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Original Article

Association of metabolic syndrome and its components with knee osteoarthritis in the older adults of Amirkola City

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Abstract

Background: Knee osteoarthritis is a very common disease that leads to mobility disabilities in older adults. In recent years, a link between metabolic syndrome and knee osteoarthritis has been reported. However, there are conflicting findings regarding this association. Our study was conducted to investigate the relationship between metabolic syndrome and its components and knee osteoarthritis in the older adults of Amirkola City.

Methods: In this case-control study, the diagnosis of knee osteoarthritis was based on the EULAR criteria. 590 older adults were examined in two groups of older adults with and without knee osteoarthritis. Both groups were compared on the frequency of metabolic syndrome and its components. Also, the variables of quadriceps femoris muscle strength, body mass index, physical activity level, and smoking were investigated as control variables between the two groups. Data was analyzed using SPSS 20 software and statistical tests of chi-square, t-test, and logistic regression. A significance level of $p< 0.05$ was considered.

Results: In this study, there was no significant relationship between knee osteoarthritis and metabolic syndrome (OR = 1.38, CI = 0.98–1.93, P = .06). Among the components of metabolic syndrome, waist circumference (P = 0.004) and blood pressure (P = 0.007) had a significant relationship with knee osteoarthritis. The variables of quadriceps femoris muscle strength, physical activity level, and age had a significant effect on knee osteoarthritis.

Conclusion: These findings show that knee osteoarthritis has no significant relationship with metabolic syndrome and its components, except for blood pressure and waist circumference.

Keywords: Knee osteoarthritis, Metabolic syndrome, Age, Blood pressure, Waist circumference.

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Knee osteoarthritis is a common musculoskeletal disorder in older adults, which manifests itself with joint pain and stiffness and, as a result, reduces individual performance and quality of life (1). Mechanical stress is considered to be the main cause of knee osteoarthritis, and the higher prevalence in old age and obesity indicates the relationship between mechanical stress and knee osteoarthritis (2). However, recently, many researchers have suggested that other factors such as genetic, neuroendocrine, and metabolic factors may also play a role in the pathophysiological mechanism of knee osteoarthritis (3). Metabolic syndrome is defined as a set of metabolic and non-metabolic disorders including high fasting blood glucose levels, high triglyceride levels, high blood pressure, low HDL-C levels, and increased waist circumference. People who have three or more criteria at the same time are diagnosed as having metabolic syndrome (4).

The basic mechanisms of the relationship between metabolic factors and osteoarthritis are not clear, but people with metabolic syndrome have a higher body mass index and inflammatory cytokines, which provide the basis for the development of osteoarthritis (5-7). Also, metabolic syndrome, as a subgroup of vascular risk factors, leads to subchondral ischemia. This may reduce gas and nutrient exchange between the subchondral bone and articular cartilage, thereby causing osteoarthritis (8, 9), but the evidence in this regard shows conflicting and ambiguous results (10-14). Limitations of previous studies have included their cross-sectional design and failure to control for potential confounding variables such as age, body mass index, and other health conditions (11, 15). Considering the importance of knee osteoarthritis in older adults, along with its complications and negative effects, and the inconsistencies found in other studies, this case-control study was conducted to investigate the relationship between metabolic syndrome and its components with knee osteoarthritis in older persons of Amirkola.

Methods

The present case-control study is a part of the second phase of the Amirkola Health and Ageing Project (AHAP), which has been ongoing since 2011 on all people aged 60 and over in Amirkla City (16). Of the 2135 older people aged 60 and over who participated in the second phase of the cohort study, a group of 295 people with knee osteoarthritis were randomly selected as a case group and a group of 295 people without knee osteoarthritis as a control group.

