



ISSN: 0975-833X

Available online at <http://www.journalcra.com>

INTERNATIONAL JOURNAL
OF CURRENT RESEARCH

International Journal of Current Research
Vol. 11, Issue, 03, pp.2154-2160, March, 2019

DOI: <https://doi.org/10.24941/ijcr.34743.03.2019>

RESEARCH ARTICLE

RISK FACTORS OF KNEE OSTEOARTHRITIS AMONG RHEUMATOLOGY UNIT ATTENDANTS IN MOSUL

*Ali Mahmood Saleem, Ashraf Kamel Abdul- Rahman Al-Nuaimiee, Salim Jasim Al-Mola

Directorate of Nineveh Health, Iraq

ARTICLE INFO

Article History:

Received 11th December, 2018
Received in revised form
24th January, 2019
Accepted 28th February, 2019
Published online 31st March, 2019

Key Words:

Osteoarthritis,
Knee Joint,
Risk Factors.

*Corresponding author:
Ali Mahmood Saleem

ABSTRACT

Background: The World Health Organization (WHO) and the United Nations have declared the decade of 2000-2010 the "Bone and Joint Decade". As life expectancy has increased throughout the world, musculoskeletal system disorders as osteoarthritis (OA) have emerged as important health care concerns for the elderly with considerable social and economic burden on all society, including developing countries. **Materials and Methods:** In order to achieve the aim of the present study, a case-control study design was adopted, and conducted in the Rheumatology Consultation Unit in Ibn-Sena Teaching Hospital in right sector of Mosul city. 200 as cases and 200 as controls were collected consecutively. Study period was from the 1st of November, 2007 to the 30th June, 2008. Data collection tool was a questionnaires used to measure general information as age in years, sex, residence, marital status and occupation. The specific information consist of history of OA, the presence of family history, history of joint trauma, stressful life events, seasonal history, the current smoking status, history of pre-existing medical disease, history of congenital anomalies and history of prolonged occupational or sport stress. Chi-square test with Odd ratio (OR) was used to the association. P-value ≤ 0.05 was considered significant. The 95% confidence interval (95% CI) were also computed. **Results:** The highest age-specific groups of cases was (55-64) years which constituted about 44%. The result of the present study indicated a highly positive significant association ($p=0.000$) between knee OA and female gender, manual working, being ever married ($OR=3.94$), and congenital anomalies ($p=0.004$). Females aged >45 years were prone to develop knee OA ($p=0.000$). A highly significant relationship was spotted regarding the history of prolonged unhealthy posture or sport stress ($OR=8.27$, $p=0.000$). Overweight and obesity are seen to duplicated the probability for knee OA. Persons with positive history of trauma were 10 times more prone to have OA. A positive association between unhealthy dietary behavior and knee OA was observed ($OR=3.09$). **Conclusions:** The OA increased steadily with age, and more in females; congenital anomalies, ever married, overweight, obesity, manual workers, history of prolong unhealthy posture or sport stress, family history, history of trauma, and unhealthy dietary behavior, all appear to play a role as risk factors in the development of knee OA.

Copyright © 2019, Ali Mahmood Saleem et al, This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Citation: Ali Mahmood Saleem, Ashraf Kamel Abdul- Rahman Al-Nuaimiee, Salim Jasim Al-Mola, 2019. "Risk factors of Knee Osteoarthritis among Rheumatology Unit Attendants in Mosul", *International Journal of Current Research*, 11, (03), 2154-2160.

INTRODUCTION

Osteoarthritis is the most common musculoskeletal disorder and the leading cause of disability among the aged people (Doherty, 2001). Also called degenerative joint disease characterized by progressive deterioration and loss of articular cartilage accompanied by proliferation of new bone and soft tissue in and around the involved joint (Dennis et al., 2005). There are inherent difficulties in obtaining incidence data for OA due to problems in defining the disease and its point of onset. The Australian burden of disease and injury study, showed a higher incidence of OA among women in all age groups (0.29%) compared to men (0.17%) (Cooper, 2000). According to this study, the incidence of radiological OA is highest among women between the ages of 65 and 74 (1.35%),

and among men aged 75 years and over (0.9%). In other studies, the incidence of OA ranges from 1% to 3.3% per year. The checklist of American College of Rheumatology criteria for the classification of knee OA, based on clinical and radiological characteristics⁽⁴⁾ is as follows:

- Knee joint pain for the most days of prior month.
- Radiographs may be normal at first but as disease progresses may show joint space narrowing, sub-chondral bone sclerosis, sub-chondral cyst, and osteophytes. Erosions are distinct from those of rheumatoid and psoriatic arthritis as they occur subchondrally along the central portion of the joint surface.

