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The association between knee osteoarthritis and polycystic ovary syndrome in postmenopausal women: preliminary results

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Abstract. – OBJECTIVE: The comorbidity of many risk factors associated with the etiology of osteoarthritis (OA) and polycystic ovary syndrome (PCOS) is commonly observed. However, to the best of our knowledge, there are no studies in literature on the relationship between PCOS history and knee OA development in postmenopausal women.

PATIENTS AND METHODS: A total of 120 postmenopausal women diagnosed with knee osteoarthritis who underwent surgical treatment in our orthopedic clinic and, 80 postmenopausal women who referred to our orthopedic clinic but did not have knee osteoarthritis were randomly included in our study. Body Mass Index (BMI) values, PCOS history and demographic data of the patients in both groups were examined.

RESULTS: PCOS was found to be an independent risk factor for OA. PCOS was 2.734 times effective in the development of knee OA, Odd ratio (95% confidence interval) = 2.734 (1.206-6.198) and *p*-value 0.016. BMI was found to be an independent risk factor for OA. BMI between 25-30 was found to be 2.783 times more effective on knee OA development when compared with BMI<25, Odd Ratio (95% confidence interval) = 2.783 (1.324-5.852) and *p*-value 0.07. In addition, BMI>30 was found to be 9.237 times more effective on knee OA development when compared with BMI<25, Odd Ratio (95% confidence interval) = 9.237 (3.992-21.374) and *p*-value <0.001.

CONCLUSIONS: The history of PCOS was found to be statistically significantly higher in the knee OA group. BMI and PCOS were found to be independent risk factors in the development of knee OA.

Key Words:
Knee osteoarthritis, Polycystic ovary syndrome, BMI, Postmenopause.

Introduction

Osteoarthritis (OA) is a degenerative disease of the knee joint (femorotibial and femoropatellar) which causes the gradual destruction of the joint cartilage. OA is a process which has an impact on daily vital physical activity caused by its effects on subchondral bone tissue, joint cartilage, connective tissue, synovial and fibrous joint capsule, cartilage tissue and periarticular muscle tissues. Symptomatic OA develops in one out of two individuals in the population until the age of 85[1]. Several factors, such as genetic, metabolic and mechanical problems can initiate this process, resulting in the loss of cartilage. Gender of the patient, ethnicity, joint instability, obesity, age and joint traumas are among the risk factors. Epidemiological studies show that knee OA rate is 58% higher in women compared with men[2]. Although it is believed that the biomechanical differences between females and males may be responsible for the higher incidence in women, there are no clear findings to support this view[3]. The difference between the genders causing this disparity between the prevalence of the disease has not been revealed yet. Sex steroids are known to have important effects on cartilage physiology, and it is known that the changes in these hormonal levels are risk factors for knee OA development[4].

PCOS is one of the endocrinal disorders commonly seen in women of reproductive age, resulting in deterioration in androgen and oestrogen levels. Its prevalence varies by region. According to Rotterdam Consensus Study Group, its prevalence is higher than 15% and its prevalence in overweight and obese women is higher than 30%[5,6]. Although there are many studies showing the association between estrogen and androgen hormones and, cartilage formation, the effect of hormones on OA development is still uncertain.

PCOS is a disease whose occurrence and development is associated with inflammatory factors and its pathogenesis has not been revealed yet. In recent studies, the levels of inflammatory markers such as CRP, interleukin -6 (IL-6) and

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tumor necrosis factor- α (TNF- α) have been shown to increase in PCOS[7,8].

Based on the existing information in literature on the effect of obesity, female gender, sex steroids and inflammatory factors in the etiology of knee OA development, the present study aims to examine the relationship between PCOS and knee OA.

