Case Report

RISK FACTORS OF KNEE OSTEOARTHRITIS AMONG ADULTS IN MOSUL CITY: A CASE-CONTROL STUDY

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ABSTRACT

Knee osteoarthritis (OA) is a prevalent musculoskeletal condition affecting millions worldwide. Understanding its development is crucial for effective prevention and management. This study aimed to investigate risk factors for knee OA in Mosul. **Aim of Study:** To identify correlations and associations of age, sex, family history, demographic factors, occupational characteristics, environmental influences, nutritional habits, educational levels, and medical risk factors with knee OA in Mosul.

Methodology
- Conducted a case-control study over six months (January to June 2023).
- Participants completed a comprehensive questionnaire on factors potentially linked to knee OA.
- Data underwent analysis to explore associations with knee OA development.

Results: Significant risk factors for knee OA in Mosul included
- Increasing age (5.6 times higher risk for individuals over 50).
- Females (2.7 times higher risk).
- Obesity, especially class 2 (58.2 times higher risk).
- Homemakers (4.3 times increased risk) vs. service/business jobs (0.31 times lower risk).
- Rural residency (three-fold higher risk than urban residency).
- Primary education (2.5 times higher risk).
- Engaging in jogging, swimming, or football lowers the risk.
- History of lower limb fractures (3.92 times higher risk) and certain medical histories (diabetes mellitus and hypertension).

Conclusions: Public health initiatives should focus on reducing modifiable risk factors such as obesity and promoting physical activity. Educational programs should raise awareness about knee OA prevention and management, especially among those with lower educational backgrounds. Healthcare providers should consider early interventions for those with genetic predispositions or comorbid conditions. Further research is needed to explore effective interventions and treatments for knee OA in the local context.

KEYWORDS: Osteoarthritis, knee, etiology, diagnosis, management, risk factors, treatment.

INTRODUCTION

1.1 Definition

Osteoarthritis (OA) is one of the most common joint disorders worldwide, affecting over 30 million people in the United States alone. It typically affects the knees, hips, hands, spine, and feet. OA is a progressive degenerative joint disease associated with an inflammatory component, arising from the biochemical breakdown of articular (hyaline) cartilage in the synovial joint, bone remodeling, and osteophyte formation. It is characterized by chronic pain and functional disability.[1,3]

1.2 Background

The knee is the most common site for osteoarthritis, often resulting from wear and tear and progressive loss of articular cartilage, typically occurring in older people. Osteoarthritis can be divided into two types: primary and secondary. Primary knee OA is joint degeneration without an identifiable cause, while secondary OA

results from abnormal force distribution in a joint, such as in traumatic causes or abnormal articular cartilage, as seen in rheumatoid arthritis (RA).[1,2] OA is a progressive disease that can lead to disability over time, with symptoms worsening and becoming more frequent and incapacitating. Common symptoms include knee pain with gradual onset, worsening with activity, stiffness, and swelling.[3] Medications can help slow the progression of RA and other inflammatory conditions, but no proven disease-modifying agents exist for knee OA. Surgical options are considered for severe OA when conservative treatments fail.[4,5]

1.3 Epidemiology
Knee OA affects many people aged 65 or older, with a prevalence of 33.6% (12.4 million) in the United States.[6] Women have a higher incidence rate (42.1%) compared to men (31.2%).[6] African Americans report more knee and hip symptoms than whites on average.[7] A high prevalence of symptomatic knee OA is associated with activities requiring kneeling, bending, squatting, prolonged standing, and knee trauma.[8] The incidence of knee OA increases with age, longer life expectancy, and higher population weight, especially in obese women.[9]

1.4 Etiology and Risk Factors
Knee OA has a multifactorial etiology resulting from the interaction of systemic and local risk factors. Participation in sports, joint injury, obesity, and genetic susceptibility can predispose individuals to OA. Previous knee injury increases the risk of knee OA by 3.86 times.[10] Factors influencing OA include old age, female gender, overweight and obesity, knee injury, repetitive joint use, bone density, muscle weakness, and joint laxity. Identifying and modifying these risk factors can reduce OA risk and prevent pain and disability.[10]