The number of men and women in both groups was the same. The older adults, who signed the informed consent form, were included in the study. Older people with incomplete information, a fracture history, associated collagen vascular diseases, trauma, and crystal arthropathies have been ruled out by a radiologist on standing knee radiographs in both anterior-posterior and lateral views, and diabetes, cancer, and kidney diseases were excluded from the study. Knee osteoarthritis was diagnosed according to the evidence-based recommendations of the European Union Rheumatology Association for the diagnosis of knee osteoarthritis (17). Accordingly, adults over 40 years of age who have knee pain during work, short-term morning stiffness, functional limitation, and one or more findings on routine assessment (crepitus, range of motion limitation, and bone enlargement) have knee osteoarthritis. The 2005 ATP III Adult Treatment Panel criteria were used to diagnose metabolic syndrome. Having three or more of the following components was considered a metabolic syndrome: systolic blood pressure ≥ 130 mmHg or the patient being treated, diastolic blood pressure ≥ 80 mmHg or the patient being treated, HDL-C is less than 40 in men and less than 50 mg/dl in women, or the patient is under treatment, triglyceride ≥ 150 mg/dl or the patient is under treatment, fasting blood sugar ≥ 100 mg/dL or the patient is undergoing treatment, and the waist circumference is greater than 88 cm for women and greater than 102 cm for men (18). Blood pressure was measured using an Omron sphygmomanometer, model 6M. Participants abstained from caffeine (coffee and tea) and tobacco for thirty minutes before the measurement. They laid supine and rested for five minutes before the blood pressure was taken. The cuff was positioned on the bare arm of the participants two to three centimeters above the elbow crease, and then the individual's blood pressure was measured twice, with the average of these two readings recorded as the patient's blood pressure (16).

To measure blood glucose and lipids, fasting venous blood sample was collected. The tests were performed by Pars Azmoun kits and the electrolyte analyzer model Response 910. Body mass index (BMI) is calculated based on the formula BMI (kg/m2) = weight (kg) ÷ height 2 (m2). Waist circumference (cm) is the distance between the upper ridge of the iliac bone and the lower part of the edge of the lower rib, parallel to the ground, and hip circumference (cm) is measured at its largest part while standing and wearing a thin dress. They were measured using a tape measure. If their difference was less than 1 cm, their average was recorded, and if it was more, both measurements were repeated (19). Weight (kg) was measured by a Seca digital scale with minimal clothing with an accuracy of 0.1 kg, and height (cm) was measured by a standing scale with an error of 0.5 cm. In this study, data on physical activity was gathered using the standard Physical Activity Survey for the Elderly (PASE) questionnaire.

This 10-item questionnaire captures the time individuals spent on walking, moderate and vigorous physical activity, home activities, and work activities over the past seven days, divided into three sections. The total PASE score was calculated by multiplying the time spent on each activity (hours/day during the past seven days) or participation in the activity (yes/no) by the PASE weight, which was determined through empirical research involving a sample of the elderly population. Finally, all PASE scores from the three sections were summed (20, 21). The strength of the quadriceps femoris muscle of both lower limbs was evaluated by an experienced physiotherapist using a dynamometer and recorded in kilograms (22). The strength

of the quadriceps muscle was measured at the maximum contraction of this muscle, and the highest strength of three measurements was considered for analysis. The reliability of the quadriceps muscle strength measurements by this tool was confirmed using the test-retest method in 20 consecutive patients, in whom the quadriceps muscle strength measurement was repeated after 30 minutes of rest. The correlation coefficient between the two tests was 0.97 (P= 0.001). The validity of the tool was tested with specified weights of metals of 5 kg, 10 kg, and 20 kg at the beginning of the study and then during the study periods (23).

For statistical analysis, at first, the data were entered into SPSS 20 statistical software. In this study, knee osteoarthritis served as the dependent variable, while metabolic syndrome and its components acted as the independent variables. An independent t-test was used to examine quantitative variables, and the chi-square test was used for two or more qualitative variables. The relationship between metabolic syndrome and its components and knee osteoarthritis was investigated through crude model logistic regression. Also, to examine the role of variables affecting knee osteoarthritis in the entire older persons, the backward multiple logistic regression test was used. A p-value of less than 0.05 was considered significant. Also, the odds ratio was examined as an effect size.

Results

In this case-control study, 590 older adults aged 60 years and older from Amirkola city were studied. The mean waist circumference, age, quadriceps femoris muscle strength, body mass index, and physical activity level were significantly different between the two groups with and without knee osteoarthritis.

