

Gender Differences in Osteoarthritis of Knee: An Indian Perspective

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ABSTRACT

Introduction: The global burden of knee osteoarthritis (KOA) is on the rise with advancing age, as life expectancy is improving worldwide. The literature shows a higher prevalence and incidence of KOA in women. The gender differences are seen not only in the developing world but also in the developed world. KOA at advanced stage can be quite disabling affecting the individuals' functioning capacity. The available treatment modalities can improve the quality of life significantly. The aim of this review is to study the gender differences in epidemiological and clinical aspects of KOA in Indian population. **Methods:** The keywords "knee osteoarthritis, Gender, India," "knee osteoarthritis, Sex, India," and "knee osteoarthritis, Prevalence, India" are used for data search for retrieving data from Indian studies in MEDLINE and Google Scholar. The broad inclusion criteria were clinical and radiological diagnosis of KOA, inclusive of both men and women and excluded articles with rheumatoid arthritis, inflammatory arthritis, and secondary causes of arthritis. **Results:** A total of 18 articles were found to fulfill the broad inclusive criteria. Majority of the articles were cross-sectional prevalence studies either done in a community setup or in tertiary care hospitals. The overall prevalence of KOA in these studies ranges from 27.1% to 66.1%, depending on the lower age limit of the study population. Postmenopausal women are affected more than premenopausal women. High body mass index, hypertension, diabetes mellitus, and osteoporosis were the common comorbid conditions. **Discussion & Conclusion:** The gender difference in the incidence and prevalence is seen in several cross-sectional studies and case series in the Indian literature. However, there is a paucity of data on clinical presentation, progression of the diseases, disability scoring at various stages of the KOA, and management.

KEYWORDS: *Epidemiology, gender, India, knee, osteoarthritis*

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INTRODUCTION

The global burden of knee osteoarthritis (KOA) is on the rise with advancing age as life expectancy is improving worldwide. The prevalence of the KOA is higher in the Asian continent compared to Europe and North America. The literature shows a higher prevalence and incidence of KOA in women with evidence in abundance.^[1,2] The gender bias is noted not only in presentation of several diseases but also in access to treatment facilities in several countries including both developed and developing countries. The cultural factors, socioeconomic status, availability of health-care facilities and geographic factors may have an impact on the prevalence of gender bias in KOA not only in India but also in the Western world too.^[3]

KOA can be described as primary or secondary degeneration of the articular cartilage of the joint. It is a multifactorial disease which causes symptoms not limited to pain, stiffness, swelling, and difficulty in walking. Clinical assessment of the knee joint, depending on the severity of the disease, shows tenderness, swelling or effusion in the knee, wasting of the quadriceps muscle, osteophyte formation, crepitus, correctable or fixed deformity, and decreased range of movement of the

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knee. Diagnosis of KOA is confirmed by a radiograph of the knee showing subchondral sclerosis, osteophytes, reduction in the joint space, subchondral cyst formation, and deformity of the knee. Kellgren–Lawrence classification is used to stage the severity of disease.^[4]

The aim of this review is to study the gender differences in epidemiological and clinical aspects of KOA in Indian population.

METHODS

The MEDLINE database was searched using keywords “knee osteoarthritis, Gender, India,” “knee osteoarthritis, Sex, India,” and “knee osteoarthritis, Prevalence, treatment, India.” The retrieved articles were manually checked for both original and review articles published in English in indexed journals. As the number of articles was few, data search extended to EMBASE and SCOPUS, which also did not retrieve articles for intended purpose. Hence, Google Scholar searched with the same keywords which had number of papers published on prevalence of KOA in various states in India. The articles retrieved from both MEDLINE and Google Scholar were manually checked. The inclusion criteria for the articles were availability of data on clinical and radiological diagnosis of osteoarthritis, data on number of both male and female participants, and also articles with pre- and postmenopausal data on KOA. The search criteria also included articles with gender variation in anthropometric data, biochemical markers, and genetic factors and excluded articles with rheumatoid arthritis, inflammatory, and secondary causes of KOA.