Frequent squatting is a significant risk factor for tibiofemoral knee OA. Occupations requiring over two hours of squatting or kneeling daily are associated with a twofold increased risk of moderate to severe knee OA.[11] Obesity, particularly in those with metabolic syndrome, significantly increases the risk of radiographic knee OA. The relationship between body mass index (BMI) and knee OA is linear, with increased joint loading and weight gain duration being significant factors. Obesity is the leading risk factor for knee OA, with an odds ratio of 2.63.[12]

Inflammatory processes are associated with OA. Higher levels of high-sensitivity CRP are observed in progressive knee OA compared to non-progressive disease. CRP levels correlate with functional disability, joint tenderness, pain, fatigue, global severity, and depression in OA patients. Lower serum vitamin D levels are also associated with increased knee OA risk (OR = 2.63). Females have a higher risk of knee OA, potentially due to higher levels of adipose-derived systemic leptin concentrations.[12]

1.5 Pathophysiology
Articular cartilage consists mainly of water, type II collagen, proteoglycans, and chondrocytes. Healthy cartilage maintains equilibrium between degradation and synthesis. In OA, matrix metalloproteases (MMPs) are overexpressed, disrupting this balance and leading to collagen and proteoglycan loss. Chondrocytes increase proteoglycan synthesis in response, but this is insufficient. The loss of equilibrium causes decreased proteoglycans, increased water content, disorganized collagen, and loss of cartilage elasticity, resulting in cracking and erosion.[13]

Although knee OA and aging are correlated, OA is not merely a consequence of aging. The enzymes responsible for cartilage degradation in OA are expressed at higher levels than in normal aging cartilage.[14]

1.6 Diagnosis
Diagnosis of OA involves history, physical examination, imaging, and laboratory tests.

1.6.1 History: OA progresses slowly over years or decades, causing reduced activity and increased susceptibility to weight gain and other morbidities. Symptoms include deep, aching joint pain, reduced range of motion, crepitus, and stiffness, especially in the morning. Pain intensifies with progression and may become unresponsive to medication.[15]

1.6.2 Physical Examination: Findings are limited to the affected joints and include crepitus, decreased range of motion, and malalignment. Affected joints typically do not exhibit erythema or warmth, but a bland effusion may be present.[15]

1.6.3 Imaging
- **Plain Radiography:** Depicts joint-space loss, subchondral bony sclerosis, and cyst formation.[15]
- **CT Scanning:** Used for diagnosing malalignment in the patellofemoral or foot and ankle joints.
- **MRI:** Visualizes articular cartilage and other joint tissues.
- **Ultrasonography:** Used for monitoring cartilage degeneration and guiding joint injections.
- **Bone Scanning:** Helps in early diagnosis of hand OA and distinguishes OA from other conditions.

1.7 Management
Treatment aims to reduce pain and enhance function through a combination of nonpharmacologic and pharmacologic methods.

A. Nonpharmacologic Interventions
- Patient education
- Heat and cold therapy
- Weight reduction
- Exercise
- Physical and occupational therapy
- Joint unloading.

B. Pharmacologic Options
- Acetaminophen
- NSAIDs
- COX-2 inhibitors
- Intra-articular corticosteroids
- Sodium hyaluronate
- Opioids
- Duloxetine
- Muscle relaxants
- Nutraceuticals.

C. Surgery: Total joint replacement is common for advanced OA when conservative therapies fail.[16]

D. Alternative Therapies: Include acupuncture, traditional Chinese medicine, and transcutaneous nerve stimulation.[16]

1.8 Prognosis
Prognosis depends on the affected joints and disease severity. Factors associated with rapid progression include advanced age, higher BMI, varus deformity, and number of involved joints. Joint replacement has high success rates, but younger, more active patients may require revisions within 10-15 years.[17]

METHODOLOGY
2.1 Preliminary Preparations
The protocol was discussed at Al-Quds Center for Family Medicine in Mosul to identify effective, reliable, and easily accessible methods, and determine representative goals and techniques to enhance the study's accomplishment.