The demographic characteristics of the participants are shown in table 1. In this study, 52.8% of the older adults with metabolic syndrome and 44.8% of the older adults without metabolic syndrome had knee osteoarthritis; the difference was not statistically significant (P= 0.06) (table 2). Also, the crude model regression analysis showed that the chance of knee osteoarthritis in older adults with metabolic syndrome was 38% higher than in older adults without metabolic syndrome. However, this relationship was not statistically significant (CI = 0.98-1.93, OR = 1.38, P = 0.06). Logistic regression analysis shows that the chance of knee osteoarthritis in older adults with a high waist circumference is two percent higher than in older adults without a high waist circumference. This relationship was statistically significant (P = 0.004). Also, the chance of knee osteoarthritis in older adults with low HDL-C is 13% higher than in older adults without low HDL-C. However, this relationship was not statistically significant (P = 0.46). Logistic regression analysis shows that the chance of knee osteoarthritis in older adults with high blood pressure is 82% higher than in older adults without high blood pressure. This relationship was statistically significant (P = 0.007). Also, the chance of knee osteoarthritis in older adults with high triglycerides is 20% higher than in older adults without high triglycerides. However, this relationship was not statistically significant (P = 0.28). Logistic regression analysis shows that the chance of knee osteoarthritis in older adults with high fasting blood sugar is one percent lower than in older adults without high fasting blood sugar. This relationship was not statistically significant (P = 0.93).

Table 1. Characteristics of quantitative variables studied in two knee osteoarthritis and control group

Variable	Without OA Mean±SD	With OA Mean±SD	P-Value
Age (years)	69.13±7.28	72.51±8.84	<0.001
waist circumference (Cm)	90.79±10.25	93.47±11.64	0.003
Systolic blood pressure (mm Hg)	141.37±21.81	144.43±22.90	0.09
Diastolic blood pressure (mm Hg)	83.65±13.63	84.80±12.78	0.29
HDL-C (mg/dl)	53.82±13.31	53.49±14.89	0.77
Triglyceride (mg/dl)	150.43±98.09	150.75±82.33	0.96
Fasting blood sugar (mg/dl)	112.27±46.82	113.16±53.16	0.82
Quadriceps femoris muscle strength (kg)	20.27±9.97	16.20±8.87	<0.001
BMI (kg /m2)	27.82±4.67	29.20±5.14	<0.01
Physical activity level (Numerical score)	104.76±61.50	77.98±48.67	<0.001

HDL-C: High-density lipoprotein-cholesterol, BMI: Body Mass Index

Table 2. Characteristics of qualitative variables studied in two groups with and without knee osteoarthritis

Variable	Odds ratio	Confidence Internal	P-Value
Metabolic syndrome	1.38	0.98 – 1.93	0.06
Waist circumference	1.02	1.00 – 1.03	0.004
HDL-C	1.13	0.82 – 1.56	0.46
Blood pressure	1.82	1.18 – 2.82	0.007
Fasting blood sugar	0.99	0.71 – 1.36	0.93
Triglyceride	1.20	0.86 – 1.66	0.28

HDL-C: High-density lipoprotein-cholesterol

A backward model logistic regression test was used to determine the role of influencing variables on knee osteoarthritis in the studied population. The variables entered into the model in the first stage included metabolic syndrome, age, body mass index, quadriceps femoris muscle strength, physical activity level, and smoking. Logistic regression analysis shows that the chance of knee osteoarthritis in older adults with high fasting blood sugar is one percent lower than in older adults without high fasting blood sugar. This relationship was not statistically significant (P = 0.93).

A backward model logistic regression test was used to determine the role of influencing variables on knee osteoarthritis in the studied population. The variables entered into the model in the first stage included metabolic syndrome, age, body mass index, quadriceps femoris muscle strength, physical activity level, and smoking. As can be seen in table 3, in the first step of logistic regression analysis, the backward model was shown by controlling the effect of control variables. These variables include body mass index, physical activity level, and quadriceps femoris muscle strength, age, smoking, and waist circumference. The chance of knee osteoarthritis in older adults with metabolic syndrome was 7% higher than in older adults without metabolic syndrome. This relationship was not statistically significant (CI = 0.70-1.64, OR = 1.07, P = 0.74). Also, the variables of age, quadriceps femoris muscle strength (OR=0.96-0.98, CI=0.94-0.001), physical activity level (CI=0.992-0.999, OR=0.995, P=0.009) had a significant role in the development of knee osteoarthritis. The smoking variable in the second step, the metabolic syndrome variable in the third step, and the physical index variable in the fourth step were removed from the model. In the last stage, four variables of waist circumference, age, and quadriceps femoris muscle strength, and physical activity level remained significant.