RESULTS

A total of 18 articles were found which fulfill the broad inclusive criteria. Majority of the articles were cross-sectional prevalence studies either done in a community setup or in tertiary care hospitals. The crude prevalence of KOA in the study population increased as the lower age limit increased. The overall prevalence of KOA in these studies ranges from 27.1% to 66.1%, depending on the lower age limit of the study population. Consistently, in all the studies, the prevalence is increased with age, significantly higher in women (51%, range: 31.6–77) than men (33.09%, range: 28.1–61.5), higher rates in urban than rural, and more common in people with higher body mass index (BMI). The lower socioeconomic class is found to have higher rates. These studies also report a higher rate of KOA in people who do less physical activity with sedentary lifestyle than those who do regular exercise with active lifestyle. Hypertension, diabetes mellitus, and osteoporosis are frequently associated comorbidities.^[5-7]

Postmenopausal women are affected more than premenopausal women.^[8] Homemakers were found to have a higher rate than professionals.^[5] The higher waist–hip ratio correlated positively with a higher risk of KOA in the females, whereas triceps skinfold thickness correlated positively in the males.

Pathophysiology

The normal articular cartilage is a complex avascular, aneural, and alymphatic nonimmunogenic tissue made of 5% cells and 95% of extracellular matrix. The ground substance is made of 75% of water held together by proteoglycans which have a protein core in aggrecan molecule. Cartilage also has numerous glycoproteins such as cartilage oligomeric matrix protein (COMP), laminin, lubricant, cartilage matrix protein, cartilage matrix glycoprotein along with degradative enzymes like matrix metalloproteinases (MMPs), collagenases, gelatinases, and membrane-associated MMPs. The collagen and water content decreases from superficial to deep zone while proteoglycan content increases in a specialized structural arrangement which helps in absorbing the shear and compressive forces without undergoing damage.

In osteoarthritis, both microscopic and macroscopic changes occur in both the cartilage and the subchondral bone. Repeated microtrauma along with the process of aging disrupts the collagen and proteoglycan meshwork resulting in a significant increase in the water content in the superficial zone of the cartilage. This change in the microenvironment in the cartilage stimulates the chondrocytes repair mechanism causing proliferation of the cells increasing DNA synthesis, increased degradative enzymes like MMPs and collagenases which causes fatigue wear microscopically followed by macrowear of the cartilage. The subchondral bone becomes stiff with interspersed cystic changes which provide uneven support to the overlying articular cartilage resulting in further mechanical damage due to high stress and low cyclical loading or low stress and high cyclical loading. There is, however, no difference between the sexes in the mechanism of micro- and macrowear of the cartilage in osteoarthritis.

DISCUSSION & CONCLUSION

Gender variance is one of the several factors affecting the prevalence of KOA. Women were having a higher incidence and prevalence of KOA irrespective of genetics, age, ethnicity, race, socioeconomic status, and demographic factors.

Genetics

Mishra *et al.*^[9] studied the role of polymorphism in growth differentiation factor-5, estrogen-specific receptor-alpha, and calmodulin-1 (CALM-1) in Indian population. They found that polymorphism in these factors has increased the disruption of cartilage and reduced mRNA and protein synthesis. This was more evident in women who have haplotype T-G-C, increasing their risk of KOA. A similar relationship is noted in Caucasian and Oriental population.

Sharma *et al.*^[10] analyzed genotypic frequencies in Indian men and women. They found a 5.41- and 16.42-fold increased risk of KOA in men and women, respectively, when carrying CT genotype, while the risk is 3.42 and 5.08 fold, respectively, when carrying TT genotype compared with CC genotype. The polymorphism of rs9382564 sequence carried higher genotype frequencies compared with controls ($P < 0.0001$) having a higher incidence of KOA in women.

Ethnicity and race

NHANES III data^[11] from the USA shows the radiographic KOA incidence of 42.1% in women and 32.1% in men. In the same study, the Kellgren–Lawrence Grades III and IV were higher in women (12.9% vs. 6.5% in men). The Johnston County Osteoarthritis Project^[12] also shows a similarly higher incidence of KOA in women and also in patients with high BMI. The incidence was higher in the non-Hispanic blacks compared to non-Hispanic whites. Bijlsma and Knahr^[13] in their study from Dutch Institute of Public Health data identified the incidence of KOA as 30.5% in women and 15.9% in men. The WHO-ILAR COPCORD study in Asian population has shown a similarly higher incidence of KOA in women.

Cui *et al.*^[1] in their meta-analysis on global incidence and prevalence of KOA in women is 1.69 (CI 95%, 1.59–1.80, $P < 0.00$) and 1.39 (CI 95%, 1.24–1.56, $P < 0.00$) times as much in males, respectively.