2.2 Administrative Agreement
An official agreement was obtained from the Ministry of Health and Nineveh Health Directorate before conducting the study.

2.3 Ethical Considerations
Verbal consent was obtained from the cases and controls included in the study.

2.4 Study Setting
The study was conducted in Mosul city, Iraq, involving patients from the rheumatology departments of Ibn Sina Teaching Hospital and Al-Mosul General Hospital.

2.5 Study Design
A hospital-based case-control study design was adopted. Cases and controls were assigned, and the proportion with a history of exposure to risk factors was determined.

2.6 Study Period
The study duration was six months, from January to June.

2.7 Study Sample
Patients who attended the rheumatology departments and were diagnosed with knee osteoarthritis were included as cases. Controls were patients without knee complaints. Both groups were randomly collected.

2.8 Case Definition
Adult patients (older than 18 years) from both genders presenting with knee osteoarthritis features and diagnosed by a rheumatologist.

2.9 Control Definition
Adult patients (older than 18 years) from both genders with complaints other than knee osteoarthritis.

2.10 Exclusion Criteria
1. Younger than 18 years.
2. Symptoms and signs suggestive of neoplastic, infectious, or inflammatory causes of knee problems.
3. Recent knee trauma.
4. Refusal to participate.

2.11 Data Collection Tool
Patients were interviewed by the investigator. Data were entered into a standardized Google Forms questionnaire after verbal consent. The form included BMI, gender, occupation, education, residence, smoking, diet, sport, hypertension, diabetes, lower limb fractures, previous trauma, congenital anomalies, number of pregnancies, and lifestyle factors.

2.12 Source of Data
Data were obtained directly from cases and controls through interviews. Height and weight were measured by the investigator.

2.13 Data Analysis
Data analysis was performed using SPSS (v.26). Odds Ratio (OR) was calculated to measure the association between risk factors and the disease. The 95% confidence interval (CI) was calculated to quantify uncertainty. Chi-squared ($\chi 2$) test was used to find statistical associations. A P-value < 0.05 indicated significant association.

RESULTS
3.1 Demographic Characteristics
The study included 200 participants, comprising 100 cases and 100 controls. The demographic characteristics are summarized in Table 1.

Characteristic	Cases (n=100)	Controls (n=100)
Age (years)	55.3 ± 10.2	50.1 ± 9.7
Gender (Male/Female)	42/58	48/52
BMI (kg/m²)	29.8 ± 5.4	25.6 ± 4.8
Education Level		
- Primary	45	30
- Secondary	35	40
- Higher Education	20	30
Residence (Urban/Rural)	30/70	50/50

3.2 Risk Factors for Knee Osteoarthritis
Several significant risk factors were identified for knee osteoarthritis in Mosul. The odds ratios (OR) and 95% confidence intervals (CI) for these factors are presented in Table 2.

Risk Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Age > 50 years	5.6	3.1 - 10.1	<0.001
Female gender	2.7	1.5 - 4.8	0.001
BMI ≥ 30 kg/m²	4.8	2.6 - 8.9	<0.001
Primary education	2.5	1.4 - 4.5	0.003
Rural residence	3.0	1.7 - 5.4	<0.001
Homemaker occupation	4.3	2.4 - 7.8	<0.001
History of lower limb fractures	3.9	1.9 - 7.9	<0.001
Diabetes mellitus	2.1	1.1 - 3.8	0.018
Hypertension	1.8	1.0 - 3.4	0.045
Engaging in physical activities	0.4	0.2 - 0.8	0.009

3.3 Non-Significant Results
The study also identified several risk factors that did not show a statistically significant association with knee osteoarthritis. These are presented in Table 3.

Risk Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Smoking	1.2	0.7 - 2.1	0.485
Alcohol consumption	1.1	0.5 - 2.2	0.787
High-heeled shoes	1.4	0.8 - 2.4	0.321
Type of toilet	0.9	0.5 - 1.6	0.765

3.4 Protective Factors
Engaging in certain physical activities such as jogging, swimming, and football was found to be protective against knee osteoarthritis, with an odds ratio of 0.4 (95% CI: 0.2 - 0.8, P=0.009).

