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THE IMPACT OF PREGNANCY ON DISTAL FEMORAL CARTILAGE- A PROSPECTIVE COHORT STUDY

GEBELİĞİN DİSTAL FEMORAL KARTİLAJ ÜZERİNDEKİ ETKİSİ-PROSPEKTİF BİR KOHORT ÇALIŞMASI

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ÖZ

Amaç: Kartilaj tahribatının, aşırı kilo, eklemlerin aşırı kullanımı ve zorlanan hareketler, yaşlanma sürecine bağlı aşınmalar, genetik faktörler gibi birçok faktörle ilişkilendirildiği görülmüştür. Obezite, osteoartrit için değiştirilebilir bir risk faktörüdür. Bu çalışmada diz eklemi kartilaj kalınlığının belirlenmesi ve gebelik sürecinin gebelikte osteoartrit gelişimine etkisinin gösterilmesi amaçlandı.

Gereç ve Yöntem: Bu çalışmaya 15-42 yaş arası 50 gebe kadın dahil edildi. Baskın diz distal femoral kartilajın ultrason görüntüsü, kemik korteksi ile suprapatellar yağ yastığı arasındaki güçlü yankısız alandan lateral kondil, interkondiler alan ve medial kondilde 1. ve 3. trimesterde ölçüldü.

Bulgular: Nullipar ve multipar gebelerin her birinin üçüncü trimester kartilaj ölçümlerinin, birinci trimester kartilaj ölçümlerine göre anlamlı derecede daha ince olduğunu bulduk (p=0,001, p=0,005, p<0,001). Yaş, sosyoekonomik düzey, eğitim düzeyi, çalışma durumu, vücut kitle indeksi ve diz kartilaj ultrason ölçümleri arasında anlamlı ilişki bulundu (p=0,001 p=0,003, p=0,002, p=0,001).

Sonuç: Bu sonuçlara göre sosyoekonomik düzey, eğitim düzeyi, çalışma durumu ve vücut kitle indeksi kartilaj kalınlığını etkileyen faktörler olmasıyla birlikte, gebeliğin üçüncü trimesterine geçişinde ve multipar kadınlarda eklem kartilaj ölçümünde anlamlı azalma, gebelik sürecinin osteoartrit gelişiminde önemli bir faktör olduğunu düşündürmektedir.

Anahtar Kelimeler: osteoartrit, gebelik, eklem, kartilaj, parite

ABSTRACT

Aim: Cartilage destruction has been associated with many factors such as overweight, excessive use of joints and forced movements, abrasion due to the aging process, and genetic factors. Obesity is a modifiable risk factor for osteoarthritis. This study aimed to determine the thickness of knee joint cartilage and demonstrate the impact of the pregnancy process on osteoarthritis development during pregnancy.

Material and Method: Fifty pregnant women aged 15-42 years, were included in this study. The ultrasound image of dominant knee distal femoral cartilage was measured at the 1st and 3rd trimesters in the lateral condyle, intercondylar area, and medial condyle from the strong anechoic area between the bone cortex and the suprapatellar fat pad.

Results: We found that the third trimester cartilage measurements for each of the nulliparous and multiparous pregnant women were significantly thinner than the first trimester cartilage measurements (p=0.001, p=0.005, p<0.001). A significant relationship was found between age, socioeconomic level, education level, employment status, body mass index, and knee cartilage ultrasound measurements (p=0.001 p=0.003, p=0.002, p= 0.001).

Conclusion: According to these results, although socioeconomic level, education level, employment status, and body mass index are factors affecting cartilage thickness, a significant decrease in joint cartilage measurement in multiparous women and the transition to the third trimester of pregnancy suggests that pregnancy is an important factor in the development of osteoarthritis.

Keywords: osteoarthritis, pregnancy, cartilage, joint, parity

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INTRODUCTION

Osteoarthritis is a non-inflammatory chronic degenerative disease characterized by progressive cartilage destruction, osteophyte formation, and subchondral sclerosis, especially in weight-bearing joints. It is most commonly seen on the knee, hip, wrist, and spine. The knee is the particularly affected joint in osteoarthritis (1).