Obesity and knee osteoarthritis

Obesity is known to be an important modifiable cause of KOA. The high BMI increases axial loading of the knee causing cartilage wear mechanically. The metabolic excess of fat also causes inflammation in the knee joint releasing degradative enzymes which lead to cartilage degeneration. Verma and Dalal^[14] in their study on COMP levels in KOA found a positive correlation between KOA and high BMI. However, there was no difference in COMP levels between men and women with KOA.

Sanghi *et al.*^[15] in their study on anthropometric measures and KOA in nonobese individuals found a higher correlation between BMI and severity of KOA.

In men, BMI and triceps skinfold thickness were positively correlated with KOA, while in women, BMI and waist–hip ratio were more strongly associated.

Menopause and its relationship with knee osteoarthritis

Chao *et al.*^[16] in their study on cartilage degeneration in women found more severe cartilage degeneration in postmenopausal women when compared to pre- and perimenopausal women ($P < 0.001$). A positive correlation is found between years from menopause and cartilage loss ($P < 0.05$). However, 25 years from menopause, there was no difference in the amount of wear of cartilage at different parts of the knee. Jung *et al.*^[17] in their nationwide cross-sectional study in South Korea reported the relationship between KOA and menopausal hormone treatment (MHT). A year of MHT has reduced the incidence in MHT group compared to non-MHT group. Women's Health Initiative in the USA found a 15% reduction in the need of knee replacement in postmenopausal women on estrogen replacement therapy. The combined estrogen and progestin therapy, however, is not associated with the risk of joint replacement.

Vitamins, osteoporosis, and knee osteoarthritis

Ghosh *et al.*^[18] in their prevalence study on osteoporosis, hypovitaminosis D, and KOA found higher rates of Vitamin D insufficiency and deficiency in women than in men in India. Breijawi *et al.*^[19] found a similar correlation between Vitamin D deficiency and KOA in Caucasian population.

Ghosh *et al.*^[18] also found that 32.65% of their study population had osteoporosis and 48.98% had osteopenia. Statistical analysis showed a significant correlation between KOA and bone mineral density. However, there was no linear relationship between radiographic KOA and osteoporosis.

The Framingham study^[20] showed an increased risk of progression with Low levels of vitamin C, which was not associated with the incidence of radiographic or symptomatic KOA.

The Johnston County Osteoarthritis group has shown a 50% reduction in risk of progression with Vitamin E, however, a controlled study has not shown any beneficial effect.^[21,22]

Disability in Indian women from knee osteoarthritis

There is a paucity of data on interventions and disability assessment in Indian studies. This review could not establish the true magnitude of the disability caused by KOA in Indian women though the available data suggest significant morbidity which is not addressed adequately

due to cultural, socioeconomic, and demographic reasons.

The recent multicenter cross-sectional study (iKare^[23]) found that majority of the patients with early KOA experience pain for less than a year. They are treated with oral medication (83.3%), intra-articular injections (29.8%), and surgical intervention (12.7%). People treated in private hospitals were more likely to have physical therapy than those treated in government hospitals. They found a similar proportion of early KOA treatment in India and North America.

Devasenapathy *et al.*^[24] in their cross-sectional analysis on 240 patients from India undergoing total knee replacement found higher disability in women compared to men. The knee injury and osteoarthritis pain scoring is higher, range of movement of the knee is less, lower muscle strength, lower objectively measured functional ability, high stair climbing time and participation restriction is higher in women than men.

In summary, the data from Indian studies on osteoarthritis are focused mainly on the prevalence and incidence of KOA. Some possible reasons could be the diversity in population, demographic and cultural differences, low literacy, and the response rate from the participants. It is understandably difficult to conduct long-term studies identifying the natural history, progression, and management. Another significant concern is loss to follow-up, which is higher in Indian studies compared to Western studies.

CONCLUSION

The gender differences in incidence and prevalence of KOA in Indian women are similar to the Western society. There is a paucity of data on clinical presentation, progression of disease, functional disability, hormone replacement treatment in postmenopausal women, and outcomes of the interventions done for KOA in Indian literature. Further research needs to be directed in addressing these issues with robust data providing evidence-based management and reducing the significant burden of the KOA in women of India.

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Conflicts of interest

There are no conflicts of interest.

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