- Synovial fluid of OA (at least 2 times repeated: clear viscous, >WBC 2000 cell/ml).
- Synovial fluid not available; age <40 years.
- Morning stiffness of the knee <30 minutes.
- Crepitus on active joint motion.

The routine laboratory work and ESR is usually normal but ESR may be elevated in patients with synovitis. Rheumatoid factor and anti nuclear antibodies studies are negative. The Synovial fluid is straw-colored with good viscosity; <WBC 2000 cell/ml; of value in ruling out crystal-induced arthritis or infection (Hunter, 2006; Stephen, 2008). OA occur because the cartilage gets worn away, some risk factors thought to be involved in this process including age, sex and genetics. Local factors include prior injury to joint, deformities, obesity and muscle weakness. Moreover, the nutrition and possibly hormones play a role (Lawrence et al., 1998). Age is the most powerful risk factor for the development of knee OA affecting more than 80% of persons older than 65 years in the United States (Iglehart et al., 1999). The recent analysis showed that obesity is linked to OA of the knee in women aged 50 years and older, Jinks et al., (2006) found that obese women with body mass index (BMI >30 kg/m²) and overweight women (BMI 25-30 kg/m²) with no knee pain at baseline had a 2.8 fold and 1.3 fold increased risk respectively.

The genetic factors probably account for at least half of all cases of OA (Kujala et al., 1999). Vitamins and arthritis have been linked for many years; vitamins A,C, and E are major antioxidants in the diet and they all have been associated in one way or another with OA (Sower, 1999). Vitamin D may also play a role in OA. These nutritional factors acting by either protecting against oxidative damage in the joint, modulating the inflammatory response affecting cellular differentiation within the arthritic joint, or altering biologic actions related to both bone and collagen synthesis (McAlidon et al., 1996). Congenital dislocation of the hip (CDH) associated with increased risk of OA, also the major joint injuries are common causes of OA, so jobs that require squatting with heavy lifting cause up to 30% of knee OA in men (Prazier et al., 1999). Muscles around the joint have several functions including movement, the maintenance of joint stability, shock absorption, and proprioception. Muscles weakness or fatigue lead to joint instability, pain and abnormal biomechanical loading on the joint, which over time result with change in cartilage and bone consistent with OA (Lane et al., 1987; Slemenda et al., 1997). The evidence is conflicting regarding ethnic differences in OA of the hip and knee. Although one study has indicated higher rates of knee OA in African American women but not men, another study from the rural south suggested no differences in OA prevalence. Ethnic differences in the risk of OA development could be explained by differences, for example in BMI, other factors may also be important in developing OA (Tepper et al., 1993; Jordan et al., 1995).

Aim: to determine the risk factors of knee osteoarthritis in Mosul among the attendants of Rheumatology Unit.

MATERIALS AND METHODS

In order to achieve the aim of the present study, a case-control study design was adopted, and conducted in the Rheumatology Consultation Unit in Ibn-Sena Teaching Hospital in right

sector of Mosul city. 200 cases with knee OA collected consecutively and asked in details about their knee OA according to the clinical criteria of OA and American College of Rheumatology criteria which used to identify patients by rheumatologist.

The inclusion criteria includes:

- Joint pain (often a deep aching pain) that is worsened by movement and improve with rest .
- Stiffness in the morning or after being inactive for not more than 15 minutes.
- Joint swelling.
- Joint that is warm to the touch.
- Muscle weakness.
- Abnormal growth of bony knobs near joint which cause deformities (x-ray findings).

Another 200 individuals who are free from any joint symptoms attending the unit are collected consecutively as controls. The period of data collection was eight months from the 1st of November, 2007 to the 30th June, 2008. Un-paired sampling technique was used in this study. Every participant in this study was interviewed by the researcher and personal consent was taken before the questionnaires proceed. The questionnaires form include general information as age in years, sex residence, marital status and occupation. The specific information consist of history of OA, the presence of family history, history of joint trauma, stressful life events (include death, accidents, divorced and loss of employment), seasonal history, the current smoking status, history of pre-existing medical disease, history of congenital anomalies and history of prolonged occupational or sport stress. Chi-square test was used to look for the presence or absence of an association. Odd ratio (OR) with it 95% confidence interval (95% CI) were also computed. P-value less than or equal to 0.05 was considered significant.

RESULTS

Study population

Frequency of main symptoms of knee OA: Figure (1) shows distribution of cases according to main symptoms of knee OA, where joint pain was the main symptom, the second one was morning stiffness, while the limited range of movement was the third, the joint swelling was the fourth.

