doi.org/10.36721/PJPS.2020.33.1.SUP.295-298.1

Association between obesity and risk of knee osteoarthritis

Bushra Khan[1]*, Obaid Yusuf Khan[2], Sitwat Zehra[1], Abid Azhar[1], and Sehrish Fatima[1]
[1]Dr. A. Q. Khan Institute of Biotechnology and Genetic Engineering (KIBGE), University of Karachi, Karachi, Pakistan
[2]Department of Genetics, University of Karachi, Karachi, Pakistan

Abstract: The study was designed to investigate the association between obesity and the risk of knee osteoarthritis, recruiting 400 knee osteoarthritis patients and an equal number of controls. After the informed consent, diagnosed patients from Jinnah Post Graduate Medical Centre, Karachi were included as "cases". Age-matched individuals without the disease were included as "controls". Sociodemographic data were taken from each participant. Characteristics were compared by odds ratio and chi-square using SPSS 20 software. Obesity (OR 3.29; 95% CI 2.40-4.51), female gender (OR 2.87; 95% CI 1.94-4.25) and family history (OR 3.61; 95% CI 2.69-4.85) were found to be significantly associated with osteoarthritis (p<0.001). Highest OR was found in case of stair climbing >10 flights/d (OR 6.08; 95% CI 4.16-8.89; p<0.001), whereas heavy lifting (>25 kg/d for > 4 hr) was observed as another major factor with OR of 5.24 (95% CI 3.54-7.75; p<0.001) that elevates the risk. The study concluded that obesity is significantly associated with osteoarthritis and obese individuals (BMI≥25 kg/m^2) are at high risk of disease development. Furthermore, family history, prolonged standing (>2 h/d for ≥1 yr), heavy lifting (>25 kg/d for > 4 hr), stair climbing (>10 flights/d) and sitting on the floor (≥5 h/d) might also be associated with knee osteoarthritis.

Keywords: Osteoarthritis, joint, osteophytes, obesity, cartilage

INTRODUCTION

Osteoarthritis (OA) is considered as the most common arthritis with low-grade inflammation of synovial joints (Berenbaum, 2013). According to WHO, 9.6% of men and 18.0% of women aged above 60 years are suffering from OA, 80% of them have movement limitations and 25% are unable to do their daily living activities (Wittenauer, 2013). It is estimated that 27 million individuals are suffering from OA in the United States while 8.5 million in the United Kingdom (Neogi, 2013). About 100 million people have OA globally with knee OA (KOA) incidence being the highest (Cross *et al.,* 2014). A recent study suggests that KOA patients are very likely to reduce their physical activities that contribute to frailty and other adverse outcomes associated with it (Wanaratna *et al.,* 2019).

The chronic disease is characterized by cartilage loss as a result of rubbing of bones together in the joint leading to pain and stiffness with impaired movement. The cartilage degradation may expose the subchondral bone to damage in later stages of the disease (Man and Mologhianu, 2014). The actual cause is unknown, but various genetic and environmental causes have been implicated including age, gender, obesity, trauma, malalignment, dysplasia and excessive joint use (Felson *et al.,* 2013). Regular heavy lifting (>25kg/d for >4 hr) and high body mass index (BMI) have also been reported for their association with KOA (Lohmander *et al.,* 2009; Palmer, 2012).

According to a recent study, low fasting concentrations of glucose (<81.98 mg/dl) and varus malalignment (femur-tibial-angle < -2.31°) were found very critical for the disease risk rather than BMI (Driban *et al.*, 2018). However, some studies suggest that obese individuals (BMI≥25 kg/m^2) show higher disease manifestations due to subchondral bone densification that is considered as a very important component for developing OA (Burr and Gallant, 2012). Besides, the correlation between subchondral trabecular bone (SCTB) microarchitectural changes and weight has also been demonstrated which shows that bone densification may lead to cartilage degeneration process (Reina *et al.,* 2017). These studies may clarify the higher prevalence of KOA in obese individuals. Therefore, the current study is based on obesity and various other risk factors' involvement in KOA development.

