.05$) . Also, the history of vaginal delivery was associated with an increased number of OA and 97.4% of women with all three types of OA had a history of vaginal delivery. While 65% of women without OA showed parity 2 or less, 76.2% of women with all three type of OA had parity more than 3, showing that the number of OA was associated with the increased number of parity (Figure 2).

Delivery mode and subsequent risk of OA by multivariate logistic regression analysis

The history of vaginal delivery was associated with an increased risk of symptomatic back OA (OR 1.75, 95% CI 1.062, 2.881), compared to the history of cesarean delivery (Table 3). There was no significant association between vaginal delivery and knee OA by symptom and radiography. However, the history of vaginal delivery was associated with decreased risk of radiographic hip OA (OR 0.184, 95% CI 0.039, 0.863).

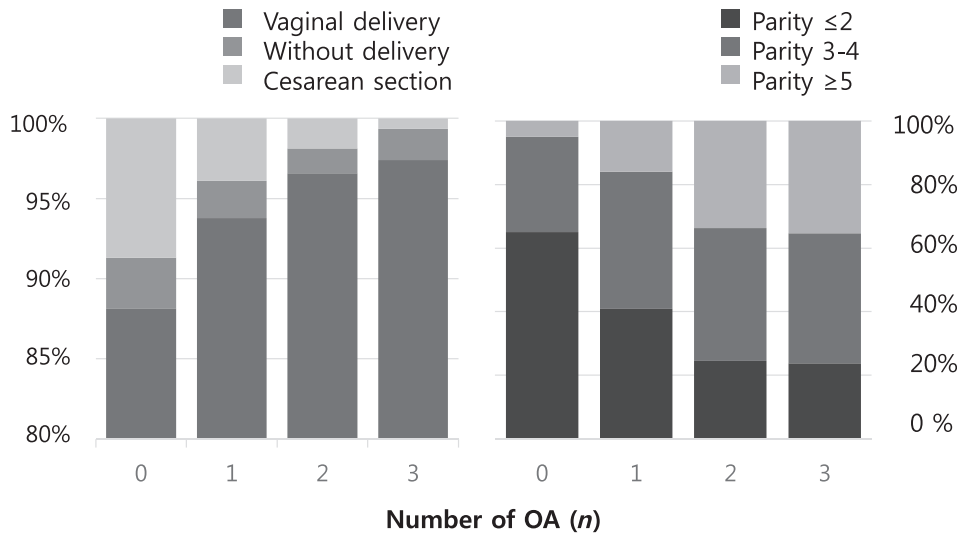

Figure 2. The proportion of delivery method type and parity according to the number of osteoarthritis (OA) site increases.

Table 2
Correlation of delivery method and parity with osteoarthritis (OA) diagnosed by radiologic finding or symptoms.

	Delivery method				Parity			
	Vaginal delivery	Without delivery	Cesarean section	*p*	≤ 2	3–4	≥ 5	*p*
Radiologic diagnosis								
Back	35.7 (1)	24.1 (4.3)	14.2 (3.2)	< 0.0001	21.3 (1.1)	37.9 (1.5)	56 (1.9)	< 0.0001
Knee	44 (1)	37.2 (5.5)	21.6 (3.4)	< 0.0001	27.2 (1.2)	46.6 (1.3)	68.8 (1.8)	< 0.0001
Hip	0.5 (0.1)	0.8 (0.8)	0.9 (0.7)	0.5746	0.5 (0.2)	0.2 (0.1)	1.2 (0.5)	0.0034
Symptomatic diagnosis								
Back	33.2 (0.9)	22.4 (4.4)	10.8 (2.4)	< 0.0001	20.3 (1.1)	35.1 (1.5)	50.9 (1.9)	< 0.0001
Knee	29.5 (0.8)	19.7 (4.2)	12.2 (2.5)	< 0.0001	18.9 (1.1)	29.9 (1.3)	46.4 (2)	< 0.0001
Hip	14.4 (0.6)	13.3 (4)	5.2 (1.6)	0.0042	9.9 (0.8)	15.3 (1)	20.3 (1.5)	< 0.0001

Parity and subsequent risk of OA by multivariate logistic regression analysis

The prevalence of symptomatic back OA in the parity 5 or more group was higher than that in the parity 2 or less group (OR 1.697, 95% CI 1.298, 2.22), which was similar in the parity 3–4 group (OR 1.397, 95% CI 1.135, 1.718). However, by radiographic diagnosis, there was no difference among three groups. The group of parity 5 or more was associated with radiographic knee OA (OR 1.328, 95% CI 1.006, 1.754). No significant association between parity and hip OA was demonstrated.