In epidemiological studies conducted around the world, symptomatic knee osteoarthritis has been reported in 10-30% of individuals over 65 years of age (2). In studies, 33% of adults and 90% of individuals over 65 years of age have been radiologically shown to have osteoarthritis (3). Osteoarthritis is approximately twice as common in females than in males (1). Cartilage destruction has been associated with many factors such as overweight, excessive use of joints and forced movements, abrasion due to the aging process, and genetic factors (4). Obesity is a modifiable risk factor for osteoarthritis (1, 4). A positive correlation was reported between an increase in body mass index (BMI) and the incidence of osteoarthritis in the knee joint (4).

The pregnancy process is associated with an increase in body mass index due to its hormonal and physiological effects. The average weight gain in a normal pregnancy is approximately 12.5 kilograms (5). However, the weight gained during pregnancy is generally higher and the risk of obesity in pregnancy increases day by day (6). This excessive weight gain triggers osteoarthritis in the long term with the increase in load on the knee joints (4). Also, the studies have reported that the increase in the number of births in women leads to a decrease in knee, tibia, and total cartilage volume and an increase in cartilage defects (7). However, there are not many studies that clearly show the change in knee joint cartilage during pregnancy.

To the best of our knowledge, this is the first study investigating changes in the characteristics of knee joint cartilage during pregnancy. This study aims to determine the effect of the pregnancy process on osteoarthritis formation by observing the change in knee joint cartilage thickness during pregnancy.

This way, by showing whether the pregnancy itself or the weight gained during the pregnancy process have an effect on the knee joint cartilage, especially to those who want 2 or more children, would allow patients to be informed in advance about this issue and should give them the opportunity to protect themselves from a future risk of osteoarthritis.

MATERIALS AND METHOD

This prospective cohort study was conducted in accordance with the Declaration of Helsinki in a tertiary referral hospital between 01.02.2016 and 01.12.2016. Ethics committee approval was obtained from the same institution (15/1069). The follow-up of 50 pregnant women between the ages of 15 and 42, who underwent regular antenatal follow-up, was performed during pregnancy. Written informed consent was obtained from all participants. Pregnant women who did not attend regular antenatal follow-ups; pregnant women with knee operation history, polycystic ovary syndrome, chronic diseases (thyroid diseases, diabetes, chronic hypertension, etc.), and with diseases that may affect knee cartilage such as rheumatoid arthritis and osteoarthritis, and with current or past drug use that may affect the cartilage structure were not included in this study. In addition, pregnant women with pregnancy-related diseases such as gestational diabetes mellitus and preeclampsia were not included in the study since some physiological changes such as edema and weight gain may be exaggerated and may lead to different results in measurements.

Weight was measured by using an electronic scale, having asked the patients to remove their shoes, socks, and heavy garments. Height was measured asking patients to remove their shoes (8). The education level was classified into three categories: primary school, high school, and university. Clinical and sociodemographic characteristics of the women were recorded.