MATERIALS AND METHODS

For executing the research work, approval was taken from both the ethical committee of Dr. A. Q. Khan Institute of Biotechnology and Genetic Engineering (KIBGE) and Institutional Review Board (IRB) of Jinnah Post Graduate Medical Centre (JPMC). Participants aged over 30 years were recruited after informed consent. Four hundred KOA patients who visited the hospital from January 2016 to December 2018 were included as "cases". Diagnostic criteria were based on the Kellgren-Lawrence (K-L) grading system. Patients with grade 2 or more (with osteophytes formation and narrowed joint space) were included. Patients were excluded if they had chronic infections such as rheumatoid arthritis, trauma, injury and other bone and joint disorders. An equal number of age-matched healthy individuals were included as "controls." The sociodemographic data of each participant were

*Corresponding author: e-mail: bushra.khan@kibge.edu.pk

recorded. BMI was measured based on the recommended criteria for Asians (Misra and Dhurandhar, 2019).

STATISTICAL ANALYSIS

The data were analyzed through SPSS 20 software. Mean with standard error of the mean (SEM) were calculated for the continuous variables. Categorical variables were presented in frequency and percentages. For comparing baseline characteristics, *p*-values were computed through chi-square for the categorical variables and student *t*-test for the numerical variables. Multivariate logistic regression analyses were used for the assessment of association between obesity and KOA risk. Other variables that were evaluated include family history, prolonged standing (>2 hr/d for ≥1 yr), heavy lifting (>25 kg/d for > 4 hr), stair climbing (>10 flights/d) and sitting on the floor for home activities (≥5 h/d). The exposure variables that remained significant at a 5% level were considered to have an independent association with the disease risk.

RESULTS

Demographic characteristics' comparisons

Demographic and clinical characteristics of the study population are shown in Table 1. The age of onset of KOA was 48.39 ± 0.57 years. The mean duration of the disease was 2.34±0.16 years. Bone spurs were observed in 198 (49.5%) while meniscal injuries in 58 (14.5%) patients. A comparison of demographic characteristics across the categories of cases and controls is presented in Table 2. The most affected age group was found between 41-50 years representing about 40% of the patients. Statistically, a significant difference was observed in the gender distribution of the patients and controls (p<0.001). KOA was found more prevalent in females as compared to males and the ratio of affected females to males was about 8:1. Besides, weight and BMI values were significantly higher in the patients as compared to controls (p<0.001). Table 3 shows the association of the study variables among cases and controls. Approximately 44% cases and 19% controls were obese (BMI≥25 kg/m^2) while 55.2% cases and 80.2% controls had BMI<25 kg/m^2.

The risk conferred by the study variables

Strongly increased KOA risk was found for obesity (OR 3.29; 95% CI 2.40-4.51; p<0.001). Odds ratio (OR) for KOA by category of obesity are shown in Table 4. Similarly, the female gender showed a significant association with KOA (OR 2.87; 95% CI 1.94-4.25; p<0.001). The risk is elevated further to 3.12 (95% CI 2.09-4.65; p<0.001) after the age adjustment. Family history has also shown a significant association with the disease risk (OR 3.61; 95% CI 2.69-4.85; p<0.001) and the risk is elevated further when adjusted for the age, gender and BMI (OR 3.93; 95% CI 2.58-5.99; p<0.001). The highest OR was found in case of stair climbing >10 flights/d (OR 6.08; 95% CI 4.16-8.89; p<0.001) whereas heavy lifting (>25 kg/d for > 4 hr) is another major factor with OR of 5.24 (95% CI 3.54-7.75; p<0.001) that elevates the risk.