Discussion

After adjusting for various sociodemographic, behavioral, and reproductive factors, several positive associations were found between symptomatic back OA, radiographic knee OA, and delivery histories, especially high parity (3 or more) and history of vaginal delivery. Radiographic knee OA was associated with high parity (5 or more), but not associated with history of vaginal delivery. This finding was correlated with the previous studies in other populations [5–8,16]. Parity was independently associated with lower cartilage volume, primarily in the tibial compartment, and higher cartilage defects in the patella compartment in women aged over 50 years [16]. In one cohort study that included around 22,000 middle-aged women undergoing a hip or a knee replacement during 6 years, Liu et al [7] found that the risk of hip and knee replacement increased by 2% and 8% per additional childbirth, respectively. As the other study suggested that childbirth was not related with hip OA, but with knee and back OA [8], our study results also did not demonstrate a positive relationship between high parity and symptomatic or radiographic hip OA, but demonstrated a positive relationship between high parity and symptomatic back OA. It seems that the combination of a considerable transient weight gain and increased joint laxity in pregnancy might explain, at least in part, the findings of an increased long-term risk of OA of the knee and back in women with multiple children, although the pathogenesis of OA is not completely understood.

The results from the previous studies between hip or lower back pain and delivery mode were also controversial [17–21]. Our study results demonstrated that the risk of radiographic hip OA is lower in vaginal delivery than cesarean delivery, although there was no significant difference in symptomatic hip OA. A recent study also suggests that vaginal delivery is not associated with a higher rate of long-term pelvic pain when compared to cesarean delivery [21]. Potential causes of pain related to cesarean delivery include uterine scar defect, ilioinguinal or iliohypogastric nerve entrapment, and pelvic adhesions [22].

It has been proposed that back pain is not related with mode of delivery and parity [21]. However, in our study, prevalence of symptomatic back OA was significantly higher in vaginal delivery than cesarean delivery. This may be due to mechanical load on the low back area (e.g., iliosacral joint) during labor and could be related with increase of back pain after midlife. To evaluate causes and relationships of back pain after vaginal delivery, more studies are needed.

Table 3
Presence of osteoarthritis (OA) according to delivery method history and parity compared to Cesarean section and parity below 2, respectively.

	OA						
	Back		Knee		Hip		OA
	Radiology	Symptom	Radiology	Symptom	Radiology	Symptom	≥ 1 type
<**Model 1**>							
Delivery history							
Vaginal delivery	1.303 (0.753, 2.255)	2.302 (1.4, 3.784)	1.053 (0.678, 1.635)	1.529 (0.943, 2.482)	0.168 (0.034, 0.841)	1.9 (0.987, 3.656)	1.451 (0.978, 2.153)
Without delivery	1.036 (0.507, 2.114	1.67 (0.814, 3.426)	1.192 (0.57, 2.493)	0.403 (0.03, 5.387)	1.25 (0.66, 2.366)	1.036 (0.507, 2.114)	1.25 (0.66, 2.366)
Cesarean section	1	1	1	1	1	1	1
Parity							
≥ 5	1.074 (0.835, 1.381)	1.951 (1.51, 2.52)	1.366 (1.043, 1.789)	1.516 (1.176, 1.954)	0.693 (0.204, 2.35)	1.157 (0.842, 1.589)	1.982 (1.332, 2.95)
3, 4	1.179 (0.971, 1.431)	1.535 (1.263, 1.866)	1.169 (0.968, 1.412)	1.18 (0.963, 1.446)	0.227 (0.071, 0.724)	1.202 (0.926, 1.561)	1.463 (1.196, 1.79)
≤ 2	1	1	1	1	1	1	1
<**Model 2**>							
Delivery history							
Vaginal delivery	1.151 (0.659, 2.01)	1.906 (1.161, 3.13)	0.928 (0.583, 1.477)	1.233 (0.737, 2.061)	0.13 (0.026, 0.64)	1.701 (0.871, 3.324)	1.299 (0.869, 1.941)
Without delivery	0.919 (0.439, 1.926)	1.365 (0.653, 2.856)	1.194 (0.58, 2.461)	0.956 (0.439, 2.08)	0.287 (0.02, 4.147)	1.785 (0.663, 4.803)	1.176 (0.583, 2.37)
Cesarean section	1	1	1	1	1	1	1
Parity							
≥ 5	0.991 (0.769, 1.276)	1.738 (1.342, 2.25)	1.29 (0.981, 1.697)	1.298 (0.999, 1.685)	0.675 (0.199, 2.287)	1.045 (0.752, 1.454)	1.798 (1.193, 2.71)
3, 4	1.108 (0.908, 1.353)	1.434 (1.174, 1.751)	1.108 (0.912, 1.345)	1.06 (0.863, 1.303)	0.22 (0.066, 0.735)	1.133 (0.866, 1.482)	1.395 (1.131, 1.721)
≤ 2	1	1	1	1	1	1	1
<**Model 3**>							
Delivery history							
Vaginal delivery	1.127 (0.645, 1.972)	1.75 (1.062, 2.881)	0.898 (0.563, 1.432)	1.216 (0.728, 2.033)	0.184 (0.039, 0.863)	1.655 (0.847, 3.234)	1.225 (0.82, 1.829)
Without delivery	0.926 (0.44, 1.951)	1.588 (0.763, 3.306)	1.267 (0.623, 2.576)	1.009 (0.465, 2.19)	0.25 (0.016, 3.898)	1.833 (0.676, 4.967)	1.28 (0.649, 2.522)
Parity							
≥ 5	0.971 (0.75, 1.258)	1.697 (1.298, 2.22)	1.328 (1.006, 1.754)	1.271 (0.973, 1.66)	0.76 (0.199, 2.913)	1.041 (0.742, 1.46)	1.79 (1.184, 2.706)
3, 4	1.089 (0.887, 1.335)	1.397 (1.135, 1.718)	1.137 (0.933, 1.386)	1.04 (0.842, 1.283)	0.254 (0.071, 0.906)	1.123 (0.857, 1.473)	1.386 (1.123, 1.71)
≤ 2	1	1	1	1	1	1	1