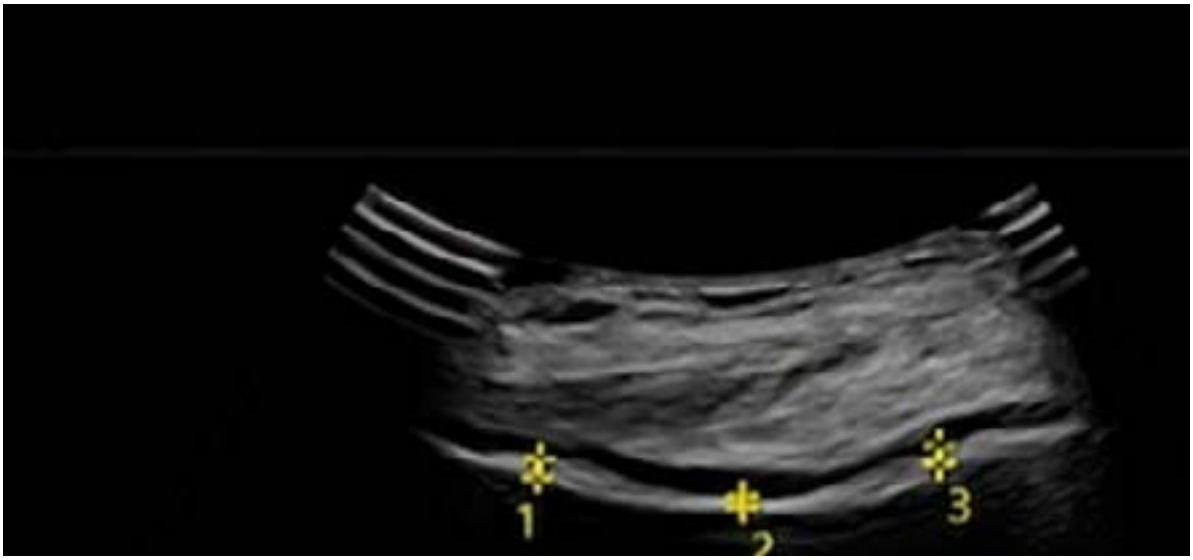
Ultrasound measurements were performed by a 5-7.5 MHz linear array transducer on an ATL HDI 5000 ultrasonography device with B-mode ultrasonography examinations by the same radiologist. An image was generated for each measurement of each patient.

For all participants, the ultrasound image of the dominant knee (defined as the stepping limb when starting to walk) was taken as the basis, and the same knee cartilage was measured at each measurement. Distal femoral cartilage measurements were made ultrasonographically with a linear probe. The patient's knee was imaged by placing the probe in an axial position on the suprapatellar region while it was in a comfortable position in maximum flexion. The measurements were obtained by measuring the lateral condyle, intercondylar area, and medial condyle from the strong anechoic area between the bone cortex and the suprapatellar fat pad at the distal femoral cartilage (9). Knee cartilage was measured in three regions: lateral tibial (1), patellar (2), and medial tibial (3) (Figure 1).

With a-priori power analysis, we calculated that the sample size needed to observe an effect size of 0.5, with a 0.05 significance and a 0.95 statistical power, was 45 patients.

Statistical analysis was performed by SPSS (Statistical Package for the Social Sciences) 22 (SPSS Inc., Chicago, IL). Descriptive analyses were given using tables of frequencies for the categorical variables and using mean and standard deviation for the normally distributed variables. The comparison of categorical variables was performed by the chi-square test, according to the relevant statistical test based on patient numbers regarding compared variables (Pearson Chi-Square Test, Yates Correction Chi-Square Test, Fisher's Final Test). Independent sample t-tests were used for the normally distributed continuous data. Paired t-tests were used for dependent continuous data statistical analysis. P values <0.05 were considered statistically significant.

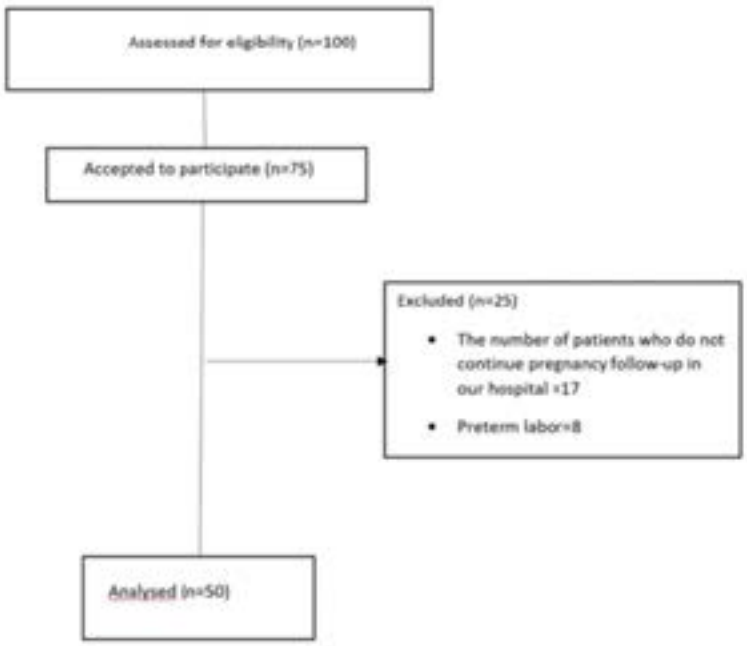
Figure 1. Ultrasonographic image demonstrating femoral cartilage measurements. (1: lateral tibial, 2: patellar 3: medial tibial)