The seasonal variation of symptoms exacerbation of knee OA:-The main season for exacerbation of knee OA symptoms according to patients claim shown in figure (2) was winter (66%), followed by spring (14%), autumn (11.5%), and the least one was summer (8.5%).

The duration of symptoms:- The most frequent duration illustrated in figure (3) was 12-24 months (42.5%) and the second one was 6-12 months (24.5%) and the third was >24 months (20%), while the remaining patients (13%) gave history of symptoms for less than 6 months duration.

Male to female ratio of knee OA according to age:- Of all 200 cases with knee OA, the male to female ratio was the lowest at age 55-64 years (1:4), followed by age 45-54 years and the highest male to female ratio was at age 25-34 years (1:2) as shown in figure (4).

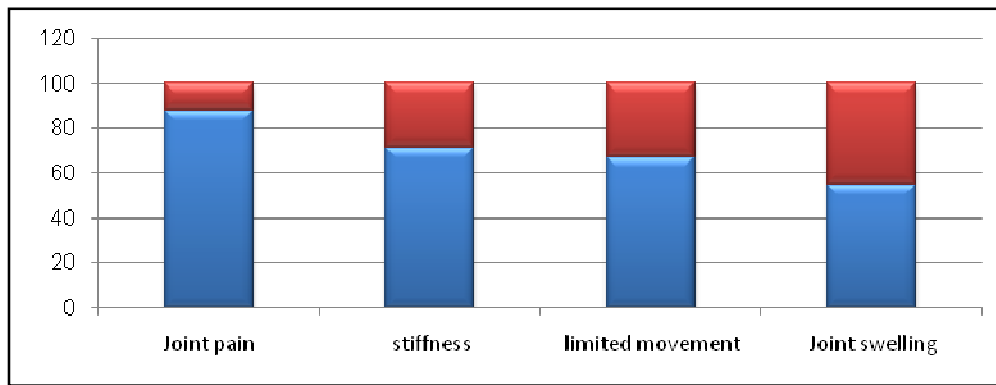


Figure 1. Frequency of main symptoms of knee OA

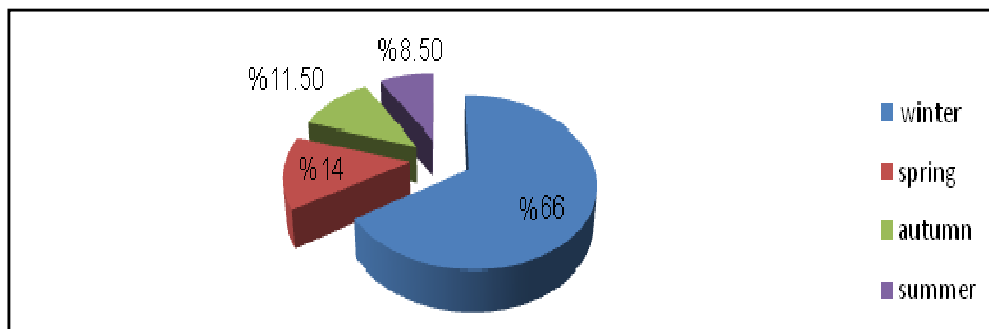


Figure 2. The seasonal variation of symptoms exacerbation of knee OA

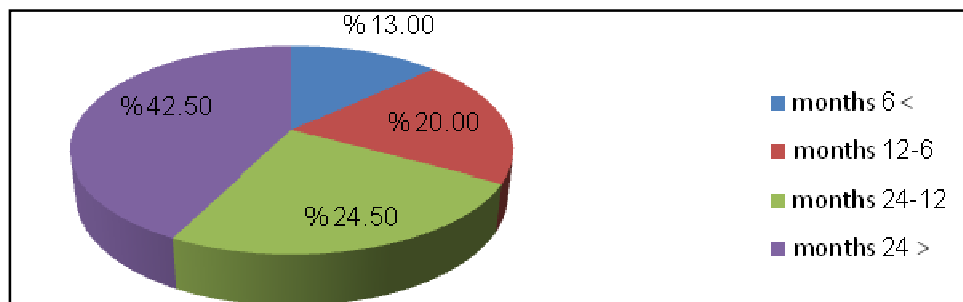


Figure 3. The duration of symptoms

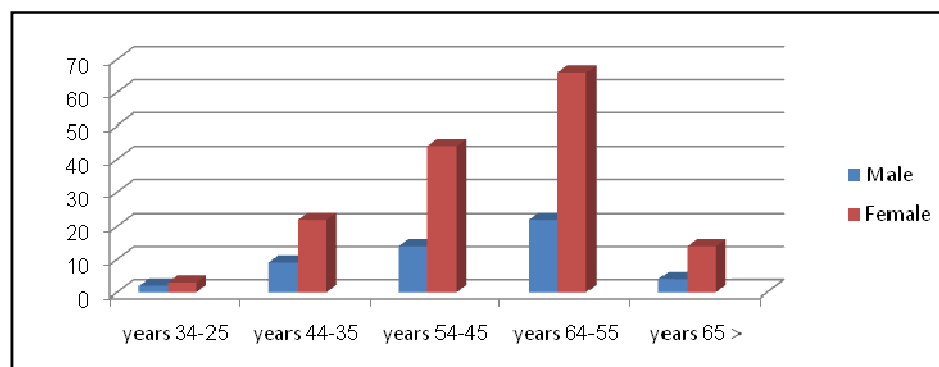


Figure 1 Male to female ratio of knee OA according to age

Table 1. Association Knee OA and the gender of the study population

Gender	Cases No. (%)	Controls No. (%)	OR	P-value*	95% C.I
Female	152(76%)	114(57%)	2.39	0.000	1.55-3.66
Male	48(24%)	86(43%)			

*Chi-square test was used, d.f=1.

Table (2): Association Knee OA and the residence of the study population

Residence	Cases No. (%)	Controls No. (%)	OR	P-value*	95% C.I
Urban	149(74.5%)	161(80.5%)	0.71	0.151	0.44-1.13
Rural	51(25.5%)	39(19.5%)			

*Chi-square test was used, d.f=1.

Table 3 Association Knee OA and the Marital Status of the study population

Marital Status	Cases No. (%)	Controls No. (%)	OR	P-value**	95% C.I
Ever married*	187(93.5%)	157(78.5%)	3.94	0.000	2.04-7.58
Single	13(6.5%)	43(21.5%)			

*Ever married include (married, widow and divorced).