Patients and Methods

In this study, a total of 150 postmenopausal patients over the age of 50 were randomly selected from the patient group who referred to our Orthopaedic clinic and who were diagnosed with grade 3 and grade 4 knee OA according to Kellegren-Lawrence criteria. These patients underwent surgical treatment between May 2015 and May 2020 and formed the Case Group (Group 1). A total of 100 postmenopausal patients over the age of 50 were randomly selected from the patient group who referred to the Orthopaedic outpatient clinic but who did not have osteoarthritis. These patients formed the Control Group (Group 2). The patients' files were reviewed and their age, BMI, PCOS history (the existence of two of the three diagnosis criteria (hyperandrogenism, ovulatory dysfunction, and PCOM) included in 2012 NIH Consensus was required for PCOS history) According to this recommendation, two out of three criteria (hyperandrogenism, ovulatory dysfunction, and PCOM) are required to diagnose PCOS[9]. The patients who had traumatic osteoarthritis, inflammatory arthritis and previous knee surgery history and the patients whose records did not have enough data were excluded from the study. In the knee OA group, 4 patients with traumatic OA; 12 patients with inflammatory arthritis; 4 patients with a history of knee surgery and 10 patients with insufficient data were excluded from the study. As for the Control Group, 20 patients with insufficient data were excluded from the study. As a result, 120 patients were included in the knee OA group and 80 patients were included in the control group.

The study was conducted in accordance with the principles of the Declaration of Helsinki.

This study was conducted as a retrospective review.

Statistical Analysis

The data were analyzed with SPSS 25 (Statistical Package for Social Sciences, IBM Corp., Armonk, NY, USA) package program. The results were considered as statistically significant at $p < 0.05$ level. Descriptive statistics were shown as mean ± standard deviation and median (minimum-maximum) for numerical values and as observation number and (%) for nominal variables. Kolmogorov Smirnov test and Shapiro-Wilks test were used to examine whether the numerical variables were distributed normally. Independent Samples *t*-test was used to reveal whether there was a statistically significant difference between the two groups in terms of the normally distributed numerical variables and, Mann-Whitney U test was used to evaluate whether there was a statistically significant difference in terms of numerical variables which were not normally distributed. Nominal variables were evaluated with Chi-square test. Binary logistic regression analysis was conducted to find out whether PCOS and BMI were effective on the development of osteoarthritis and oddsratios (OR), 95% confidence interval (95% CI) and *p*-values of each variable were noted.

Results

A total of 120 postmenopausal female patients were included in the knee OA group and 80 postmenopausal female patients were included in the control group of the study. Mean age of the patients in the knee OA group was found as 63.4±6.79 while mean age of the patients in the control group was found as 63.61±6.19.

PCOS prevalence was 35.0% (n=42) for the patients in knee OA group and 12.5% (n=10) for the patients in control group. Statistically significant difference was found between the patient and

Table I. Incidence of polycystic ovary syndrome (PCOS) history in knee osteoarthritis (OA) and control group.

Groups	PCOS historyn (%)		Total n (%)	*p*-value
	Yes	No		
Knee OA	42 (35.0%)	78 (65.0%)	120 (100.0%)	$p = 0.001$
Control	10 (12.5%)	70 (87.5%)	80 (100.0%)	

Table II. The association between knee osteoarthritis (OA) and control groups and body mass index (BMI).

Groups	BMI n (%)			Total n (%)	*p*-value
	< 25	25-30	> 30		
Knee OA	19 (15.8%)	39 (32.5%)	62 (51.7%)	120 (100.0%)	$p < 0.001$
Control	40 (50.0%)	28 (35.0%)	12 (15.0%)	80 (100.0%)	

control group in terms of the presence of PCOS (p=0.001) (Table I).

Of the postmenopausal women included in the study, 29.5% (n=59) were BMI<25, 33.5% (n=67) were BMI 25-30 and 37% (n=74) were BMI >30. In knee OA patients, mean BMI was 31 (19-43) while those in the control group had a mean BMI of 24.5 (18-35). Statistically significant difference was found between the patient and control group in terms of BMI groups (p<0.001) (Table II). PCOS and BMI distributions in knee OA and control group are shown in Table III. PCOS was found as an independent risk factor for knee OA. PCOS was found to be 2.734 times more effective on knee OA development, Odd Ratio (95% confidence interval) = 2.734 (1.206-6.198) and p-value 0.016. BMI was found as an independent risk factor for knee OA. BMI=25-30 was found to be 2.783 times more effective on knee OA development when compared with BMI<25, Odd Ratio (95% confidence interval) = 2.783 (1.324-5.852) and p-value 0.07. In addition, BMI>30 was found to be 9.237 times more effective on knee OA development when compared with BMI<25, Odd Ratio (95% confidence interval) = 9.237 (3.992-21.374) and p-value <0.001.