RESULTS

A total of 75 randomly selected singleton pregnant women who accepted to participate were included in the study. However, in the following weeks, 17 pregnant women who did not continue their pregnancy follow-up in our hospital and 8 pregnant women who had preterm labor had to be excluded (Figure 2).

Figure 2. Flow diagram of pregnant patients participating in the study.



The comparison of the main characteristics of the nulliparous and multiparous women is given in Table1.The mean BMI of the first trimester and third trimester of multiparous participants was significantly higher than that of the nulliparous participants. The average height of the multiparous and nulliparous women who participated in the study was found to be similar, and multiparous women began the pregnancy process more overweight than nulliparous pregnant women in the first trimester and ended this process with more weight (Table 1). The mean age of theparticipants was 26.2 (17 – 37), and 8.0% of these women were working (Table 1).

Table 1. Comparison of the main characteristics of the nulliparous and multiparous

		Nulliparous (n=18) Mean±SD	Parous (n=32) Mean±SD	P value
Age (years)		23.0±4.2	28.6±5.4	0.001*
Menarche age (years)		14.6±1.2	13.2±1.4	0.159*
First gestational age (years)		22.5±3.7	20.3±3.2	0.215*
Smoking status %		16.7	21.9	0.730**
BMI (first trimester)		24.2±5.4	27.5±6.6	0.044*
BMI (third trimester)		30.8±6.3	33.6±6.8	0.018*
Education level %	Primary school	44.4	62.5	
	High school	33.3	34.4	
	University	22.2	3.1	0.087**

*Independent sample t-test, **Chi-square test

The correlation of education level, employment status, socioeconomic status, and smoking status with knee joint cartilage measurements is shown in Table 2.

Table 2. Correlation of education level, employment status, socioeconomic status, and smoking status with knee joint cartilage measurements

	Education status		Employment status		Socioeconomic level		Smoking status	
	Rho*	P**	Rho*	P**	Rho*	P**	Rho*	P**
Patella1st trimester	0.871	0.002	0.054	0.001	0.164	0.003	0.011	0.325
Patella 3rd trimester	0.099	0.003	0.079	0.005	0.325	0.003	0.013	0.324
Medial tibial 1st trimester	0.025	0.000	0.125	0.000	0.119	0.012	0.012	0.963
Medial tibial 3rd trimester	0.019	0.039	0.112	0.021	0.132	0.015	0.065	0.587
Lateral tibial 1st trimester	0.078	0.041	0.325	0.004	0.369	0.002	0.061	0.139
Lateral tibial 3rd trimester	0.312	0. 012	0.621	0.001	0.254	0.000	0.018	0.123

*Rho: correlation coefficient,**Spearman's correlation analysis

First and third-trimester femoral cartilage ultrasound measurements of participant nulliparous and multiparous pregnant women were compared, and the mean femoral cartilage measurements in all three regions (patella, medial tibial, lateral tibial) were found to be similar between nulliparous and multiparous women (Table 3).