Table 3. Logistic regression analysis to determine the role of influencing variables on knee osteoarthritis in the total elderly population under investigation.

Variable	First step			Last step		
	Odds ratio	Confidence Internal	P-Value	Odds ratio	Confidence Internal	P-Value
Metabolic syndrome	1.07	0.70 – 1.64	0.74	-	-	-
Waist circumference	1.02	0.99 – 1.05	0.097	1.04	1.02– 1.06	<0.001
BMI						
≤25	1			-	-	-
25 – 29.99	1.57	0.87 – 2.83	0.12	-	-	-
≥30	1.83	0.85 – 3.95	0.11	-	-	-
Quadriceps femoris muscle strength	0.96	0.94 – 0.98	0.001	0.96	0.94 – 0.98	<0.001
Physical activity level	0.99	0.992 – 0.999	0.009	0.99	0.991 – 0.998	0.002
Smoking	1	0.56 – 1.77	0.98	-	-	-

Variable	First step			Last step		
	Odds ratio	Confidence Internal	P-Value	Odds ratio	Confidence Internal	P-Value
Age						
60 – 64	1			1		
65 - 69	1.94	1.09 – 3.44	0.02	1.99	1.13 – 3.50	0.01
70 – 74	3.72	1.90 – 7.26	<0.001	3.79	1.97 – 7.29	<0.001
75 - 79	3.59	1.56 – 8.23	0.003	3.39	1.52 – 7.56	0.003
≥80	2.68	0.94 – 7.62	0.015	3.23	1.25 – 8.36	0.01

BMI: Body Mass Index

Discussion

The results of the present study showed that knee osteoarthritis has a significant relationship with blood pressure and waist circumference. However, knee osteoarthritis has no significant relationship with metabolic syndrome, HDL-C, triglycerides, and fasting blood sugar. In the following, each of the above cases and comparisons with other studies will be mentioned more fully.

In the present study, it was shown that the chance of knee osteoarthritis in older adults with metabolic syndrome was 38% higher than in older adults without metabolic syndrome. After controlling for confounding variables, the chance of knee osteoarthritis in older adults with metabolic syndrome was seven percent higher than in older adults without metabolic syndrome. However, the relationship between metabolic syndrome and knee osteoarthritis was not statistically significant, which is consistent with previous studies (26-24). A study by Daqing Nie et al. shows that metabolic syndrome is not an independent risk factor for knee osteoarthritis (27). Some studies (28, 29), showed that metabolic syndrome increases the likelihood of osteoarthritis, but this association did not remain significant after adjusting for confounding factors such as weight and BMI. Some studies show that metabolic syndrome is associated with high degrees of knee osteoarthritis (30), so the absence of a significant association between metabolic syndrome and knee osteoarthritis in our study may be attributed to the association of metabolic syndrome with severe knee osteoarthritis, which was not investigated in our research. Also, the high prevalence of metabolic syndrome in older adults in Amirkola compared to other regions may affect the results. In East Asian countries, the prevalence of metabolic syndrome is between 10 and 20%, according to WHO and ATP III definitions (31, 32). In the Iranian population, the overall prevalence of this syndrome is 29% according to ATP III (33), but the prevalence of the metabolic syndrome, according to the definition of ATP III 2005 in the city of Amirkola was 71.9% (32). Also, the studies of Dong-xing Xie et al. (14), and Lee et al. (10) have shown a significant relationship between metabolic syndrome and knee osteoarthritis.

In our study, it was shown that the chance of knee osteoarthritis in older adults with a high waist circumference is 2% higher than in older adults without a high waist circumference; this relationship was statistically significant. It was also shown in the logistic regression analysis of the backward model that waist circumference has an effective role in knee osteoarthritis (CI=1.00-1.06, OR=1.04, p<0.0001). Past studies (29, 34, 35) have shown that waist circumference has a significant relationship with knee osteoarthritis.