** Chi-square test was used, d.f=1.

Table (4): Association Knee OA and the occupation of the study population

Occupation	Cases No. (%)	Controls No. (%)	OR	P-value***	95% C.I
Manual worker*	170(85.0%)	139(30.5%)	2.48	0.000	1.52-4.06
Non-manual worker**	30(15.0%)	61(69.5%)			

*Manual workers (manual skilled, partially skilled and unskilled)

** non-manual workers (professional, semi- professional and non manual skilled)

***Chi-square test was used, d.f=1.

Table 5. Association Knee OA and the smoking habit of the study population

Smoking Habit	Cases No. (%)	Controls No. (%)	OR	P-value*	95% C.I
Smokers	57(28.5%)	52(26.0%)	1.13	0.574	0.73-1.76
Non-smokers	143(71.5%)	148(74.0%)			

*Chi-square test was used, d.f=1.

Table 6. Association Knee OA and the age and gender of the study population

Age > 45 years	Cases No. (%)	Controls No. (%)	OR	P-value*	95% C.I
Female > 45 years	131(86.2%)	60(52.6%)	5.61	0.000	3.11-10.12
Female < 45 years	21(13.8%)	54(47.4%)			
Male > 45 years	38(79.2%)	55(63.9%)	2.14	0.067	0.94-4.88
Male < 45 years	10(20.8%)	31(36.1%)			

*Chi-square test was used, d.f=1.

Table (7): Association Knee OA and the History of prolong unhealthy posture or sport stress of the study population

History of prolong unhealthy posture or sport stress	Cases No. (%)	Controls No. (%)	OR	P-value*	95% C.I
Present	65(32.5%)	11(5.5%)	8.27	0.000	4.20-16.26
Absent	135(67.5%)	189(94.5%)			

*Chi-square test was used, d.f=1.

Table (8): Association Knee OA and the BMI of the study population

BMI	Cases No. (%)	Controls No. (%)	OR	P-value*	95% C.I
Overweight and obesity	154(77.0%)	115(57.5%)	2.47	0.000	1.60-3.81
Normal BMI	46(23.0%)	85(42.5%)			

*Chi-square test was used, d.f=1.

Table 9. Association Knee OA and history of trauma of the study population

History of trauma	Cases No. (%)	Controls No. (%)	OR	P-value*	95% C.I
Present	68(34.0%)	4(2.0%)	9.78	0.000	4.86-19.71
Absent	132(66.0%)	196(98.0%)			

*Chi-square test was used, d.f=1.