Discussion

Sex steroids are believed to have a significant role on cartilage physiology. When Cynomolgus monkeys underwent oophorectomy, they showed OA-specific histopathological changes, suggesting that oestrogen has a protective effect on cartilage health[10]. However, there is no clear data on the regenerative potentials of sex steroids on knee OA incidence, progression, and affected cartilage.

PCOS is the most common endocrinopathy in women of reproductive age and its aetiology and long-term negative effects have not been fully clarified. In PCOS, tumour necrosis factor alpha and interleukin-6, which are serum inflammatory markers increasing the risk of OA, increase. The risk increases as BMI and insulin resistance increase[11]. High IL-6 and TNF-a levels have been shown to be increased risk factors in the progression or radiographic knee OA[12]. In our study, a statistically significant association was found between knee OA development and PCOS history. Obesity is common in PCOS patients[5,6]. Obesity has been shown to be a significant risk factor in knee OA patients[13]. In PCOS, the prevalence of Type 2 DM, hyperlipidemia and metabolic syndrome increase compared with normal healthy women[14,15]. In the comorbidity of obesity and OA, components such as metabolic syndrome, type 2 diabetes and hyperlipidemia, which commonly accompany obesity, are also believed to contribute to the OA pathogenesis[16]. A statistically significant association was found between BMI and knee OA in our study.

The exogenous use of oestrogens has been shown to be beneficial in OA treatment in an-

Table III. Cross relationship of knee osteoarthritis and control groups and BMI and PCOS history.

Groups			BMI n (%)			Total n (%)	*p*-value
			< 25	25-30	> 30		
Knee OA	PCOS History	Yes	3 (7.1%)	12 (28.6%)	27 (64.3%)	42 (100.0%)	$p < 0.001$
		No	16 (20.5%)	27 (34.6%)	35 (44.9%)	78 (100.0%)	
		Total	19 (15.8%)	39 (32.5%)	62 (51.7%)	120 (100.0%)	
Control	PCOS history	Yes	5 (50.0%)	3 (30.0%)	2 (20.0%)	10 (100.0%)	
		No	35 (50.0%)	25 (35.7%)	10 (14.3%)	70 (100.0%)	
		Total	40 (50.0%)	28 (35.0%)	12 (15.0%)	80 (100.0%)	

imal models[17,18] and to have positive effects on knee joint cartilage volume in postmenopausal women who received HRT for more than 5 years[19]. It is a known fact that men have higher cartilage volume than women and have hyperandrogenemia in PCOS. We believe that the comorbidity of knee OA and PCOS is associated with increased frequency of obesity, type 2 DM and increased inflammatory markers in PCOS. Further studies are required on the possible positive effects of increased androgen and oestrogen levels on cartilage volume in PCOS. Diagnosing and treating PCOS patients in the reproductive period may prevent many morbidities including the knee OA. Although many long-term health problems have been defined in PCOS, there are no studies on its association with OA and it is hoped that our study will attract attention on this issue.

Limitations

The present study has some potential limitations. The data were evaluated from the Orthopaedic clinic of a tertiary hospital (a group of patients who mostly referred or were referred with the thought of surgical treatment). Therefore, there may be more serious OA cases than the primary health care services. The OA, PCOS and BMI in this population may be different from the normal population. However, to the best of our knowledge, since our study is the first one in literature evaluating the association between PCOS and knee OA independently from BMI, it will contribute to literature.

Conclusions

In conclusion, a statistically significant association was found between knee OA and PCOS history in our study, as well as a statistically significant association between knee OA and BMI. BMI and PCOS were found as independent risk factors in knee OA development. The link behind the relationship between PCOS and knee OA is not fully understood, and further studies are required to identify the underlying mechanisms.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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