Table 1: Descriptives of all study variables

Group	N (%)
Gender	
Female	657 (82.1)
Male	143 (17.9)
Obesity status	
BMI<25 kg/m^2	542 (67.8)
BMI≥25 kg/m^2	258 (32.2)
VAS*	6.31 ± 0.06
WOMAC*	55.2 ± 0.75
Disease duration (yr)	2.34 ± 0.16
KL grade	
2	319 (79.7)
3	41 (10.3)
4	40 (10.0)
Affected joint sites	
Knee	359 (89.8)
Knee and hip	5 (1.2)
Knee and hand	28 (7.0)
Knee with multiple joints	8 (2.0)

VAS*: Visual Analogue Scale
WOMAC*: Western Ontario and McMaster Universities Osteoarthritis Index

DISCUSSION

Obesity and OA, both are chronic conditions. Obesity is considered the major problem globally and its burden has been rising at an alarming rate (Seidell and Halberstadt, 2015). During a single stance, three to six times body weight is exerted across the knee joint. Therefore, increased body weight may exert additional burden across the joint in obese individuals (Felson, 1995).

Several studies have reported a significant association of obesity with musculoskeletal disorders which shows that bone size might be critical for OA development (Kortt and Baldry, 2002). Increased BMI may enhance the subchondral bone size of knee and the joint surface area may expand to respond to the higher loads (Ding *et al.,* 2005). Besides, denser subchondral bone may also increase the mechanical stresses on the cartilage in weight-bearing joints that narrow down the joint space. Similarly, the study supports that obesity might be a potent risk factor of KOA as more than 44% of the patients were obese (Dorais *et al.,* 2018). The risk conferred in obese individuals is approximately 3 times higher than individuals with BMI<25kg/m^2. However metabolic activities and joint biomechanics may also play

Table 2: Baseline characteristics of cases and controls

Parameters	Controls	Cases	*p-value
Age (Mean ± SEM)	48.45 ± 0.52	50.44 ± 0.49	-
Male/Female	101/299	42/358	<0.001
BMI (kg/m^2)	26.10 ± 0.25	38.10 ± 0.45	<0.001

SEM: Standard Error of Mean, BMI: Body Mass Index, **p*- value was calculate using t-test and chi-square test.

Table 3: Distribution and association of the study variables among cases and controls

Study variables	Controls	Cases	*p-value
BMI<25 kg/m^2	321 (80.2%)	221 (55.2%)	<0.001
BMI≥25 kg/m^2	79 (19.8%)	179 (44.8%)	
Age group (31-40 yr)	137 (34.2%)	82 (20.5%)	-
Age group (41-50 yr)	119 (29.8%)	163 (40.8%)	-
Age group (51-60 yr)	104 (26.0%)	98 (24.5%)	-
Age group (61-70 yr)	40 (10.0%)	57 (14.2%)	-
Family history of OA	165 (41.2%)	287 (71.7%)	<0.001
Prolonged standing >2 h/d for ≥1 yr	233 (58.3%)	300 (75.0%)	<0.001
Heavy lifting >25 kg/d for > 4 hr	258 (64.5%)	362 (90.5%)	<0.001
Stair climbing >10 flights/d	236 (59.0%)	359 (89.8%)	<0.001
Sitting on the floor ≥5 h/d	218 (54.5%)	277 (69.2%)	<0.001

**p*-value was calculated using chi-square test.

Table 4: Factors associated with the occurrence of KOA (n=800)

Characteristics	OR (95% CI)	p- value	*AOR (95% CI)	p- value
Male	1		1	
Female	2.87 (1.94-4.25)	<0.001	3.12 (2.09-4.65)	<0.001
BMI<25 kg/m^2	1		1	
BMI≥25 kg/m^2	3.29 (2.40-4.51)	<0.001	3.79 (3.02-4.86)	<0.001
Family history (No)	1		1	
Family history (Yes)	3.61 (2.69-4.85)	<0.001	3.93 (2.58-5.99)	<0.001
Prolonged standing >2 h/d for ≥1 yr (No)	1		1	
Prolonged standing >2 h/d for ≥1 yr (Yes)	2.15 (1.59-2.96)	<0.001	2.20 (1.39-3.47)	<0.05
Heavy lifting >25 kg/d for > 4 hr (No)	1		1	
Heavy lifting >25 kg/d for > 4 hr (Yes)	5.24 (3.54-7.75)	<0.001	6.76 (4.44-10.33)	<0.001
Stair climbing >10 flights/d (No)	1		1	
Stair climbing >10 flights/d (Yes)	6.08 (4.16-8.89)	<0.001	5.68 (3.86-8.36)	<0.001
Sitting on the floor ≥5 h/d (No)	1		1	
Sitting on the floor ≥5 h/d (Yes)	1.88 (1.40-2.51)	<0.001	2.05 (1.51-2.78)	<0.001