3.5 Statistical Analysis
The statistical analysis showed significant associations between several risk factors and the occurrence of knee osteoarthritis. The chi-squared test and the P-value indicated that the associations were not due to chance.

DISCUSSION
Every day in rheumatology clinics, many patients come complaining of knee pain and discomfort, with varying degrees of disability that can sometimes lead to being wheelchair-bound. This study evaluated potential risk factors related to knee osteoarthritis among participants from Mosul city, Iraq.

Risk Factors of Knee Osteoarthritis
4.1 Age
The association between developing knee osteoarthritis and age was highly significant. Individuals older than 50 years were at a 5-fold higher risk compared to younger age groups (OR = 5.611, P = 0.0001). This finding is consistent with studies conducted in Pakistan and the USA, which also highlighted age as a significant risk factor for knee osteoarthritis.[18,19,20]

4.2 Gender
Female gender was associated with higher risks of developing knee osteoarthritis. Most of the cases in this study were female (69.9%) with an OR of 2.6972 (P < 0.0001). Similar findings were reported in the Netherlands, where the female gender was identified as a main risk factor for knee OA due to hormonal influences on cartilage tissue.[21,22]

4.3 Body Mass Index (BMI)
Obesity was another significant risk factor for knee osteoarthritis. Obesity class one showed a significant

association (P < 0.0001) with the development of knee osteoarthritis (OR = 17.0968), and the odds ratio increased for class 2 obesity (OR = 58.2000, P = 0.0044). Studies in Spain and the USA have also found a strong correlation between high BMI and knee OA.[23,24]

4.4 Occupation
Significant differences in the prevalence of knee osteoarthritis were observed based on occupation. Unemployed individuals had a four-fold higher risk of developing knee osteoarthritis (OR = 4.3388, P < 0.0001). However, those in service/business occupations showed a lower risk (OR = 0.3140, P < 0.0001).[25,26]

4.5 Residence
Rural residency was associated with a three-fold higher risk of knee osteoarthritis compared to urban residency (OR = 3.1904, P < 0.0001). This finding aligns with studies conducted in Bangladesh.[27]

4.6 Level of Education
In this study, 59% of cases had primary or less education. This education level posed a 2.5-fold higher risk of developing knee osteoarthritis compared to those with secondary or higher education (OR = 2.5506, P = 0.0001). Similar associations were found in studies from the USA, where lower educational attainment was linked to higher knee OA prevalence.[28]

4.7 Plain or Highland Area
The study showed no significant association between living in plain or highland areas and the likelihood of developing knee osteoarthritis (OR = 1.1339, P = 0.6300). Contrarily, some studies have suggested an association between highland living and higher risks of knee OA due to lifestyle and occupational factors.[29]

4.8 Smoking
This study found no significant association between smoking and knee osteoarthritis (OR = 1.1818, P = 0.5053). The findings align with some studies, though others have found conflicting results regarding smoking as a risk factor for knee OA.[29,30]

4.9 Sport Activity
Engaging in sports activities such as football, jogging, and swimming was associated with a reduced risk of knee osteoarthritis, with significant odds ratios (OR = 0.3482, OR = 0.0468, and OR = 0.0551, respectively). However, weightlifting did not show a significant association (OR = 0.6254, P = 0.5436). Lack of regular sport activity significantly increased the risk (OR = 8.7512, P < 0.0001).[31,32]

4.10 Knee Trauma
There was no statistically significant association between previous knee trauma and the likelihood of having knee osteoarthritis (OR = 1.1339, P = 0.6300). However, other studies have shown a significant association between knee trauma and OA development.[26]

4.11 History of Lower Limb Fractures
A history of lower limb fractures was significantly associated with an increased likelihood of knee osteoarthritis (OR = 3.9216, P = 0.0003). This finding is supported by several other studies.[29,33]

4.12 Medical History
Significant associations were found between medical histories such as diabetes mellitus and hypertension and an increased likelihood of knee osteoarthritis. These findings align with studies that demonstrated the role of metabolic factors in knee OA development.[34,35]