Table 10. Association Knee OA and congenital anomalies of the study population

Congenital anomalies	Cases No. (%)	Controls No. (%)	OR	P-value*	95% C.I
Present	17(8.5%)	4(2.0%)	4.55	0.004	1.50-13.78
Absent	183(91.5%)	196(98.0%)			

*Chi-square test was used, d.f=1.

Table 11. Association Knee OA and the Family history of the study population

Family history	Cases No. (%)	Controls No. (%)	OR	P-value*	95% C.I
Present	103(51.5%)	35(17.5%)	5.01	0.000	3.16-7.91
Absent	97(48.5%)	165(82.5%)			

*Chi-square test was used, d.f=1.

Table 12. Association Knee OA and the unhealthy dietary behavior of the study population

Unhealthy dietary behavior	Cases No. (%)	Controls No. (%)	OR	P-value**	95% C.I
Unhealthy*	151(75.5%)	119(59.5%)	3.09	0.001	1.36-3.21
Healthy	49(24.5%)	81(40.5%)			

*unhealthy dietary behavior include (hgh calories diet, high fatty diet, less minerals and vitamins diet)

**Chi-square test was used, d.f=1.

Table 13. Association Knee OA and the systemic diseases of the study population

Systemic diseases	Smoker No. (%)	Non-smoker No. (%)	OR	P-value*	95% C.I
Yes.					
Hypertension	16(8.0%)	15(7.5%)	1.07	0.852	0.51-2.23
Diabetic Mellitus	13(6.5%)	14(7.0%)	0.92	0.440	0.42-2.01
Cardiovascular diseases	8(4.0%)	11(5.5%)	0.71	0.480	0.28-1.81
Renal diseases	12(6.0%)	15(7.5%)	0.65	0.430	0.22-1.88
More than one disease	6(3.0%)	3(1.5%)	2.03	0.321	0.50-5.24
No.	157(78.5%)	151(75.5%)	1.18	0.470	0.72-1.88

*Chi-square test was used, d.f=1.

Analysis of risk factors: Table (1) indicates a highly significant association (OR=2.39, p=0.000) between knee OA and female gender, they constitutes 76% of cases, while in controls, the female represents 57% only

Table (2) reveals that 74.5% of cases and 80.5% of controls were resident in an urban areas. No significant difference between cases and controls regarding their residence (OR 0.71, p=0.151). The ever married constitutes 93.5% of cases, while in controls it is down to 78.5%. the odd ratio indicates that being ever married was a risk factor or development of knee OA with very high significant manner (OR=3.94, p=0.000) as displays in Table (3). The present result shows that 85% of cases and 30.5% of controls were manual workers. The rest were non-manual workers as demonstrated in Table (4). Positive relationship between manual workers and knee OA was noticed (OR=2.48, p= 0.000). Table (5) indicates no association is present between smoking and development of knee OA (p=.0574). The data in Table (6) shows that females aged more than 45 years is more prone to develop knee OA than younger age women (OR= 5.61, p=0.000). represented 86.2% of cases, while in controls, females aged more than 45 years represented 52.6%. In contrast, in males also older age seems to be risk factor in the development of knee OA, however this relationship is not significant (OR=2.14, p=0.067). The data in Table (7) shows a high significant relationship (p=0.000) between History of prolong unhealthy posture or sport stress and the development of knee OA of a risky way (OR=8.27). Table (8) illustrates a highly significant association (p=0.000) between abnormal BMI and the development of knee OA. Overweight and obese cases are two times prone to develop knee OA than controls (OR= 2.47). One third of cases and 2% of controls give positive history of trauma, with a risk up to ten times in significant association

(OR=9.78, p=0.000) as displays in Table (9). Table (10) displays a significant relationship (p=0.004) between the congenital anomalies and the development of knee OA with (Or=4.55). Table (11) shows that the positive family history of OA was found to be a risk factor in the development of knee OA (OR=5.01). about one half of cases give positive family history where as, only 17.5% of the controls give the positive history of OA. Table (12) indicates that three quarter of cases were consume unhealthy diet and 59.5% of corresponding controls group were also consume unhealthy diet. This result in a significant association between unhealthy dietary behavior and the development of knee OA (OR=3.09). Table (13) demonstrates the effect of the systemic disease and the development of knee OA such as hypertension, diabetic mellitus, cardiovascular diseases, and renal diseases. No evident association could be concluded from this Table .