OR: odds ratio, CI: confidence intervals, *AOR: adjusted odds ratio for all variables

a crucial role in KOA acceleration besides the body mass (Driban *et al.,* 2018).

The female gender showed a significant association with KOA risk. The gender-based risk was more than twice and increased to three times after the age adjustment that represents three times higher disease risk in older females. It might be due to the accelerated cartilage degradation after menopause. As estrogen hormone deficiency in females after menopause lowers the cartilage turnover process thereby increases the disease risk on aging (Yu *et al.,* 2019).

Family history also exhibited three times more disease risk because of the considerable involvement of inheritance in OA (Zhang *et al.,* 2011). Moreover, poor socioeconomic factors including prolonged standing (>2h/d for ≥1 yr), heavy lifting (>25 kg/d for >4hr), stair climbing (>10 flights/d) and sitting on the floor for home activities (≥5 h/d) showed higher association with the disease risk. The risk conferred by prolonged standing (>2 h/d for ≥1 yr) was two times higher with further increase in the risk upon adjustment for age, gender, and BMI. Likewise, heavy lifting (>25kg/d for >4hr), stair climbing (>10 flights/d) and sitting on the floor for home activities

(≥5 h/d) also exhibited considerable risk when adjusted for age and gender (Dahaghin *et al.,* 2009; Jensen, 2008; Seidler *et al.,* 2008). It might be due to the lack of awareness and fewer opportunities to maintain a healthy lifestyle or access to healthcare centers (Wanaratna *et al.,* 2019). Throughout the study, BMI was found as a consistent predictor of KOA such as the risk conferred by heavy lifting (>25 kg/d for > 4 hr) and stair climbing (>10 flights/d) was extremely high when adjusted for BMI. These findings reveal the significant contribution of obesity in KOA development. However, the area of obesity and KOA risk still requires further investigations.

CONCLUSION

The study found that obesity is significantly associated with KOA and obese individuals (BMI≥25 kg/m^2) are at risk of disease development. Besides, family history, prolonged standing (>2h/d for ≥1 yr), heavy lifting (>25kg/d for >4 hr), stair climbing (>10 flights/d) and sitting on the floor (≥5 h/d) might also be associated with increased risk of KOA.

REFERENCES

Berenbaum F (2013). Osteoarthritis as an inflammatory disease (osteoarthritis is not osteoarthrosis!). *Osteoarthr Cartil.,* **21**(1): 16-21.

Burr DB and Gallant MA (2012). Bone remodelling in osteoarthritis. *Nat. Rev. Rheumatol.,* **8**(11): 665.

Cross M, Smith E, Hoy D, Nolte S, Ackerman I and Fransen M (2014). The global burden of hip and knee osteoarthritis: Estimates from the global burden of disease 2010 study. *Ann. Rheum Dis.,* **73**(7): 1323-1330.

Dahaghin S, Tehrani Banihashemi SA, Faezi ST, Jamshidi AR and Davatchi F (2009). Squatting, sitting on the floor, or cycling: Are life long daily activities risk factors for clinical knee osteoarthritis? Stage III results of a community based study. *Arthritis Care Res.,* **61**(10): 1337-1342.

Ding C, Cicuttini F, Scott F, Cooley H and Jones G (2005). Knee structural alteration and BMI: A cross sectional study. *Obes Res.,* **13**(2): 350-361.