Table 3. First and third trimester femoral cartilage ultrasound measurements of participant nulliparous and multiparous pregnant

women	Nulliparous (mm)	Parous (mm)	P value
Patella 1st Trimester	2.20(0.8)	2.10(0.9)	0.701
Patella 3rd Trimester	2.1(0.7)	1.99(0.6)	0.628
Medial tibial 1st Trimester	1.71(0.9)	1.41(0.6)	0.142
Medial tibial 3rd Trimester	1.32(0.4)	1.22(0.4)	0.532
Lateral tibial 1st Trimester	1.59(0.4)	1.41(0.3)	0.186
Lateral tibial 3rd Trimester	1.50(0.3)	1.35(0.4)	0.220

Independent sample t-test

There was a statistically significant difference in femoral cartilage measurements between the first trimester and third trimester in all three regions. The femoral cartilage measurements in all three regions of the third trimester were found to be thinner than the first trimester measurements of the participants (Table 4).

Table 4. Comparison of ultrasound measurements between first and third trimesters of participant pregnant women

	Joint ultrasound measurement (mm)	P value
Patella 1st Trimester Patella 3rd Trimester	0.104(0.02)	0.000
Medial tibial 1st Trimester Medial tibial 3rd Trimester	0.266(0.08)	0.005
Lateral tibial 1st Trimester Lateral tibial 3rd Trimester	0.078 (0.01)	0.001

Paired sample t-test

DISCUSION

In our study, we examined the impact of the pregnancy process on osteoarthritis development in the knee joint. We found that the third trimester cartilage measurements for each of the nulliparous and multiparous pregnant women were significantly thinner than the first trimester cartilage measurements ($p=0.001$, $p=0.005$, $p<0.001$). In addition, we determined a significant relationship between age, socioeconomic level, education level, employment status, body mass index and knee cartilage ultrasound measurements ($p=0.001$ $p=0.003$, $p=0.002$, $p= 0.001$).

Osteoarthritis is seen twice as often in women than in men. The risk of osteoarthritis increases with age. Osteoarthritis has been associated with certain genetic and internal diseases such as hypertension, hyperuricemia, diabetes mellitus, and PCOS (10). For this reason, we used the presence of diseases that may affect the knee joint as one of the exclusion criteria in our study. According to a study conducted on PCOS patients in Turkey, the femoral cartilage thickness of PCOS patients was found to be significantly thinner than in BMI matched control patients (11). Therefore, PCOS patients were excluded from the study due to the fact that PCOS could affect knee joint cartilage.

The mean age of nulliparous pregnant participants was 23, while the mean age of multiparous pregnant participants was 28.6, and no statistically significant relationship was found with the occurrence of osteoarthritis. Autopsy studies show that degenerative joint changes begin to appear in the second decade. X-ray findings start in the third decade and progress with age (12). These results are a strong aspect of our study to prevent the impact of the effect of increased age on the joint cartilage, since the evaluation was perfomed on a similar age group.

Studies have clearly shown the relationship between socioeconomic status, education level, working status and osteoarthritis (13-15). Similarly, we found that women with low socioeconomic status and education levels had lower knee cartilage measurements.

There are contradictions in the literature regarding the relationship between smoking status and osteoarthritis; while some show that the risk of osteoarthritis increases in smokers (16), some say that there is a protective effect from osteoarthritis because of increased glycosaminoglycans and collagen in smokers (17, 18), and some reports state that there is no significant difference between smokers and nonsmokers (19). In our study, the knee cartilage ultrasound measurements of smokers generally did not differ from non-smoking pregnant women. However, most pregnant women do not smoke as much as non-pregnant women; this may be the reason for this insignificance.

The relationship between parity and osteoarthritis has been demonstrated by recent studies (20). In their study, Wei et al. clearly demonstrated that increased parity causes knee joint patellar cartilage degeneration (7). Similarly, Wise et al. reported that the risk of osteoarthritis significantly increased in those who had a parity of four or higher (21). This relationship showed that the negative effect on knee cartilage was more prominent with the increasing number of live births. In our study, we did not find any significant difference between nulliparous and multiparous pregnant women in medial tibial, lateral tibial, and patellar cartilage ultrasound measurements in both the first trimester and third trimester. We thought this could be due to the low number of patients and the number of patients with parity above three in our study. However, in a study conducted in 14 nulliparous and 14 multiparous patients, it was shown that the risk of osteoarthritis increased as a result of the alteration of cartilage mechanics in multiparous patients (22). In addition, a study suggested that there is a relationship between abortion and knee osteoarthritis, and that it may increase knee osteoarthritis (23).