DISCUSSION

Joint pain is common among older people in the community and is a major cause of disability (Roos, 2005). Identifying modifiable risk factors should be given a high priority, and many studies investigate the relation between potential risk factors and joint OA (Bongers, 2001; Croft et al., 1996). In the present study, male to female ratio of cases was 1:3, this result was in agreement with that of Pencharz et al 2002. The mean age of cases of knee OA was 54 years, this result coincides with the finding of Christensen et al. (2007) the study conducted in 2007, who showed that the mean age of cases of knee OA was 53.5 years, while Fidelix ea al, 2006 indicated that the mean age of knee OA was 51 years which was slightly lower than those obtained in our study⁽²³⁾. Urban or rural residence carries no risk for the development of knee OA, the relatively low percentage of rural sample; in both cases and

controls is probably due to difficult geographical access to the services in the city. Being ever- married (married, widowed and divorced) patients was risky factor in the development of knee OA (OR=3.94), this agreed with the finding of Davis et al. 1991, in a case-control study; they observed a significant association between marital status and symptoms and signs of knee OA (OR=4, $p=0.000$), this is probably due to the burden of marriage and its products. The analysis of results regarding occupation showed a positive relationship between manual work and the development of knee OA (OR=2.49, $p=0.000$), indicating a significant positive association between occupational and individual activities and the current status of knee damage, this may be explained on the basis of the manual worker having more mechanical burden on the knee joint leading to development of more knee OA. This result was in agreement with that of Soeroso and Santoso 2005, and Klusmann and Gebhardt (2007) in a case-control study conducted in 2007, both observed a significant association between occupational hazards and symptoms and signs of knee OA. The result of the present work indicated no association between smoking and the development of knee OA (OR=1.13, $p=0.574$), while Felson et al. (1989) 1989 found that smoking is a protective factor for developing OA of knee (OR=0.74, CI: 0.55-0.98). there is no biological explanation of why smoking may protect against OA. Smoke may affect cartilage directly, or its putative osteopenic effect may protect joints by making subchondral bone more deformable to impact loads or smoking may prevent weight gain and protect the mechanical stress to joints. Hart and Spector 1993, in a cross sectional study among women did not find any significant association (OR=1.34, CI: 0.68-2.34) between smoking and the presence of knee OA. A significant association was found between females age more than 45 years and the risk of having knee OA in the present study with (OR= 5.61, $p=0.000$, CI: 3.11-10.1), in contrast, in males this relationship was not significant (OR=2.14, $p=0.67$, CI: 0.94-4.88). this finding was supported by the result of Gill et al. 2002, and also agree with finding obtained by Soeroso and Santoso in a case-control study conducted in Indonesia in 2005, the significant association observed between female age more than 45 years and risk of knee OA (OR=9.34), and found no significant association between male age more than 45 years and the risk of knee OA (Soeroso, 2005).

A highly significant relationship ($p=0.000$) was found between history of prolonged unhealthy posture and sport stress and the development of knee OA (OR=8.27, CI:4.20-16.26); this result agreed with the finding of Sandmark⁽³⁰⁾ 2006. This idea is that more prolonged unhealthy posture and sport stress lead to further damage in the knee joint contour and precipitate more OA of the knee joint. The result of the present study indicated that a highly significant relationship ($p=0.000$) between abnormal BMI (include overweight and obesity) and the development of knee OA. These results are supported by findings of Nevitt⁽³¹⁾ 2002, and the study of Ray 2007, in his cross-sectional work conducted in New York ($n=100$) where 82 women and 18 men with unilateral or bilateral knee OA were examined. They reported a high BMI is present in most adults with knee OA. Moreover, being overweight may affect knee joint impact rates and pain incrementally. Having high body weights may heighten the risk for bilateral knee joint, as well as hip joint OA. On the other hand Al Arfaj 2002, in his cross-sectional study in Saudi Arabia ($n=400$) reported that excess weight was strongly associated with knee OA in women, with weaker link for men. Dawson et al. 2003, in his case-control study in United Kingdom found being overweight before 40 years