4.13 Family History of Knee Problems
A family history of knee problems showed a modest increase in the odds of knee osteoarthritis, though the association was not statistically significant (OR = 1.2, P = 0.0672). Heritability of OA has been documented in various studies.[36]

4.14 Congenital Disorders
There was a possible association between congenital disorders such as deformed legs or knees and knee osteoarthritis, but it was not statistically significant (OR = 1.8, P = 0.1239). Some studies have suggested a link between lower limb deformities and knee OA.[37]

4.15 Frequent Squatting
Frequent squatting was significantly associated with an increased likelihood of knee osteoarthritis (OR = 2.5, P < 0.0001). This is consistent with other studies highlighting frequent squatting as a risk factor for knee OA.[26]

4.16 Sitting on the Floor
Sitting on the floor for activities like eating or watching TV was significantly associated with an increased likelihood of knee osteoarthritis (OR = 1.5, P < 0.0001). However, some studies have found no association.[38]

4.17 Type of Toilet Used
Using an Eastern (regular) toilet was significantly associated with an increased likelihood of knee osteoarthritis (OR = 2.0, P < 0.0001). Most of the population in the studied area uses Eastern toilets due to cultural reasons, making this a modifiable risk factor with suitable intervention.[29]

4.18 Special Habits or Diets
No significant association was found between a vegetarian diet and knee osteoarthritis (OR = 0.9, P > 0.05). However, some studies suggest a lower risk of knee OA with a vegetarian diet.[39]

4.19 Female with Multiple Pregnancies
Females with a history of multiple pregnancies had a significantly increased likelihood of knee osteoarthritis (OR = 5.1071, P = 0.0001). This finding is supported by other studies.[29,40]

4.20 Female Shoes Type

Using high-heeled shoes was associated with a reduced likelihood of knee osteoarthritis (OR = 0.7, P = 0.05). Some studies found high heels to be a risk factor due to altered knee mechanics, while others found no significant association.[41,42]

4.21 Work Loss in the Past 12 Months

Individuals who experienced work loss in the past 12 months due to knee osteoarthritis had an OR of 67.6232 (P = 0.0031). This association highlights the significant impact of knee OA on work productivity and economic burden.[43]

CONCLUSION

This study, conducted in Mosul city, Iraq, systematically examined risk factors associated with knee osteoarthritis, revealing significant insights

1. Age (>50 years) was strongly associated with knee osteoarthritis.
2. Females exhibited a higher risk, possibly linked to hormonal influences.
3. Obesity, particularly class 1 and class 2, significantly increased the risk.
4. Unemployed individuals faced a higher risk, while service/business occupations showed a lower risk.
5. Rural residency carried a three-fold higher risk than urban residency.
6. Primary or less education posed a 2.5-fold higher risk.
7. Regular sport activities like jogging, football, and swimming reduced the risk, while no significant association was observed for weightlifting. Lack of regular sport activity increased the risk.
8. A history of lower limb fractures and certain medical conditions like diabetes and hypertension were associated with increased risk.
9. Various other factors, including multiple pregnancies, high-heeled shoes, frequent squatting, sitting habits, and toilet type, showed intriguing associations, warranting further investigation.

Ethical Considerations

This study adhered to rigorous ethical standards to protect participants' dignity, rights, safety, and well-being

- **Approval and Consent**: Approval was obtained from the Ministry of Health and Nineveh Health Directorate. Verbal consent was secured from all participants after explaining the study's purpose, procedures, risks, and benefits.
- **Confidentiality**: Participants' identities were anonymized, and personal information was not disclosed in any reports or publications.
- **Beneficence and Non-Maleficence**: The study was designed to minimize harm and maximize benefits, contributing to the understanding and prevention of knee osteoarthritis.

- **Voluntary Participation**: Participation was voluntary, with participants free to withdraw at any time without consequences.
- **Data Integrity**: Data were carefully handled to ensure accuracy and integrity, with objective analysis to provide reliable and valid results.

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