Although the exact mechanism of the relationship between osteoarthritis and obesity has not yet been fully determined, studies report the existence of mechanical and metabolic factors in this relationship (36). Studies have shown that adipose tissue secretes adipokines such as leptin, adiponectin, visfatin, and resistin (37). The study by Dumond et al. shows that the level of leptin in the synovial fluid of patients with osteoarthritis is higher than that of normal people, and leptin plays an important role in the pathophysiology of osteoarthritis (38). Existing studies suggest that leptin may be related to inducing the expression of several pro-inflammatory factors and destructive enzymes (39-41). Also, the abnormal and high production of leptin in osteoblasts of the subchondral bone of the joint of people with osteoarthritis leads to disruption in the secretion of alkaline phosphatase, β-TGF, osteocalcin, and collagen type 1 in these cells (42). The local increase in leptin concentration directly affects the proliferation and differentiation of osteoblasts, and it has been shown in studies that by increasing the systemic concentration of leptin, bone production is indirectly suppressed by a

mechanism related to the hypothalamus (43). In addition, the accumulation of cholesterol in cartilage can impair the outflow function of cartilage, thereby causing osteoarthritis (44, 45). The results of the present study show that the chance of knee osteoarthritis in older adults with high blood pressure is 82% higher than in older adults without high blood pressure. This relationship was statistically significant (P= .007). Recent studies have shown that blood pressure has a significant relationship with knee osteoarthritis (25, 26, 34). The relationship between high blood pressure and joint degenerative changes can be explained by the fact that cartilage is an avascular tissue. Therefore, disruption of blood flow causes interference in the exchanges between nutrients and oxygen and leads to further destruction of cartilage (8).

There is a hypothesis that the vascular pathology of small subchondral vessels can lead to local ischemia and subsequent osteoarthritis (8, 46). Le Clanche et al. (47) investigated a possible pathologic pathway between hypertension and osteoarthritis in one study and attributed the association between hypertension and osteoarthritis to a reduction in the capacity of cells to produce nitric oxide, as hypertension causes narrowing of blood vessels (48). which leads to decreased blood flow in subchondral bone, thereby compromising nutrient and oxygen exchange and cartilage destruction (8). This subchondral ischemia can also induce osteocyte apoptosis in the subchondral bone, which again can lead to osteoclast recruitment and subchondral bone loss (49). Some past studies show contradictory results (25, 34).

Our results show that the chance of knee osteoarthritis in older adults with high triglycerides is 20% higher than in older adults without high triglycerides. But this relationship was not statistically significant, which is similar to previous studies (50-52). A study by Zhang et al. showed that high levels of triglycerides can cause inflammation, which in turn can cause joint damage (53). Also, the studies of Marko Nemet et al. (54) and Sanchez-Santos MT et al. (13) showed that high triglyceride levels have a significant relationship with knee osteoarthritis. In the present study, there was no significant relationship between fasting blood sugar and knee osteoarthritis, which is consistent with the results of previous studies (51, 55). The study by Sopasakis VR et al. showed that supraphysiological concentrations of glucose lead to glucose uptake, hyaluronan synthesis, and matrix integrity and induce anti-inflammatory effects by promoting cartilage repair in chondrocytes studied in vitro (56). Studies by Marko Nemet et al. (54) and Kumar Dubey et al. (57) show that fasting blood sugar has a significant relationship with knee osteoarthritis.

In the present study, the chance of knee osteoarthritis in older adults with low HDL-C is 13% higher than in older adults without low HDL-C. However, this relationship was not statistically significant. This result is similar to the results of other studies (25, 50, 51). The anti-inflammatory and antioxidant properties of HDL-C are important for maintaining joint health, and low levels of HDL-C may lead to increased inflammation and oxidative stress in the knee joint and contribute to the development and progression of osteoarthritis (58). Also, an increase in free fatty acids and a decrease in HDL may play an important role in endothelial dysfunction and a decrease in vascular reactivity (59). Also, the studies of Dong-xing Xie et al. (14) and Min Zhou et al. (60) showed that HDL-C has a significant relationship with knee osteoarthritis. Limitations and Strengths: Due to the case-control study design, the causal relationship between variables remained unclear. The instrument used in our study to diagnose knee osteoarthritis does not provide information on disease severity for grading purposes. Furthermore, confounding factors such as diet and occupation were not controlled for in this study. However, our study's strength was its control of variables such as physical activity level, quadriceps femoris muscle strength, and smoking as confounders. The findings of our study show that knee osteoarthritis has no significant relationship with metabolic syndrome and its components, except blood pressure and waist circumference.

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Conflict of interests: The authors declare that there are no conflicts of interest.

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