increased risk of knee OA. Raynauld et al. 2005, in his prospective study of 107 persons with high BMI (exposed) who were followed clinically and radiologically via quantitative magnetic resonance imaging for 24 months in Canada found high BMI was a significant predictor of fast cartilage volume loss in comparison to non-exposed group. Indeed, our study and the mentioned studies indicate a strongly implicated excess body mass in the pathogenesis of knee OA and its associated disability. Al Youzbaki (2008), in a case-control study of 76 women age > 50 years with knee OA (cases) in comparison with 116 women age > 50 years not having knee OA as a control group, conducted in Mosul in 2007, found a strong association (OR=8.88) between obesity and the development of knee OA. Highly significant association between previous trauma of the knee joint and the development of knee OA was found in the present study (OR=9.78, $p=0.000$); this result agreed with the finding of Baliunas et al. (2002). The idea that previous trauma leads to more distortion of normal anatomy of knee joint and to further OA changes of joint. The result of the present study indicated a significant relationship ($p=0.004$) between congenital anomalies and the development of knee OA (OR=4.55). Felson et al.⁽³⁸⁾, in a case-control study of 120 patients with knee OA and 100 control subjects, conducted in 1991 found a strong association (OR=3.65, CI: 1.60-11.20) between congenital anomalies and the development of knee OA. Positive family history of OA is found to be a risk factor in the development of knee OA (OR= 5.01, CI: 1.36-3.21). about one half of cases (51.5%) give positive history in general. Spector et al 1996, found a weak positive association between family history of OA and knee OA, the explanation of this result may be due to small sample size in that study ($n=100$) (Spector, 1996). The results of the present work showed a positive association between unhealthy dietary behavior and the development of knee OA (OR=3.10). these results are supported by Sowers and Lachance (1999) in a case-control study of 250 patients with knee OA and 210 control subjects conducted in 1999, who found a positive association (OR=2.20, CI: 1.40-3.11) between unhealthy dietary behavior and the development of knee OA, and also agreed with the finding of Mc Alindon et al. (1996). Al Youzbaki (2008) also found a strong association ($p=0.000$). Regarding the relationship between systemic diseases and the development of knee OA, the present study revealed no significant association.

REFERENCES

- Al Youzbaki DB. 2008. Sociological Risk Factors in the Development of Knee Osteoarthritis Among Women > 50 years, Case control study in Mosul. Iraq journal of community medicine, serial no. 1425 (Accepted, April/27/2008.)
- Al-Arfaj AS. 2002. Radiographic osteoarthritis and obesity. *Saudi Med J*, 23: 938-942.
- Altman R., Asch E., Bloch DA., et al., 2002. development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. *Diagnostic and therapeutic Criteria Committee of American Rheumatism Association. Arthritis Rheumatology*, 29:1039-1049.
- Baliunas AJ., Hurwitz DE., Ryals AB. et al., 2002. Increased knee joint loads during walking are present in subjects with knee osteoarthritis. *Osteoarthritis Cartilage*, 10: 573-579.
- Bongers PM. 2001. The cost of shoulder pain at work. *BMJ*, 322:64-65.
- Christensen R., Bartels EM., Astrup A., Bliddal H. 2007. The effect of weight reduction in obese patients diagnosed with