Dorais M, Martel-Pelletier J, Raynauld JP, Delorme P and Pelletier JP (2018). Impact of oral osteoarthritis therapy usage among other risk factors on knee replacement: a nested case-control study using the Osteoarthritis Initiative cohort. *Arthritis Res Ther.,* **20**(1): 172.

Driban JB, McAlindon TE, Amin M, Price LL, Eaton CB and Davis JE (2018). Risk factors can classify individuals who develop accelerated knee osteoarthritis: Data from the osteoarthritis initiative. *J Orthop Res.,* **36**(3): 876-880.

Felson DT (1995). Weight and osteoarthritis. *J Rheumatol.,* **43**: 7-9.

Felson DT, Niu J, Gross KD, Englund M, Sharma L and Cooke TD (2013). Valgus malalignment is a risk factor for lateral knee osteoarthritis incidence and progression: Findings from the Multicenter Osteoarthritis Study and the Osteoarthritis Initiative. *Arthritis Rheum.,* **65**(2): 355-362.

Jensen LK (2008). Knee osteoarthritis: Influence of work with heavy lifting, kneeling, climbing stairs or ladders, or combining kneeling/squatting with heavy lifting. *Occ. Environ Med.,* **65**(2): 72-89.

Kortt M and Baldry J (2002). The association between musculoskeletal disorders and obesity. *Aust. Health Rev.,* **25**(6): 207-214.

Lohmander LS, de Verdier MG, Rollof J, Nilsson PM and Engstrom G (2009). Incidence of severe knee and hip osteoarthritis in relation to different measures of body mass: a population-based prospective cohort study. *Ann Rheum.,* **68**(4): 490-496.

Man GS and Mologhianu G (2014). Osteoarthritis pathogenesis a complex process that involves the entire joint. *J. med life.*, **7**(1): 37-41.

Misra A and Dhurandhar NV (2019). Current formula for calculating body mass index is applicable to Asian populations. *Nutr Diabetes.*, **9**(1): 3.

Neogi T (2013). The epidemiology and impact of pain in osteoarthritis. *Osteoarthr Cartil.,* **21**(9): 1145-1153.

Palmer KT (2012). Occupational activities and osteoarthritis of the knee. *Br Med Bull.,* **102**: 147-170.

Reina N, Cavaignac E, Pailhe R, Pailliser A, Bonnevialle N and Swider P (2017). BMI related microstructural changes in the tibial subchondral trabecular bone of patients with knee osteoarthritis. *J. Orthop. Res.,* **35**(8): 1653-1660.

Seidell JC and Halberstadt J (2015). The global burden of obesity and the challenges of prevention. *Ann Nutr Metab*., **66**(Suppl.2): 7-12.

Seidler A, Bolm-Audorff U, Abolmaali N and Elsner G (2008). The role of cumulative physical work load in symptomatic knee osteoarthritis a case-control study in Germany. *J Occup Med Toxicol*., **3**(1): 14.

Wanaratna K, Muangpaisan W, Kuptniratsaikul V, Chalermsri C and Nuttamonwarakul A (2019). Prevalence and Factors Associated with Frailty and Cognitive Frailty Among Community-Dwelling Elderly with Knee Osteoarthritis. *J. Community Health,* **44**(3): 587-595.

Wittenauer R, Smith L and Aden K (2013). Background paper 6.12 osteoarthritis. *World Health Organization*., 1-31.

Yu J, Mursu E, Typpo M, Laaksonen S, Voipio HM and Pesonen P (2019). MMP-3 and MMP-8 in rat mandibular condylar cartilage associated with dietary loading, estrogen level, and aging. *Arch Oral Biol.,* **97**: 238-244.

Zhang W, McWilliams DF, Ingham SL, Doherty SA, Muthuri S and Muir KR (2011). Nottingham knee osteoarthritis risk prediction models. *Ann Rheum Dis.,* **70**(9): 1599-1604.