Obesity is defined as an osteoarthritis risk factor due to excessive load on the knee joints. There are many studies in the literature showing that there is a direct relationship between increased BMI and increased risk of osteoarthritis (24). In our study, the mean BMI of the first trimester and third trimester of multiparous participants was significantly higher than that of nulliparous participants. In both groups, a difference of approximately six units was found between the first trimester and the third trimester in both nulliparous and multiparous women. This showed that multiparous and nulliparous women had similar weight gain during pregnancy, and this was an indication of the fast weight gain of the participants during pregnancy. Our study showed that third trimester lateral tibial, medial tibial, and patellar cartilage measurements for each of the nulliparous and multiparous pregnant women were significantly thinner than the first trimester lateral tibial, medial tibial, and patellar cartilage measurements. This was attributed to the increase in BMI between the first and the third trimester. Although increased sex hormones such as estrogen and progesterone have a protective effect on cartilage during the pregnancy process, we think that increased BMI due to increased weight gain, increased load on the joint and excessive decrease in physical activity thins the knee joint cartilage thickness in the third trimester. However, it is known that there is a significant amount of weight loss in the first month, especially after the expulsion of the fetus and its attachments, the energy consumed by breastfeeding, and the disappearance of edema (25). We think that this thinning in the knee joint cartilage may revert to first trimester measurements in the third trimester by decreasing the load on the knee joint from losing excess weight. To understand whether cartilage ultrasound measurements are reversible, ultrasound measurements of the patients at the end of the postpartum period (after 40 days) are needed. In our study, it was not possible to reevaluate patient groups due to patient-related reasons, but we are confident that future studies will clarify this thesis.

Recently, the use of ultrasound in the detection of osteoarthritis has become widespread (26-28). In a study conducted by the EULAR study group on the use of ultrasound (USG) in osteoarthritis, USG was shown to be more sensitive than conventional radiography in detecting osteophytes and joint space narrowing in hand osteoarthritis (29). In a study, it was concluded that ultrasound, as an easily accessible, inexpensive and radiation-free modality, is helpful in revealing the factors associated with pain in knee osteoarthritis (30). The USG method was

found to be more sensitive than MRI, x-ray, and arthroscopic techniques (31).

This is the first study evaluating the changes in the characteristics of knee joint cartilage during pregnancy. However, in current USG imaging, the lack of standard scoring systems for the identification, detection, and grading of changes in osteoarthritis and structural damage, subjectivity in selection and interpretation of images, and the need for studies to determine the validity and reliability of USG in evaluating the pathology of osteoarthritis restrict the use of USG in the diagnosis of osteoarthritis. The patients included in this study were selected from the antenatal outpatient clinic, and no randomization was made. The patients who consented to participate were recruited, which could produce a selection bias. In order to minimize the risk of observer bias, only one sonographer made all the measurements. One limitation of our study was the lack of postpartum evaluation which was not performed due to patients` incompatibility and non-attendance.

In conclusion, according to these results, although the socioeconomic level, education level, empolyment status, and body mass index are factors affecting cartilage thickness, a significant decrease in joint cartilage measurement in multiparous women and the transition from the first trimester to the third trimester of pregnancy suggests that pregnancy is an important factor in the development of osteoarthritis.

We believe that more studies are needed with an increase in the number of participating patients, repeating the measurements at the end of the puerperium period, and adding non-pregnant women to the study group, which will contribute to our study in the future. Early diagnosis of osteoarthritis positively impacts public health by providing early intervention and early initiation of necessary life changes in patients. Therefore, women considering pregnancy should be informed that high weight gain and increased parity during pregnancy increase the risk of osteoarthritis.

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