- knee osteoarthritis (OA): a systemic review and meta-analysis. *Ann Rheum Dis.*, 66(4): 433-439.
- Cooper C., Snow S., Alidon TE. et al., 2000. Risk factors for the incidence and progression of radiographic knee osteoarthritis. *Arthritis Rheumatology*, 43: 995-1000.
- Croft P., Pope D., Silman A. 1996. The clinical course of shoulder pain: prospective Cohort study in primary care. *BMJ*, 313:601-602.
- Davis MA., Ettinger WH., Neuhaus JM., Mallon P. 1991. Knee osteoarthritis and physical functioning: Evidence from the Nhanes I epidemiologic follow up study. *J Rheumatol*, 18:591-598.
- Dawson J., Juszczka KE., Thorogood M. et al., 2003. An investigation of risk factors for symptomatic osteoarthritis of the knee in women using a life course approach. *J Epidemiol Comm Hlth*, 57: 823-830.
- Dennis L. Eugene B., Anthony S., Stephen L., Dan L., Larry J. 2005. Harrison manual of medicine 16th ed, Mc Graw-Hill United States of America 794-800.
- Doherty M. 2001. Risk factors for progression of knee osteoarthritis. *The lancet*, 358: 9284-9775.
- Felson DT., Anderson JJ., Naimark A., Hannan MT., Kannel WB., Meenan RF. 1989. Does smoking protect against osteoarthritis?. *Arthritis Rheum*, 32 :166-172.
- Felson DT., Hannan MT., Naimark A., Berkeley J., Gordon G., Wilson PW. et al., 1991. Occupational physical demands, knee bending, and knee osteoarthritis: results from the Framingham Study. *J Rheumatol.*, 18:1587-1592.
- Fidelix TSA., Soares BG., Trevisani VM. 2006. Co-Chrane Data base Systemic Review fo Osteoarthritis. *Ann Rheum Dis.*, 10: 1465-1858.
- Gill T., Taylor A., Chittleborough C. 2002. Overweight and obesity as risk factors for arthritis. *Arthritis Foundation of South Australia*. 2002.
- Hart DJ., Spector TD. 1993. Cigarette smoking and risk of osteoarthritis in women in general population. *Ann Rheum Dis.*, 52:93-96.
- Hunter DJ. 2006. Imaging outcomes and their role in determining out comes in Osteoarthritis and rheumatoid arthritis. *Arthritis Rheumatology*, 12(1):40-46.
- Iglehart JK. 1999. The American health care system expenditures. *N Engl J Med.*, 340:70-76.
- Jinks C., Jordan K., Croft P. 2006. Disabling knee pain – another consequence of obesity: results from a prospective cohort study. *BMC Public Health*, 6:258.
- Jordan JM., Linder GF., Renner JB., Fryer JG. 1995. The impact of arthritis in rural populations. *Arthritis Care Res.*, 8:242-250.
- Klussmann A., Gebhardt H. 2007. Individual and occupational risk factors for knee osteoarthritis-study protocol of a case control study. *Arthritis Rheum*, 49(7):1333-1339.
- Kujala UM., Leppavuori J., Kaprio J., Kinnunen J., Peltonen L., Koskenvuo M. 1999. Joint-specific twin and familial aggregation of recalled physician diagnosed osteoarthritis. *Twin Res.*, 2:196-202.
- Lane NE., Bloch DA., Wood PD., Fries JF. 1987. Aging long-distance running, and the development of musculoskeletal disability. A controlled study. *Am J Med.*, 82:772-780.
- Lawrence RC., Helmick CG., Arnett FC., Felson DT., Giannini EH., Heyse SP., et al. 1998. Estimates of the prevalence of arthritis and selected musculoskeletal disorders. *Arthritis Rheumatology*, 111(1):22-29.
- McAlidon TE., Felson DT., Zhang Y., Hannan MT., Aliabadi P., Weissman B. et al., 1996. Relation of dietary intake and serum levels of vitamin D to progression of osteoarthritis of the knee among participants in the Framingham study. *Ann Intern Med.*, 125:353-359.
- Nevitt MC. 2002. Obesity outcomes in disease management: clinical outcomes for osteoarthritis. *Obes Res.*, 10 :33S-37S.
- Pencharz JN., Grigoriadid E., Janz GF., Bombardier C. 2002. A critical appraisal of clinical practice guidelines for the treatment of lower limb osteoarthritis [Review]. *Arthritis Res.*, 4(1): 36-44.
- Prazier JE., Harper R., Munro J., Walters SJ., Snaith ML. 1999. Genetic and condition- specific outcome measures for people with osteoarthritis of the knee. *Rheumatology*, 38:870-877.
- Ray M. 2007. Obesity profiles with knee osteoarthritis: Correlation with pain, disability, disease progression. *Obesity*, 15: 1867-1874.
- Raynauld JP., Martel-Pelleetier J., Berthiame MJ., et al., 2005. Long term evaluation of disease progression through the quantitative magnetic resonance imaging of symptomatic knee osteoarthritis patients: correlation with clinical and radiographic changes. *Arthritis Res Ther.*, 8: 21.
- Roos EM. 2005. Joint injury causes knee osteoarthritis in young adults. *Curr Opinion Rheumatology*, 17:195-200.
- Sandmark H. 2006. Primary osteoarthritis of the knee in men and women as a result of lifelong physical load from work. *Scand J Work Environ Health*, 26(1): 20-25.
- Slemenda C., Brandt KO., Heilman DK., Mazzuca S., Braunstein EM., Katz BP., Wolinsky FD. 1997. Quadriceps weakness and osteoarthritis of the knee. *Ann Intern Med.*, 127:97-104.
- Soeroso J., Santoso G. 2005. Risk Factors of Symptomatic and Asymptomatic Osteoarthritis of the Knee. *Folia Medica Indonesiana*, 41(2): 343-364.
- Sower MF., Lanchance L. 1999. Vitamins and arthritis, the role of vitamins A, C, D, and E. *Rheum clin North Am.*, 25:315-332.
- Spector TD., Cicuttini F., Baker J., et al., 1996. Genetic influences on osteoarthritis in women: a twin study. *BMJ*, 312: 940-943.
- Stephen J. 2008. Current Medical Diagnosis and Treatment. *Arthritis Rheumatology*, 710-790.
- Tepper S., Hochberg MC. 1993. Factors associated with hip osteoarthritis: data from the First National Health and Nutrition Examination Survey (NHANES-I). *Am J Epidemiol*, 137:1081-1088.