Model 1: Adjusted by age, waist circumference (WC).
Model 2: Adjusted by age, WC, smoke, alcohol intake, exercise, income, education.
Model 3: Adjusted by age, WC, smoke, alcohol intake, exercise, income, education, parity, delivery method.
Values are presented as odds ratio (95% confidence interval).

Although there is no proven intervention for preventing and treating pelvic and back pain in pregnancy, further research might be needed to relieve pressure on the back area during pregnancy and labor, to decrease the long-term risk of back OA [22]. The recent study using a computational approach to understand therapeutic effects of pelvic belts suggests mechanism of pelvic belts on sacroiliac joint ligaments [23].

The limitation of our study is that we described symptomatically possible OA as symptomatic OA. So, the prevalence of OA became too high. However, the diagnosis of OA is known to be complicated by numerous factors. These include a lack of specific physical or laboratory findings and discrepancies between symptoms and the results of radiographic examinations. Consequently, OA is frequently diagnosed by an overall clinical impression based on the patient's age and history, location of the joint abnormalities, and radiographic findings. Clinical criteria for the back OA do not exist, because there are many reasons for back pain. The criteria for the diagnosis of hip OA have been suggested by the American College of Rheumatology, including both clinical and radiographic information [24]. They include hip pain and at least two of the following: an erythrocyte sedimentation rate of < 20 mm/h, radiographic evidence of femoral or acetabular osteophytes, and radiographic evidence of joint-space narrowing (superior, axial, or medial). In addition, the clinical criteria for knee OA by the American College of Rheumatology include articular knee pain for most days of the prior month, in addition to at least three of the following: crepitus on active joint motion, morning stiffness < 30 minutes duration, age > 38 years, bony enlargement of the knee on examination, bony tenderness of the knee on examination, and no palpable warmth [25]. The discordance between radiographic OA and the occurrence of knee pain in the general population has been well documented [26]. It is possible to have symptomatic OA without radiographic OA, and vice versa. As Hannan et al [27] reported, when we analyze clinical research data, chronic arthralgia should be considered as criteria for OA. Therefore, we tried to include chronic joint pain from KNHANES data to include all possible OA patients who need to see a doctor, although this can lead to overestimation. Due to our broad definition of symptomatic OA, a positive relationship between vaginal delivery and symptomatic back OA in this study needs more evidence in the future. However, we can expect that delivery history is related with back pain, because high parity more than 3 also increased the risk of symptomatic OA.

In conclusion, parity is associated with an overall risk of back, knee, or hip OA and independently associated with radiographic

knee OA. Vaginal delivery is positively associated with symptomatic back OA, but negatively associated with radiographic knee OA, compared to cesarean delivery. Further study is needed to evaluate mechanisms between delivery mode and subsequent OA. As lifespan increases, to decrease symptomatic or mechanical OA for middle- or old-aged women, further studies might be needed to support weight loading which increases by trimester advance, and decrease spinal deformity by pregnancy and delivery.

Conflicts of interest

The authors declare that they have no competing interests.

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